

## OP1 0002 Is Tumour Staging Possible by Hydrocolonic Sonography?

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**Introduction** By filling the bowel with water, a precise study of the bowel wall is possible using ultrasonography: this technique is known as hydrocolonic sonography. A normal bowel wall consists of five layers that can be recognised on ultrasound. The first echogenic and the second echopoor layer correspond to the mucosa. The third echogenic layer is the submucosa, the fourth echopoor layer the muscularis and the fifth echogenic layer the serosa. The aim of the study was to investigate whether hydrocolonic sonography can allow a correct preoperative staging of colon tumours.

**Methods** After a laxative orthograde intestinal lavage and a retrograde instillation of water into the bowel, a transabdominal sonographic examination is performed with the 5 and 7.5 MHz transducer. To achieve an optimal distention of the bowel and to suppress the urge for elimination, 20 mg scopolamine is given intravenously. A tumour is classified as T1 when it invades the mucosa and submucosa, T2 when the infiltration is confined to the muscularis, T3 when the infiltration extends to the serosa and T4 when there is invasion of other organs or perforation to the visceral peritoneum. 320 patients underwent a hydrocolonic sonography after informed consent. The proposed staging was compared to the pathologic anatomy of the resected specimen.

**Results** 36 colon tumours were detected by hydrocolonic sonography and confirmed by colonoscopy. 16 were localised in the sigmoid, 4 in the descending colon, 10 in the transverse colon and 6 in the ascending colon. 15 were substenosing tumours. In three patients the hydrocolonic sonography detected a synchronic small polyp which was confirmed pre- or postoperatively. One tumour was classified as T1, 2 as T2, 15 as T3, 18 as T4. Two of the distal sigmoid (0–25 cm) tumours were understaged as T3. The sensitivity of staging by hydrocolonic sonography was 94.4%, when excluding the distal tumours 100%.

**Conclusion** Hydrocolonic sonography is an easy, cheap and sensitive technique which allows a correct preoperative staging of colon tumours. For the distal sigmoidal and rectal tumours an echo-endoscopic approaches still necessary. The usefulness of staging of colon tumours is until now not proven, but future therapeutic approach (e.g. laparoscopic surgery) may benefit of it. Radiology and ultrasound: Diagnosis } "Is Tumour Staging Possible by Hydrocolonic Sonography?"

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## OP2 0008 Virtual Colonoscopy — A Pig Model for Optimization of Study Parameters

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**Purpose** The increasing incidence of colorectal cancer calls for a simple, safe, accurate and cost-effective screening technique. However, the general acceptance of available screening methods remains disappointingly low. Virtual colonoscopy is an exciting new imaging modality, combining spiral CT scanning with newly developed virtual reality computer software. The reconstructed images simulate the endoluminal view obtained by the endoscopists and also allows visualization of colons where passage of a colonoscope is impossible. However, the optimal scanning parameters and inter-study variation is currently poorly defined. The aims of the present study were to determine the feasibility of a pig model to address some of these problems.

**Methods** A 80 cm proximal segment of pig colon was resected and lavaged thoroughly. After partial eversion, artificial polyps were created by invagination of the mucosa and suture of the base. A set of one large "index" polyp and two smaller polyps ranging from 2 to 9 mm were positioned at intervals throughout the colon segment. The bowel was completely surrounded by 6 liters of ultrasound gel and was placed in a Picker PQ5000 spiral CT scanner and a series of scans obtained with various parameter changes according to a predefined protocol. A continuous volume CT dataset was reconstructed and reformatted into the virtual endoscopy presentation (Epi-scope<sup>®</sup>), and the virtual reality images were reviewed by two independent observers.

**Results** Preliminary data indicate that optimal resolution is obtained by a combination of reduced slice thickness, slow table speed and increased kV and mA. For practical purposes, it appears that the most important factor is minimizing slice thickness. Additional data are currently being collated with respect to inter-observer and inter-study variability.

**Conclusions** This simplified pig colon model appears to be a useful tool to study the technical aspects of virtual colonoscopy, and an important adjunct to clinical studies in humans. Endoscopy, general: Instrumentation, diagnosis Radiology and ultrasound: Diagnosis Endoscopy, specific: Colon, rectum } "Virtual Colonoscopy / A Pig Model for Optimization of Study Parameters"

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## OP2 0010 A Randomized Trial Comparing Endoscopic Balloon Dilatation (EBD) and Endoscopic Sphincterotomy (EST) for Removal of Bile Duct Stones (BDS)

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**Aim** EST is effective for removal of BDS but carries a 10% risk for acute complications. Furthermore, the long-term effects of loss of biliary sphincter function after EST are unknown. EBD of the biliary sphincter may be an alternative to EST since it has a potentially lower risk for acute complications, such as bleeding, and preserves the function of the biliary sphincter. EBD, however, may be less effective than EST and may carry an increased risk for pancreatitis. We performed a randomized trial comparing EST and EBD in 202 consecutive patients with BDS.

**Methods** EBD was performed with a 8 mm Maxforce' dilatation balloon (Microvasive, Boston). EST was performed according to standard guidelines. Mechanical lithotripsy (MLT) was allowed to fragment stones prior to extraction. In case of failed stone removal after EBD, a secondary EST was performed during the same ERCP. Primary outcome was the rate of complete stone removal in one ERCP. Treatment outcome was assessed at 24 hours and 30 days by personal interview, questionnaires and blood tests. Complications were graded by a panel of experts who were blinded to the treatment allocation.

**Results** EBD (N = 101) EST (N = 101) Median stone number (range) 2 (1–14) 1 (1–15) Median stone diameter (mm) 10 (3–36) 9 (4–27) Direct success 81/92 Success after sec. EST 9/92 N.A. Overall success 90/92 MLT (\*p < 0.005) 31/92 \* 13/92 Acute pancreatitis 7/70 Other acute complications 10/17

**Conclusions** After EBD, BDS of all sizes can be completely removed in one ERCP in 80% of cases (81/101). If necessary, secondary EST can further increase success rate up to 89% (90/101). The overall success rate of EBD is hereby comparable to that of EST (91%). MLT is more often required after EBD than after EST. The risks for pancreatitis after EBD and EST seem to be comparable. EBD is an effective and safe alternative to EST for patients with BDS. Endoscopy, specific: Biliary Endoscopy, general: Complications Liver and bile ducts, 2: Gallstones, formation, treatment } "A Randomized Trial Comparing Endoscopic Balloon Dilatation (EBD) and Endoscopic Sphincterotomy (EST) for Removal of Bile Duct Stones (BDS)"

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## "P P 1 0022" P 1 0022 **Lung Cancer Staging — Comparison of Endoscopic Ultrasound and Mediastinoscopy Cost Effectiveness for Assessing Lymph Node Involvement**

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**Purpose** The use of endoscopic ultrasonographic (EUS) guidance for fine needle aspiration (FNA) of mediastinal lymph nodes has become an important adjunct in the staging of bronchogenic carcinoma. In many cases, it may be an alternative to mediastinoscopy (MED), but the cost-effectiveness of the techniques has not been compared.

**Methods** A decision model was developed to compare EUS/FNA and MED in patients with known or suspected lung cancer to stage the mediastinum. Based on available literature, the baseline estimates for negative predictive value of EUS/FNA and MED were 0.87 and 0.91, respectively. Baseline cost estimates, derived from prevailing Medicare reimbursement rates, were \$ 20 000 for thoracotomy, \$ 7 400 for mediastinoscopy and \$ 765 for EUS with FNA. The mean life expectancy for resected non-disseminated disease was 5 years, and for non-resectable disease 1 year. Baseline pickup-rate of EUS and MED was 0.59. Sensitivity analysis was performed on all probabilities and utilities. in the model.

**Results** Using our baseline estimates, cost/efficacy analysis favored EUS/FNA over mediastinoscopy with a marginal cost/effectiveness of \$ 130 000.-/year of survival. The average cost per year survival was \$ 3,810.- and \$ 6,471.- in the EUS/FNA and MED arm, respectively. The cost-effectiveness advantage of EUS/FNA increases when enlarged lymph nodes are documented prior to the sampling procedure.

**Conclusion** This decision analysis, strongly favors EUS/FNA over mediastinoscopy for staging of patients with lung cancer. The advantage is even more pronounced when lymph nodes are visualized before the procedure. Echoendosonography: EchoendoscopyEndoscopy, general: Instrumentation, diagnosisClinical practice: Management strategy }" "Lung Cancer Staging / Comparison of Endoscopic Ultrasound and Mediastinoscopy Cost Effectiveness for Assessing Lymph Node Involvement"

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## "P P 1 0023" P 1 0023 Accuracy of a 20 MHz Radial Probe in Staging Small Digestive Tumors

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Department of Digestive Diseases, Hospital E Herriot, Lyon, France Staging of small cancers of the digestive wall is essential for the choice between surgery and local treatment. While endoscopic ultrasound (EUS) is the best available staging method, metastatic lymph nodes detection is not optimal with EUS in such setting. High frequency probe could allow the distinction between mucosal (T1m) and submucosal cancer (T1sm), only the latest having a significant risk of metastatic nodes, especially in esophageal cancer. The aim of this study was thus to evaluate the accuracy of a 20 MHz prototype probe in staging small digestive tumors.

**Methods** The prototype from Olympus Co is similar to GFUM 20 but has 2 frequencies 7.5/20 MHz. It was used from December 94 to May 96, in 136 patients. In these 136 patients, 12 with uT1 or uT2 tumors were operated on, allowing comparison between EUS results and the operative specimen. Tumor localization was esophagus (n = 4), cardia (n = 1), stomach (n = 2), ampulla of Vater (n = 1), rectum (n = 4).

**Results** For T1 vs T2 staging (8 pT1 and 4 pT2), accuracy of Olympus prototype 20 MHz was 92% (11/12). The only error concerned a large (5 cm) polypoid rectal villous tumor classed uT2, in fact pT1. For N staging (7 pN0, 4 pN1, 1 not staged – local excision), accuracy of EUS was 73% (8/11). In an esophageal cancer, a small (4 mm) paratumoral lymph node was considered metastatic; the lymph node, was indeed found at pathology but was benign. The 2 last errors concerned small metastatic nodes missed by EUS respectively in an esophageal cancer staged uT1sm (partial invasion) and in a rectal cancer staged uT2 (4 mm node seen at EUS considered as benign). For the distinction T1m vs T1sm, visualization of the muscularis mucosae was possible only in esophageal and gastric cancer (5 T1, 3 pT1sm and 2 pT1m). Accuracy was 3/5 cases (2 T1sm, 1 T1m). There were 1 overstaging (uT1sm pT1m for a squamous cell carcinoma of the esophagus) and 1 understaging (uT1m, pT1sm for a gastric carcinoma at the level of the angulus).

**Conclusions** The 20 MHz probe was accurate for the TN staging of small GI cancers. It could improve the distinction between mucosal and submucosal cancer in gastric and esophageal tumors, but more experience is needed to increase fiability. Echoendosonography: Echoendoscopy Endoscopy, general: Instrumentation, diagnosis Oncology, specific: Oesophagus } "Accuracy of a 20 MHz Radial Probe in Staging Small Digestive Tumors"

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## "P P 1 0028" P 1 0028 **Palliative Treatment of Malignant Esophageal Stenosis with Tygon Plastic Prostheses**

\*S. Bohnacker, U. Seitz, K.F. Binmoeller, M. Hinner, H. Seifert, F. Thonke, N. Soehendra

Dept. of Endoscopic Surgery, University Hospital Hamburg, Germany Palliative endoscopic treatment of malignant esophageal stenosis with plastic stents has been reported to have the following disadvantages: 1. high procedural complication rates, 2. high dislocation rates, 3. exclusion of patients with cervical stenoses (distance to upper esophageal sphincter (UES) < 2 cm). We evaluated a modified design and implantation technique of plastic tygon stents with the aim of determining whether these disadvantages apply.

**Methods** All patients underwent palliative treatment of dysphagia resulting from obstructing malignancies of the esophagus. Stents were made of Tygon and came in 3 sizes (9, 12 and 14 mm). The stent length was tailored to the stenosis. The funnel was short; a proximal funnel could be added as well as flaps at the distal end to prevent caudal and cranial dislocation, respectively. Bougienage was performed stepwise, usually over several sessions (dilatation to 33 F, 38 F, 42 F for 9, 12, and 14 mm stents, respectively). The stent was loaded onto a bougie, then inserted over a guide wire without fluoroscopy under iv sedation.

**Results** Between 7/94 and 1/96 54 consecutive patients with inoperable malignant esophageal stenoses (11 upper, 12 middle and 31 lower) were treated by endoscopic insertion of Tygon plastic stents. Implantation was performed after a median of 2 (1–4) sessions of bougienage. Two 9 mm, 35 12 mm and 17 14 mm stents were implanted. In 10 patients the stent was inserted 1 cm below the UES. In 2 of these patients the stent had to be replaced within 24 h because of thoracic pain or immediate dislocation. Perforation or bleeding did not occur. During a median follow-up of 55 d (9–407), 88% of patients reported improvement, or at least no progression, of dysphagia. Fifteen patients required further interventions: 8 had stents repositioned or replaced due to dislocation, pain or pressure-induced ulcer, 4 required recanalisation for bolus obstruction, and 3 treatments for tumor overgrowth. Eight patients who had persistent dysphagia and/or inappetence received nutrition via a duodenal feeding tube or PEG.

**Conclusions** Previously described disadvantages of plastic stents in treatment of patients with malignant esophageal stenosis can be overcome with modifications of stents and implantation technique. The results of treatment with these stents are comparable to those of self-expanding metal stents, but their costs are much lower. Endoscopy, specific: OesophagusOncology, specific: Oesophagus } " Palliative Treatment of Malignant Esophageal Stenosis with Tygon Plastic Prostheses "

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"P P 1 0029" P 1 0029 **Treatment of Malignant Stenosis of the Esophagus by Placement of Self-Expanding Coated Stents (SECS). Results in 35 Patients**

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**The purpose** of this study was to assess the placement, tolerance and efficacy of SECS for malignant stenosis of the esophagus.

**Patients and Methods** From december 1993 to january 1996, placement of SECS was attempted in 35 patients (29 men and 6 women) with a mean age 61 years (range 43 to 86 years). The indication was squamous cell carcinoma of the esophagus (SCCE) with stenosis in 13 cases, SCCE with eso-bronchial fistula (EBF) in 15 cases, an adenocarcinoma of esophagus (AE) with stenosis in 4 cases, a bronchial carcinoma with EBF in 2 cases and 1 extrinsic compression by a bronchial cancer. 3 types of SECS were used. "Song" type were placed in 31 patients, "Boston Scientific" type in 3 patients and "Endocoil Instent" in 1 patient.

**Results** Dilatation of the esophagus stenosis beyond bougie n° 12.8 was not required prior to placement. The SECS was properly placed in 34/35 patients. In 1 case, it was impossible to open the SECS (Song type). Early migration occurred in 3 cases (8.5%) 3–7 days after placement. Hard thoracic pain occurred in 4 cases (3 Song+ 1 Endocoil) and in 1 case (Endocoil stent) it was necessary to remove the stent. The success rate for fonctionnal SECS was 30/35 (85.7%). 16/17 EBF were closed but only 15/16 were able to resume intake of both solids and liquids. The success rate for SECS in case of EBF is 15/17 (88.2%). SECS obstruction occurred in 1 case 6 months after the placement, the SECS (Song type) was removed and an other was placed. Three patients are still alive at 2, 3 and 8 months after placement. The mean duration of patency of SECS for these patient was 2.5 months (range: 1–14 months) and for the patients with EBF mean duration of patency of SECS was 3.5 months.

**Conclusion** This easily inserted SECS constitutes a significant advance for endoscopic management of esophageal stenosis and EBF. Endoscopy, general: Instrumentation, therapyOncology, specific: Oesophagus } "Treatment of Malignant Stenosis of the Esophagus by Placement of Self-Expanding Coated Stents (SECS). Results in 35 Patients"

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## "P P 1 0030" P 1 0030 **Metal Stent for Palliative Treatment of Recurrent Dysphagia in Esophagojejunostomy**

\*P. Ricci, F. Farroni, G. Mariotti, A. Maselli, S. Mosca, R. Ricci, F. Barzi

Digestive Endoscopy, Dept. of Surgery, Dept. of Radiology, University of Perugia, Italy After "curative" resection of gastro-esophageal carcinoma, late severe dysphagia almost invariably indicates loco-regional recurrence. Surgery and radiation therapy are not commonly used because of the associated high morbidity and mortality rates. The only option for most pts. is palliative treatment for rapid relief of dysphagia and restoration of passage of fluids and solids. The best treatment is intubation with self-expanding metal stents for an easy and safe insertion and effective palliation. Six pts., all males, mean age 70 years-old (range 58–79) who had total gastrectomy for esophageal malignancies with recurrent anastomotic stricture underwent palliative treatment with self-expanding metal stent (4 Ultraflex Microvasive, 1 covered Ultraflex Microvasive, 2 silicone covered Gianturco Zestents). The median tumor length was 6.5 cm. (range 5–9 cm.). Two pts. were on TPN for aphagia. Before intubation all pts. received dilation. Four pts. were treated with LASER. Stent insertion was technically successful in all pts. with good symptomatic relief. Complications: 1 stent migration in esophagus (Gianturco) after 3 months with additional placement of Ultraflex stent which gave satisfactory results; severe pain in 1 pt. (Gianturco) who had also delayed massive bleeding after 21 days. Median survival was 90 days (range 21–294). One pt. is still alive after 45 days. The insertion of self-expanding metal stent is an optimal palliative treatment for pts. with anastomotic recurrent cancer. Ultraflex stent in our small series seems to work better for its pliability in esophagojejunostomy recurrence. Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } "Metal Stent for Palliative Treatment of Recurrent Dysphagia in Esophagojejunostomy"

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## "P P 1 0031" P 1 0031 **Self-Expandable Covered Stents for Esophageal Fistulas**

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Esophageal fistulas complicate 15% of esophageal cancers and are associated with severe morbidity and mortality. Their management is particularly difficult when a stricture is absent (e.g. after radiotherapy), rendering stent placement non feasible or inefficient.

**Aim** To prospectively assess the feasibility and efficacy of esophageal fistula sealing with (1) self-expandable covered stents and (2) salvage treatments.

**Patients and Methods** From December 1993 to April 1996, stent placement was attempted in 19 patients [male: 12, age: 61 – 18 yrs (range: 6–82)] with esophageal fistulas. These were related to primary or secondary esophageal cancer (N = 12) as well as a variety of benign disorders (N = 7). The lesion was proximal in 4, mid-esophageal in 10, distal in 3 and at the gastro-esophageal junction in 2. Strictures (present in 8 cases) were dilated up to 15 mm. Covered Ultraflex<sup>®</sup> (N = 14), Wallstent<sup>®</sup> (N = 3) and Wilson-Cook Z<sup>®</sup> (N = 2) stents were inserted under general anesthesia and fluoroscopic control. Salvage treatments used for initial failures of fistula sealing as well as recurrent fistulas consisted of repeated stent insertion or injection of tissue adhesive (Histoacryl<sup>®</sup>) or fibrin sealant (Tissucol<sup>®</sup>).

**Results** Stent insertion and correct positioning were successful in all cases. No procedure-related complications were noted. Fistula sealing was evidenced by esophagogram with Ultraflex<sup>®</sup> or other stents in 14/14 and 1/5 cases ( $p = 10^{-3}$ , 2-tailed Fischer exact test), respectively. Failures to seal fistula were due to passage of fluids between the esophageal wall and stent (N = 3) or early stent migration (N = 1). Although salvage treatments (glue injection, N = 2 or repeated stent insertion, N = 2) achieved fistula sealing as assessed by esophagogram in 3 additional cases, only 1 patient could resume oral intake without aspiration. Among 15 patients with fistula sealing evidenced on their first esophagogram, 12 could start oral intakes while the 3 other patients died early after stent placement. After a mean F/U of 127 – 131 days (range 18–498), fistula sealing remained complete (solids + liquids) in 10/12 (83%) cases and partial (solids only) in 1 (8%) case. This result was achieved with salvage treatments which were attempted in 5/6 cases of recurrent fistulas. These were due to stent migration (N = 2), covering rupture (N = 1), spontaneous fistula enlargement (N = 1), passage of liquids between the esophageal wall and stent (N = 1), bouginage of a stricture due to mucosal hyperplasia.

**Conclusion** Ultraflex<sup>®</sup> covered stent is more effective than other covered metallic stents in sealing esophageal fistulas. This is probably due to the softness of meshes which embed in the esophageal wall, avoiding passage of liquids around the stent. After sealing, fistula may recur for a variety of reasons and can often be successfully treated with well-fitted salvage treatment modalities. } "Self-Expandable Covered Stents for Esophageal Fistulas"



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## "P P 1 0033" P 1 0033 ""Wallstent"" Self Expanding Protheses for Palliation of Malignant Dysphagia

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Hospital de Navarra, Pamplona, Spain Implantation of self expanding stents in the palliative treatment of malignant esophageal strictures has become a widespread established procedure. We report our experience with esophageal ""Wallstent"" for palliation of malignant esophagocardial tumors.

**Material and Methods** 35 patients, 26 males/9 females, aged between 41 and 81 years, were referred for endoscopic palliation of malignant dysphagia. All patients had contraindications for radical surgery. 31 patients had squamous cell carcinoma and 4 cardiac adenocarcinoma. Three patients had an esophagobronchial fistula (EBF). 36 ""Wallstent"" protheses were inserted (one patient required two overlapped stents) after balloon dilation to a diameter of 12–15 mm and under continuous fluoroscopy. In patients with EBF, silicone covered stents were implanted. No dilation was needed after stent placement as the stent widens by its own expansile force.

**Results** Technical success with correct stent placement was achieved in all patients without major complications. Immediate improvement of dysphagia was observed in all cases and patients were discharged within the first 48 hours. Dysphagia recurred in 6 cases due to tumor overgrowth and a new stent was placed overlapping the first. In patients with EBF a complete seal was achieved and no stent migration was observed.

**Conclusions** 1. Wallstent esophageal protheses offer excellent palliation of malignant dysphagia 2. Covered silicone stents have proved to be safe and effective in patients with EBF. 3. Dilation requirements are modest due to the small diameter of the delivery catheter and stent own expansile force. Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } ""Wallstent"" Self Expanding Protheses for Palliation of Malignant Dysphagia"

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## "P P 1 0034" P 1 0034 **Prognostic Factors in Patients with Malignant Esophageal Stenosis and Palliative Treatment with Self-Expanding Mesh Stents**

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<sup>1</sup> St\{e4dtisches Krankenhaus S\{fcd, L\{fcbeck, Germany We previously reported on the prognostic parameters in patients with esophagogastric carcinoma during laser treatment (Endoscopy 21, 254). The palliative endoscopic treatment of malignant stenoses of the upper gastrointestinal tract by self-expanding mesh stents is an alternative and novel procedure. Factors influencing clinical outcome and survival rates in these patients have not yet been defined. From July 1992 to August 1995 40 patients (11 females, 29 males, mean age 63 (22–82) yrs.) were treated with 51 mesh stents (Ultraflex<sup>R</sup> 35, Wallstent<sup>R</sup> 16). Survival rates (Kaplan Meier) were analyzed with regard to the degree of dysphagia (grades 0–3), Karnofsky's score, additional therapy by chemo- and radiotherapy. Complication and reintervention rates have also been analyzed. Dysphagia improved significantly in all patients within 24 hours (2.1 – 0.7 pre vs. 0.5 – 0.7 post implantation;  $p < 0.05$ ). Survival of patients without residual dysphagia was prolonged (180 – 31 vs. 137 – 26;  $p < 0.05$ ). During a median follow-up period of 60 days (range 51–116 days) 23 patients (53%) reported a worsening of dysphagia which could be relieved by endoscopic reintervention in 21 (91%) of them. 15 of 28 patients (54%) with primary weight loss stabilized or increased their body weight and experienced superior survival (234 – 49 vs. 179 – 22,  $p < 0.05$ ). A subgroup receiving additional radio-chemotherapy (T<sub>3</sub>N<sub>1</sub>M<sub>0</sub>) survived longer compared to a matched subgroup without additional therapy (499 – 83 days vs. 166 – 22 days;  $p < 0.001$ ). Acute complications within 7 days included insufficient stent expansion ( $n = 15$ ) and epigastric or retrosternal pain ( $n = 8$ ); severe complications (bleeding, perforation) did not occur. Survival of patients with stenosing esophageal carcinoma and mesh stent implantation is prolonged significantly by additional cancer therapy, early stabilisation of body weight and without residual dysphagia. Oncology, specific: Oesophagus Oncology, general: Therapy Endoscopy, specific: Oesophagus } "Prognostic Factors in Patients with Malignant Esophageal Stenosis and Palliative Treatment with Self-Expanding Mesh Stents"

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## "P P 1 0038" P 1 0038 **Combined Endoscopic Treatment of Nonresectable Esophageal Carcinoma**

\*W. Otto, P.M. Paczkowski, W. Gackowski, B. Najnigier, A. Karwowski

Medical Academy of Warsaw, Warsaw, Poland Over 30 patients are treated each year for squamous cell esophageal carcinoma in our Department. More than 80% of them present with TNM stage III/IV. The purpose of the study was to introduce and evaluate laser endoscopy and stenting, combined with additional radiotherapy as a method of palliation in these cases. One hundred patients (36 F, 64 M, m.a. 68) have been treated prospectively since 1991. They were qualified to the procedure because of advanced age, extensive carcinoma infiltration, concomitant disease excluding surgery or loss of more than 20% of body weight. The procedure consisted of endoscopic Nd:YAG laser vaporization alone in 37 patients and laser vaporization followed by radiotherapy in 63 patients. In 12 of them a self-expanding prosthesis was introduced to the recanalized part of the esophagus. Efficacy of the procedure, time of survival and quality of patients' life were evaluated. There were 14 deaths (14%) related to the procedure itself, 6 of them caused by esophagus perforation and 8 – related to the failure in recanalization. In 86 patients recanalization was achieved, although in 23 was not complete. In the latter group the quality of life was poor and just 16% of patients survived more than 6 months (no 1-year survival). In the remaining 63 patients, who underwent radiotherapy (12 of whom were prothesised) quality of life was good or acceptable and 39% of them survived more than 12 months. The longest period of survival is 19 months in 6 patients. We conclude that endoscopic laser treatment is useful for palliation of nonresectable esophageal carcinoma. Satisfactory results may be achieved if it is applied relatively early and is followed by additional radiotherapy. Stenting simplifies the procedure and helps to maintain the patency of recanalized occlusion. Endoscopy, specific: Oesophagus Oncology, specific: Oesophagus } "Combined Endoscopic Treatment of Nonresectable Esophageal Carcinoma"

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"P P 1 0039" P 1 0039 **Real Benefits in Conventional Vs. Expandable Stents for Esophageal Cancer: In What Cases?** H. Mart'ednez, N. Chopita, N. Landoni, A. Jmelnitzky

**La Plata University Medical School, Hospital San Mart'edn, Gastroenterology Service, La Plata, Argentina**

**Aims** To compare our experience with conventional endoscopic stents for palliative management of esophageal cancer with our results in a recent series using self-expanding metal stents, related to early mortality and morbidity, survival and cost-benefit relation.

**Material and Method** from November 1992 up to July 1995, 25 patients underwent palliative treatment for esophageal cancer receiving 32 self-expanding metal stents: 9 Strecker, 16 Gianturco-Rosch, 6 Wallstent and 1 esophacoil type. Results were compare with a series of 60 patients receiving plastic prosthesis.

**Results** Plastic stents Self-expanding stents N = 60 n (%) N = 25 n (%) Early mortality 10 (16.6) 1 (4.0) Early morbidity 4 (6.6) 2 (8.0) Late mortality 4 (6.6) 1 (4.3) Late morbidity 17 (28.2) 5 (21.7) Survival (4 months) 4.8 6.0

**Conclusions** In our experience self-expanding esophageal stents seem to show a trend to a lesser early mortality than the classic type, without significative difference in other parameters; due to the great difference in costs (10 times) in Argentine, we suggest to reserve self-expanding stents for patients with difficult malignant stenosis not easily amenable to other methods and with fistulas Endoscopy, specific: Oesophagus } "Real Benefits in Conventional Vs. Expandable Stents for Esophageal Cancer: In What Cases?"

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"P P 1 0041" P 1 0041 **Diagnosis and Treatment of Superficial Esophageal Carcinomas**

\*T. Kawano, K. Yoshino, K. Nagai, H. Inoue, M. Endo

First Department of Surgery, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan We studied the accuracy of pretreatment diagnosis of the superficial esophageal carcinomas (SECs) and the reliability of endoscopic esophageal mucosectomy (EEM), and discuss a strategy for the treatment of SEC.

**Patients and methods** 191 patients with SEC treated by esophagectomy in our department during a recent 11 year period and 71 patients with SEC or dysplasia treated by mucosectomy were evaluated retrospectively.

**Results** Clinicopathological study of patients with mucosal carcinoma revealed the rare occurrence of lymph node metastasis (1.1%) and no lymph node metastasis in patients with tumors showing no vascular involvement. On the other hand, many patients with submucosal carcinoma had lymph node metastasis. The accuracies of pretreatment diagnoses of the depth of tumor invasion and lymph node metastasis by a combination of endoscopic observation, endosonography, and computed tomography were 86% and 75%, respectively, which were considered to be unsatisfactory. On the other hand, specimens obtained by mucosectomy offered precise and detailed information about tumor extension, i.e. depth of tumor invasion, vascular involvement, etc. Moreover, mucosectomy using the negative pressure method was not difficult and was safe for wide mucosal lesions.

**Conclusion** Almost all mucosal cancers of the esophagus should be treated by esophagus-preserving methods, and endoscopic mucosectomy should play a role not only as a therapeutic modality, but also as an important diagnostic tool for use in patients with SEC in which invasion is suspected of being at the mucosal or superficial submucosal layer. Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Instrumentation, therapy } "Diagnosis and Treatment of Superficial Esophageal Carcinomas"

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## "P P 1 0044" P 1 0044 A New Instrument for Endoscopic Esophageal Mucosectomy

\*T. Kawano, K. Nagai, H. Inoue, K. Yoshino, M. Endo, K. Takeshita<sup>1</sup>

First Department of Surgery and Endoscopic Division, Tokyo, Japan

<sup>1</sup> Tokyo Medical and Dental University School of Medicine, Tokyo, Japan  
Endoscopic esophageal mucosectomy (EEM) is somewhat difficult because the esophagus is a narrow tubular organ. We devised a technique for EEM using a transparent overtube with negative pressure (np-EEM, Dig. Endosc., 1991). We altered the commercially available tube for this technique and performed EEM. However, alteration of the tube is troublesome, and now the tube for np-EEM is commercially available (Multipurpose guide tube (MDU type), Create Medic Inc., Tokyo, Japan,; MP tube). Here we describe the MP tube and how to use it.  
Instrument and techniques: The MP tube is made totally of silicone, is almost transparent, 60 cm in length, 15.5/12.0 mm in outer/inner diameter, and has a proximal balloon for making intraluminal negative pressure, a distal outer balloon for hemostasis after EM, a working channel, and a side hole for mucosectomy. The preparation is the same as for usual endoscopy, and the MP tube overlaid on the panendoscope is inserted after endoscopic observation.

**Introduction** The protruding mucosa induced by negative pressure and submucosal saline injection is strangulated by the snare and cut with high frequency current.

**Results** We performed EEM using an MP tube in 23 patients. The tube enabled us to achieve a relatively wide (2.5–3.5 cm times; 2.0–3.0 cm in size) mucosectomy and repetitive mucosectomy was also easy. No perforations and no uncontrollable bleeding occurred.

**Conclusion** A multipurpose guide tube (MDU type) is very useful when performing EEM with the negative pressure method. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } "A New Instrument for Endoscopic Esophageal Mucosectomy"

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"P P 1 0045" P 1 0045 **The Non Surgical Chemoradiation Protocol of Advanced Esophageal Cancer: Is Endoscopic Laser Helpful?** R. Lambert,

\*P. Jacob, G. Bernard, F. Desseigne, F. Mornex, F. Descos

Federation Digestive, Hospital E. Herriot, 69453, Lyon, France This randomized prospective study aims to determine whether, in the non surgical chemoradiation treatment of advanced esophageal cancer, a single session of laser esophageal desobstruction after the first chemotherapy course will improve symptoms, tumor response or survival.

**Methods** From 1992 to 1993, 20 patients (16 men and 4 women, mean age, 62 years; age range, 46–79 years) with advanced esophageal squamous cell cancer were submitted to a non surgical chemoradiation protocol with 5 chemotherapy courses (5FU-CDDP) and 3 radiation courses (20, 20 and 10 Gy). All patients had dysphagia (grade 1 or 2 in the Atkinson scale). They were randomized in 2 groups. –

**Group I** 10 patients with chemoradiation alone – sex: 7 men, 3 women, mean age: 60 y, mean weight: 62 kgs, dysphagia score 1.4, EUS stage: uT3, N+ in 8, uT4, N+ in 2. –

**Group II** 10 patients with laser and chemoradiation – 9 men, 1 woman, mean age 63 y, mean weight 63 kgs, dysphagia score 1.4, EUS stage: uT3, N+ in 6, uT4, N+ in 4). A single Nd YAG laser session (mean: 3370 Joules) was performed after the first chemotherapy session. Criteria in the follow up were: – at 2 months: dysphagia score and EUS response – at 6 months: Weight variation, mean number of dilation sessions, tumor response as complete or incomplete (macroscopic and histological) – Finally the death rate during follow up and median survival were evaluated.

**Results** The average follow-up was the same in the 2 groups (45 months). At 2 months, the mean improvement in dysphagia score were 0.7 and 1.2 respectively in groups I and II. A reduction in EUS staging was notified in 4 patients in groups I (40%) and 5 in group II (50%). At 6 months, no significant weight variation between the 2 groups was notified. The mean N° of dilation sessions was 3.1 in group I and 2.1 in group II. The tumor response was complete in 3 patients in each group (30%). During follow up, death rate was 80%, in group I and 100% in group II. The median survival was higher in group II (14.5 months) than in group I (7 months), but this difference was not significant (Wilcoxon test).

**Conclusions** in advanced esophageal cancer, an endoscopic laser session in addition to the chemoradiation protocol results in a slight improvement of the dysphagia score, no change in the rate of complete tumor response. The increased median survival rate is not associated in a reduction of the high death toll. Its main justification is the relief of dysphagia in the initial period; the procedure is therefore recommended in polypoid obstructive tumors only. Oncology, specific: Oesophagus Endoscopy, specific: Oesophagus } "The Non Surgical Chemoradiation Protocol of Advanced Esophageal Cancer: Is Endoscopic Laser Helpful?"



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## "P P 7 0161" P 7 0161 **Lymph Node Detection by Ultrasound within the Hepatoduodenal Ligament in Patients with Primary Biliary Cirrhosis**

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Dept. of Internal Medicine, JW Goethe University, Frankfurt, Germany

**Purpose** Viral, bacterial infections and enterotoxins have been proposed as etiopathological factors causing primary biliary cirrhosis (PBC). Therefore we prospectively investigated the number and size of lymph nodes (LN) within the hepatoduodenal ligament (HDL) in 35 consecutive patients with PBC and in 30 healthy controls.

**Methods** Sonographic detection of LN within the HDL was validated in 20 human bodies including histological examination of the respective LN to exclude malignant infiltration. In the present study the LN ventral of the portal vein (PV) and between the PV and inferior vena cava were evaluated by high resolution ultrasound (Acuson 128, 3.5 MHz) in 35 consecutive patients with primary biliary cirrhosis (age: 56 – 9 years) and in 30 healthy controls (30 – 8 years) in a 15° degree left lateral position in a standardized fashion by one examiner. The area (ellipse function) of all LN detected was recorded for each region. The stages I–IV of PBC were biochemically and histologically proven in all patients.

**Results** In 32/35 patients (91.4%) and in 28/30 healthy controls (93.3%) adequate visualisation of the region of the HDL was achieved. LN were detected in 30/32 patients with PBC (93.8%) and in 12/28 controls (46.4%). The mean LN area size was 461 – 325 mm<sup>2</sup> in the PBC group and 81 – 45 mm<sup>2</sup> in the controls ( $p < 0.0001$ ). Number and size of the lymph nodes showed no significant correlation to liver function tests.

**Conclusion** Enlarged lymph nodes within the hepatoduodenal ligament are sonographically detectable in almost all patients with PBC. This lymph node enlargement could reflect extrahepatic immunological activity and could be helpful in the diagnosis of PBC. Radiology and ultrasound: Diagnosis Liver and bile ducts, 1: Chronic non viral hepatitis Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Lymph Node Detection by Ultrasound within the Hepatoduodenal Ligament in Patients with Primary Biliary Cirrhosis"

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## "P P 7 0162" P 7 0162 **Intraductal Ultrasound (IDUS) and ERCP — A New Diagnostic Dimension?**

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Department of Medicine B, University of Muenster, Germany

Endoscopic retrograde cholangiopancreatography (ERCP) is able to depict diseases affecting the pancreatobiliary tract fluoroscopically. To allow a diagnosis additional information on adjacent tissue is useful. Intraductal ultrasonographic imaging (IDUS) with newly developed probes is feasible during ERCP. During ERCP ultrasound miniprobes (Aloka, Microvasive, Endosonics) with diameters of 3.5 up to 6.2 French were inserted via the working channel of a routine duodenoscope (Olympus JF1T20). 53 patients underwent intraductal ultrasound with these probes. In 32 patients (17 women, 15 men) the probe was inserted into the biliary tract, in 21 patients (9 women, 12 men) into the pancreatic duct. IDUS of the tail of the pancreas was possible in 48%, of the body in 90% and of the head of the pancreas in 95%. Due to ultrasound frequencies of 12.5 to 30 MHz imaging of stenoses in microscopic dimension of a magnifying glass was possible. Malignant infiltration of the pancreatic duct appeared inhomogeneously echopoor, whereas carcinoma of the bile duct appeared echodense. Lymph nodes of a size of 5 mm in diameter adjacent to the bile duct were visualized. Infiltration of the tumor into the portal vein system is detectable. However, the high ultrasound frequency of the probes limits the penetration depth. Thus the extension only of large tumors could not be demonstrated completely. Rotation of the cable in mechanical probes sometimes limits the flexibility of the probes. On average intraductal ultrasound examination during ERCP took 4:16 minutes (1:23 up to 13:36). There was no indication of any injury to the duct system or the pancreas. Intraductal ultrasound of the pancreatobiliary tract is a secure, easy and quick examination which can be performed during ERCP. IDUS gives important supplementary information on the periductal tissue. Controlled studies to compare the diagnostic value of IDUS with that of conventional techniques (EUS, CT) are currently underway.

Endoscopy, specific: Biliary Echoendosonography: Echoendoscopy Echoendosonography: Therapy } "Intraductal Ultrasound (IDUS) and ERCP / A New Diagnostic Dimension?"

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"P P 7 0163" P 7 0163 **Endoscopic Ultrasound and Helical CT Scan for Bilio-Pancreatic Cancer: Preliminary Prospective Study of 40 Patients** F. Jellouli, O. Keriven-Souquet, L. Henry, B. Napol'e9on, B. Pujol, P.J. Valette, T. Ponchon,

\*J.C. Souquet

Department of Digestive Diseases, Hospital E Herriot, Lyon, France Endoscopic ultrasound (EUS) is nowadays a recognized method for bilio-pancreatic imaging: it has been shown superior to CT scan for the diagnosis of small pancreatic tumors and tumor staging. Helical CT scan is a promising improvement, that could increase the efficiency of CT. Here we prospectively compared these 2 methods for the study of bilio-pancreatic carcinomas.

**Methods** 50 patients referred for EUS (search of bilio-pancreatic tumor) were prospectively included. EUS (Olympus JF or GF M20) were performed under intravenous sedation. For helical scan (Philips SR 7000), patients absorbed 1000 ml water and received IV 15 mg Tiemonium. A first acquisition (general examination of the pancreas) was obtained with 10 mm continuous slices. A second acquisition (fine imaging of the pancreas) was obtained 30 s after contrast injection with thirty-five 3 mm continuous slices. A third acquisition (study of veins) was obtained 80 sec after the injection with 10 mm continuous slices. EUS and helical CT were performed independantly within 48 hours, in a randomized order and with the same level of clinical background. Results were compared to the final diagnosis obtained by surgery, cytoponction or follow-up.

**Results** Final diagnosis was obtained in 40 patients (surgery in 13, cytology in 8, follow-up superior to 8 months in 19 – ERCP in 11). It consisted in bilio-pancreatic tumors in 16 (pancreatic adenocarcinoma, n = 8; cholangiocarcinoma, n = 4; ampulloma, n = 2; pancreatic endocrine tumor, n = 1; mucinous ductal ectasia, n = 1) and non tumoral diseases in 24 patients (ampullary sclerosis, n = 2; bile duct stone, n = 3; chronic pancreatitis, n = 4; pancreatic cyst, n = 5; no abnormality, n = 10). For the diagnosis of bilio-pancreatic tumor (absence or presence of such a tumor), EUS was right in 38/40 cases (95%) while helical CT was right in only 27/40 cases (68%). For determining the true nature of the visualized tumor, EUS was accurate in 11/14 cases (79%) and helical CT in 6/9 only (67%). For lymph node staging, in the 9 patients operated on and evaluable, EUS was correct 6 times and helical CT 4 times. For the determination of vascular invasion (present in 3 cases, absent in 11 cases), helical CT was always right, while EUS missed invasion of the mesenteric vein by a pancreatic adenocarcinoma in one case.

**Conclusions** while helical CT scan appeared an improvement in comparison to classical CT scan, it remained inferior to EUS in this preliminary study regarding the diagnosis of bilio-pancreatic tumor. Echoendosonography: EchoendoscopyOncology, specific: Pancreas }"  
"Endoscopic Ultrasound and Helical CT Scan for Bilio-Pancreatic Cancer: Preliminary Prospective Study of 40 Patients"

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## "P P 7 0164" P 7 0164 **Cholangioscopic Ultrasonography in the Diagnosis of Extrahepatic Bile Duct Carcinoma**

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<sup>1</sup> Second Department of Internal Medicine, Nagoya University School of Medicine, Japan  
Ultrasonograms, obtained using a 20-MHz mechanical linear ultrasound probe under cholangioscopic guidance, were analyzed to develop criteria for assessing the depth of carcinomatous invasion of extrahepatic bile duct (EHBD). We studied ultrasonograms of 25 in vitro EHBD walls, including 12 normal and 13 carcinoma specimens. Using this probe, we performed percutaneous transhepatic cholangioscopic ultrasonography (PTCSUS), in 25 patients with EHBD carcinoma. Ultrasonograms suitable for evaluating the depth of tumor infiltration were obtained in 23 of 25 patients (92%). Overall accuracy of PTCSUS was 91.3% in 23 patients, including 1 case of T1, 8 of T2, 14 of T3. Understaging of a T2 carcinoma and of a T3 carcinoma occurred in 1 (12.5%), and 1 cases (7.1%), respectively. The probe produced higher resolution ultrasonograms than present methods. This study indicates that PTCSUS with the ultrasound probe may become a clinically useful procedure for preoperative staging of EHBD carcinoma. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Biliary Echoendosonography: Echoendoscopy } "Cholangioscopic Ultrasonography in the Diagnosis of Extrahepatic Bile Duct Carcinoma"

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## "P P 7 0165" P 7 0165 Endoscopic Ultrasonography in the Evaluation of Dilated Common Bile Duct of Unexplained Origin in Transabdominal Ultrasonography

\*Y. Song, U. Yilmaz, A. Serin, dc. Saritas, G. Temu'in, B. Sahin

Dept. of Gastroenterology, Y'cksek Ihtisas Hosp., Ankara, Turkey Abdominal ultrasonography (US) is the procedure of the first choice in the demonstration of a dilated common bile duct (CBD), but the cause can be determined in only two third of patients. The aim of this prospective study was to assess the value of EUS in detecting the cause of CBD dilatation in the patients in whom US failed or revealed equivocal results to diagnose the cause of dilatation.

**Methods** Between June 1995 and May 1996, ninety consecutive patients (54 women, 36 men, range 21–74 years) who had enlarged (the diameter 7 mm or more) CBD of unexplained origin during US examination were included in this study. Twenty-eight patients had had previous cholecistectomy. All patients underwent EUS examination. Final diagnosis was determined by endoscopic retrograd cholangiopancreatography (ERCP) with or without sphincterotomy (n = 53) or surgical exploration (SE) (n = 23).

**Results** The following diagnoses were correctly made by EUS: choledocholithiasis in 38, tumor of the papilla of the Vater in 8, benign distal stricture in 8, distal cholangiocarcinoma in 4, choledochal cyst in 2, ova of *Ascaris* in 1 patient. In two patients, ERC did not show choledocholithiasis seen by EUS. In one patient, EUS did not show choledocholithiasis seen by ERC. The diagnosis of distal cholangiocarcinoma was not confirmed by ERC in one patient. In two patients, the transducer could not be inserted into the second duodenum because of duodenal stenosis. EUS findings were normal in 23 patients, except for CBD dilatation. In 9 of the 23 patients, EUS result was confirmed by ERC. ERCP or SE was not performed in the remaining 14 patients. Excluding the 14 patients who had only dilated CBD, EUS provided an accurate explanation for CBD dilatation in 70 of the 76 patients (92%). We conclude that EUS is a highly accurate modality for the detection of the cause of CBD dilatation. EUS can demonstrate the type, location and extent of biliary obstruction. Endoscopy, specific: Biliary Echoendosonography: Echoendoscopy Radiology and ultrasound: Diagnosis }"  
"Endoscopic Ultrasonography in the Evaluation of Dilated Common Bile Duct of Unexplained Origin in Transabdominal Ultrasonography"

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## "P P 7 0166" P 7 0166 **Percutaneous Transhepatic Ultrasound-Guided Puncture of the Gallbladder for Acute Cholecystitis**

\*M. Ichikawa, O. Takahara, A. Ishihara, H. Hamada, A. Toyoshima, J. Kanou

Department of Internal Medicine, Anjo Kosei Hospital, Anjo, Japan  
The aim of the present study was to assess experience with percutaneous transhepatic ultrasound-guided puncture of the gallbladder (PTUPG) in resolving the acute episode of cholecystitis.

**Patients and methods** Thirty-one consecutive patients (18 men, 13 women) with a clinical diagnosis of acute cholecystitis (25 cholelithiasis, 13 acalculous) underwent the procedure on an emergency basis. The median age was 61 years (range 39–84). Twelve of the 31 patients were considered high-risk patients. PTUPG was performed as a bedside procedure under local anaesthesia. Under ultrasonic guidance, a 21-gauge PTC needle was used. After complete aspiration of the gallbladder, the PTC needle was withdrawn. All patients were taking antibiotics systematically before and after the procedure.

**Results** PTUPG was performed successfully and rapid resolution of symptoms occurred in almost all patients. Sixty-six percent of aspirates were positive for a variety of organisms. No complications related to the puncture were seen.

**Conclusion** PTUPG should be considered a simple, safe and efficacious means of conservative management of the patient with acute cholecystitis. Liver and bile ducts, 2: Gallstones, formation, treatment  
Radiology and ultrasound: Diagnosis  
Radiology and ultrasound: Therapy }  
"Percutaneous Transhepatic Ultrasound-Guided Puncture of the Gallbladder for Acute Cholecystitis"

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"P P 7 0167" P 7 0167 **Usefulness of Endoscopic Ultrasonography for Detecting Gallbladder and Common Bile Duct Lesion in Patients with Anomalous Connection of Pancreato-Biliary Ducts**

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Divisions of Internal Med. of Gastroenterology, Iwate Prefectural Central Hospital

Divisions of Pathology

**Introduction** The relation between carcinoma of the gallbladder and an anomalous connection of pancreato-biliary ducts is well known. We encountered 24 cases of anomalous connection of the pancreato-biliary ducts [9 males, 15 females, mean age 46.7 (range 18 – 76)]. Eleven cases demonstrated choledochal cysts, but 13 cases demonstrated common bile duct (CBD) with no dilatation. Associated conditions included gallbladder (GB) cancer in 7, CBD cancer in 3, CBD stone in 3, pancreatitis in 8.

**Aim and Method** To evaluate the diagnostic efficacy of endoscopic ultrasonography (EUS) for anomalous pancreato-biliary ducts 11 patients which had undergone EUS preoperatively, were reviewed.

**Result** Abdominal ultrasonography (US) was performed in 24 cases. US revealed GB wall thickness (n = 7), GB polyp (n = 2), GB tumor (n = 9), GB tumor with stone (n = 1), debris (n = 2), comet echo (n = 1), and no abnormality (n = 1). EUS was performed in 11 cases. Using EUS, we could detect GB or CBD tumor in 5, GB polyp in 2, and thickening of the first GB layer in 4. EUS images were compared with histological findings of surgical materials in each case. Pathological findings were GB cancer in 3, CBD cancer in 1, hyperplasia of the gallbladder wall in 1, and adenoma in 2, being compatible with EUS findings. Four patients with thickening of the first GB layer had GB cholesterosis. Although EUS showed a common channel of an anomalous connection of pancreato-biliary ducts was successful in 9 of 11 (82%).

**Conclusion** EUS produces better images of the GB and CBD in patients with anomalous connection of pancreato-biliary ducts than US does. Thorough evaluation of the common channel by EUS, however, was not possible and additional evaluation with ERCP (endoscopic retrograde cholangiopancreatography) is required. Liver and bile ducts, 2: Biliary cysts, atresia  
Endoscopy, specific: Biliary Echoendosonography: Echoendoscopy } "Usefulness of Endoscopic Ultrasonography for Detecting Gallbladder and Common Bile Duct Lesion in Patients with Anomalous Connection of Pancreato-Biliary Ducts"

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## "P P 7 0168" P 7 0168 **Magnetic Resonance Cholangiography (MRC) in Cholestatic Jaundice**

\*G. Macarri, G. Feliciangeli, A. Giovagnoni<sup>1</sup>, C. Guidarelli, V. Berdini, L. Costarelli<sup>1</sup>, A. Benedetti, F. Orlandi

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<sup>1</sup> Dept. of Radiology, University of Ancona, Ancona, Italy The MRC allows a tridimensional visualization of biliary tree based on Fast Spin Echo sequences. Its clinical value has not been evaluated yet. *Aim* of this study was to prospectively evaluate the diagnostic accuracy of MRC in the cholestatic jaundice. *Patients and Methods.* 34 consecutive patients (19 male, median age 66.1 years, range 39–85 years) with cholestatic jaundice (total bilirubin > 5 mg/dl), elevated serum indexes of cholestasis and common bile duct diameter > 7 mm as determined by ultrasonography have been enrolled. MRC and ERCP were performed on the same day by investigators unaware of the results of the other procedure. ERCP with or without surgery was used as the diagnostic gold standard. *Results.* MRC and ERCP were carried out in 32 of 34 patients. Choledocholithiasis (13 patients), somatostatinoma (1 pat), ampullary adenocarcinoma (2 pat), pancreatic adenocarcinoma (5 pat), haemobilia (1 pat), benign stricture of the common bile duct (CBD) (2 pat), carcinoma of gallbladder wall (1 pat), cholangiocarcinoma (1 pat) and 6 patients with normal biliary tree have been admitted to the study. MRC was negative in 4/6 patients with normal biliary tree (specificity 66.6%) and was positive in 24/26 patients with abnormalities of biliary tree (sensitivity 92.3%). Particularly MRC identified 10/14 patients (71.5%) with filling defect of CBD and 12/13 patients with stenosis (92.3%). In 2 cases of CBD stricture at MRC, small extractable stones were present at ERCP. Overall Positive Predictive Value (PPV) was 92.3%. No side effects at MRC were observed. *Conclusions.* Our results show that in patients with cholestatic jaundice MRC was very sensitive to show CBD abnormalities but less accurate to define their nature. Major limitation of MRC is its inability to offer therapeutic intervention. Radiology and ultrasound: Diagnosis Endoscopy, specific: Biliary }  
"Magnetic Resonance Cholangiography (MRC) in Cholestatic Jaundice"

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## "P P 7 0169" P 7 0169 **Magnetic Resonance Cholangiopancreatography, Alternative Method in Bile Duct Obstruction Diagnosis**

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**Purpose** Magnetic resonance cholangiopancreatography (MRCP) was evaluated and assessed as an alternative to endoscopic ultrasonography (EU), endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTC).

**Methods** MRCP was performed in 46 patients using half fourier single shot turbo spin echo sequence (HASTE sequence) with coronal, oblique or sagittal images. The imaging time was 18 seconds (breath-hold) for sequential acquisition of multislice technique with 5 mm slice thickness. All the patients presented clinical symptoms and/or biochemical studies consistent with gallstone disease and/or bile duct obstruction or pancreatic disease. Final diagnosis was established with surgery (n = 35) ERCP (n = 10) EU (n = 10) PTC (n = 3)

**Results** In gallstone disease (n = 20) the sensitivity of MRCP was 82% for gallbladder calculi; 89% for choledocholithiasis. Common bile duct and main pancreatic duct were seen in 100% patients, cystic duct in 64%. Biliary tree obstruction by tumors (n = 16) was showed by MRCP in all cases. In chronic pancreatitis (n = 5) common bile duct dilatations, pancreatic duct features and pseudocyst formations were visualized. Accurate level of benign biliary stricture (n = 5) was demonstrated.

**Conclusion** MRCP is a useful non invasive tool for the evaluation of bile duct obstruction. It may replace percutaneous transhepatic cholangiography and can be an alternative when endoscopic retrograde cholangiopancreatography or endoscopic ultrasonography are unsuccessful. Pancreas: Pancreatitis, chronic Liver and bile ducts, 2: Bile formation, cholestasis Radiology and ultrasound: Diagnosis } "Magnetic Resonance Cholangiopancreatography, Alternative Method in Bile Duct Obstruction Diagnosis"

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## "P P 7 0170" P 7 0170 Is Magnetic Resonance Cholangiopancreatography Able to Take the Place of Endoscopic Retrograde Cholangiopancreatography?

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**Introduction** By the technical development of magnetic resonance tomography (MR) there are efficient devices available for MR-cholangio-pancreatography (MRC-P) in the meantime. For the first time their high resolution makes a direct comparison to the established endoscopic retrograde cholangio-pancreatography (ERC-P) possible. In an initial series the clinical value of this non-invasive imaging technique in diseases of the bile and pancreatic duct system could be evaluated.

**Methods** As MR-tomograph a 1.5 Tesla Gyroscan (Philips<sup>R</sup>) for static MRC-P with special adapted turbospinechosequences was available. MRC-P was performed with a T2-weighted IR-sequence with a layer of 3 mm and a 1.5 mm overlapping tomography in coronary orientation and respiratory triggering and an IR-delay time of 90 ms.

**Results** In 22 patients MRC-P was performed, in 9 of them a malignant process was diagnosed (3x Klatskin-tumors, 3x bile duct carcinomas, 2x pancreatic carcinomas, 1x carcinoid of the pancreas). In 3 patients a chronic pancreatitis was found, in 2 with liver cirrhosis a thin intrahepatic bile duct system was shown, in 4 alterations of the extrahepatic bile duct system after orthotopic liver transplantation were demonstrated. A stenosis of the common bile duct could be proved in 3 patients after laparoscopic cholecystectomy, in 1 patient a CBD-stone. In 20 of those patients an ERC was performed. In 18 cases was a right positive correlation, in 2 a wrong negative result of the MRC. With MRC-P the pancreatic duct could be sufficiently demonstrated only in 8 patients. In localisation and definition of bile duct stenoses MRC and ERC are comparable. In the definition of the extension of Klatskin-tumors MRC is better than ERC. In general imaging of the papillary near duct segments is of better quality in ERC than in MRC.

**Conclusions** MRC as a non invasive imaging procedure is qualified for planning therapeutic ERC and PTC-techniques as well as for review of endoscopic placed drainages especially in cases with Klatskin-tumors. MRC makes a very important contribution to visualise hepatic branches that are not demonstrable with ERC due to tumor growth. Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic Radiology and ultrasound: Diagnosis } "Is Magnetic Resonance Cholangiopancreatography Able to Take the Place of Endoscopic Retrograde Cholangiopancreatography?"

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"P P 7 0171" P 7 0171 **Usefulness of Endoscopic Ultrasonography in Diagnosing Elevated Lesions of the Gallbladder: With Emphasis on Its Usefulness in the Diagnosis of Adenomyomatosis**

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**Purpose** The usefulness of endoscopic ultrasonography (EUS) in diagnosing elevated lesions of the gallbladder, especially its usefulness in distinguishing adenomyomatosis (ADM) from other gallbladder diseases, was assessed in comparison with other imaging techniques.

**Subjects and Methods** The subjects of this study were 30 patients who underwent cholecystectomy following the detection of elevated lesions of the gallbladder by EUS at our department between April 1992 and March 1996. The EUS-based diagnosis of elevated lesions of the gallbladder was compared with their histopathological diagnosis. For cases where a diagnosis of ADM was made histopathologically, we compared the accurate diagnosis rate, the wall hypertrophy detection rate and the Rokitanski-Aschoff sinus (RAS) detection rate using abdominal ultrasonography, abdominal CT, ERCP and EUS.

**Results** The diagnosis made by EUS was cholesterol polyp in 10 cases, adenoma in 1 case, ADM in 11 cases, cancer in 7 cases and not detected in 1 case. The histopathological diagnosis was cholesterol polyp in 9 cases, adenoma in 1 case, ADM in 11 cases, cancer in 6 cases and others in 3 cases. Thus, the EUS-based diagnosis had an accuracy of 70.0%. For the 11 cases where a diagnosis of ADM was made histopathologically, the accurate diagnosis rate was 54.5% by ultrasonography, 18.2% by abdominal CT, 63.6% by ERCP and 81.8% by EUS.

**Conclusion** 1. EUS was found to be useful in qualitative diagnosis of elevated lesions of the gallbladder. 2. A diagnosis of ADM seems reasonable if its three major signs of ADM (a 3 mm or greater hypertrophy of the gallbladder wall, the presence of two or more RAS within a 1 cm segment of the gallbladder wall, preservation of the three-layer structure of the gallbladder wall) are detected using EUS. Endoscopy, specific: BiliaryEchoendosonography: Echoendoscopy }  
"Usefulness of Endoscopic Ultrasonography in Diagnosing Elevated Lesions of the Gallbladder: With Emphasis on Its Usefulness in the Diagnosis of Adenomyomatosis"

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## "P P 8 0172" P 8 0172 **Ampullary Carcinoma: Analysis of Prognostic Factors for Survival**

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**Aim** To evaluate ampullary carcinoma survival prognostic factors by studying a series of patients who underwent ERCP for obstructive jaundice.

**Methods** From 1989 to 1995, 49 consecutive patients (33 M and 16 F; median age 70, range 34–92 years) with ampullary carcinoma were diagnosed by ERCP and histology and followed-up (mean follow-up 639 days, range 1–2370). The following data were retrospectively reviewed for all patients: clinical data, laboratory results (bilirubin, ALP, GGT, ASAT, ALAT, amylase, hemoglobin, leucocyte count), imaging investigations (UES, CT), ERCP data (endoscopic findings, CBD fluoroscopic findings, sphincterotomy and/or endobiliary stent), histologic findings, operative procedures (pancreaticoduodenectomy, surgical bypass procedure, endoscopic biliary drainage). Survival rates were calculated by using the Kaplan-Meier method, the Log-Rank test was utilized for the univariate analysis of the survival curves and the Cox regression model for the multivariate survival analysis.

**Results** In the total group the 1- and 3-year survival was 66% and 30% respectively. By using univariate analysis, factors affecting negatively survival were: age > 60 ( $p < 0.1$ ), leucocyte count > 10000 ( $p < 0.0005$ ), poor differentiation grade of the tumor ( $p < 0.1$ ), surgical or endoscopical biliary drainage ( $p < 0.02$ ). By multivariate analysis factors influencing survival were: age > 60 R.R. = 8.28 (95% C.I. 1.52–45.08), leucocyte count > 10000 R.R. = 52.24 (95% C.I. 5.99–455.61), moderate or poor tumor differentiation R.R. = 2.94 (95% C.I. 1.25–6.91). Operative procedures were not significantly associated with survival but a strong collinearity between age and operative procedures existed.

**Conclusions** No ERCP findings had influence on survival. A significant correlation was found between age, high leucocyte count (showing cholangitis), tumor differentiation and survival. Oncology, specific: Liver, biliary Endoscopy, general: Instrumentation, therapy } "Ampullary Carcinoma: Analysis of Prognostic Factors for Survival"

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## "P P 8 0174" P 8 0174 Tumors of the Papilla of Vater — Improvement of Diagnostic Imaging by Intraductal Ultrasound (IDUS)

\*J. Menzel, E.-Ch. Foerster, J. Konturek, W. Domschke

Department of Medicine B, University of Muenster, Germany An adenoma-carcinoma-sequence also applies to adenomas of the papilla of Vater. ERCP alone does not provide any information on infiltrative growth. Imaging of polypoid processes of the papilla of Vater has an influence on the choice of therapeutical procedures. Endoscopic ultrasound (EUS) is usually limited in detection small processes. High-frequency ultrasonic probes adjusted to the dimension of the pancreatic and biliary tract can, if applied during ERCP, visualize the peripapillary tissue at highest resolution. Ultrasound miniprobes (Aloka', Microvasive') 2 mm in diameter (6 French) were inserted via the operating channel of a routine duodenoscope (Olympus JF1T20) during ERCP. 35 patients (18 female, 17 male; \d8 65 years, from 31 up to 85) with polypoid processes of the papilla of Vater were examined. The sonomorphologic images were compared with biopsy and if available with the resection specimen. IDUS was correlated with findings of EUS as well as with the CT findings. Using sonographic frequencies of 12.5 up to 30 MHz the peripapillary tissue was demonstrated in microscopic dimension of a magnifying glass. Malignant infiltration of the papilla of Vater was depicted sonographically inhomogenous and echopoor in echoes whereas benign papillary stenosis were shown homogenously echodense. Insertion of the probe and ultrasonic examination during ERCP took 5 minutes on average, indications of any trauma to the papilla or the surrounding tissue could not be found. Eight of the 35 patients underwent surgery: Three had a carcinoma, five an adenoma of the papilla of Vater. Sensitivity of IDUS was 100%, specificity 80% and accuracy 87%. Endoscopic ultrasound (EUS): sensitivity 12%, specificity 40%, accuracy 37%; CT scan: sensitivity, specificity and accuracy 0%. Though only a limited number of patients has been evaluated by intraductal ultrasound up to now, imaging of the papilla of Vater with IDUS seems to be superior to conventional imaging techniques in diagnosing polypoid processes of the papilla. IDUS provides a view behind the surface and visualizes the adjacent tissue at high resolution. Controlled studies have been initiated to define the value of IDUS in the diagnostic procedure concerning diseases of the papilla of Vater. Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic Echoendosonography: Therapy } "Tumors of the Papilla of Vater / Improvement of Diagnostic Imaging by Intraductal Ultrasound (IDUS)"

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## "P P 8 0176" P 8 0176 **New Approach to the Endoscopical Treatment of Benign Tumors of the Terminal Part of Choledochus (TPCH)**

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**Purpose** The present study was designed to develop and investigate the new method of endoscopical excision of benign tumors of the TPCH.

**Methods** Between III/91 and IV/96 endoscopical operations were performed in 39 patients with the benign tumors of TPCH. There were 11 men and 28 women; age from 31 to 85. The leading clinical manifestations were: pancreatitis (16) and biliary hypertension (23) with obstructive jaundice (16). The sizes of tumors were from 3 {\\b4} 4 mm to 8 {\\b4} 15 mm. Histological types were: 28 cases of adenomas (mainly villous forms) and 11 cases of polyps (mainly adenomatous forms). Tumors were treated by endoscopical monopolar electrocoagulation with preliminary endoscopic sphincterotomy (EST) and insertion of pancreaticoduodenal stent. Due to this method the excision of the tumors was completed without direct damage of the main pancreatic duct (MPD) orifice. The prolonged insertion of pancreaticoduodenal drainage (for 4–6 months) prevented last formation of the strictures of the MPD orifices. During two last years double biliary and pancreatic stents were inserted in 7 cases for 4–6 months after excision of the tumors to prevent stenosis of the both orifices. All manipulations were performed with apparatus and accessories of the firm ""Olympus"" (Jp.).

**Results** In all cases the tumors were deleted. Mild forms of acute pancreatitis as early complications were developed in 3 cases. There were no mortality. Recoagulations of the remains of tumor tissue were made in 10 cases during the next 1–5 months after control endoscopical interventions. There were no relapses of the tumors and cases of malignant transformation during the next 0.5–5 years. EST and virsungotomy were performed in 9 cases after 5–12 months later the first excision because of the stenosis of the orifices of choledochus (5) and MPD (4). There were no mortality and complications in this group of patients. Signs of biliary hypertension disappeared in all cases, pancreatitis in mild forms retained in 4 cases out of 16, so the efficiency of treatment of pancreatitis was 75%. In 7 patients with double stents there were no cases of restenosis.

**Conclusion** Presented method of TPCH tumors treatment is effective and safe. According to our experience it will be sufficient to insert double biliary and pancreatic stents after excision of large size tumors (more than 5 mm in diameter) for 4–6 months to prevent stenosis of the orifices of choledochus and MPD. Oncology, specific: Liver, biliary Endoscopy, general:

Instrumentation, therapyEndoscopy, specific: Biliary }" "New Approach to the Endoscopical Treatment of Bening Tumors of the Terminal Part of Choledochus (TPCH)"

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## "P P 8 0177" P 8 0177 **Reliability of Preoperative Biopsy in the Diagnosis of Ampullary Malignancy**

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Department of Digestive Surgery and Transplant Unit, CHR Pontchaillou, Rue Henri Le Guilloux, 35033 Rennes, France The choice treatment of malignant ampulloma is pancreaticoduodenectomy. Before engaging in such major surgery, some clinicians prefer to have histological confirmation of malignancy. In case of negative biopsies, surveillance, ampullectomy and endoscopic sphincterotomy have been advocated.

**Patients and methods** 35 patients with adenocarcinomas of the Ampulla of Vater confirmed by pathological analysis of the surgical specimens (3 ampullectomies, 31 pancreaticoduodenectomies, 1 total pancreatectomy) underwent preoperative endoscopic biopsy. There were 22 males and 13 females with a mean age of 62.5 – 9.5 years. Jaundice, abdominal pain, poor general health status and gastrointestinal bleeding were present in 19, 21, 22 and 8 patients respectively.

**Results** Specimens showed protuberant and hemorrhagic papillary tumor (n = 17), a pseudovillous tumor (n = 2), an enlarged papilla (n = 5), a common bile duct dilatation (n = 4), a common bile duct nodule (n = 4) and a papillary obstruction (n = 1). Data was not available for 2 patients. 17 of 35 biopsies showed infiltrating adenocarcinoma, 1 biopsy having been obtained only after sphincterotomy. Biopsies showed an adenovillous tumor suspect of malignant transformation, an unspecified suspect lesion and a positive smear in 1 case each. Other biopsies showed mild (n = 1), medium (n = 2), or severe dysplasia (n = 4), benign tumors (n = 4), inflammation (n = 1) and hyperplasia (n = 1). No anomalies were noted in 2 patients.

**Conclusion** In some patients preoperative endoscopic biopsies are capable of ascertaining malignancy for tumors of Vater's ampulla. However the possibility of malignancy should not be discarded in the presence of a negative biopsy and patients should be denied the benefits of resective surgery solely on the basis of a negative biopsy. Oncology, specific: Liver, biliary Clinical practice: Management strategy } "Reliability of Preoperative Biopsy in the Diagnosis of Ampullary Malignancy"

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## "P P 9 0181" P 9 0181 A Endoscopic Survey of Colonic Diverticuloses in Singapore

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**Objective** We studied the prevalence and characteristics of colonic diverticuloses in patients undergoing colonoscopy performed by the Division of Gastroenterology in the National University Hospital, Singapore, from January 1992 to April 1995.

**Methodology** The results of colonoscopy performed on 1628 patients (mean age 52, range 13 to 91, 51% males, 82% Chinese, 7% Indians, 4% Malay) were reviewed. Patient data, indications for colonoscopy and the presence or absence of diverticuli were obtained from structured recording forms.

**Results** 118 (7%) patients (98 Chinese, 5 Malays, 6 Indians) had diverticuli in at least one part of the colon. This group was significantly older (mean age 62 yrs vs 51 yrs,  $p < 0.001$ ) and there were more males (61% vs 50%,  $p = 0.02$ ) than those without diverticuli. There were 30 patients (25%) with left-sided diverticuloses only, 73 (62%) with right sided diverticuloses only, 3 (3%) had involvement of the transverse colon only, 11 (9%) had both left-and right-sided diverticuli, and one patient had diverticuli in all parts of the colon. Patients with right-sided diverticuli were younger (59 yrs vs 68 yrs,  $p = 0.001$ ) and there were more Chinese (92% vs 67%,  $p = 0.009$ ) than patients with left sided involvement. There were no differences in the indications for colonoscopy in patients with and without diverticuli, and in patients with right-sided vs left-sided diverticuli.

**Conclusions** (1) The prevalence of diverticuloses in this survey of colonoscopic examinations was 7.2%, which is lower than previously published local autopsy and barium studies. This could be because endoscopy may be a less sensitive method for detecting diverticuloses. Also, ours being a medical series seldom include patients with suspected diverticulitis. (2) Patients with diverticuloses tend to be older and male. (3) Right-sided diverticuloses is commoner in Singapore, and these patients are younger and more likely to be Chinese. Endoscopy, specific: Colon, rectum Clinical practice: Epidemiology (non cancer) } "A Endoscopic Survey of Colonic Diverticuloses in Singapore"

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## "P P 9 0183" P 9 0183 **Endoscopy Defines the Therapeutical Options of Non Occlusive Ischemic Colitis**

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**Introduction** While the occlusive form of ischemic colitis (IC) is caused by embolic or thrombotic vessel occlusions, the reason for the non occlusive form is often a cardiogenic circulation deficit of the colon nearly almost in intensive care patients. Diagnosis of the non occlusive form can be proved angiographically only exceptionally. Aim of our study is the evaluation of endoscopy for diagnosis and treatment of this IC.

**Patients** From 7/91 to 10/95 in 236 intensive care patients with different primary diseases 373 colonoscopies due to prolonged intestinal atony and meteorism (thereof 122x diarrhoea and blood loss per anum) were performed under emergency circumstances. 210 patients needed artificial respiration due to their cardiorespiratory situation and they were dependent on catecholamines. 78 patients were female, 158 male, mean age: 58.6 years (min. 28–max. 78).

**Results** All 236 patients suffered from a colonic pseudoobstruction with massive meteorism (Ogilvie's-syndrome). Endoscopy demonstrated in 41.9% minor signs of ischemic damage: 22.0% (n = 52) showed a lividity with erosive aphthous lesions (grade I), 19.9% (n = 47) flat, non confluent ulcerations (grade II). Severe ischemic alterations were found in 22.9%: 15.7% (n = 37) with deep confluent ulcerations over the total colon (grade III) and 7.2% (n = 17) with gangrenous findings, sometimes with perforation (grade IV). Rare findings (chronic inflammatory bowel disease, neoplasia) in n = 6 (2.5%). In 32.7% a definitive classification of the colonic damage was not possible due to not eliminable stool masses. As therapy in all patients a colon decompression could be performed, in n = 154 (65.3%) with application of an indwelling decompression tube.

**Conclusions** While the cause of IC with vessel occlusion is to be proved angiographically, the non occlusive IC can only be diagnosed endoscopically. The endoscopic classification of the non occlusive IC defines the severity and therapeutical option: In IC grade I and II a primary endoscopic therapy with follow-up controls will be successful besides other measures; in grade IV a primary surgical intervention dependent of the operability is always indicated. In the intermediate stage grade III an individual decision in coordination with the surgeon is necessary. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Colon, rectum } "Endoscopy Defines the Therapeutical Options of Non Occlusive Ischemic Colitis"

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## "P P 9 0189" P 9 0189 **Endoscopic and Pathological Examination of Colorectal Lesions in Immunocompromized Hosts**

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**Purpose** This study aimed to characterize pathological and immunohistochemical findings in the colonoscopic biopsy specimens obtained from two cases of graft versus host disease-associated colitis after bone marrow transplantation and one case of cytomegalovirus (CMV) induced colitis.

**Materials and Method** The examined cases included a 13-year old male with acute lymphocytic leukemia (case 1) and a 13-year old male with non Hodgkin lymphoma (case 2) who had watery diarrhea and anal bleeding after bone marrow transplantation and a 42-year old female with aplastic anemia who had hemorrhagic diarrhea after immunosuppressive therapy with ALG, CsA, anabolic steroids, and G-CSF (case 3). Colonoscopic biopsy specimens were obtained from the lesion and were immunohistochemically stained with monoclonal antibodies against CD3, CD45RO, L26, and CD43.

**Results** Colonoscopic examination showed hemorrhage, edema, and erosion in the rectum and sigmoid colon in case 1 and 2. Histological sections of biopsies (HE) showed apoptotic lesions on crypt basement membrane. Most infiltrating cells were matured memory T lymphocytes with CD43 and CD45RO. In case 3, colonoscopy revealed solitary ulcer with round wall in the anterior wall of the rectum. Histological section (HE) disclosed two CMV inclusion bodies around the venules in the lymphocyte infiltrated region, and anti-HRP-C7 antibody was positive in the serum. We diagnosed the lesion as rectal ulcer formed by CMV reactivation.

**Conclusion** In immunocompromized hosts with intestinal hemorrhage, detailed histological examination of colonoscopic biopsies may be useful in understanding the pathogenesis of colonic lesions as well as decision of therapeutic plans. Intestinal disorders: Anorectal disordersIntestinal disorders: Anorectal disorders: childrenEndoscopy, specific: Colon, rectum }"  
"Endoscopic and Pathological Examination of Colorectal Lesions in Immunocompromized Hosts"

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"P P 11 0208" P 11 0208 **The Role of Ultrasound (US) in the Detection of the Colonic Cancer in the Elderly**

\*C. Petrogiannopoulos, A. Zacharof, A. Tzoumani, J. Panagopoulos, N. Papageorgiou, J. Poulidakos

2nd Department of Medicine, Hellenic Red Cross Hospital, Athens, Greece Usually colonic malignancies are investigated with barium enema (BE) colonoscopy or both of it.

**The aim of the study** was to evaluate the efficacy of the ultrasound (US) of the abdomen in the detection of these colonic lesions in elderly people.

**Material and methods** We studied 42 old patients (32 men and 10 women m. age 78 – 6 years old) who were suspected for colorectal cancer. Ultrasound of the abdomen has been performed before doing BE or colonoscopy.

**Results** A colonic lesion was identified on US in 39/42 (92.8%) patients. In 36/42 (85.7%) this was correct for the site and nature of the lesion. In four patients the nature was correct but the site was fault and in three patients which had cancer in the sigmoid colon with BE, the lesion was missed on US.

**Conclusions** The above data show that with US we can detect the colonic cancer in 85.7% of patients. It cannot be the main examination but it can complete the BE or the colonoscopy and it may be very useful in the elderly or in a difficult patient. A bigger number of patients is required to confirm the exact value of this noninvasive procedure. Oncology, specific: Colon, rectum Radiology and ultrasound: Diagnosis } "The Role of Ultrasound (US) in the Detection of the Colonic Cancer in the Elderly"

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"P P 11 0209" P 11 0209 **Comparison of Endorectal MR Imaging and Transrectal Ultrasound with Pathology in Rectal Tumors**

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<sup>2</sup> I Department of Radiology, University of Cologne, Germany *Purpose* To study the accuracy and limitations for staging rectal lesions by comparing endorectal MR imaging with transrectal ultrasound and histopathological correlation. *Material and Methods* 19 patients with known rectal lesions underwent MR imaging with an endorectal surface coil and transrectal ultrasound. All patients underwent biopsy before imaging. *Results* Transrectal ultrasound and endorectal MR imaging allowed an evaluation of the normal rectal wall and separation of its layers. The depth of wall invasion by rectal tumors was correctly staged with MR in 16/19, with Ultrasound in 17/19 and with both methods in 15/19 tumors. In the detection of perirectal adenopathy use of ultrasound as well as MRI enabled correct identification of positive perirectal nodes only in 1/3 patients; both imaging methods gave one false positive and one false negative result. *Conclusion* Endorectal imaging methods are especially helpful for staging in patients with an adenoma or a T1 tumor where the abdomino-perineal resection of the rectum can be avoided. While MR imaging is more expensive technically as well as financially as compared to endorectal ultrasound, it is well accepted from clinicians due to objective documentation of findings. Radiology and ultrasound: Diagnosis } "Comparison of Endorectal MR Imaging and Transrectal Ultrasound with Pathology in Rectal Tumors"

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"P P 11 0210" P 11 0210 **Hidrocolonic Ultrasonography in the Detection of Tumoral Processes in the Inferior Gastrointestinal Tract**

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**Objectives** To determine the value of hidrocolonic ultrasound (H.U.) in the detection of proliferative lesions in the colon and to compare it with other techniques of already proven value.

**Material and Methods** We performed a prospective blinded trial including 155 patients (82 males and 73 females) with ages ranging from 33 to 94 years (average of 58) and clinical, analytical criteria suggesting the existence of colonic proliferative lesions. Patients with rectal mass or those with deficient bowel preparation were excluded. Ultrasound findings were compared to those obtained by colonoscopy (133 cases) and by barium RX studies (22 cases) and all diagnoses were always confirmed by histologic exams.

**Results** 165 patients were studied. 50 of them had cancer and 46 of these 50 were diagnosed by H.U. (92%) 26 had polyps > 7 mm. and 15 of these polyps were diagnosed by H.U. H.U. failed to detect all the polyps < 7 mm.. The overall sensitivity, specificity, positive predictive value, negative predictive value for identifying colon carcinoma were 92%, 98%, 95.8% and 96.2% respectively and for polyps > 7 mm. were 78.9%, 100%, 100% and 97.1% respectively. The mean time for examination was 14 minutes. Tolerancy was good in 114 patients (73.5%), 29 showed a slight discomfort (18.7%) and 12 (7.7%) showed a great discomfort. There were no complications. 49.7% of the patients had complete studies and 68.6% had satisfactory studies.

**Conclusions** H.U. is an innocuous, fast, well tolerated technique for detecting colonic proliferative lesions > 7 mm. Its usefulness was limited for detecting lesion < 7 mm. H.U. can be considered as a useful complementary technique to other more expensive and invasive such as barium RX studies and colonoscopy. Radiology and ultrasound: Diagnosis } "Hidrocolonic Ultrasonography in the Detection of Tumoral Processes in the Inferior Gastrointestinal Tract"

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## "P P 11 0211" P 11 0211 **Endoscopic Ultrasonography in the Diagnosis of Submucosal Lesions of the Large Intestine**

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**Purpose** Submucosal tumors and extraluminal tumorous compression by neighboring organs and lesions are sometimes difficult to detect by x-ray or endoscopic examinations. In this study, we discuss the usefulness of endoscopic ultrasonography (EUS) in the diagnosis of submucosal lesions of the large intestine by the determination of their imaging characteristics.

**Materials and Methods** From September 1989 to April 1996, EUS was performed in 44 patients who were suspected to have submucosal lesions in the large intestine by x-ray and endoscopic examinations. The EUS systems used in this study were the Olympus CF-UM3/UM20 and the Aloka MP-PN 15-08L (ultrasound probe). Of the 44 patients, 26 were confirmed histologically by endoscopic or surgical resections, and their EUS images were compared with resected materials.

**Results** Lipomas (n = 15) were visualized as hyperechoic masses located in the submucosa. Lymphangiomas (n = 9) were visualized as cystic lesions with septal structures located in the submucosa. The ultrasonographic images of leiomyomas (n = 6), leiomyosarcomas (n = 3) and enteric endometriosis (n = 7) were all hypoechoic lesions located in the muscularis propria. Leiomyosarcomas tended to be larger and more inhomogeneous than leiomyomas (mean 47 mm: 14 mm). The shape of enteric endometriosis was round like myogenic tumors when the size was small; but large lesions were shaped like a spindle or a half-moon. On the other hand, myogenic tumors were lobulated. EUS images of recurrence of colorectal carcinomas (n = 3) showed hypoechoic masses with irregular borders in the muscularis propria. Appendiceal mucocele (n = 1) was extraluminally observed as a hypoechoic mass with hyperechoic spots.

**Conclusion** EUS is useful in the diagnosis of submucosal lesions of the large intestine and can have an important role in the choice of therapy as it provides precise information about their sizes, layers of origin and nature. Echoendosonography: Echoendoscopy } "Endoscopic Ultrasonography in the Diagnosis of Submucosal Lesions of the Large Intestine"

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"P P 11 0212" P 11 0212 **Evaluation of Endosonography for the Diagnosis of Rectal Cancer**

\*N. Joksimovik, V. Serafimoskic, M. Neshkovski, D. Trajanovski, M. Miloshevski, R. Popova Jovanovska, J. Mishevcki, M. Genadieva, K. Stardelova

Clinic of Gastroenterohepatology, Medical Faculty, Skopje, Macedonia Between March 1990 and May 1996, endosonography was used as a complementary method in 377 patients with symptoms as perianal pain, rectal bleeding, change in bowel habit and tenesmus that had been investigated at the Clinic. Rectal cancer was diagnosed by endoscopy and pathohistologically confirmed in 221 cases. Endosonography was performed in all cases and I Grade neoplastic infiltration was found in 17 cases (resectable cases), II Grade neoplastic infiltration (resectable cases) in 75 cases and III Grade neoplastic infiltration (irresectable cases) in 129 cases. Endosonographic findings have been correlated with the pathohistological specimens after surgery, according the modified Dukes classification for rectal cancer, and high accuracy was obtained (92%). In 156 out of 377 patients, endosonography revealed 69 uterine tumors, 58 prostate tumors, 21 ovarian tumors, 3 perirectal abscesses, 2 Hirschsprung's disease, and volvulus of the sigmoid colon in one patient. The utility of endosonography is evident, the method is non-invasive, there are no contraindications, permits precise evaluation of the rectal cancer extension as well as the diseases of the neighboring organs. Oncology, specific: Colon, rectum Echoendosonography: Echoendoscopy } "Evaluation of Endosonography for the Diagnosis of Rectal Cancer"

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## "P P 11 0213" P 11 0213 **Evaluation of Endoscopic Ultrasonography for the Diagnosis of Early Colorectal Cancer Invasion**

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The purpose of this study was to evaluate the effectiveness of endoscopic ultrasonography (EUS) in the differential diagnosis between mucosal and submucosal invaded colorectal cancer (so called early colorectal cancer). Colorectal cancer limited to the mucosa (m-cancer) can be treated completely by only endoscopic polypectomy, but submucosal invaded cancer (sm-cancer) have a risk of lymphnode and distant metastasis except of lesions with minute invasion into the submucosa, so most sm-cancers were suitable for surgical operation.

**Subjects & Methods** We performed EUS for 75 lesions of m-cancers and 65 lesions of sm-cancers. EUS diagnosis of the depth of invasion were compared with histological findings of the resected specimens. The instruments employed were CF-UM3 (7.5 MHz and 12 MHz) and UM-3R (20 MHz) (Olympus).

**Results** 1) The depth of invasion of early colorectal cancer was accurately diagnosed by EUS in 89% (67/75 lesions) in m-cancers and 74% (48/65 lesions) in sm-cancers respectively. Generally early colorectal cancer with mucosal or minute submucosal invasion (Group A) are treated endoscopically and cancer with massive submucosal invasion (Group B) are suitable for surgical operation. The differentiation between Group A and Group B was possible in 92% (129/140 lesions) successfully. 2) The correct diagnostic rates for lesions of the descending – ascending colon was 78% (21/27 lesions), which were poor when compared to the others. Diagnostic accuracy of each macroscopic form of the lesion were almost of the same. 3) The reasons of incorrect assessment for diagnosing early colorectal cancer invasion by EUS were microscopic tumor infiltration, peritumorous fibrotic reactions and incomplete visualization of the lesions.

**Conclusion** It was concluded that EUS is useful in diagnosing the depth of early colorectal cancer invasion and in planning therapeutic methods (endoscopic polypectomy or surgical operation).  
Oncology, specific: Colon, rectum  
Echoendosonography: Echoendoscopy }  
"Evaluation of Endoscopic Ultrasonography for the Diagnosis of Early Colorectal Cancer Invasion"

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## "P P 11 0214" P 11 0214 Prognostic Value of Endosonographic Staging in Anal Carcinoma

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**Aim** to compare the prognostic values of pretherapeutic clinical and endosonographic stagings for squamous cell anal carcinoma.

**Methods** From sept 87 to june 95, 57 patients with squamous cell anal carcinoma (51 F, 6 M, mean age 63 years, range 42–88), were evaluated by transorectal ultrasonography (TRUS), before combined chemotherapy and radiotherapy treatment. We used a 7 Mhz Bruel & Kjaer echoprobe. Clinical staging was assessed by digital evaluation according to the UICC 87 classification.

**Results**I – Nine tumors in clinical stage cN0 had an involvement of lymph nodes at ultrasound examination. All lymph nodes missed at clinical evaluation were located at more than 8 cm from the anal margin. 10% of cT1 tumors had lymph node involvement at ultrasound examination, versus none of the tumors staged uT1. II – Three years disease specific survival rates failed just short of being significantly different between uN0 and uN1 stages (97.4% vs 85.4%), whereas the difference was far from being significantly different between cN0 and cN1 stages (91.2% vs 88.2%). III – Concordance between cT and uT stages was low ( $\kappa = 0.37$ ) and none of the two classifications was more accurate in predicting patients outcome, perhaps due to the low number of cancer related deaths (5) during the follow-up.

**Conclusions** TRUS is more accurate than digital evaluation in detecting peri-rectal lymph node involvement, specially for nodes distal to the anal margin. As this factor seems to be the most closely related to the patients survival in our study, TRUS appear warranted in the pretherapeutic staging of squamous cell anal carcinoma. Echoendosonography: Therapy } "Prognostic Value of Endosonographic Staging in Anal Carcinoma"

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## "P P 11 0215" P 11 0215 **Magnifying Colonoscopic Findings Reflect Mucosal Inflammation in Ulcerative Colitis Patients**

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**Purpose** We sometimes encounter a discrepancy between conventional colonoscopic findings and histological activity in ulcerative colitis (UC) patients. Therefore, in the present study, we evaluated the pit pattern of rectal mucosa affected with UC using magnifying colonoscopy (MCS) and compared the MCS findings with histological findings or the levels of IL-6 and soluble IL-6 receptor (sIL-6R) secreted in the organ culture supernatants.

**Patients and Methods** Twenty-nine UC patients (13 males and 16 females, mean age 33 years) were evaluated. Ten patients had total colitis, 13 had left-sided colitis and 6 had proctitis. After preparation with polyethylene glycol electrolyte lavage, the rectal mucosa was observed by MCS (Fujinon EC410CM) after 0.1% methylene blue staining. The pit pattern was classified into 4 grades; Grade 1: small round pits with regular arrangement, Grade 2: slightly deformed and large pits with slight irregular arrangement, Grade 3: various shaped pits with irregular size and arrangement, Grade 4: scattered pits with various shape and size.

**Results** MCS-grades showed a correlation with histological inflammatory indexes (mononuclear cell infiltration, polymorphonuclear cell infiltration, enterocyte loss, crypt inflammation, glandular atrophy and goblet cell depletion). MCS-grades also showed a correlation with IL-6 levels (ng/mg biopsy protein; median, Grade 1: 93, Grade 2: 410, Grade 3: 634, Grade 4: 592) and sIL-6R levels (median, Grade 1: 6.3, Grade 2: 34.0, Grade 3: 59.9, Grade 4: 68.4) in the organ cultures.

**Conclusion** MCS grades reflect histological inflammation and inflammatory cytokine activity. MCS may be useful in the follow-up and evaluating drug effects in UC patients. Intestinal disorders: IBD diagnosis, monitoring Endoscopy, general: Instrumentation, diagnosis } "  
"Magnifying Colonoscopic Findings Reflect Mucosal Inflammation in Ulcerative Colitis Patients"

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"P P 11 0216" P 11 0216 **Effect of Addition of Cisapride to Colonoscopy Preparation with Polyethylene Glycol Solution. A Prospective Single-Blind Randomized Trial**

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Department of Internal Medicine and Gastroenterology, University of Bologna, Italy

**Purpose** We assessed the effect of the addition of cisapride (CIS) to colon lavage with polyethylene glycol (PEG) solution.

**Methods** In a prospective single-blind study, 157 consecutive outpatients scheduled for total diagnostic colonoscopy were prepared with two different regimens. The day before endoscopy, the patients (pts) were randomly allocated to two different cleansing preparations: a) 73 pts (37 M, 36 F: 56.3 – 16.0 yrs, mean age – SD) received 4 litres of PEG solution; b) 84 pts (34 M, 50 F: 56.6 – 16.1 yrs) received PEG as above with the addition of oral CIS 20 mg b.i.d. Before colonoscopy, pts completed a questionnaire about the presence and severity of four symptoms: abdominal cramps, nausea, vomiting and dizziness (scale from 0 to 3: 0: absent, 1: mild, 2: moderate, 3: severe). The quality of colon cleansing was semiquantitatively scored 0 to 3 (0: poor, 1: fair, 2: good, 3: excellent) by an endoscopist who was unaware of the administered preparation.

**Results** The presence of symptoms (score  $\geq 1$ ) and the frequency of good-excellent colon cleansing (score  $\geq 2$ ) are shown in the table. Preparation Cramps Nausea Vomiting Dizziness Cleansing (no. pts) % % % % PEG (73) 6.8 34.5 11.0 8.2 54.8\* PEG + CIS (84) 9.5 24.7 4.8 7.1 75.3\*\*  $p < 0.01$ . Mann-Whitney U test.

**Conclusions** The addition of cisapride to the colonic preparation with PEG solution results in a significantly better colon cleansing, without significant changes in symptoms related to PEG ingestion. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Preparation, management Endoscopy, specific: Colon, rectum } "Effect of Addition of Cisapride to Colonoscopy Preparation with Polyethylene Glycol Solution. A Prospective Single-Blind Randomized Trial"

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"P P 11 0217" P 11 0217 **The Clean Colon — Is Cisapride Useful in Preparation for Colonoscopy?** A. Nagorni, T. Tasic, H. Milovanovic, S. Petrovic-Nagorni

Clinic for gastroenterology Faculty of medicine Nis, Yugoslavia The clean colon is important factor for safety and accurate diagnostics during colonoscopy. Sometimes, residual fecal or/and liquid contents make colonoscopy difficult for performing. Cisapride is a powerful prokinetic drug and has been shown to enhance propulsive motor activity of the entire gastrointestinal tract, including colon. The aim of our study was to analyse the role of cisapride in preparation of patients for colonoscopy, measuring volumes of residual liquid content in colon after preparation with 3 liters of electrolyte lavage solutions. There were 2 groups of patients: I group – 52 patients in whom 10 mg cisapride was administered 30 minutes before preparation with electrolyte lavage solutions, II group – 51 patients in whom cisapride was not administered. Residual liquid was aspirated through working channel of colonoscope and volumes were measured in ml. In I group fecal contents were observed in 4 (7.6%) patients and residual liquids in 7 (13.4%) patients. Residual liquids were measured 10 to 150 ml (mean 35 ml). In group II, fecal contents were observed in 9 (17.6%) patients and residual contents in 22 (43.1%) patients. Residual liquids were measured 35 to 350 ml (mean 85 ml). Patients in group II had statistically more frequent residual liquids than patients in cisapride group – group I ( $p < 0.05$ ). Residual liquid volumes were higher in group II than in cisapride group ( $p < 0.05$ ).

**Conclusion** Enhancement of the colon propulsive motor activity by cisapride improves preparation for colonoscopy with electrolyte lavage solutions. Colonoscopic preparation with addition of cisapride may reduce time for performing and may reduce risk for complications during colonoscopy. Endoscopy, general: Preparation, management Endoscopy, specific: Colon, rectum } "The Clean Colon / Is Cisapride Useful in Preparation for Colonoscopy?"

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**"P P 11 0218" P 11 0218A Randomized Prospective Trial Comparing 45 and 90-ml Oral Sodium Phosphate with X-Prep in the Preparation of Patients for ColonoscopyS. \dcnal,**

\*\dc.B. Dogan, Z. \d6zt\fcrk, M. Cindoruk

Gazi University, Faculty of Medicine, Department of Gastroenterology, Ankara, TurkeyForty-six patients were randomized to receive either 45 or 90-ml oral sodium phosphate (NaP) (Fleet Phospho-Soda), or X-Prep (a Senna preparation) before elective colonoscopy to compare the quality of colon cleansing, ease of preparation, and gastrointestinal intolerance. Before colonoscopy, one of us administered a questionnaire to the patient to assess how well the preparation was tolerated (scale from 1 to 5: 1 = easy, to 5 = unable to finish) and about the presence of four symptoms: abdominal pain, nausea, vomiting, and dizziness. The quality of colon cleansing was graded by two gastroenterologists (1 = excellent, 2 = good, 3 = fair, 4 = poor), who were unaware of how the patient was prepared or tolerated the preparation. The overall quality of bowel preparation with 90-ml oral NaP was better than with X-Prep and 45-ml NaP ( $p < 0.01$ ). Patients found preparation with NaP to be easier than X-Prep ( $p < 0.002$ ). No difference was seen in the incidence of abdominal pain, nausea, vomiting or dizziness. In the 90-ml NaP group, a significant rise in sodium and chloride occurred. However, increments were not greater than 5%. Hyperphosphatemia was noted with NaP, but was transient, and no concomitant decrease in calcium was seen. We conclude that, in the groups of patients studied, 90-ml NaP is a safe colonic cleansing agent that is better tolerated and more effective than others. Endoscopy, general: Preparation, management }" "A Randomized Prospective Trial Comparing 45 and 90-ml Oral Sodium Phosphate with X-Prep in the Preparation of Patients for Colonoscopy"

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## "P P 11 0219" P 11 0219 Urgent Colonoscopy for Melena in Children

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**Background** Colonoscopic examination is the first choice for melena in adult patients today. But for children's cases it was very difficult to perform colonoscopic examination because of that their lumen were narrow and fragile, and children could not well understand the necessity of the examination. Recently, as the improvement of endoscopic instruments and insertion technics, we are able to do it easily. So in the present study, we evaluated the usefulness of urgent colonoscopy for melena in children. We studied the cases of 47 children with melena who received colorectal endoscopy at our department during a five period between August 1989 and July 1993. Of these 47 children, 36 (77%) were found to have some underlying disease. Colorectal polyps were seen in 6 cases (including 5 cases of juvenile polyps). Colorectal polyps were the most frequent underlying disease for children between 1 and 5 years of age. Ulcerative colitis and Crohn's disease were seen in the children in their early youth (over 11 years of age). Lymphfolliculosis had the highest prevalence (7 cases) in the population studied. This disease was seen in all age group, with a particularly higher incidence in infants younger than 12 months. Colorectal endoscopy seems to provide a useful means for the diagnosis and treatment of melena in children. Intestinal disorders: Anorectal disorders: children Endoscopy, general: Endoscopy: children Endoscopy, specific: Colon, rectum } "Urgent Colonoscopy for Melena in Children"

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## "P PP0 0224"PP0 0224 **Diagnosis of Invasion of Superficial Esophageal Carcinomas by Infrared Electronic Endoscopy**

\*H. Iishi, K. Iseki, M. Tatsuta

Department of Gastrointestinal Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan Superficial esophageal carcinomas (SEC) were defined as those which were confined to the mucosa or the submucosal layer with or without lymph nodes metastasis. The depths of involvement of SEC were classified as follows: m<sub>1</sub>, intraepithelial; m<sub>2</sub>, intramucosal not in contact with the muscularis mucosae; m<sub>3</sub>, intramucosal in contact with the muscularis mucosae; sm, submucosal. Because SCE confined to m<sub>1</sub> or m<sub>2</sub> seldom have lymph nodes metastasis, they are thought to be curable by endoscopic resection only. Therefore, it is very important to differentiate SEC of m<sub>1</sub> or m<sub>2</sub> from others. However, it is not always easy to diagnose their depths exactly, especially in intramucosal cancers. Infrared images were obtained through the electronic endoscope (GIF-Q200IR, Olympus) in which the infrared cut filter was removed, combined with the light source in which the narrow band filter for infrared range was inserted before the xenon lamp. After the routine endoscopic examination including iodine staining, i.v. bolus injection of 2 – 5 mg/kg body weight of indocyanine green (ICG) was given to intensify the infrared images. We examined 14 SEC in 12 patients (10 males and 2 females) by the infrared electronic endoscopy. In all of 8 SEC of m<sub>1</sub> or m<sub>2</sub>, the entire lesions were uniformly stained after ICG injection. However, in 6 SCE of m<sub>3</sub> or sm, the lesions were partially stained after ICG injection. In conclusion, the infrared electronic endoscopy is very useful in differentiation of SCE of m<sub>1</sub> or m<sub>2</sub> from those of deeper invasion. Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, diagnosis } "Diagnosis of Invasion of Superficial Esophageal Carcinomas by Infrared Electronic Endoscopy"

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## "P PP0 0225"PP0 0225 Endoscopic Injection of Mitomycin Adsorbed on Carbon Particles for Advanced Esophageal Cancer: A Pilot Study

\*M. Ortner, A. Buchali, F. Noak, S. Dinges, S. Schreiber, J. Wirth, H. Lochs

4th Med. Department, Charit'e9 Univ., Berlin, Germany

**Background** Dysphagia is the main problem for patients with advanced nonresectable esophageal tumors. Local palliation can be achieved by laser therapy, brachytherapy or stent placement. The

**Aim** of this study was to evaluate the efficacy of local injections of mitomycin adsorbed on activated carbon particles (MMC-CH) in nonresectable esophageal carcinomas. The primary outcome parameter was time to local tumor progress, secondary parameters were dysphagia, Quality of Life (Karnofsky index) and survival time.

**Methods** 10 Patients with esophageal carcinoma stage IV (age: median 58 a (95% CI: 42–78), tumor length 10.7 (5–15)) received four weekly injections of 10–15 mg MMC-CH via a 5 mm sclerotherapy needle into endoscopically visualised tumor. Tumor staging (chest CT, endosonography, gastroscopy, esophagogramm), symptom scores, and life quality index, were performed before and bi-monthly after therapy. The results were compared with 10 historical controls from the same center (4 Stage IV, 6 stage III, age 67 a (55–96), tumor length 6 cm (4–10)) who were treated immediately before the study by implantation of nitinol stents (Ultraflex, Boston Scientific Inc.).

**Results** Local injections were tolerated well with no side effects. Median time to local tumor progress was longer in the MMC-CH group (Fig.). Dysphagia ( $p = 0.0012$ ) as well as Karnofsky Index ( $p = 0.0034$ ) improved after MMC-CH (Table). By stenting dysphagia improved as well ( $p = 0.03$ , Table) but Karnofsky index did not change ( $p = 0.21$ ). Median survival time after MMC-CH therapy was 16 weeks (11.7–20.4) versus 4.5 weeks (2.7–14.9) after stenting ( $p = 0.019$ ).

**Conclusions** Endoluminal MMC-CH therapy seems to be an effective, well tolerated treatment for nonresectable esophageal tumors which inhibits local tumor progress, improves dysphagia and quality of life. A randomised, prospective study is currently conducted.

030000000000 } Table Dysphagia score Karnofsky ind. Before MMC-CH 2.5 (1.3–3.3) 60 (71–75) After MMC-CH 0.5 (0.1–1.1) 80 (77–87) Before stent 3.00 (2.1–3.2) 80 (65–86) After stent 2.00 (1.0–2.6) 70 (58–78) Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, therapy } "Endoscopic Injection of Mitomycin Adsorbed on Carbon Particles for Advanced Esophageal Cancer: A Pilot Study"

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## "P PP0 0226"PP0 0226 **Is Radiation Useful after Photodynamic Therapy (PDT) of Superficial Esophageal Cancer?**

\*Ph. Jacob, R. Lambert, M. Diculescu, F. Descos

Department of Digestive Diseases, Hospital E. Herriot, Lyon, France Endoscopic treatment of superficial (T1) esophageal cancer has been proposed as an alternative to surgery, however T1 tumors often enter the submucosa having then a risk (around 35%) of lymphatic invasion. Therefore, a benefit could be expected from a complement regional therapy (radiation). This retrospective non randomized study aims to determine whether radiation after PDT improved the response rate of a superficial esophageal cancer and the 5 year survival rate (5 y.SR)

**Methods** From 1986 to 1995, 80 patients (74 men and 6 women – age: mean = 63 y. range = 41–82 y.) with squamous cell cancer in the esophagus, staged UT1 N0 at endoscopic ultrasonography, were included in a protocol based upon endoscopic destruction by PDT. The photosensitizer (Photofrin, QLT Canada, 2 mg/kg, or Hematoporphyrin Derivative, Quentron, Australia, 2.5 mg/kg) was injected 72 h. before laser irradiation with 630-nm dye laser (200/300 J/cm<sup>2</sup> of tumor surface). –

**Group I** no other treatment was proposed in 40 patients –

**Group II** a course of radiotherapy was applied two months later (45 Gy) in the other 40 patients. The tumor response at 6 months was estimated complete in presence of normal or cicatricial endoscopic pattern and negative biopsies. The treatment was repeated in patients with incomplete response. Global and Disease Specific 5 y. SR were computed according to the Kaplan-Meier method.

**Results in all patients** the mean follow up was 40 months; the respective values for the Global and Disease Specific 5 y. SR were 45.1% – 6.3% and 71.2% – 6.4%.

**Results by groups** The Complete Response rate at 6 months were similar in Group I (79.4%) and in Group II (86.4%). Recurrences occurred after the initial complete response in 9 out of 27 patients in Group I and in 5 out of 32 in Group II. The Global 5-y. SR was 48% – 9% in Group I and 38% – 8% in Group II. The respective values of the Disease-Specific 5 y. SR were 70% – 9% and 71% – 8%.

**Complications** – in relation to PDT: esophageal stricture in 22 and cutaneous photosensitization in 7. – in relation to radiation (Group II): radiodermatitis in 3 and pericarditis in 2.

**Conclusions** The 45% Global 5 y. SR suggests that endoscopic treatment (PDT) is an acceptable alternative to surgery in superficial (UT1, N0) esophageal squamous cell cancer. This study does not show a benefit from addition of radiotherapy after endoscopic treatment. Oncology, specific: Oesophagus } "Is Radiation Useful after Photodynamic Therapy (PDT) of Superficial Esophageal Cancer?"



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## "P PP0 0238"PP0 0238 Investigation on Endoscopic Treatment of Early Gastric Cancer

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**Purpose** Evaluation of the endoscopic treatment of early gastric cancer.

**Material and method** The cases included in this study were 131 in total, 101 cases received Endoscopic Resection (ER) only, 16 cases were followed by surgical resection and the rest 14 cases received Laser therapy after ER. The indication for Resection ""en bloc"" was determined by the depth of invasion and the size of the lesion.

**Results** In the protruded type, 22 of the 30 lesions limited to the mucosa (m-cancer) less than 10 mm were resected totally. In relation to the lesions invading the submucosal layer (sm-cancer), 1 case was resected totally and the other one underwent piecemeal resection. Among the lesions of 11–20 mm in size, 12 cases were resected totally and the rest 15 cases were piecemeal resected. 31 of 43 of the depressed lesions less than 10 mm were resected totally and in the rest 12 cases piecemeal resection was performed. Evaluating the recurrence rate of these lesions, we found that 6 cases were multiple cancers and in 4 cases a new focus was detected during the follow up after ER. This represents about 8% of the total.

**Conclusions** Considering the efficacy of the ER, no local recurrence or distal metastasis were found in those which the surgical margin was sufficient. It was possible to resect horizontally even the m-cancers by piecemeal resection. In the piecemeal resected cases there is the possibility of local recurrence so we consider necessary to add surgical resection or at least continue a sufficient follow with those patients not allowed to received surgical treatment. Furthermore we encourage to continue following the patients, even those with total resection because of the possibility of newer findings. Oncology, general: TherapyEndoscopy, general: Instrumentation, therapyEndoscopy, specific: Stomach, duodenum } "Investigation on Endoscopic Treatment of Early Gastric Cancer"

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## "P PP0 0255"PP0 0255 **Follow-Up with Colonoscopy after Polypectomy. A 15 Years Prospective Study**

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**Introduction** The adenoma-carcinoma sequence is now well established. This fact has provided a basis for the excision of all polyps detected at colonoscopy. Indeed the risk for invasive colorectal cancer may be lowered by this polypectomy. The risk of new polyps is high after polypectomy and these patients are at risk for further colorectal cancer.

**Objective** The aim of this study was to evaluate the incidence of metachronous polyps after polypectomy and to identify factors of recurrence.

**Methods** 840 patients (582 male and 258 female with a median age of 58 years) with no prior history of polyps or colon cancer had a complete colonoscopy with removal of all polyps detected and were included in a follow-up study. 1339 polyps were excised (mean 1.59 – 0.96 polyps/patient, range 1 to 5), 2% were juvenile polyps, 11% of patients had only hyperplastic polyps and 87% had at least one adenoma (105 patients had a malignant adenoma, 67% with non invasive carcinoma, 23% with invasive carcinoma). The mean time of follow-up was 53.6 months (range 3 to 120) for the 72% of patients who had at least one endoscopic control examination (mean 2.6, range 1 to 12).

**Results** The cumulative rate of metachronous polyps was 12% at 1 year, 30% at 2 years, 50% at 3 years, 62% at 5 years and 76% at 10 years. Most of these new polyps were small (mean 4.93 – 3.45 mm) adenomas with mild dysplasia. Number of adenomas at index colonoscopy and age of patients at entry were the only risk factors for further adenomas ( $p < 0.001$ ). 5% of patients developed adenomas with severe dysplasia. The only risk factor for severe lesions was the number of adenomas at entry ( $p < 0.02$ ). Sexe, family history, nature (villous or not), grade of dysplasia and size of polyp were of no value in predicting the occurrence of further adenomas or severe lesions.

**Conclusions** The cumulative risk of polyps after polypectomy is about 50% at 3 years. Age and number of adenomas at index colonoscopy were the only predictive factors of metachronous polyps. As the surveillance should not be increased with age of the patient, the follow-up strategy should depend on the number of polyps at index colonoscopy. Oncology, general: Screening, preventionEndoscopy, specific: PancreaticEndoscopy, general: Instrumentation, therapy }" "Follow-Up with Colonoscopy after Polypectomy. A 15 Years Prospective Study"

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## "P PP0 0257"PP0 0257 **Correlation between Colonoscopy and CT-Based Virtual Endoscopy (VE) in Detecting Space-Occupying Lesions of the Colon**

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**Purpose** Colonoscopy is currently regarded as the most accurate technique of diagnosing colonic lesions, but an ideal method would be safe, simple, sedationless and non-invasive. Recently, a new technique has been described which combines abdominal spiral CT scanning and virtual reality computer technology — known as virtual colonoscopy (VC). The reconstructed images provide a simulation of the interior of the colon as viewed by endoscopy. The purpose of our study was to compare VC to conventional colonoscopy in patients with suspected or known space-occupying lesions of the colon.

**Patients/methods** Seventeen patients, in whom there was a high likelihood of colonic polyps or cancer, underwent a non-contrast spiral CT scan (Picker PQ5000) of the abdomen after regular colonoscopy bowel preparation. The colon was distended by rectal air insufflation via an enema tube, and i.v. glucagon was administered to paralyze the bowel. A continuous volume CT dataset of the abdomen was reconstructed and reformatted into the VE presentation (Epi-scope<sup>®</sup>) by one of the investigators blinded to the results of other imaging. A regular colonoscopy was performed on the same day by an experienced endoscopist, and the studies were documented with standardized videotape recording.

**Results** VC correctly identified the three patients with normal findings on colonoscopy, one patient with fecal loading, four with diverticulosis and all four lesions > 8 mm in diameter. VC failed to detect all but one polyp < 8 mm. Also, there were two false positive diagnoses on VC, which were an "ascending colon structure" (focal spasm) and a "cecal polyp" (prominent ileocecal valve).

**Conclusions** Our initial results show that virtual colonoscopy is technically feasible and capable of detecting lesions > 8 mm in size. Current technology may miss small polyps but with further developments in computer software, virtual endoscopy may supplant colonoscopy in the detection of space-occupying lesions of the colon. Endoscopy, general: Instrumentation, diagnosisRadiology and ultrasound: DiagnosisEndoscopy, specific: Colon, rectum }"  
"Correlation between Colonoscopy and CT-Based Virtual Endoscopy (VE) in Detecting Space-Occupying Lesions of the Colon"

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## "P PP0 0258"PP0 0258 Endosonographic Evaluation of Fistula-In-Ano

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Success of surgery for anal fistula depends on accurate assessment of the fistula. Unidentified primary opening is a significant factor associated with recurrence. In the literature, the site of primary opening is identified by anal endosonography (AES) in 30 to 80% cases. Our aim is to report our experience with AES evaluating 40 cases of suspected perianal abscesses and fistulas.

**Methods** From November 1994 to April 1996, 40 patients admitted to our hospital with the preoperative diagnosis of perianal sepsis were evaluated with the aid of AES (Br\fccl and Kjaer type 1846 anal endoprobe with a 7-MHZ transducer). The primary opening was determined as the contact between fistula tract and internal sphincter. EAS findings were then compared with surgical findings with respect to Park's classification.

**Results** AES identified a fistula/abscess in 35 patients. At surgery, 32 patients were found to have abscess/fistula in ano: 10 high and 16 low transsphincteric fistulas, 2 intersphincteric abscesses and 4 complex fistulas. In 8 cases, no fistula was identified: Verneuil disease (n = 1), sepsis of perineal gland (n = 2), infected fissure (n = 1), miscellaneous (n = 4). The sensitivity, specificity, and positive and negative predictive value of AES in the diagnosis of anal fistulas/abscesses were 100%, 62.5%, 91.4% and 100%. There was an exact correlation between operative and AES findings with regard to the location of primary opening in 30/32 patients (93.7%) and to the relationship between the fistula level and the sphincter mechanism in 23/26 patients (88%) with high or low transsphincteric fistula.

**Conclusions** AES is a simple and inexpensive technique which is able to assess correctly the location of primary opening and thus to decrease the rate of fistula-in-ano recurrence. The good correlation according to Park's classification allows to predict and to influence operative techniques. Intestinal disorders: Anorectal disordersEchoendosonography: Therapy }"  
"Endosonographic Evaluation of Fistula-In-Ano"

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## "P PP0 0261"PP0 0261 **Transvenous Obliteration of Porto-Systemic Shunt (Tops) for Control of Solitary Gastric Varices**

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**Purpose** Gastric varices (GV) are usually associated with gastrosplenic shunt. Using this hemodynamic factor, the author performed TOPS, a new method for eradicating GV. In this study we present techniques of TOPS and evaluate the efficacy between TOPS and endoscopic injection sclerotherapy (EIS).

**Patients** 43 patients with solitary GV were included in this study. 28 patients of them were examined by TOPS and 15 patients were treated with EIS.

**Methods of TOPS** Each patient received insertion of balloon-catheter through right internal jugular vein and balloon was finally located at shunt vessel as blood outlet of GV that is connected to greater circulation. The shunt vessel was obliterated by retrograde transvenous infusion of 5% ethanolamine oleate (EO).

**Results** Disappearance of GV was recognized in all patients in the EIS group (100%), and 26 patients in TOPS group (92.9%). The rate of rebleeding in the EIS group within 1 year, 3 year, and 5 year was 42%, 57%, and 57%, respectively. Both rebleeding and recurrence of varices did not occurred in all patients in the TOPS group through observation period (1 month–44 months, mean 17.8 months). The average volume of sclerosant per session was 18.4 ml in the EIS group, and 22.7 ml in the TOPS group. The duration of the treatment showed significant difference between the EIS and TOPS groups (2.8 weeks vs. 2.46 days). The patients whose GV were associated with inferior phrenic vein or pericardial vein in addition to main shunt vessels received significantly higher volume of EO than the patients in whom GV were not associated with those vein (33 ml vs. 13.3 ml).

**Conclusions** These results suggest that TOPS as self-retaining catheter method is useful in controlling blood flow of shunt vessels. TOPS could reduce the duration of therapy and eradicate GV without recurrence. Clinical practice: Management strategyLiver and bile ducts, 1: Cirrhosis: portal hypertensionEndoscopy, specific: Stomach, duodenum } "Transvenous Obliteration of Porto-Systemic Shunt (Tops) for Control of Solitary Gastric Varices"

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## "PP0 0263" A New Multiple-Band Ligator (Speedband) for the Endoscopic Treatment of Esophageal and Gastric Varices — Preliminary Results in 63 Applications of a Prospective Ongoing Study

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New multiple-band ligators promise to remarkably simplify endoscopic ligation therapy of bleeding esophageal varices because of no need for an overtube and the rapid consecutive release of 5–8 bands without repeated withdrawal of the endoscope from the esophagus. In the following we report on our preliminary results of 63 applications in 27 pts using the Speedband multiple-band ligator set in a prospective ongoing study for esophageal and gastric varices.

**MMP** From July 4, 1995 to May 3, 1996 27 pts. (m = 19, f = 8; age m = 51 – 33 y, 35–75; Liv. Ci. Child A/B 24, Child C 3) were included into a first prospective one-arm treatment protocol using the "Speedband" (5 -) multiple-band ligator for hemostasis or prevention of re-bleeding (eradication) from esophageal (EV) or esophago-gastric varices (EGV). 1 set (5 bands) per session was used to limit cost practice-oriented (– 100 US \$/set). Because we initially observed an early loss of bands within 24 h after correct placement (DMW 1995: 1300–1; DDW 1996#186), control endoscopies were scheduled for: 1 d post and every 5–7 d until ulcer healing or eradication. Retreatment schedule: lig. ulcers 4 mm + varices > grade I; EV or GV or RCS. Controls every 6 weeks after eradication.

**Results** In 63 treatment sessions 309 bands were applied. (4.7 – 0.95; 3–5). 9 patients had EV only, 18 patients had EGV (9 Sarin I; 2 type II; 7 type I + II). 16 sess. were carried out for acute bleeding, 47 for sess. for eradication treatment. 6 of 16 acute bleeders had active bleeding at index endoscopy ("Fo.la/b"). Definitive hemostasis: 15/16 bleeders. 1 pat. with EGV II rebled from an untreated gastric varix. Loss of bands during treatment: 9/309 (3%), the following day 31% (0–100%). However, no adverse effects on rebleeding rate and eradication so far. Follow-up: m 81 d (73 d; 2–252 d) with 20 pts. eradicated after m 2.1 (0.7; 1–4) sessions. 3 patients died without signs of rebleeding. Recurrences of EV/GV: 6/20 pts. (22%), m 101 d (61; 45–203) after initial eradication => 4/6 pts. eradicated after +1 treatm. session.

**Conclusions** Endoscopic variceal ligation using the Speedband multiple-band ligator is a fast and reliable method for hemostasis and eradication of bleeding EV and EGV. Contrary to conventional sets also the ligation of gastric varices (EGV Sarin type II) proved safely possible in 9 pts.. A partially observed loss of bands (m 31%) within 24 h after initially correct placement showed up to now no adverse effects concerning rebleeding rate and time/effect of eradication, probably due to variceal thrombosis after initial trauma of the wall. The study is ongoing. Prospective, randomized trials in a larger number of patients are needed to confirm these very promising preliminary data. Endoscopy, specific: Oesophagus/Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy } "A New Multiple-Band Ligator (Speedband) for the Endoscopic Treatment of Esophageal and Gastric Varices / Preliminary Results in 63 Applications of a Prospective Ongoing Study"

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**"P PP0 0270"PP0 0270 Comparison of Magnetic Resonance Cholangio-Pancreaticography (MRCP) with ERCP; Ultrasound; CT and Endoscopic Ultrasound in Patients with Bile Duct StricturesC. Zillinger,**

\*T. R\`f6sch, H. Helnberger, S. Fr\`fchmorgen, P. Born, H.D. Allescher, P. Gerhardt, J.R. Siewert, M. Classen

Dept. of Internal Medicine II, Radiology and Surgery, Technical University of Munich, GermanyMRCP is a new non-invasive technique for visualization of the pancreatobiliary tree. The present study was designed to evaluate its diagnostic accuracy in patients with suspected bile duct strictures in comparison to ERCP and other diagnostic procedures such as ultrasound (US), computed tomography (CT) and endoscopic ultrasound (EUS).In this ongoing prospective study, 75 patients have been included so far, and complete data are available for 36 cases (17 male/19 female, age 33 to 86 years). Patients with suspected obstructive jaundice due to malignant and benign biliary stricture (stones were excluded) were examined by MRCP, ERCP or PTC, CT, US and EUS. Various parameters such as visualization of the stricture, determination of its nature (benign/malignant) and origin (biliary or pancreatic), tumor detection and staging were recorded. Control of findings was by histology (biopsy or surgery), unequivocal signs of malignancy such as liver metastases and/or by follow-up, especially in cases with a benign disorder.21, 11, and 4 patients had malignant, benign biliary obstruction, or a normal pancreatobiliary tract (liver disease). All procedures were performed in all patients except for 1 case of ERCP (not possible) and CT each (rejected by the patient); 13 patients did not undergo EUS for various reasons (mainly patient refusal). MRCP, ERC/PTC, CT, US and EUS reached the following results: Diagnosis of level of obstruction — accuracy 97%, 97%, 91%, 88%, 97%. Diagnosis of malignancy was correct in 88%, 86%, 80%, 60% and 72%. Diagnosis of biliary versus pancreatic origin was correct in 90%, 88%, 84%, 69% and 74%.These results show that MRCP can replace diagnostic ERCP in most cases and can even provide additional information such as about tumor staging. The diagnostic information provide by CT and EUS were consistently inferior. Radiology and ultrasound: DiagnosisEndoscopy, specific: BiliaryEndoscopy, specific: Pancreatic }" "Comparison of Magnetic Resonance Cholangio-Pancreaticography (MRCP) with ERCP; Ultrasound; CT and Endoscopic Ultrasound in Patients with Bile Duct Strictures"

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"P PP0 0271"PP0 0271 **A Clinical Evaluation of MRCP (MRcholangiopancreatography), Compared with ERCP in 60 Cases**

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**Purpose of the study** To determine the role and efficacy of MRCP, we considered the possibility of substituting MRCP for ERCP for the diagnosis of biliary and pancreatic diseases.

**Methods used** 60 patients with suspected biliary or pancreatic disease were examined. Of these 60 patients, ranging from 21 y.o. to 88 y.o. (average 63.3 y.o.), there were 27 males and 33 females. The type of MRI instrument was the Magnetom Impact Expert (1.0T, Siemens). MRCP was performed with a sequence of Half fourier single shot turbo spin echo (HASTE), and the images were processed by using a Maximum intensity projection (MIP) algorithm. The cases investigated were as follows: diseases of common bile duct – 21 cases, diseases of GB – 27, diseases of the pancreas – 10, and others – 4. All patients were imaged with MRCP within 1 month prior to the attempted ERCP or PTC. MRCP and ERCP images were evaluated together with additional clinical information. When ducts were abnormal, probable causes were categorized as follows: localized duct stenosis, calculus disease, duct anomalies, tumor and cystic disease. First we discussed abnormal findings according to the previous classification, and then discussed the diagnosis.

**Summary of results** We were able to diagnose each disease as follows. The accurate diagnoses for GB diseases were 70.4% (19 in 27 cases) by ERCP, but 92.6% (25 in 27 cases) by MRCP. Similarly, for common bile duct diseases the statistic showed 92.5% (20 in 21 cases) by MRCP. [Especially the diagnosis for CBD stones was 100% by MRCP, while it was 93.7% by ERCP (15 in 16 cases).] For pancreatic diseases and others the diagnosis showed 100% accuracy both by MRCP and ERCP.

**Conclusion reached** MRCP is an excellent method for diagnosis in biliary and pancreatic diseases, especially in the diagnosis of stones. Endoscopy, general: Instrumentation, diagnosisEndoscopy, specific: BiliaryRadiology and ultrasound: Diagnosis } "A Clinical Evaluation of MRCP (MRcholangiopancreatography), Compared with ERCP in 60 Cases"

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## "P PP0 0273"PP0 0273 **Treatment of Common Bile Duct Lithiasis, Laparoscopy Versus Endoscopy: Results of a Preliminary Prospective Randomized Trial**

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**Aim of the study** Treatment of common bile duct lithiasis (CBDL) associated with gallbladder lithiasis can be carried out, either in one laparoscopic operation (A) or by laparoscopic cholecystectomy with pre-operative endoscopic sphincterotomy (B). The aim of this randomized trial was to evaluate feasibility and morbidity of each approach.

**Patients and Methods** Between January 1994 and September 1995, among 300 cholecystectomies which began by laparoscopy, 86 CBDL high risk patients defined by clinical (jaundice, pancreatic pain) or biological or ultrasonographic (CBD > 7 mm) data were identified and endoscopic ultrasonography was performed. Criteria of exclusion were severe acute pancreatitis or uremic angiocholitis. Randomization between A and B was performed in the case of an endoscopic ultrasonographic image of CBDL. Intra-operative cholangiography was systematic. Trans-cystic extraction was always attempted, otherwise longitudinal choledocotomy with choledocoscopy was carried out. Thirty-two patients (27 F, 5 M), average age 64 years (40–83), average ASA-score 2.3, were included in this study. There were 14 hepatic colics, 4 cholecystitises, 9 angiocholitises and 5 pancreatitis.

**Results** Sixteen patients of each option were comparable in age, weight, ASA-score and clinical presentation. Mean hospital stay (A vs B) after first act on CBD (8.7 d – 0.7 vs 9.9 d – 1.3), was not different (NS). Morbidity of option A was, residual CBDL, which was treated by post-operative sphincterotomy; a 69 year old cirrhotic man, ASA-score 3, died on day 9. Six conversions into laparotomy were necessary in option A (1 cholecysto-colic fistula, 1 cancer of gallbladder, 3 pediculitises and one failure of cholangiography). One moderate post-sphincterotomic pancreatitis and one re-operation for hemorrhagia of gallbladder's bed were recorded as morbidity of option B. There was no conversion into laparotomy for this last option.

**Conclusions** Feasibility of laparoscopic CBDL's treatment in one intervention, is only 60%. Despite no significant differences in outcome due to small size of both groups, endoscopic stone removal prior laparoscopic cholecystectomy seems confer advantage to patients who desire cholecystectomy by laparoscopic methods. Endoscopy, specific: BiliaryEchoendosonography: EchoendoscopyLaparoscopic surgery: Therapy }" "Treatment of Common Bile Duct Lithiasis, Laparoscopy Versus Endoscopy: Results of a Preliminary Prospective Randomized Trial"

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## "P PP0 0275"PP0 0275 **Needle Knife Papillotomy, A Prospective Study**

\*M. Taha, W. Schimming, U. Schentke

1st Dept. of Internal Medicine, Technical University, Dresden, GermanyOur department is a referral center for difficult or therapeutic ERCP. We studied the success rate and safety of needle knife papillotomy (NKP) retrospectively during two years (1993 and 1994) and prospectively from 01/1995 to 05/1996 within a total number of 1319 endoscopic sphincterotomies (ES).

**Methods** the needle knife (Olympus KD 10 Q) was used to perform gentle cuts from the papillary orifice in an upward 11 o'clock direction, when several attempts to selectively cannulate the bile duct had failed (4–5 attempts 1993/94 and 2–3 in 1995/96).

**Results** success and complication rates Period No. ES No. NKP Success of Complications NKP after NKP1993/94 765 79 (10.3%) 86% 12.7% 1995/96 554 119 (21.5%) 91% 5.9% Success of NKP is defined as free cannulation of the common bile duct with the standard or wireguided catheter. Sphincterotomy was then completed to perform therapeutic maneuvers. The complications were mostly mild pancreatitis, 2 minor bleedings and 3 small perforations. No deaths or emergency surgery occurred.

**Summary** during the second (prospective) period, the percentage of needle knife papillotomy has doubled, but the complication rate halved and the success rate increased.

**Conclusion** needle knife papillotomy (without pancreatic duct stenting) is a safe and useful method, but has an improvement curve even in experienced hands. Liver and bile ducts, 2: Gallstones, formation, treatmentEndoscopy, general: Instrumentation, therapyEndoscopy, specific: Biliary }" "Needle Knife Papillotomy, A Prospective Study"

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"P PP0 0276"PP0 0276 **Extracorporeal Shock-Wave Lithotripsy (ESWL) of Pancreatic Ductal Stones** W. Johanns, J. Janssen,

\*L. Greiner

Medical Clinic A, Municipal Hospital Wuppertal, University of Witten-Herdecke, Germany

**Introduction** Formation of stones in the pancreatic duct can lead to obstruction and maintain obstructive chronic pancreatitis. Endoscopic-operative measures (papillotomy, stone extraction) are of limited use in the case of large or impacted stones or ductal strictures. We used pancreatic ESWL as an alternative to surgical intervention to treat patients with symptomatic pancreatic duct stones, which were not primarily extractable by endoscopy.

**Patients/Methods** 45 patients (m = 25, f = 20) suffering from chronic calcifying pancreatitis were treated by ultrasound-guided ESWL (500–13500 shock-waves, 14–22 kV). Only 13 patients had solitary stones. The average diameter of the largest stone in each case was 11 (5–25) mm. The mean diameter of the dilated pancreatic duct was 9 (5–28) mm. Endoscopic papillotomy was carried out in 44 patients. Fragments not passed spontaneously after ESWL were extracted endoscopically. 30 patients presented with exocrine pancreatic dysfunction; 6 patients had overt diabetes mellitus and 5 patients presented with impaired glucose tolerance. The average duration of follow up was 23 (3–70) months.

**Results** Disintegration of the obstructing calculi was possible in all cases. Completely stone-free ducts were achieved in 23 and a significant reduction in the width of the pancreatic duct in 37 cases. 38 patients became asymptomatic or reported a significant reduction in pain. During the follow-up period 23 patients gained weight and pancreatogenic steatorrhoea ceased. In two patients a pathological glucose tolerance test returned to normal. In 3 cases recurrent stones developed. These were again successfully treated. 4 patients had to undergo surgery in the further course. No major complications were observed.

**Conclusion** Pancreatic ESWL in combination with endoscopy is an effective procedure for non-surgical management of symptomatic pancreaticolithiasis. Removal of the ductal obstruction provides effective pain relief and is frequently accompanied by a reduction in pancreatic exocrine dysfunction. Improvement in endocrine function may even be seen in individual cases. Pancreas: Pancreatitis, chronic } "Extracorporeal Shock-Wave Lithotripsy (ESWL) of Pancreatic Ductal Stones"

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"P PP0 0279"PP0 0279 **The Feasibility of Upper GI Endoscopy Performed through the Nose Using Thin Videoendoscope**J.-F. Rey<sup>1</sup>, D. Duforest<sup>1</sup>, T.A. Marek<sup>2</sup>

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<sup>2</sup> Silesian Medical Academy, Katowice, Poland

**Background and aim** Sedation for upper GI endoscopy is inseparably connected with increase in costs and possible adverse effects of the procedure. The attempts to improve the tolerance of upper GI endoscopy without sedation were based mainly on using thinner scope and very recently on change of the traditional oral to the nasal route of insertion. The aim of the study was to assess the tolerance of diagnostic upper GI endoscopy performed with very thin prototype of electronic videoendoscope, Olympus XGIF-N200H.

**Patients and methods** The first part of the study, made on 10 volunteers, comprised the comparison of the tolerance of endoscopy performed through the nose versus standard oral route. The assessment was made by means of questionnaire, filled-in by volunteers directly after the procedure, in 0–10 scale. Examinations were videotaped for further confirmation of the endoscopic correctness of the procedure, done by independent endoscopist. In the second part, the nose-gastroscopy was performed on the series of consecutive patients, who refused the sedation. Failure of scope insertion, failure of completing the procedure and patients' recommendations for further examinations were noted.

**Results – part I** In one patient the insertion through the nose failed; she was excluded from the further analysis. The overall tolerance of the procedure did not differ for both routes of insertion (median score: 7 for oral as well as for nasal introduction;  $p = 0.612$ ), but the gagging occurred much less frequently during endoscopies performed by nose (1/9 vs. 6/9;  $p = 0.050$ ).

**Results – part II** The attempts of nose-gastroscopy were made in 283 patients. In 19 (6.7%) insertion was impossible. In additional 6 (2.1%) patients marked discomfort was the reason for continuing the procedure under sedation. In remaining 256 (91.2%) endoscopy was successfully completed. Out of them, 237 (91.8%) patients accepted the new route of insertion for (possible) follow-up endoscopies. The gagging, which is the main cause of intolerance of unsedated oral gastroscopy, occurred only in 15 (5.7%) patients.

**Conclusions** The technological progress (very thin endoscope) and the psychological breakthrough (new route of scope insertion) could open the new possibility of decreasing costs of examination while maintaining its tolerance — the thin-scope nose-panendoscopy. Endoscopy, general: Instrumentation, diagnosis } "The Feasibility of Upper GI Endoscopy Performed through the Nose Using Thin Videoendoscope"

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## "P PP0 0280"PP0 0280 **The Role of Balloon Catheter Dilatation in the Management of Benign Gastric Outlet Stenosis**

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**Purpose** For long time, gastric outlet obstruction was managed surgically. Since 1981, we have performed 106 dilatations in 46 patients with gastric outlet obstruction of various origins. In the present paper we discuss the results and the effectiveness of this form of therapy.

**Methods** Dilatation was performed with either double or single lumen (TTS) balloon catheter. For insertion of the double lumen balloon catheter, a guide wire was passed through the stenosis. The single lumen balloon catheter was introduced through the gastroscope. Recently, a big channel gastroscope and high pressure TTS balloon catheter was used. In post vagotomy obstructions, we used a special 20–25 mm diameter balloon catheter. Dilatations were performed under endoscopic or x ray control or both.

**Results** 106 balloon catheter dilatations were done in 46 patients. Out of these, dilatation was a final solution in 25 patients, while 21 patients required surgery after dilatation. Dilatation was most effective in cases of gastric outlet stenosis complicating Billroth I, Billroth II, modified Whipple surgery or vagotomy. Complications: temporary arterial bleeding in one case and perforation in two cases. The effectiveness of dilatation therapy is presented in table below:

Causes of obstruction	Balloon dilatation	Surgery	Total	Post Billroth I or Billroth II	9 0
Corrosive ingestion	3	10	13		
Pyloric or duodenal ulcer	5	5	10		
Postvagotomy	4	1	5		
Modified Whipple operation	3	3	6		
Malignancy (stent implanted)	1	5	6		
Total number of patients:	25	21	46		

**Conclusions** Our results suggest that balloon catheter dilatation in gastric outlet obstruction has both diagnostic and therapeutic value. The dilatation therapy in many cases proved alternative to surgery. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Stomach, duodenum Clinical practice: Management strategy }" "The Role of Balloon Catheter Dilatation in the Management of Benign Gastric Outlet Stenosis"

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## "P PP0 0281"PP0 0281 **Preliminary Results of Endoscopic MR Imaging for Assessment of Esophageal and Rectal Cancer**

\*D. Kulling, D. Feldman, C. Kay, K. Spicer, R. Hawes

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**Background** In contrast to the endorectal surface coil used to assess pelvic tumors, the new magnetic resonance (MR) endoscope has the appearance and all the features of a standard endoscope. We are currently performing a prospective trial on patients with esophageal and rectal cancer, comparing this instrument to endoscopic ultrasound (EUS) in local disease staging. This report presents our preliminary results.

**Methods** After placement of the MR-endoscope (XGIF MR 30, Olympus, Tokyo, Japan) under direct visualization next to the tumor in patients with esophageal (n = 3) or rectal (n = 1) cancer, imaging was conducted on a 1.5 Tesla scanner. Sequences performed were T1-weighted spin echo (SE), T2-weighted fast spin echo and T1-weighted SE after gadolinium injection. The radiologists reading the endoscopic MR images were blinded for any other staging examination. Assessment of T- and N-stages was compared to EUS.

**Results** The procedure was well tolerated with no complication. In one patient with esophageal cancer, due to misinterpretation of the localizer image, the area scanned was beyond the range of the MR-endoscope coil, resulting in insufficient image quality. In the other cases, endoscopic MR and EUS revealed identical tumor expansion (1 {\b4} T2, 2 {\b4} T3) and peritumorous lymph node metastases (3 {\b4} N1). In two patients EUS showed additional pathologic lymph nodes beyond the range of the MR-endoscope coil.

**Conclusions** These preliminary results on endoscopic MR imaging showed high quality images of anatomic details and local cancer depiction in patients with esophageal and rectal tumors. Considering current advantages (three dimensional reconstruction, combination with body coil imaging for M-staging) and awaited technical improvements (real time imaging, open gantry system) of MR imaging, the MR-endoscope is a promising tool for staging of esophageal and rectal cancer. Endoscopy, general: Instrumentation, diagnosisEndoscopy, specific: OesophagusEndoscopy, specific: Colon, rectum }" "Preliminary Results of Endoscopic MR Imaging for Assessment of Esophageal and Rectal Cancer"

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"P P 13 0331" P 13 0331 **H. Pylori Infection and Basal Gastrin Levels in Duodenal Ulcer Patients and in Subjects with Normal Endoscopy**

\*J.P. Gisbert, D. Boixeda, T. Vila, R. Cantón, I. Baleriola Alvarez, V. Moreira, Martedn C. de Argila

"Ramón y Cajal" Hospital, Madrid, Spain

**Purpose** To study basal gastrin levels in duodenal ulcer (DU) patients and those with normal endoscopy, according to

**H. pylori** status.

**Methods** Eighty-four DU patients and 164 with normal endoscopy were studied. Biopsy specimens were taken from both gastric antrum and body, and investigated for microbiology (Gram stain and culture) and histology (H&E stain). Serum basal gastrin levels were measured (RIA; Becton-Dickinson).

**Results** In DU patients the percentage of chronic gastritis was higher ( $p < 0.001$ ) than in

**H. pylori**{ - } patients with normal endoscopy, and similar to

**H. pylori**{ + } patients. **In patients with normal endoscopy, those infected with *H. pylori* had higher ( $p = 0.02$ ) gastrin levels (m – SD) than non-infected (64 – 34 vs 51 – 14 pg/ml) and similar to DU patients (62 – 20 pg/ml). In the multiple regression model analysis *H. pylori* infection was the only variable which correlated with gastrin levels (regression coef.: 9.48 [SE = 4.59]; multiple correlation coef.: 0.22 [ $p = 0.008$ ]). Additional variables (age, sex, presence of DU lesion) were not correlated with gastrin levels. Patients with chronic gastritis had higher gastrin levels ( $p < 0.01$ ) than those with normal histologic mucosa.****Conclusion** *In patients with normal endoscopy, those infected with {*

*H. pylori* had significantly higher basal gastrin levels than non-infected subjects, and similar to DU patients (all of them *H. pylori*{+}). Therefore, hypergastrinaemia seems to be associated with *H. pylori* infection and is not a distinctive feature of DU disease. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "H. Pylori Infection and Basal Gastrin Levels in Duodenal Ulcer Patients and in Subjects with Normal Endoscopy"

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"P P 13 0332" P 13 0332 **Basal Pepsinogen I Levels and *H. Pylori* Infection in Duodenal Ulcer Patients and in Subjects with Normal Endoscopy** D. Boixeda,

\*J.P. Gisbert, T. Vila, L. De Rafael, C. Redondo, Mart'edn C. de Argila, C. Arocena

""Ram\ 'f3n y Cajal"" Hospital, Madrid, Spain

**Purpose** To study basal pepsinogen I (PGI) levels in patients with duodenal ulcer (DU) and with normal endoscopy, according to

**H. pylori** status.

**Methods** Seventy-nine DU patients and 120 with normal endoscopy were studied. Mean age and sex distribution was: 45 – 15 vs 48 – 13 years; and 75% vs 64% males, respectively. In DU patients biopsy specimens were taken from both gastric antrum and body and investigated for microbiology (Gram stain and culture) and histology (H&E stain). In patients with normal endoscopy, samples were obtained only for microbiologic study. Serum basal PGI levels were measured (RIA; Sorin-Biomedica).

**Results** In patients with normal endoscopy, those infected with

**H. pylori** had higher ( $p < 0.001$ ) PGI levels (m – SD) than non-infected patients (81 – 22 vs 54 – 11 ng/ml). PGI levels in DU patients were 106 – 35 ng/ml, which represents a higher value ( $p < 0.001$ ) than in normal endoscopy group (both in

**H. pylori+** and **H. pylori{-}** patients). **In the multiple regression model analysis PGI levels were correlated with *H. pylori* infection ( $r = 27$ ;  $EE = 6$ ), presence of DU lesion ( $r = 26$ ;  $EE = 4$ ) and smoking ( $r = 9$ ;  $EE = 4$ ).** *Conclusion* Basal PGI levels were significantly higher in DU patients than in {

*H. pylori* infected patients with normal endoscopy. Non-infected patients had the lowest PGI values. Therefore, an additional factor seems to exist (besides *H. pylori*) to explain the classically described hyperpepsinogenaemia in DU patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Basal Pepsinogen I Levels and *H. Pylori* Infection in Duodenal Ulcer Patients and in Subjects with Normal Endoscopy"

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## "P P 13 0334" P 13 0334 Prevalence of Duodenal Bulb Gastric Metaplasia and Helicobacter Pylori in Turkey

\*\dc.B. Dogan<sup>1</sup>, C. Tun\er<sup>1</sup>, A. Dursun<sup>2</sup>, U. Kandilci<sup>1</sup>

<sup>1</sup> Gazi University, Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey

<sup>2</sup> Gazi University, Faculty of Medicine, Department of Pathology, Ankara, Turkey Helicobacter pylori (H. pylori) infection causes chronic-active gastritis and is associated with peptic ulceration. However, the link between gastric H. pylori colonization and duodenal ulcers is not well understood. It has been proposed that H. pylori can adhere to the duodenal mucosa where there is gastric metaplasia, survive, and cause focal duodenitis and ulceration. But, duodenal bulb gastric metaplasia and helicobacter pylori are not consistently present in patients with duodenal ulcer, and their frequency have been reported to vary widely from 8% to 92%, and 16% to 83% of patients with duodenal ulcer, respectively. The aim of this study was to investigate the prevalence of duodenal bulb gastric metaplasia and H. pylori in Turkey. 216 patients with duodenal ulcer and 103 with non-ulcer dyspepsia (NUD) were included. Endoscopic mucosal biopsies were done at corpus, antrum, and duodenum, and, if present, ulcer margin. The specimens were stained with periodic acid-Schiff, hematoxylin-eosin, and warthin-starry to examine for gastric metaplasia, mucosal inflammation, and H. pylori, respectively. Prevalence of H. pylori in gastric mucosa was higher in patients with duodenal ulcers (97.6%) than in patients with NUD (57.3%) ( $p < 0.001$ ). Also in the duodenal mucosa of non-ulcer sites, and the ulcer margin of patients with duodenal ulcers, the detection rates (16.8% and 39.20%) were higher than those in the duodenal mucosa of patients with NUD (2.9%) ( $p < 0.001$ ). Gastric metaplasia was present 36.8% and 81.60% in the non-ulcer sites and the ulcer margin of patients with duodenal ulcers, and 13.59% in the duodenal mucosa of patients with NUD ( $p < 0.001$ ). These data suggest that H. pylori is a possible pathogen for duodenal ulcer by duodenal colonization probably via gastric metaplasia in Turkey. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Instrumentation, diagnosis } "Prevalence of Duodenal Bulb Gastric Metaplasia and Helicobacter Pylori in Turkey"

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## "P P 13 0337" P 13 0337 Effect of Chronic Acid Inhibition on Duodenal Bulb Gastric Metaplasia and Helicobacter Pylori

\*\dc.B. Dogan<sup>1</sup>, C. Tun\er<sup>1</sup>, A. Dursun<sup>2</sup>, U. Kandilci<sup>1</sup>

<sup>1</sup> Gazi University, Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey

<sup>2</sup> Gazi University, Faculty of Medicine, Department of Pathology, Ankara, Turkey Gastric metaplasia (GM) has been demonstrated in the duodenal bulb in patients with duodenal ulcer (DU), representing the result of severe inflammation at the ulcer site. These changes have been shown to be related to acid secretion and may regress on acid reduction by highly selective vagotomy. It has also been found that DU patients on continuous pharmacological acid suppression exhibit a lower prevalence of GM in comparison with intermittently treated patients, although not supported by some. The aim of this study was to evaluate the effect of H<sub>2</sub> receptor antagonists on GM in patients with DU. We studied 216 DU patients (130 M, 86 F; 39.7 – 13.4 yrs, m – SD) and 103 healthy controls (35 M, 68 F; 39.4 – 13.7 yrs). DU patients included: 168 patients with active DU (group 1); 26 with healed DU, continuously treated with famotidine (20 mg/nocte), for 3 to 12 months (group 2) and 22 for 2 to 10 years (group 3). Multiple endoscopic biopsies were obtained from the gastric corpus, antrum and the duodenal bulb of each subject. Sections of biopsy tissue were stained with periodic acid-Schiff, hematoxylin-eosin, and warthin-starry to examine for GM, mucosal inflammation, and H. pylori, respectively. Prevalence of gastric and bulber H. pylori, and GM were 85.7%, 31.5%, 71.4% in group 1; 80.8%, 26.9%, 65.4% in group 2; 81.8%, 13.6%, 50% in group 3; and 57.3%, 2.9%, and 13.6% in healthy controls, respectively. Prevalence of GM and bulber H. pylori in group 3 was lower than group 1 (p < 0.05). However, there was a lack of correlation between the duration of drug use and both of them. We concluded that chronic continuous inhibition of gastric asid secretion by H<sub>2</sub> receptor antagonists decreases of prevalence of GM and bulber H. pylori in DU patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: Instrumentation, diagnosis } "Effect of Chronic Acid Inhibition on Duodenal Bulb Gastric Metaplasia and Helicobacter Pylori"

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"P P 14 0388" P 14 0388 **Randomised Controlled Trial of Pre Endoscopy Screening for H. Pylori in the Management of Dyspepsia**

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**Background** It remains unclear whether endoscopy is necessary in the management of H. pylori negative dyspepsia in young patients. In this randomised controlled trial we have tested a hypothesis that endoscopy does not influence the management outcomes of H. pylori seronegative patients under the age of 45 presenting with dyspepsia. The strategy of not endoscoping young H. pylori seronegative dyspeptic subjects will be considered viable if following management by their General practitioners (GPs), no difference is detected at 6 months in symptoms, disability, GP visits and use of medications when an endoscopy group is compared with a group who are endoscoped.

**Design** 417 patients under the age of 45 years referred to a direct access endoscopy service were screened with a validated questionnaire and H. pylori serology (Helico-G ELISA). A cut off level of 6.3 u/ml had been previously determined to be suitable for screening. 154 patients (56% male) had serology titres below 6.3 u/ml and were randomised to have either endoscopy or no endoscopy. All patients were returned to their GPs for further management. Patients with a history of weight loss of more than 1/2 stone in 6 months, dysphagia, anaemia or persistent vomiting or on regular NSAIDs were excluded. Six month assessment was by postal questionnaire.

**Results** Of the 119 due for six month review, 94 (79%) have returned their questionnaires. Endoscopy (50) No endoscopy (44) P Symptom score 1.6 – 0.08 1.5 – 0.08 0.67 Disability score 0.8 – 0.13 0.8 – 0.17 0.64 Days off work 4.3 – 2.24 2.3 – 1.49 0.78 GP visit 1.9 – 0.58 1.9 – 0.61 0.88 GP prescriptions 13/38 (34%) 17/39 (44%) 0.54 Self medications 19/45 (42%) 27/44 (61%) 0.11 Referral to specialist 5/41 (11%) 14/44 (32%) 0.03 Referral for endoscopy 2

**Summary** There was no difference in symptoms, disability, GP visits, and prescriptions between the two groups. There was trend for the endoscoped group to take more days off work, however the non endoscoped group were referred more often for specialist consultations.

**Conclusions** It is safe to manage young H. pylori negative dyspeptic patients without endoscopy. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Randomised Controlled Trial of Pre Endoscopy Screening for H. Pylori in the Management of Dyspepsia"

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"P P 16 0408" P 16 0408 **Chronic Atrophic Gastritis in Children & Adolescents with Upper Dyspeptic Syndrome**

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The aim of this study was to evaluate clinical, endoscopic & histological findings of chronic atrophic gastritis in children & adolescents. In 1993–1995, 138 pts (63 girls & 75 boys), aged 6–18, were investigated for upper dyspeptic syndrome. Upper endoscopy with forceps biopsy from antrum for histological investigation, (hematoxylin/eosin & Giemsa for detection of *Helicobacter pylori* – H.p.) was applied in these pts. In 24 pts was investigated corpus biopsy. Gastritis were graduated by Sidney system. Gastritis was established in 123/138 (89.13 + 5.3%) antral biopsy & in 16/24 corpus biopsy (66.67 + 18.86%). In 33/138 of these biopsy partial atrophy was found. Clinical features of these pts were non specific. Endoscopic findings were: eritematousexudative gastritis in 93.94% & only in 6.06% – atrophic gastritis. Associated pathology was chronic duodenitis in – 81.82%, chronic esophagitis – in 66.67%, duodenogastric reflux – 22.27%, gastroesophageal reflux & duodenal ulcer – in 15.15% ( $p > 0.05$ ). Histopathologically atrophic gastritis was partial & antral. H.p. was detected in 42.42% of these pts ( $p > 0.05$ ). It be concluded that chronic atrophic gastritis is not rare in upper dyspeptic children & adolescents. It is a histopathological diagnosis. Atrophic gastritis is minimal, antral often associated with H.p. in childhood. Oesophageal gastric duodenal disorders: EGD disorders in children Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Endoscopy, general: Endoscopy: children } "Chronic Atrophic Gastritis in Children & Adolescents with Upper Dyspeptic Syndrome"

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## "P P 16 0414" P 16 0414 **Pediatric Biopsies; Morphology and Gene Expression Compared along the Duodenum during Development**

\*E.H. Van Beers, E.H.H.M. Rings, A.W.C. Einerhand, J.A.J.M. Taminiou, H.S.A. Heymans, J. Dekker, H.A. B\fcller

Pediatric Gastroenterology and Nutrition, Academic Medical Center, Amsterdam, The Netherlands

**Purpose** To compare mucosal morphology as well as gene expression in pediatric duodenal biopsies from sites proximal and distal to the papilla of Vater during development in patients with upper gastrointestinal complaints.

**Methods** Duodenal biopsies were obtained from 85 pediatric patients (aged 3 months–18 yrs) with informed consent and permission of the medical ethical committee. Complaints or symptoms included, diarrhea, celiac disease, oesophageal reflux, H. pylori, and G. lamblia. The two locations from which biopsies were taken were proximally and distally from the papilla of Vater and at least 15 cm apart along the duodenum. The study group included white-Caucasian (68) and non white-Caucasian (17) individuals. We used four categories to allocate crypt-villus morphology. Lactase (L) and sucrase-isomaltase (SI) gene expression was measured quantitatively at the mRNA level using Northern analysis and semi-quantitatively at the protein level on paraformaldehyde-fixed tissue using specific monoclonal antibodies [1] and the PAP-technique [2]. Results were assessed double blind using light microscopy.

**Summary** We report a wide inter-individual variability for all the characteristics studied. However, when biopsies from two locations along the duodenum of a single individual are compared with respect to each of the above criteria (morphology, L and SI gene expression amounts and patterns), similarity for each single trait was at least 93%.

**Conclusion** Duodenal biopsies taken distally or proximally relative to the papilla of Vater yield very similar results for morphology and L and SI gene expression if taken from a single individual. This appeared to be independent from age, race, and disease. However, there was considerable variation between individuals for each of the measured characteristics. These findings indicate that the mucosa along the duodenum is rather similar within, but not among, individuals. This would imply that the diagnostic value of proximal and distal biopsies from the duodenum are comparable.

Reference: Hauri, HP, Sterchi, EE, Bienz, D, Fransen, JAM, and Marxer, A (1985) J. Cell Biol. 101; 838.

Van Beers, EH, AI, RH, Rings, EHHM, Einerhand, AWC, Dekker, J, B\fcller, HA. (1995) Biochem. J. 308; 769–775. Endoscopy, general: Endoscopy: children Endoscopy, specific: Stomach, duodenum Clinical practice: Quality assurance } "Pediatric Biopsies; Morphology and Gene Expression Compared along the Duodenum during Development"

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"P P 17 0425" P 17 0425 **Macroscopic and Histopathologic Extent of Disease in Patients with Ulcerative Colitis at Diagnosis and Follow-Up** Bjørn Moum<sup>1</sup>, Anders Ekbohm<sup>2</sup>, Morten H. Vatn<sup>3</sup>

<sup>1</sup> Dept Med, Fredrikstad, Oslo, Norway

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<sup>2</sup> Dept Cancer Epidemiol Uppsala, Sweden

**Background** Colonoscopy has replaced barium enemas as the mean to determine extent of disease in patients with ulcerative colitis (UC). Normally, the extent of disease is determined by direct visualisation of the mucosa, but biopsies are also used with an increased frequency. Very little is known to what extent these two ways to assess extent of disease correlates and if the correlation differs with time of diagnosis and during follow-up.

**Aim** To determine the changes in extent of disease assessed both by direct visualisation and by histopathological changes in the mucosa at the time of diagnosis and after one year follow-up in a cohort of incident cases of UC patients.

**Material and methods** All new cases of UC in a defined population were identified during a four year period (496 patients). 384 patients (78%) were available for follow-up and subjected to a second colonoscopy with representative biopsies taken both from normal and affected mucosa.

**Results** After one year there was macroscopical signs of progression in 14%, 22% showed regression and additionally 30% had a normal colonoscopy. The histopathological changes from diagnosis until follow-up showed progression in 20%, 24% showed regression and in addition 24% had normal histopathologic findings. Histopathologic examination entailed a more extensive disease compared to direct visualisation in 4% at diagnosis and in 28% at follow-up, while direct visualisation entailed a more extensive disease than histopathologic examination in 18% at diagnosis and 12% at follow-up. Best correlation at both diagnosis and follow-up was seen in pancolitis (99% and 88% respectively).

**Conclusion** From our results it is obvious that there is an increasing difference between macroscopic and histopathological involvement in UC patients at follow-up one year after diagnosis. It remains to be evaluated in further studies to what extent histopathological involvement is a better marker than macroscopic changes for the long-time prognosis. Intestinal disorders: IBD diagnosis, monitoring Endoscopy, specific: Colon, rectum } "Macroscopic and Histopathologic Extent of Disease in Patients with Ulcerative Colitis at Diagnosis and Follow-Up"

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"P P 17 0432" P 17 0432 **Measurement of Mucosal Blood Flow in Ulcerative Colitis by Means of Endoscopic Laser Doppler Flowmetry**

\*M. Cianci, G. Gizzi, V. Villani, K. Jadallah, G. Elia, A. Ferri, R. Corinaldesi

Department of Internal Medicine and Gastroenterology, University of Bologna, Italy  
The aim of our study was to evaluate colonic mucosal blood flow in patients with ulcerative colitis (UC), using endoscopic laser-doppler flowmetry (ELDF). We studied 20 UC patients (14 M, 6 F: 36 – 8 yrs; mean age – SD) and 18 healthy controls (HC) (10 M, 8 F: 38 – 5 yrs). The Laser-doppler flowmeter used was the Laserflow BPM-403, Vasamedics USA. Four ELDF measurements were taken from the rectosigmoidal mucosa and expressed in flux units (FU) (ml/min in 100 cc of tissue). Finally, skin blood flow was measured at the forearm for 5 minutes. The mucosal/skin flow ratio (MUSK index) was calculated. Results were expressed as mean values – SD and analyzed by ANOVA test. The average of mucosal blood flow (MBF) and MUSK index (MI) was significantly increased in UC patients compared to HC (MBF: 38.1 – 11.2 vs 15.5 – 2.7,  $p < 0.02$ ; MI: 20.1 – 6.8 vs 9.1 – 2.9,  $p < 0.05$ ). The following table illustrates the ELDF measurements and MUSK index related to the mucosal inflammatory activity in UC.

Inflammatory mucosal activity	No. Pts	Mucosal Blood Flow (FU)	MUSK index
Remission	5	24.6 – 3.1*	12.8 – 1.7*
Mild	7	35.2 – 6.1*	18.3 – 2.6*
Moderate-severe	8	53.9 – 8.8**	28.1 – 3.9**

\* $p < 0.05$  vs following value of MBF and MI. \*\* $p < 0.05$  vs all other values of MBF and MI. Our results show a significant increase of mucosal blood flow in UC patients compared to HC. The increase of mucosal blood flow in UC patients is directly related to the mucosal inflammatory activity. The MUSK index seems to be reliable in distinguishing between normal and abnormal mucosa in different degrees of inflammatory activity. Endoscopy, general: Instrumentation, diagnosis  
Endoscopy, specific: Colon, rectum  
Intestinal disorders: IBD diagnosis, monitoring }  
"Measurement of Mucosal Blood Flow in Ulcerative Colitis by Means of Endoscopic Laser Doppler Flowmetry"

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## "P P 19 0486" P 19 0486 Comparison of Ultrasound-Secretin Test and Sphincter of ODDI Manometry in Patients with Acute Recurrent Pancreatitis

\*M.P. Brunori, V. Di Francesco, L. Rigo, G. Angelini, P. Bovo, M. Filippini, B. Vaona, L. Frulloni, M. Tebaldi, P.C. Farris, T. Grasso, G. Cavallini

Gastroenterology Unit, University of Verona, Italy Sphincter of Oddi manometry (SOM) is considered the gold standard for evaluating sphincter of Oddi dysfunction (SOD). It has recently been demonstrated that the Ultrasound-Secretin test (US-S), proposed as a non-invasive test for the study of SOD, yields an high percentages of pathological findings in ARP patients. The aim of this study was to compare the results of the US-S test with SOM findings in a consecutive series of patients with ARP. Twenty-three patients admitted to our GI unit (12 M, 11 F; mean age 41 – 13 years) suffering from ARP underwent US measurement of the main pancreatic duct in the baseline situation and at one-min intervals for 60 min after maximal stimulation with secretin 1 UI/Kg. The test was considered pathological when the duct was still dilated at 20 min. Within one week interval the same patients were submitted to SOM. The procedure was performed endoscopically by using a perfused three or two lumen catheter connected to a computerised system (Polygram Synectis, Sweden). Intraduodenal pressure was taken as a zero reference. In 12 patients Caerulein 0.05 \b5g/Kg i.v. bolus was administrated during SOM. A stenosis was defined in the presence of > 40 mmHg basal pressure, dyskinesia when paradoxical response to Caerulein or abnormal phasic contraction amplitude (> 300 mmHg), frequency (> 7/min) or propagation (> 50% retrograde) were present. Compared to SOM findings US-S sensitivity and specificity for SOD were 87.5% and 71.4% respectively. SOMUS-S Normal Stenosis Dyskinesia Normal 5 1 1 7 (30.4%) Abnormal 2 10 4 16 (69.6%) 7 (30.4%) 11 (47.8%) 5 (21.7%)

**Conclusions** 1) most patients with ARP present a documentable SOD both at US-S and SOM; 2) results at US-S are strongly concordant with the SOM findings, therefore US-S may offer a valid alternative to the more expensive and invasive manometric procedure for assessing SOD. Pancreas: Pancreatitis, acute Pancreas: Pancreatitis experimental } "Comparison of Ultrasound-Secretin Test and Sphincter of ODDI Manometry in Patients with Acute Recurrent Pancreatitis"

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**OT11 0542 Fibrin Sealant (Beriplast<sup>R</sup>) V.s. Polidocanol 1% in the Endoscopic Treatment of Bleeding Gastroduodenal Ulcers** E.A.J. Rauws<sup>1</sup>, P. Rutgeerts<sup>2</sup>, P. Wara<sup>3</sup>, A. Hoos<sup>4</sup>, E. Solleder<sup>4</sup>, M. Praus<sup>4</sup>, Beriplast study team<sup>5</sup>, J. Halttunen<sup>6</sup>, G. Dobrilla<sup>7</sup>, G. Richter<sup>8</sup>, R. Prassler<sup>9</sup>, C. Soederlund<sup>10</sup>, A. Saggioro<sup>11</sup>, M. Matikainen<sup>12</sup>, J. Kjaeve, M. Osnes, P. Swain

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<sup>7</sup> I-Bolzano

<sup>8</sup> D-Augsburg

<sup>9</sup> D-Minden

<sup>10</sup> S-Stockholm

<sup>11</sup> I-Mestre

<sup>12</sup> SF-Tampere

N-Tromsø

N-Oslo

GB-London A prospective, randomized, stratified, open and controlled study was performed in 19 centres in 9 European countries. Patients suffering from an endoscopically verified gastroduodenal ulcer bleeding (spurting/oozing/visible vessel) (Forrest IA, IB, IIA) were randomly allocated to receive either single sclerotherapy (polidocanol 1%) or single injection therapy with fibrin sealant (FS) or repeated therapy with FS. A daily endoscopic control was performed until the ulcer base was hematin covered or clean (Forrest IIC or III). A minimum in patient observation period of 5 days and a safety follow-up of one month were required. The primary objective was the comparison of repeated application of FS v.s. sclerotherapy with polidocanol in terms of rebleeding rates after initial hemostasis. Rebleeding was defined as visually (endoscopically) verified bleeding from the same source. Per protocol analysis was performed on 737 patients. The overall incidences of rebleeding were for polidocanol 21.3%, FG single 17.2% and FG repeated 12.1%. This result was statistically significant in favour of repeated therapy with FS in comparison to polidocanol (2-sided p-value 0.020). Safety analysis

as well as evaluation of laboratory parameters and clinical variables revealed no specific risk for either treatment group. As approximately 50% of all rebleedings occurred within 24 hours after initial hemostasis, elective early re-endoscopy with prophylactic retreatment might be beneficial. Endoscopy, general: GI bleeding } "Fibrin Sealant (BeriplastR) V.s. Polidocanol 1% in the Endoscopic Treatment of Bleeding Gastroduodenal Ulcers"

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## OT24 0562 Intraductal Papillary Mucinous Tumors of the Pancreas (IPMT): Accuracy of Preoperative Imaging and Long Term Follow-Up in a Large Series of Operated Patients

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IPMT of the pancreas are rare and few data are available about the accuracy of preoperative imaging and long term outcome after surgery.

**Aims** To assess: 1. the accuracies of preoperative findings by Computed Tomodensitometry (CT), Endoscopic Retrograde Pancreatography (ERP) and Endoscopic Ultrasonography (EUS) related invasive malignancy and pancreatic extension of the disease, by comparison to resected specimens. 2. the long term outcome after supposed curative surgery.

**Patients and Methods** Forty seven patients (34 M, 13 F, mean age: 63 (35–81), operated between 1980 and 1995, with a definite pathological diagnosis of IPMT were included in this retrospective study. CT (n = 25), ERP (n = 29) and EUS (n = 21) available examinations were each reviewed by 2 physicians unaware of the patients to assess invasive malignancy and pancreatic extension. Surgical resected specimens were reviewed by 2 experienced pathologists. Postoperative follow-up was analysed using the Kaplan-Meier method.

**Results** Tumors were diffuse or overlapped resection margin in 51% (24/47) cases. IPMT showed histological features with invasive carcinoma in 43% (20/47) patients, with severe dysplasia in 21% (10/47) and with non severe dysplasia in 36% (17/47). The overall accuracies, for the distinction between invasive and non invasive tumors by CT, ERP and EUS, were respectively 76% (19/25), 79% (23/29) and 76% (16/21). The extension of IPMT were correctly assessed by CT, ERP and EUS in respectively 67%, 57% and 62% cases. The overall 3 years free disease survival was 79%, but only 21% in the group of patients operated with features of invasive carcinoma (p < 0.001). In these latter 20 patients, 12 malignant recurrences and 7 deaths related tumors occurred.

**Conclusions** This study underlines the need for an early surgical resection in patients with suspected IPMT of the pancreas, because: – the high rate of invasive carcinoma, – the insufficiency of preoperative imaging to correctly assess malignancy and – the poor outcome of patients operated with features of invasive carcinoma. Oncology, specific: Pancreas }"  
"Intraductal Papillary Mucinous Tumors of the Pancreas (IPMT): Accuracy of Preoperative Imaging and Long Term Follow-Up in a Large Series of Operated Patients"

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## OT24 0563 Small Pancreatic Cysts Are Clinical Precancerous Condition? — Analysis of K-Ras Gene Mutation in the Pancreatic Juice-

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The mutations of K-*ras* codon 12 (MR) was found in the majority of pancreatic adenocarcinomas (PC), and has also been identified in the pancreatic duct with hyperplasia in association with chronic pancreatitis (CP). Therefore some of these CP may be considered to be early precursors of PC. Recently we sometimes found MR in pancreatic juice (PJ) in patients with small pancreatic cyst. Therefore in the present study, we evaluate whether small pancreatic cysts are precancerous condition by the view point of MR in PJ. From November 1994 to December 1995, endoscopic aspiration cytology of PJ was performed in 52 consecutive patients suggested pancreatic diseases. PJ was collected through an endoscopic cannulation into the pancreatic duct. Analysis of the MR was performed using the enriched polymerase chain reaction—single-strand conformation polymorphism technique and confirmed by direct sequencing. MR were detected in 13 of 15 patients with PC, and in 7 of 13 patients with CP. In 16 patients with benign small pancreatic cyst, MR were also detected in 11. None of the 8 normal control had MR. Main mutational patterns in patients with benign small pancreatic cyst included GTT, GAT, and CGT, which were the same as those found in the cases of PC. MR occurred frequently in PJ of patients with benign small pancreatic cysts. Their mutational rate was higher than that of CP cases. We have already detected several cases of *in situ* PC in patients with small pancreatic cysts. These results suggested that patients with benign small cysts may be at high risk for the development of PC.

Oncology, general: Molecular biology, genetics  
Oncology, specific: Pancreas  
Endoscopy, specific: Pancreatic }

"Small Pancreatic Cysts Are Clinical Precancerous Condition? / Analysis of K-Ras Gene Mutation in the Pancreatic Juice-"

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OT26 0569 **Microlithiasis of Common Bile Duct in Patients with Acute Biliary Pancreatitis (ABP) — An Indication for Endoscopic Treatment** A. Nowak, M. Kohut, E. Nowakowska-Dulawa, R. Kaczor, T.A. Marek

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**Aim** The use of endoscopic sphincterotomy in the treatment of ABP patients with no common bile duct stones (CBDS) is not generally accepted. The aim of this study was to investigate the presence of CBD microlithiasis in patients with AP of biliary origin and no CBDS.

**Material and methods** 117 consecutive patients with ABP and no CBDS on ERCP, performed as an urgent (< 24 hours of admission) procedure, (70 – gallbladder stones, 47 post-cholecystectomy), treated between January 1994 and May 1996 were included to the study. 67 consecutive patients with no CBDS found in ERCP and no AP served as controls. The presence of CBD microlithiasis (CBDM) was calculated according to Juniper and Benson, in CBD bile collected during ERCP.

**Results** The frequency of CBD microlithiasis in ABP and controls: ABP – acute biliary pancreatitis, GBS – gallbladder stones, PC – post-cholecystectomy, A – acute episode of ABP, H – history of ABP, T-total. GBS PC ABP no ABP no A H T ABP A H T ABPCBDM (+) 58 5 63 8 28 8 36 22 (90%) (40%) (77%) (37%) CBDM ({ -}) 6 1 7 12 4 7 11 37 p < 0.001 p < 0.001

**Conclusions** 1. In patients with ABP and no CBDS on ERCP, CBD microlithiasis is observed in the vast majority of patients, especially during the acute attack of the disease. 2. Microscopic examination of CBD bile taken during ERCP in an useful diagnostic tool. 3. The presence of CBD microlithiasis in the majority of ABP patients suggests the necessity of endoscopic treatment in every case of acute biliary pancreatitis, also with no CBDS present on ERCP. Pancreas: Pancreatitis, acute Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Microlithiasis of Common Bile Duct in Patients with Acute Biliary Pancreatitis (ABP) / An Indication for Endoscopic Treatment"

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## OT31 0579 Botulinum Toxin (BT) in Achalasia: How Predictable is the Therapeutic Response?

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CHU Nantes, Ghent, Belgium Although results of BT seem slightly less favorable than those achieved with balloon dilation, the non invasive nature of BT makes it an attractive alternative as the first choice treatment of achalasia. In order to optimize the therapeutic strategy we tried to identify in a cohort of patients prospectively treated with BT factors which may represent useful predictors of therapeutic response. *Methods.* Intrasphincteric injections of Botox<sup>®</sup> (4 × 20 U) were performed in 55 symptomatic patients with manometrically-proven achalasia (28 men; mean age 53 yrs; mean duration of symptoms 39 months; 18 with previous dilation). Dysphagia, regurgitation and chest pain were scored on a 0–3 scale (3 = every meal, 2 = daily, 1 = occasionally) before and 6 months after injection. At 6 months, remission was defined by severity score (S) ≤ 3, and failure by relapse (S > 3) after 2 injections or loss to follow-up. Analysis of risk factors was performed between remission and failure groups (Student t-test, Mann-Whitney test and Chi<sup>2</sup> test). *Results* (Table, m – SD). Remission (n = 33) Failure (n = 22) PAge (yrs) 56 – 15 50 – 14 0.125 Time to diagnosis (months) 41 – 45 37 – 52 0.915 Weight loss (kg) 5.2 – 6.4 7.0 – 6.7 0.324 Severity score 4.9 – 2.0 5.5 – 1.4 0.183 LOS pressure (mm Hg) 28 – 12 25 – 12 0.429 Amplit. of waves (mm Hg) 39 – 34 35 – 32 0.562 Oesophageal diameter (cm) 4.6 – 1.4 4.1 – 1.3 0.260 Previous dilation (n) 12 6 0.480 Male/Female 18/15 10/12 0.510 *Conclusions.* Although there was a trend for older patients to have a better outcome after BT, none of the parameters tested were found to be predictive of the therapeutic response. Acknowledgements to SNFGE, CHU Nantes and Allergan France. Oesophageal gastric

duodenal disorders: Oesophageal disorders, non refluxMotility, specific: OesophagusEndoscopy,  
general: Instrumentation, therapy }" "Botulinum Toxin (BT) in Achalasia: How Predictable is  
the Therapeutic Response?"

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## "P P 21 0595" P 21 0595 Endoscopic Ultrasound (EUS) Staging of Adenocarcinomas (A) Developed on Barrett's Esophagus (BE)

\*P. Ruzsniwski, M.H. Sayegh, P. Dahan, A. Sauvanet, J.F. Fl'e9jou<sup>1</sup>, V. Vilgrain<sup>2</sup>, J. Belghiti, P. Bernades

<sup>1</sup> Federation of Hepato-Gastroenterology, Departments of Anatomopathology, 92118 Clichy Cedex, France

<sup>2</sup> Radiology, Hospital Beaujon, 92118 Clichy Cedex, France EUS is an accurate procedure for the staging of epidermoid esophageal cancer. The presence of Barrett's epithelium, lymph-node and cardiac involvement may account for differences in EUS performance in the staging of ABE.

**Aim of the study** to determine the sensitivity of EUS for the assessment of parietal and lymph-node involvement, and for tumoral staging (UICC classification) in patients with ABE.

**Patients (pts) and Methods** 43 pts with ABE operated on between January 1987 and December 1994 in one center; EUS performed before surgery. Results of EUS were compared to anatomical findings in surgical specimen.

**Results** staging was complete in 33 pts, but intraversable stenosis was encountered in 10 pts. 1 – Traversable tumors: a) T-stage accuracy: 17 of 19 T1, 4 of 5 T2, 5 of 8 T3 and 1/1 T4 tumors were correctly assessed by EUS, i.e. an accuracy of 81%. Among T1 lesions (accuracy: 90%), EUS was unable to distinguish those limited to the mucosa from those involving the submucosa. b) N staging: 22 of 25 No, 5 of 8 N+ were correctly assessed, i.e. EUS sensitivity and specificity were 75 and 80%, respectively. Tumoral staging according to the UICC classification was correctly determined in 72% of the pts (stage I: 16 of 19; stage IIa: 3 of 5; stage IIb: 1 of 2; stage III: 3 of 7). 2-Intraversable stenoses (10 pts): EUS accuracy decreased dramatically to 20% for T staging. Sensitivity and specificity of EUS for N staging were 57 and 100%, respectively; tumoral UICC staging was correct in 30% of the pts. *Conclusion.* EUS is a useful for preoperative staging of traversable ABE. It is an accurate procedure to assess parietal and lymph-node involvement. EUS accuracy decreases in pts with intraversable tumors, most of which are at T3 or T4 stage. Echoendosonography: Echoendoscopy Oesophageal gastric duodenal disorders: EG Reflux Oncology, specific: Oesophagus } "Endoscopic Ultrasound (EUS) Staging of Adenocarcinomas (A) Developed on Barrett's Esophagus (BE)"

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**"P P 21 0597" P 21 0597 Barrett's Patients Developing Gastric Polyps during Acid Suppression are at Greater Risk for Esophageal Dysplasia A. Svoboda, S. Tillisch-Svoboda**

Sansum Medical Clinic, Santa Barbara, CA, USA Endoscopic surveillance of patients with specialized columnar epithelium and intestinal metaplasia in the tubular esophagus is indicated because of the rapidly increasing incidence of adenocarcinoma of the esophagus (and cardioesophageal junction). The development of large (over 1 cm) gastric hyperplastic polyps in such patients on long-term omeprazole therapy, and their disappearance or reduction in size and number associated with stopping or decreasing the dosage of omeprazole, prompted a retrospective and prospective review of Barrett's patients followed by the author. 121 patients with short segment Barrett's (less than 3 cm) were further compared with 82 patients with long segment classical Barrett's (over 3 cm). The increased occurrence of non-neoplastic gastric polyps was statistically significant in Barrett's patients (17.4%,  $p = 0.0001$ ), and this was especially true in those treated with proton pump inhibitors. All moderate and high-grade dysplasia (nine) and most low-grade dysplasia (twenty-six of forty seven) occurred with long segment Barrett's. A majority of gastric polyps (59%) occurred with long segment Barrett's. A finding of gastric polyps is associated with a greater risk of esophageal dysplasia (36% versus 19%,  $p = 0.032$ ). The development of gastric polyps during acid suppression therapy appears to be a side effect of therapy and possibly helps select a group at greater need for careful surveillance. Oncology, general: Screening, prevention Oncology, specific: Oesophagus Endoscopy, specific: Oesophagus } "Barrett's Patients Developing Gastric Polyps during Acid Suppression are at Greater Risk for Esophageal Dysplasia"

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"P P 23 0624" P 23 0624 **Dilation of Benign Oesophageal Strictures with Savary-Guilliard Bougies in Outpatients** A. Konstantinide,

\*K. Paraskeva, V. Vamvakousis, A. Germanopouls, N. Scandalis

Gastroenterology department, General Hospital of Athens, Greece

**Aim** To show that endoscopic dilation of benign esophageal strictures is effective and safe for outpatients.

**Patients** During the last 2.5 years, 27 patients, 15 male and 12 female, aged 29–84 with benign oesophageal strictures underwent endoscopic dilation. The cause of the stricture was: reflux oesophagitis in 16 patients, sclerotherapy in 7, caustic injury in 3 and surgery in 1 patient. The site of the stricture was: in the upper oesophagus 3, in the middle 2 and in the distal 22 cases.

**Method** Endoscopic evaluation of the nature, site and extent of the stricture, plus biopsies in all patients and barium radiology in 4 patients. Savary-Guilliard bougies were used over guidewire. After the procedure, the patients were kept under observation for 1–2 hours and then discharged with instructions about liquid food 5 hours later, omeprazole 40 mg/day and keeping in touch in case of adverse events.

**Results** Each time 4–6 S-G bougies were used, gradually increased in size. The procedure was repeated 2–4 times with 3 weeks intervals in between, to be continued in case of dysphagia. All dilation procedures were 117 (4.3 per patient). There were no complications or adverse events.

**Conclusion** Endoscopic dilation of benign oesophageal strictures with S-G bougies is effective and safe and patients' hospitalization is not necessary. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } "Dilation of Benign Oesophageal Strictures with Savary-Guilliard Bougies in Outpatients"

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## "P P 24 0626" P 24 0626 **Oesophageal Dilatation for Caustic Stenosis in Childhood: Study of 19 Patients**

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Endoscopy Unit of Pediatric Hospital of Coimbra, Coimbra, Portugal

**Introduction** After the ingestion of a strong caustic agent, oesophageal stenosis remains relatively frequent. Oesophageal repetitive dilatation is usually regarded as an effective therapy but, because large paediatric series are infrequent, there are many doubts about the periodicity of sessions, efficacy and duration of the treatment and rate of complications. We present our results of dilatation therapy for corrosive oesophageal stenosis.

**Methods** We reviewed retrospectively our experience (January 1986–May 1996). The dilatations were performed, under sedation or under general anesthesia, in a regimen of day care. The dilatator guide was introduced under endoscopic control. Two different materials were used: until 1987 metallic bougies and since 1987 Savary bougies.

**Results** One hundred and forty children with accidental ingestion of caustic, were endoscopically evaluated for the suspect of oesophageal burn: One of them developed severe complications — oesophageal and gastric necrosis requiring oesophageal replacement — and 19 patients developed oesophageal stenosis. To treat stenosis, 265 sessions of dilatation were performed (median: 10, with SD: 8.35, min.: 2 max: 33). Nine of the 19 children achieved cure with mechanical dilatation: the duration of the treatment was 5 months (median, with SD: 5, min.: 2, max: 16) and the number of dilatations was 9 (median, with SD: 6.95, min.: 2 max: 27). Four of 19 children were operated on because oesophageal dilatations were unsuccessful: the duration of the treatment was 8.5 months (median, with SD: 4.9, min.: 1 max: 13) and the number of dilatations was 18 (median, with SD: 8.81, min.: 4 max: 23). Six children are currently under dilatation therapy: 4 of those children, are on a regular program, with a monthly periodicity; the duration of treatment was respectively 4 months, in 2 cases and 15 months in the other case. The other two children are treated when dysphagia occurs; the duration of the treatment/number of sessions was respectively 18 months/19 dilatations and 48 months/33 dilatations. Oesophageal perforation occurred in 1.13% of the dilatations. All were treated with gastric aspiration, nothing by mouth and antibiotics, and all survived.

**Conclusion** Dilatation therapy for oesophageal caustic stenosis achieved a 50% cure rate. When performed by an experienced team it is safe, but is also time consuming because, to achieve cure, repetitive dilatations are necessary and duration of treatment is long. Endoscopy, general: Instrumentation, therapy Endoscopy, general: Endoscopy: children Endoscopy, specific: Oesophagus } " Oesophageal Dilatation for Caustic Stenosis in Childhood: Study of 19 Patients"

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## "P P 24 0627" P 24 0627 **Caustic Injuries of Upper Gastrointestinal Tract (UGIT) in Patients Admitted to an ICU**

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Ingestion of caustic agents can cause severe injury to the esophagus and stomach which continues to be a medical and surgical management problem.

**Purpose** To evaluate patients admitted to an ICU with caustic injuries and correlate the severity of endoscopic lesions with complications developed.

**Methods** We retrospectively reviewed 23 patients admitted to an ICU, (11 women and 12 men with a mean age of 45 years), during a 4 year period (February 1992–February 1996), with caustic injuries of the UGIT. Statistical analyses were done using the chi-square test.

**Results** Caustic ingestion was accidental in 12 patients (52%) and suicide attempt in 11 (48%). The type of agent was acid – 9, alkali – 11, medicament – 1 and unknow – 2. The most frequent symptoms were: odynophagia – 82%, hematemesis and epigastric pain – 43%, chest pain – 26%. In 14 patients occurred oropharyngeal lesions independent the UGIT lesions ( $p = 0.8$ ). Endoscopy revealed: caustic esophagitis grade I-2, II A-7, II B-10 e III-4; gastritis grade I-4, II-10, III-9 (Zargar Classification). The mean hospitalization time was 11 days. Infection developed in 8 patients (sepsis in 4) with no significant correlation with the burn grades. All patients were treated with omeprazol and sucralfate, 17 did antibiotics, 5 corticosteroids and 12 needed parenteral nutrition. 100% of grade III and 40% of grade II B injuries developed esophageal stenosis ( $p = 0.02$ ), and 2 patients (1 grade III and 1 II B gastric burns) developed pyloric stenosis ( $p = 0.27$ ). Therapeutic endoscopy were done successfully in 5 patients. Of the 3 patients who needed surgery (total esophagectomy – 2; esophagectomy and gastrectomy – 1) all died.

**Conclusions** (1) Oropharyngeal lesions had no significant correlation with UGIT injuries; (2) Infection was the most frequent immediate complication, not correlated with the severity of injuries; (3) Only patients with grade IIB and III developed stenosis; (4) Therapeutic endoscopy were successful in 62%; (5) Caustic injuries can be potentially fatal. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux  
Endoscopy, specific: Oesophagus  
Endoscopy, specific: Stomach, duodenum } "Caustic Injuries of Upper Gastrointestinal Tract (UGIT) in Patients Admitted to an ICU"

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"P P 24 0628" P 24 0628 **Oesophageal Dilatation for Caustic Stenosis in Childhood: Study of 19 Patients** M. Francelina Lopes<sup>1</sup>, Aurélio Reis<sup>1</sup>, M. Rute Cunha<sup>2</sup>, A. Nogueira Brandão<sup>2</sup>, A. Mendes Antunes<sup>2</sup>

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**Introduction** After the ingestion of a strong caustic agent, oesophageal stenosis remains relatively frequent. Oesophageal repetitive dilatation is usually regarded as an effective therapy but, because large paediatric series are infrequent, there are many doubts about the periodicity of sessions, efficacy and duration of the treatment and rate of complications. We present our results of dilatation therapy for corrosive oesophageal stenosis.

**Patients and methods** We reviewed retrospectively our experience (January 1986–May 1996). The dilatations were performed, under sedation or under general anesthesia, in a regimen of day care. The dilatator guide was introduced under endoscopic control. Two different materials were used: until 1987 metallic bougies and since 1987 Savary bougies.

**Results** One hundred and forty children with accidental ingestion of caustic, were endoscopically evaluated for the suspect of oesophageal burn: One of them developed severe complications — oesophageal and gastric necrosis requiring oesophageal replacement — and 19 patients developed oesophageal stenosis. To treat stenosis, 265 sessions of dilatation were performed (median: 10, standard deviation: 8.35, min.: 2 max: 33). Nine of the 19 children achieved cure with mechanical dilatation: the duration of the treatment was median: 5 months, standard deviation: 5, min.: 2, max: 16 and the number of dilatations was median: 9, standard deviation: 6.95, min.: 2 max: 27. Four of 19 children were operated on because oesophageal dilatations were unsuccessful: the duration of the treatment was median: 8.5, standard deviation: 4.9, min.: 1 max: 13 and the number of dilatations was median: 18, standard deviation: 8.81, min.: 4 max: 23. Six children are currently under dilatation therapy: 4 of those children, are on a regular program, with a monthly periodicity; the duration of treatment was respectively 4 months, in 2 cases and 15 months in the other case. The other two children are treated when dysphagia occurs; the duration of the treatment/number of sessions was respectively 18 months/19 dilatations and 48 months/33 dilatations. Oesophageal perforation occurred in 1.13% of the dilatations. All were treated with gastric aspiration, nothing by mouth and antibiotics and all survived.

**Conclusion** Dilatation therapy for oesophageal caustic stenosis achieved a 50% cure rate. When performed by an experiment team it is safe but is also time consuming because, to achieve cure, repetitive dilatations are necessary and duration of treatment is long. } "Oesophageal Dilatation for Caustic Stenosis in Childhood: Study of 19 Patients"

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"P P 28 0671" P 28 0671 **Endoscopic Diagnosis of Esophageal Varices Using an Endoscopic Image Processor (EVIP-230)**

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**Purpose** Following recent advances in the treatment of esophageal varices, these varices assume diverse morphological features after treatment or upon recurrence. For this reason, detailed endoscopic assessment of varices is now more important than ever. We recently assessed the usefulness of an endoscopic image processor (OLYMPUS Endoprocessor EVIP-230) as a means of endoscopic diagnosis of esophageal varices.

**Subjects and Methods** The subjects of this study were 45 patients with esophageal varices who underwent endoscopy at our department after October 1995. By the time of endoscopic assessment, 15 cases had received no treatment and 14 cases had undergone treatment, in other 16 cases, endoscopy was performed both before and after treatment. The endoscopic images were subjected to adaptive structure enhancement or IHb color enhancement or both on a real time basis or some time later after the data was stored on optomagnetic disc.

**Results** Image processing was very useful in assessing the efficacy of treatment and the post treatment morphology of varices, especially in examining the presence/absence and location of small vessels. During the follow-up period, varices recurred in 2 cases. In both cases, the morphology of recurrent varices could be predicted in advance, by processing produced difficulties in making a judgment of Red color sign or to follow the time course of varices.

**Conclusion** The Endoprocessor EVIP-230 was very useful as a means of endoscopic diagnosis of esophageal varices. However, so that the time course of varices could be followed and the data could be compared among patients treated at different facilities, it seems necessary to process images after assessing the raw images and to standardize the color of processed images. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Oesophagus } "Endoscopic Diagnosis of Esophageal Varices Using an Endoscopic Image Processor (EVIP-230)"

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## "P P 28 0672" P 28 0672 Endoscopic Evaluation of Solitary and Scattered Varices and Analysis of Clinical Features

\*T. Fukuda, S. Okamura, A. Tsutsui, S. Taoka, M. Sogabe, H. Matunaga, Y. Ohkita, N. Muguruma, S. Hayashi, T. Okahisa, H. Shibata, S. Ito

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**Purpose** The pathogenesis and clinical significance of solitary or scattered varices of the upper or middle esophagus, not contiguous to any varix of the lower esophagus, have not yet been fully clarified. We recently carried out endoscopic assessment of these varices and analyzed the clinical features of patients with these varices.

**Subjects and Methods** Between 1991 and 1995, routine endoscopic examinations of the upper gastrointestinal tract were carried out on 6128 individuals. Of these individuals, 31 cases (18 males and 13 females, and 61.3 years old on average) were found to have solitary or scattered varices (53 lesions in total). The clinical features and endoscopic findings of these cases were analyzed. 12 cases (25 lesions) were followed up.

**Results** Varices were more often solitary (20 cases, 64.5%) than scattered (11 cases, 35.5%). Blue varices were seen in 19 cases (61.3%), and white varices in 11 cases (35.5%). One case (3.2%) had both blue and white varices. Varices were dome-shaped in 23 cases (74.2%) and "Quonset hut"-shaped in 8 cases (25.8%). Of all cases studied, only 8 cases (25.8%) had underlying disease which could cause ordinary esophageal varices (e.g. portal hypertension, congestive heart failure and SVC obstruction). 4 cases had chronic hepatitis and another 4 cases had liver cirrhosis. Disease of the upper gastrointestinal tract, which accompanied varices, include chronic gastritis (13 cases) and gastric polyps (6 cases). When 12 cases were followed up for 10.4 months on average, 10 cases showed no change in the size or number of varices, one case showed a size reduction, and another one case had disappeared.

**Conclusion** On the basis of the results we obtained, we think it is unlikely that the factors known to cause ordinary esophageal varices are responsible for the onset of solitary or scattered varices. These varices seem to be attributable to: (1) dilatation of submucosal vessels due to local fragility or compression, or (2) increase in local blood flow. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Endoscopy, specific: Oesophagus } "Endoscopic Evaluation of Solitary and Scattered Varices and Analysis of Clinical Features"

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"P P 28 0673" P 28 0673 **The Use of Endoscopic Ultrasonography in the Study of the Azygos Vein in Patients with Esogastric Varices**

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In the course of portal hypertension portosystemic collaterals develop, which may lead to the formation of esophagogastric varices (EGV). The most important collateral system is the coronary-gastroesophageal-azygos system. Thus, the azygos vein may be used for quantification of variceal blood flow. In this study the azygos vein was examined by endoscopic ultrasound (EUS) including Color-Doppler EUS. Eighteen patients having esophageal varices due to chronic liver disease were included. Eleven of them had no history of variceal bleeding while 7 had at least one attack of variceal bleeding. They were subjected to EUS examination using the Pentax FG-UA echoendoscope with a Hitachi EUB display unit; a system allowing the performance of duplex Doppler and colour flow mapping in vascular structures. Further 13 cases not suffering from chronic liver disease or varices were used as a control group and were subjected to the same examination. In all patients and controls subjects the azygos vein was sought; its diameter and the velocity inside were measured. Both the diameter and the maximal velocity in the azygos vein were found to be higher among portal hypertensive patients than control subjects ( $p < 0.01$ ). These two parameters were also found to be higher among non-treated portal hypertensive patients than those who have been subjected to injection sclerotherapy (4 patients) without reaching statistical significance. Echoendosonography: Echoendoscopy Liver and bile ducts, 1: Cirrhosis: portal hypertension } "The Use of Endoscopic Ultrasonography in the Study of the Azygos Vein in Patients with Esogastric Varices"

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## "P P 28 0674" P 28 0674 **Prognostic Determinants of Endoscopic Treatment of Esophageal Varices**

\*P.K. Kupcsulik, Zs. Les, L. D'f6ng'f6lo", P. Kokas, K. Pinkola

1st Dept of Surgery, Semmelweis Univ. of Medicine, Budapest, Hungary 3210 patients with esophageal varices and portal hypertension due to liver cirrhosis underwent endoscopic sclerotherapy between 1980–95. In a prospective nonrandomised trial standardized protocol for treatment of esophageal varices was applied consecutively. Lethality of elective treatment of 1734 patients bleed previously was 0.07 percent. The small number of lethal cases excludes relevant analysis of risk factors for this group of patients. 16.2 percent of 1476 cases admitted for acute variceal bleeding died. Analysis of independent variables for acute lethal outcome showed patient related and treatment related risk factors of different significance. Child-Pugh status, jaundice, rapid formation or progression of ascitic fluid during bleeding, onset, blood requirement in the first 24 hours, bleeding phase, hemorrhoids are the most characteristic patient related factors influencing early survival. Despite of standardized technique, skill in endoscopy, training of ICU personal play defining role in outcome. Failure of immediate control of rebleeding, optimal timing of repeated sclerotherapy, hesitation for urgent surgery, hypoxia have a significant negative prognostic value. For long term survival regular endoscopic control, lack of rebleeding, stop with alcohol consumption, continuous Propranolol therapy are of significant value. 2 year survival of patient regularly controlled is 92 percent, while that of patients without is 41 percent respectively. At 5 year actuarial survival of patients treated with Propranolol after sclerotherapy (73 percent) is significantly better than that of controls (58 percent) Managed care of patients treated by endoscopic sclerotherapy offers clinically acceptable results. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding Endoscopy, specific: Oesophagus } "Prognostic Determinants of Endoscopic Treatment of Esophageal Varices"

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## "P P 28 0675" P 28 0675 Duplex Doppler U.S. as a Useful Technique for Detecting Propensity for Bleeding from Oesophageal Varices

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**Objectives** To determine if ultrasonography (U.S.) Duplex Doppler color can help us establish the patients with higher risk of gastrointestinal (GI) bleeding among those with cirrhosis and oesophageal varices (O.V.) grade III–IV.

### Material and Methods

**Patients** 46 patients with cirrhosis and O.V. grade III–IV. 34 males and 12 females, with ages ranging from 38 to 73 years (average 59). 23 alcoholic, 18 HVC+, 5 alcoholic plus HVC+. We evaluated mean velocities, maximum velocity, flow pattern and flow direction in the portal, splenic veins and their collaterals. We also measured the Congestion Index (C.I.) in the portal vein and the resistivity index in the hepatic artery. Patients were followed up for a period of 14 months (2–18). U.S. Duplex Doppler color was performed at the beginning of the follow up. U.S. findings were evaluated at the end of the trial and comparison was established between two different groups. Group 1 included patients with no episodes of GI bleeding and group 2 included patients with GI bleeding from O.V.

**Results** 9 patients (19.5%) presented with GI bleeding from O.V. during the follow up. There were no differences between the two groups in terms of mean velocity, maximum velocity and flow pattern found in the portal vein, splenic vein and their collaterals. Patients with previous episodes of bleeding from O.V. had a higher Congestion Index (0.09 vs. 0.05) ( $p < 0.05$ ) and a significant lower mean velocity in the portal vein (10 vs. 14) ( $p < 0.05$ ).

**Conclusions** The measurement of the C.I. and the mean velocity in the portal vein using U.S. Duplex Doppler color is of great value to differentiate which patients among those with O.V. grade III–IV at greater propensity for variceal haemorrhage. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis } "Duplex Doppler U.S. as a Useful Technique for Detecting Propensity for Bleeding from Oesophageal Varices"

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"P P 28 0676" P 28 0676 **MR Angiography to Evaluate Patients with Esophago-Gastric Varices before and after Endoscopic Sclerotherapy**

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**Purpose** To evaluate the usefulness of MR angiography (MRA) in the evaluation of patients with esophageal varices (EV) and/or gastric varices (GV) before and after endoscopic injection sclerotherapy (EIS). In particular, we sought 1) to determine whether MRA was useful in detecting both varicose lesions and portal collaterals, and 2) to evaluate therapeutic response to EIS.

**Methods** MRA was performed in 15 patients with EV and/or GV before and after EIS. For each patient 25–35 axial images were obtained during a single breath-holding using a fast spoiled GRASS pulse sequence. Data were reconstructed by using a two-dimension time-of-flight (TOF) algorithm.

**Results** MRA detected varicose lesions in all 6 patients with GV and in 9 of 10 patients with EV of grade F2 or higher. However, MRA detected EV of grade F1 in only 1 of 5 patients. There were no false-positive diagnoses when compared with standard endoscopic findings. MRA revealed left gastric vein in 5 patients. The sensitivity of MRA for the depiction of left gastric vein was 80% (4 of 5 patients) when compared with findings during the portal phase of superior mesenteric arteriography. In 6 patients with persistent MR evidence of EV after EIS, EV recurred on follow-up endoscopy, although in 1 of 6 patients EIS showed complete eradication of varices endoscopically. EV recurred in 2 of 4 patients with no varices detected with both MRA and endoscopy after EIS; this recurrence correlated with the persistence of left gastric vein. MRA has a better predictor of the prognosis of GV than endoscopy, because EIS causes GV to swell for a few weeks after the procedure.

**Conclusion** MRA is a non-invasive technique that appears to be useful for detection of varices and other portal collaterals in patients undergoing EIS. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, specific: Oesophagus Radiology and ultrasound: Diagnosis } "MR Angiography to Evaluate Patients with Esophago-Gastric Varices before and after Endoscopic Sclerotherapy"

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## "P P 28 0677" P 28 0677 Gastric Varices: Predictors for Bleeding

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Division of Gastroenterology, National Cheng Kung University, Tainan, Taiwan

**Background and Aim** Gastric varix is an important cause of death in patients with liver cirrhosis and portal hypertension. No conclusive factors were identified as predictors for bleeding. In order to discover the factors which are suggestive of impending or possible gastric variceal bleeding, we conducted this retrospective study.

**Patients and Methods** From May 1989 to August 1995, two hundred and forty patients were diagnosed to have gastric varices in our endoscopic unit. Eighty-four patients were excluded due to suboptimal image quality for reviewing or lack of follow-up information. The gastric varices were described as form, location, and red color sign according to the classification of Hashizume

**et al.** Bleeding group was defined as (1) active bleeding or presence of blood clot over varices during endoscopic examination, and (2) lack of other bleeding sources. Non-bleeding group was defined as no bleeding episode occurred one month before and after endoscopic examination. The endoscopic characteristic and demographic data were collected for analysis.

**Results** The study included 156 patients. They were divided into bleeding and non-bleeding groups. Bleeding Non bleeding *P* value Patient number (M:F) 31 (20:11) 125 (93:32) Age (yr) 50.6 – 17.8 50.6 – 17.3 Etiology (cirrhosis:HCC:others) 22:6:3 89:29:7 Location anterior (%) 4 (14%) 19 (17%) NS posterior (%) 6 (22%) 6 (5%) NS greater curvature (%) 13 (46%) 72 (65%) NS lesser curvature (%) 5 (18%) 14 (13%) NS Form: Form 1 (%) 6 (21%) 72 (60%) < 0.001 Form 2 (%) 11 (38%) 35 (29%) Form 3 (%) 12 (41%) 13 (11%) Red color sign (%) 17 (55%) 12 (10%) < 0.001 **Conclusion** The form and the red color sign are significantly predictors for gastric variceal bleeding in our patients. If patients were identified to have these signs, they may need treatment to prevent bleeding. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding } "Gastric Varices: Predictors for Bleeding"

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## "P P 28 0678" P 28 0678 **Assessment of Variceal Hemorrhage in Cirrhotic Patients: A Comparison of Doppler Flowmetry, Endoscopy and Clinical Parameters**

\*C.H. Wang, L.R. Mo, R.C. Lin, J.Y. Kuo, K.K. Chang

Department of Internal Medicine, Tainan Municipal Hospital, Tainan, Taiwan, R.O.C.

**Background** Esophageal varices are part of the system of spontaneous portosystemic collaterals that develop in portal hypertensive states. The risk of esophageal hemorrhage was thought to be closely associated with variceal size and other clinical features. However, no firm data are yet available. The aim of this study was to find more parameters to establish a causal relationship with variceal hemorrhage.

**Methods** We collected 47 cirrhotic patients (29 males, 18 females, mean age: 56.5 – 12.7 yrs) with (n = 17) and without (n = 30) variceal hemorrhage. The assessment parameters were evaluated as followings: (1) age, (2) modified Child's classification (an index of liver dysfunction based on serum albumin and bilirubin levels, prothrombin time, ascites, and encephalopathy), (3) characteristics of varices which were classified endoscopically as suggested by the Japanese Research Society for Portal Hypertension (e.g. color, red color sign, location and form) which were further devised as a simple scoring system, (4) number of varices which were also observed by endoscopy, (5) "congestion index" of portal vein (the ratio between the cross-sectional area and the blood flow velocity which was performed by abdominal Doppler examinations).

**Results** "Congestion index" of portal vein was significantly associated with characteristics of varices ( $r = 0.53$ ,  $p < 0.0001$ ), and numbers of varices ( $r = 0.41$ ,  $p = 0.006$ ). The points of variceal scoring system in hemorrhage group (n = 17) were significantly more than non-hemorrhage group (n = 30) ( $p < 0.0001$ ). Also, numbers of varices in hemorrhage group were significantly more than non-hemorrhage group ( $p = 0.009$ ). Logistic regression analysis revealed that characteristics of varices was the independent predictor of variceal hemorrhage.

**Conclusions** "Congestion index" obtained via Doppler ultrasonography have a clinical role in noninvasive detection of severity and numbers of varices. Endoscopic appearances of varices have a predictive value of variceal hemorrhage. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, specific: Oesophagus Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux } "Assessment of Variceal Hemorrhage in Cirrhotic Patients: A Comparison of Doppler Flowmetry, Endoscopy and Clinical Parameters"

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**"P P 28 0680" P 28 0680 Portal Hemodynamics after Long-Term Endoscopic Sclerotherapy of Esophageal Varices in Advanced Liver Cirrhosis K. Boulanov**

Institute of Clinical and Experimental Surgery, Kiev, Ukraine Endoscopic sclerotherapy (ES) of bleeding esophageal varices proved to be the treatment of choice in patients with advanced liver cirrhosis. Changes of portal hemodynamics caused by ES were studied in 30 cirrhotic patients (Child-Pugh class B – 14, C – 16), who had bled from large (> 5 mm) esophageal varices. All of them were assigned to elective long-term ES, which consisted of combined intra- and paravariceal injections of 3% sodium tetradecylsulfate using free-hand technique. Sessions of ES included 3–5 injections performed every other day and were repeated every 6 month. Complications were of minor importance. Portal venous flow (PVF) was measured using duplex Doppler system before and after sessions. Patients' follow-up ranged from 12 to 36 months. Mean values of PVF showed evidence of significant increase after ES from 437.0 to 580.2 ml/min ( $P < 0.05$ ), but demonstrated a tendency to reduction before the next session. Complete obliteration of esophageal varices was observed after 4 sessions of ES in 18 patients (60%). At the end of the follow-up, PVF in this group was higher compared with that in patients with persistent varices (591.0 versus 476.6 ml/min). Considerable decrease of blood ammonia nitrogen level confirmed effective interruption of gastroesophageal collateral pathways. Thus, long-term ES in patients with advanced liver cirrhosis produces significant stable rise in PVF, providing that complete eradication of esophageal varices is achieved. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy Radiology and ultrasound: Diagnosis } "Portal Hemodynamics after Long-Term Endoscopic Sclerotherapy of Esophageal Varices in Advanced Liver Cirrhosis"

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## "P P 28 0689" P 28 0689 Correlation between Endoscopic Findings and Histology in Portal Hypertensive Gastropathy

\*C. Gheorghe, G. Aposteanu, L. Gheorghe, Al. Oproiu

Center of Gastroenterology, Fundeni, Bucharest, Romania The aims of this prospective longitudinal study were: to evaluate the relation between classic histology on endobioptic specimens and endoscopic patterns of portal hypertensive gastropathy (PHG); to investigate the histology as predictor of PHG evolution, from mild (mPHG) to severe (sPHG) and overt bleeding. Between 1989–1996, 225 pts with hepatic cirrhosis (CH) were evaluated for the study. We used endoscopic inclusion criteria for mPHG/sPHG allocation. We detected 137 PHG pts, of whom 98 pts completed the study (19 pts lost; 20 pts. excluded by means of exclusion criteria). The follow-up program comprised endoscopy-endobiopsies using a standard protocol; the specimens were processed routinely, stained with haematoxylin-eosin and blindly examined; examinations were performed at 6/12 mo. interval (small/large varices) till the end of the study or patient's death. The mean follow-up period was 42 – 24 mo. mPHG was found initially in 86 pts (87.7%) and sPHG in 12 pts (12.2%). During the follow-up, 18 mPHG pts developed sPHG. On admission, there were 41 pts (41.8%) with positive histological criteria for PHG (vascular ectasia) and 57 (58.2%) pts with negative histology. Positive histology correlated with endoscopic pattern of sPHG (cherry red spots) ( $p = 0.009$ ). In the group of mPHG, the positive histology correlated with evolution from mPHG to sPHG: there were 12 positive and 6 negative histology pts in the group of evolving mPHG to sPHG ( $p = 0.005$ ). Overt bleeding occurred in 12/98 and correlated with positive histology: 10 positive vs 2 negative histology pts ( $p = 0.03$ ). Cumulative bleeding probability at 42 mo. was 48% vs 93% in severe/mild PHG (Kaplan-Meier method). The correlation between histology and PHG evolution from mild to severe and overt bleeding may imply the progression of vascular ectasia from the submucosa to mucosa (endobiotically intercepted) in the natural history of PHG. We may conclude that, especially in mPHG, endobiopsies are necessarily in prediction of the natural course of PHG. Endoscopy, specific: Stomach, duodenum Liver and bile ducts, 1: Cirrhosis: portal hypertension }"  
"Correlation between Endoscopic Findings and Histology in Portal Hypertensive Gastropathy"

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"P P 28 0692" P 28 0692 **Endoscopic Doppler Flow Ultrasonography in Portal Hypertension  
— First Results**

\*J. Janssen, W. Johanns, C. Jakobeit, L. Greiner

Medical Clinic A, Municipal Hospital Wuppertal, University of Witten-Herdecke, Germany *Introduction.* This pilot study was performed to explore the facilities of endoscopic ultrasound (EUS) including Doppler flow measurement with regard to patients at risk of bleeding from portal hypertension. *Methods.* 20 patients with known portal hypertension were examined by upper gastrointestinal endoscopy and EUS with a 7.5 MHz curved array transducer (Pentax FG 32 UA/Picker CS 192). 10 patients had no prior bleeding episode (group A), 10 patients had undergone sclerotherapy after variceal hemorrhage (group B) and two patients of the latter group could be examined before and after transjugular intrahepatic portosystemic shunting. Variceal size and mean values of three Doppler flow measurements of representative varices were recorded. *Results.* Subepithelial esophageal varices could be detected in 18 patients by endoscopy and in 13 patients by EUS, whereas gastric varices were found in 6 patients by EUS versus two patients in endoscopy. Paraesophageal varices (n = 14) and paragastric varices (n = 6) were seen by EUS only. Distribution pattern of varices was unsystematic between the two groups. Mean flow values and flow range hardly differed between the two groups in paraesophageal, gastric and paragastric varices. Mean velocity tended to be higher in subepithelial varices in group B but could not be measured reliably in 5 of 13 patients because of small vessel diameter. In two patients mean velocity fell by about 10 cm/s after transjugular intrahepatic portosystemic shunting. *Conclusion.* In comparison with endoscopy, EUS is superior in detecting intramural gastric varices but inferior in diagnosing subepithelial esophageal varices. Paraesophageal and paragastric varices can be demonstrated by EUS only. Doppler flow measurement in subepithelial varices cannot reliably be done in vessels of less than 1.5 mm in size. The similar velocity range in both groups reveals that flow does neither necessarily reflect intravascular pressure nor indicate patients at risk of bleeding. Nevertheless the impressive fall in flow after transjugular intrahepatic portosystemic shunting in two patients is the result of lowering portal hypertension. Further systematic research is mandatory. Liver and bile ducts, 1: Cirrhosis: portal hypertension Echoendosonography: Echoendoscopy } "Endoscopic Doppler Flow Ultrasonography in Portal Hypertension / First Results"

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"P P 28 0694" P 28 0694 **Modification of Mucosal Blood Flow in Portal Hypertensive Gastropathy. A Laser-Doppler Flowmetry Study**

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The aim of our study was to estimate quantitative variations of gastric mucosal blood flow in patients affected by portal hypertensive gastropathy (PHG), using endoscopic laser-doppler flowmetry (ELDF). We performed ELDF in 11 patients (8 M: 56 – 12 yrs; 3 F: 60 – 9 yrs; mean age – SD) with PHG related to post-hepatitis cirrhosis and in 10 healthy controls (HC) (6 F: 48 – 4 yrs; 4 M: 50 – 9 yrs). All patients had PHG localized in the corpus and antrum (6 mild; 5 severe); 5 had esophageal varices (F1–F2) never undergone sclerotherapy. There was no history of  $\beta$ -blockers treatment. The laser-doppler flowmeter (Laserflow BPM-403, Vasamedics, USA) was connected to a perendoscopic laser probe and placed perpendicularly toward the mucosal surface. Two measurements were taken from the greater and lesser curvature of the corpus and antrum and expressed in flux units (ml/min in 100 cc of tissue). Finally, skin blood flow was measured at the forearm for 5 minutes. The mucosal/skin flow ratio (MUSK index) was calculated. Results were expressed as mean values – SD and analyzed by student's *t* test. The results showed a significant increase of the mucosal blood flow (MBF) and MUSK index (MI) in patients with PHG compared to HC (MBF: 30.53 – 4.18 vs 16.41 – 1.23,  $p < 0.02$ ; MI: 9.3 – 0.5 vs 5.49 – 0.86,  $p < 0.05$ ) and in severe PHG compared to the mild form (MBF: 35.84 – 3.3 vs 26.51 – 5.4,  $p < 0.05$ ; MI: 11.08 – 1.6 vs 7.8 – 1.4,  $p < 0.05$ ). We conclude that both MBF and MI are significantly increased in PHG. The increase of these haemodynamic parameters seems to be directly related to the severity of PHG. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Stomach, duodenum Liver and bile ducts, 1: Cirrhosis: portal hypertension }

"Modification of Mucosal Blood Flow in Portal Hypertensive Gastropathy. A Laser-Doppler Flowmetry Study"

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"P P 28 0695" P 28 0695 **Evaluation of Changes in Portal Hypertensive Gastropathy (PHG) Following Endoscopic Treatment of Varices with Endoscopic Sclerotherapy (ES) or Band Ligation (EL)**

\*M. Primignani, M. Materia, M. Bianchi, P. Preatoni, R. de Franchis

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IRCCS Ospedale Policlinico, Milan, Italy Conflicting data exist on the evolution of PHG-related lesions in patients undergoing ES, and little is known about the relationship between PHG and EL.

**Aim** to evaluate the initial prevalence and severity of PHG in patients undergoing ES or EL, the evolution of gastric mucosal lesions during the course of these therapies, together with PHG-related bleeding events during follow-up.

**Methods** 55 patients with portal hypertension, mostly cirrhotics with previous variceal bleeding, underwent ES or EL. PHG was assessed by recording the 4 elementary signs of the NIEC classification (mosaic pattern, red points, cherry-red spots, black-brown spots). PHG was classified as mild, (mosaic pattern alone), or severe, (red signs or black-brown spots).

**Results** 27 patients received ES, 28 EL. Baseline clinical and demographic data were similar in the 2 groups. Initial prevalence of PHG was 55% (mild 44%, severe 11%) in ES, and 68% (mild 39%, severe 29%) in EL patients ( $P = \text{N.S.}$ ). Varices were eradicated in 18 ES patients (67%) with a mean of 6.1 – 3.1 sessions, and in 18 (64.2%) EL patients, with a mean of 2.9 – 1.1 sessions. Worsening of PHG occurred in 9/27 (33.3%) ES and 7/28 (25.0%) EL patients ( $P = \text{N.S.}$ ). Regression from severe to mild PHG was found in 2 (7%) ES and 3 (11%) EL patients ( $P = \text{N.S.}$ ). The rates of progression and of regression of PHG lesions were uniform throughout follow-up in both groups. Rebleeding occurred in 10/27 (37%) ES, and in 11/28 (39%) EL patients ( $P = \text{N.S.}$ ). PHG was the cause of bleeding in 2 (7%) EL patients only.

**Conclusions** In patients undergoing ES or EL, worsening of PHG-related mucosal lesions occurs in 25–35% of cases, while improvement occurs in 5–10% of cases. The effect of the two treatments on PHG is virtually identical, and uniform throughout follow-up. Bleeding related to PHG lesions is relatively uncommon. Liver and bile ducts, 1: Cirrhosis: portal hypertension }"  
"Evaluation of Changes in Portal Hypertensive Gastropathy (PHG) Following Endoscopic Treatment of Varices with Endoscopic Sclerotherapy (ES) or Band Ligation (EL)"

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"P P 29 0704" P 29 0704 **Role of ERCP before and after Laparoscopic Cholecystectomy**

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King Fahad National Guard Hospital, Riyadh, Saudi Arabia

**Purpose** To evaluate the usefulness of ERCP and endoscopic sphincterotomy (EST) in patients undergoing laparoscopic cholecystectomy (LC) with suspicion of choledocholithiasis and in the management of complications resulting from LC.

**Methods** This is a retrospective analysis of our experience at King Fahad National Guard Hospital, a tertiary care and referral center for hepatobiliary disease. Between January 1992 and December 1995 a total of 717 ERCP and 1221 LC were performed. 257 ERCP were performed on 225 patients who underwent LC, 230 were done before LC and 27 after LC. Age range was 10–85 years (mean 43.5 years). There were 77 (34%) males with mean age of 51.7 years and 148 (66%) females with mean age of 39 years.

**Results** Over all success rate for ERCP was 92% (96% for diagnostic and 88% for therapeutic outcome). Choledocholithiasis was found in 79 patients (40%). Prediction of choledocholithiasis based on abnormal liver chemistries was accurate in 28%, in 47% of cases when based on ultrasound criteria and it reached 70% when based on both. From 40 cases of acute biliary pancreatitis, choledocholithiasis was found in 8 (20%). Indications for ERCP post LC included 8 retained stones, 8 cases of bile leaks, (7 of which treated endoscopically) and 4 major duct injuries which required surgical repair. Complications encountered were two cases of significant bleeding post EST and 3 cases of mild pancreatitis.

**Conclusion** ERCP and EST are effective and safe in the diagnosis and management of choledocholithiasis and facilitate the role of LC. The procedures are also valuable in the diagnosis and management of most complications resulting from LC. Clinical practice: Management strategy Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Role of ERCP before and after Laparoscopic Cholecystectomy"

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"P P 29 0708" P 29 0708 **Endoscopic Papillary Dilatation and Nasobiliary Drainage for Bile Leak after Laparoscopic Cholecystectomy**

\*M. Ito<sup>1</sup>, T. Ooyama, S. Sezai, T. Abe, Y. Sakurai, F. Ikegami, K. Kamisaka, K. Ito<sup>2</sup>, S. Agawa, Y. Ishihara

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<sup>2</sup> Dept. of Surgery, The Kanto Teishin Hospital, Tokyo 141, Japan  
Laparoscopic cholecystectomy carries an increased risk for bile duct injury than open cholecystectomy does. Most frequent complications are minor bile leaks such as cystic duct leak which have been usually treated with papillotomy and/or stent insertion for several weeks. Recently papillary balloon dilatation has received attention and replaced papillotomy in some cases. We investigated the usefulness of papillary balloon dilatation and nasobiliary drainage in patients of bile leak after laparoscopic cholecystectomy. *Patients and Methods.* During four-year period, 450 patients underwent laparoscopic cholecystectomy. Bile duct injuries recognized after the operation were reviewed. When bile leak was noted at postoperative ERCP, we preferred to perform papillary balloon dilatation and nasobiliary drainage for a week. *Results.* Five patients of bile leaks from cystic duct stump and one patient of right hepatic duct leak were diagnosed by ERCP and successfully treated with papillary balloon dilatation and nasobiliary drain. The drainage tube was withdrawn about a week later when no leak was shown by nasobiliary tube cholangiography. The remaining one patient was noted to have transection of the common bile duct and treated with hepaticojejunostomy. *Conclusions.* Endoscopic papillary dilatation and nasobiliary drainage is another safe and useful treatment for bile leakage after laparoscopic cholecystectomy. Endoscopy, specific: Biliary } "Endoscopic Papillary Dilatation and Nasobiliary Drainage for Bile Leak after Laparoscopic Cholecystectomy"

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"P P 30 0723" P 30 0723 **Evaluation of 12 Cases of Anomalous Arrangement of Pancreaticobiliary Ductal System (AAPBDS)**

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**Aim** This study was carried out in order to demonstrate that Anomalous Arrangement of Pancreaticobiliary Ductal System (AAPBDS) was closely associated with carcinoma in the biliary tract.

**Methods and Results** Between January 1988 and April 1994, Endoscopic-Retrograde-Cholangio-Pancreatography (ERCP) was performed in our hospital for 935 cases, of which 12 cases were diagnosed as AAPBDS. The ages of these cases ranged from 40 to 70 years; 4 cases of age in the 40s, 4 in the 50s, 3 in the 60s and one in the 70s. Ultrasonography (US), Endoscopic Ultrasonography (EUS), Computed Tomography (CT) and Angiography were performed for these 12 patients, 4 of whom had a carcinoma in the biliary tract. Patients consisted of 3 females aged 44–68 years and one male 40-year-old: an average age of 50 years. On the other hand, operation could be carried out in 9 of 12 patients diagnosed as AAPBDS by ERCP and EUS. The value of amylase in the bile of the 9 patients was extremely elevated. From these findings, the presence of AAPBDS in these patients could be confirmed.

**Conclusions** It should be noted that the average age, in the case having biliary tract carcinoma with AAPBDS, was 20 years younger than those who had the carcinoma without AAPBDS. Concerning the fact that 4 cases (33%) with complicated carcinoma in the biliary tract, minute examination of AAPBDS by ERCP and EUS should be required before surgery. Liver and bile ducts, 2: Biliary cysts, atresia Endoscopy, specific: Biliary Radiology and ultrasound: Diagnosis }

} "Evaluation of 12 Cases of Anomalous Arrangement of Pancreaticobiliary Ductal System (AAPBDS)"

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"P P 32 0746" P 32 0746 **Association of Melanosis Coli and Colorectal Neoplasms?** G. Nusko, B. Schneider, Ch. Wittekind, E.G. Hahn

Depts. of Medicine I & Pathology, University of Erlangen and Inst. of Biometrics, Medical School of Hannover, Germany Melanosis coli has been considered for a long time as a harmless pigmentation of the colorectum associated with the use of anthranoid laxatives. Recent experimental and clinical studies (Gut 1993; 34: 1099–1101) showed the evidence of a possible association of melanosis coli and colorectal neoplasms.

**Methods** A total of 2229 consecutive patients underwent total colonoscopy at the Dept. of Medicine I of the University of Erlangen. The findings of the initial colonoscopic examination were analysed. The median of age of patients was 55 years. 1213 (54%) patients were male and 1016 (46%) female. The association of melanosis coli, laxative use and colorectal neoplasms was analysed retrospectively and statistically assessed using the Mantel-Haenszel test for linear association.

**Results** Melanosis coli was found in 102 (4.6%) patients. Hyperplastic polyps were found in 198 (8.9%), adenomas in 441 (19.8%) and carcinomas in 60 (2.7%) patients. Colorectal polyps were significantly associated with melanosis coli ( $p = 0.0002$ ). The relative risk of melanosis coli for tubular adenomas was 1.8 (95% CI: 1.3–2.6), for tubulovillous adenomas 2.03 (95% CI: 1.1–3.8). An association of melanosis coli and villous adenomas was not found, and the association with carcinoma was not significant (RR 1.1; 95% CI: 0.4–3.4). Melanosis coli was significantly associated with anthranoid laxative use ( $p = 0.00004$ ). The relative risk of laxative use for tubular adenomas was 1.6 (95% CI: 1.3–2.1). Laxative use and tubulovillous or villous adenomas or carcinomas were not significantly associated. Colorectal adenomas found in patients with melanosis coli were predominantly located in the proximal colon ( $p = 0.0002$ ) and were significantly smaller ( $p = 0.00001$ ) than in patients without melanosis coli. No significant differences were found in the grade of dysplasia between patients showing melanosis coli and those without. Colorectal carcinoma was not associated with melanosis coli or laxative use.

**Conclusions** Melanosis coli and anthranoid laxative use can not be considered as a significant risk factor in the development of colorectal carcinomas. Colorectal adenomas associated with melanosis coli are small and proximal located polyps. Polyps do not contain the melanin-like pigment. The association of colorectal adenomas and melanosis coli can be explained by the easiness of detecting even smaller polyps as a white point within a dark coloured colonic mucosa. Oncology, specific: Colon, rectum Oncology, general: Screening, prevention }  
"Association of Melanosis Coli and Colorectal Neoplasms?"

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**Aim** To compare the results of endoscopic anal dilatation (EAD) with those of lateral internal sphincterotomy (LIS) for the treatment of fissure-in-ano.

**Patients and Methods** 62 patients, 35 F (mean age 43 yrs, range 20–72) and 27 M (mean age 42 yrs, range 16–82) were referred to our Department for treatment of fissure-in-ano. Anal dilatation was performed with a two-valved anoscope (RichardWolf 884900) under local anesthesia in an ambulatory setting. A complete dilatation is achieved when anoscope's valves are parallel, reaching a distance of 4.5 cm., and is maintained for 4 minutes. Patients follow-up was at 30 days and at 12–24 months. There was therapeutic response when the symptoms completely disappeared, another treatment procedures were not necessary or fissure epithelization could be demonstrated at anoscopy.

**Results** At 30 days 55 patients (95.2%) were free of symptoms and the treatment was considered successful. 4 patients did not come to the visit and other three shew a persistent fissure at anoscopy. All of them were excluded from the study. After a mean interval of 19 months (range 12–24), we contacted one more time with our patients. 47 of them replied: 46 were asymptomatic (97.8%). The other one recurred and underwent surgical treatment. At last, 4 were considered failures, in three of them EAD was not effective (4.8%), and the other one had a late recurrence (2.2%). No complications (incontinence, bleeding or discharge) were described.

**Conclusions** We compared our results with those of LIS reported and we verified that EAD is equivalent to LIS for anal fissure treatment and, furthermore, it is associated with fewer complications. So we think: 1) EAD is the choice procedure for patients with anal fissure, and so more in elder people in which LIS carries a higher complication rate and 2) Indications for LIS should be reserved for those patients with persistent or recurred fissure, and patients in which a proper dilatation can not be accomplished because of a fibrous anal stenosis. Intestinal disorders: Anorectal disorders Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Colon, rectum } "Endoscopic Treatment for Anal Fissure"

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"P P 35 0791" P 35 0791 **High Frequency Endosonography of the Female Perineum**

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St Mark's Hospital, London, UK

**Purpose of the study** Recent technical improvements in anal endosonography, notably a 10 MHz transducer, have increased resolution requiring re-assessment of the normal anatomy.

**Patients and methods** 50 consecutive nulliparous females of median age 31.5 (range 19–65 yrs) were investigated. Anal endosonography was performed using a B&K Medical 3535 ultrasound scanner with 1850 endoprobe and 10 MHz transducer (focal length 1.5–4 cm).

**Results** A significant correlation with age was found only with the subepithelial thickness high in the canal ( $r^2$  0.113,  $p$  0.0179), and internal sphincter in the high ( $r^2$  0.3024,  $p$  < 0.0001) and mid canal levels ( $r^2$  0.2543,  $p$  0.0002). The longitudinal muscle (95% CI 2.2–2.5 mms) could be distinguished as a distinct layer in all the females, and formed part of the anterior muscle ring in 42/50 (84%). The superficial transverse perineal muscles were demonstrated in 39 (78%). Aberrant muscle slips from the external anal sphincter, simulating defects, in 4/50 (8%). The 95% CI thickness of the anterior muscle ring was 4.4–5.2 mms.

**Conclusion** Improved sonographic resolution has allowed for the first time all the layers of the anal canal to be visualised in the female. Normal parameters have been established for a baseline for comparison to patients with damaged sphincters. Echoendosonography: Echoendoscopy Radiology and ultrasound: Diagnosis Intestinal disorders: Anorectal disorders } "High Frequency Endosonography of the Female Perineum"

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## "P P 35 0792" P 35 0792 **Vaginal Endosonography in the Diagnosis of Anorectal Disease**

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Depts. of Surgery and Gastroenterology, University Hospital "Vrije Universiteit", Amsterdam, the Netherlands

Anal endosonography is an established procedure in the evaluation of anorectal disease. However, vaginal endosonography (VE) is able to image the anal sphincters without distortion by the probe and can serve as an alternative if anal endosonography (AE) is not possible. In this study we described the pelvic floor anatomy with VE and we evaluated the additive value of VE in diagnosing anorectal disease. Between October 1994 and August 1995 AE as well as VE was performed in 81 women (26 fecal incontinence, 21 perianal abscess/fistula, 5 constipation, 6 IBD, 2 proctalgia, 21 other). In 23 cases, both with VE and AE the thickness was assessed of the internal (IST) and external anal sphincter (EST), the puborectal muscle (PRT) and the submucosa (SMT). Diagnostic improvement after vaginal endosonography was defined as obtaining more information due to clearer images with VE or due to limiting factors regarding anal endosonography (for example pain or anal stenosis). VE visualised the anal sphincters clearly in 67 of 81 cases. The dorsolateral part of the external anal sphincter was most difficult to image. IST (2.9 vs. 1.7 mm,  $p < 0.001$ ), PRT (8.7 vs. 7.6 mm,  $p = 0.001$ ) and SMT (5.8 vs. 2.4 mm,  $p < 0.001$ ) were significantly increased compared to AE, while EST (5.7 vs. 7.5,  $p < 0.001$ ) was significantly decreased. Anal and vaginal sphincter measurements correlated significantly. Differences existed by measuring the anal sphincters in an undistorted fashion and under a different angle with VE. Diagnostic improvement was seen in 18 (22%) of 81 cases. This was achieved especially in disorders of the rectovaginal septum, such as anterior sphincter defects and anovaginal sepsis.

**In conclusion** Vaginal endosonography is capable of imaging the anal sphincters in an undistorted fashion and has the potential of adding to the diagnosis of anorectal disease.

Echoendosonography: Therapy Motility, specific: Colon, anorectum Radiology and ultrasound: Diagnosis } "Vaginal Endosonography in the Diagnosis of Anorectal Disease"

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"P P 38 0869" P 38 0869 **Mucosal Tissue Activated Oxygen-Producing Capacity in Endoscopic Redness of Gastric Mucosa by Chemiluminescence Assay** Kouichi Furukawa, Terasu Honma, Hirotaka Motoyama, Hiroyuki Enomoto, Yoshihisa Tsukada, Toru Takahashi, Hitoshi Asakura

3rd Department of Internal Medicine, School of Medicine, Niigata Univ.

**Objective** Redness of the gastric mucosa noted by endoscopy is thought to reflect circulatory dynamics and inflammation at the affected areas. It is felt worthwhile therefore to study the degree of severity of mucosal inflammation in redness with or without erosion, superficial reddening and congestive gastropathy.

**Methods** Biopsy specimens taken from gastric mucosal lesions of 13, 12 and 13 patients, with endoscopically proven erosion, superficial reddening and congestive gastropathy (redness group) respectively and from the normal appearing gastric mucosa of 21 subjects for a non-redness (control) group (gastric body in 15 and pyloric region in 6) were used in the study. Mucosal tissue activated oxygen-producing capacity (ChL) was measured by luminol-dependent chemiluminescence method. Furthermore, histological changes of biopsy specimens categorized according to the Sydney system of gastritis classification were compared in ChL and polymorphonuclear leukocyte infiltration assessed by Erik et al.'s index among these lesions.

**Results** As to mucosal lesions, ChL was found to be significantly increased in erosive mucosa, but not significantly different in mucosal areas exhibiting superficial reddening or congestive gastropathy from the control. Assessed by the Sydney system of gastritis classification, ChL had a correlation with the degree of severity of inflammation but no significant association with any of the degree of inflammatory cell infiltration, atrophy, intestinal metaplasia and *Helicobacter pylori* (HP) infection. ChL, when assessed by Erik et al.'s index, was demonstrated to have a positive trend with increasing severity of mucosal infiltration by inflammatory cells, predominantly neutrophils.

**Conclusion** This study showed that superficial reddening of the gastric mucosa and congestive gastropathy unlike redness with or without erosion were not accompanied by inflammatory changes, suggesting participation of other factors than inflammation in the pathogenesis of the mucosal lesions. It seems that the presence of HP in the affected gastric mucosa does not always accompany by inflammation. Measurement of ChL by luminol-dependent chemiluminescence method was considered to be useful for evaluating the degree of severity of mucosal inflammatory cell infiltration, mainly by neutrophils, because it can be expressed numerically. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: Inflammation Endoscopy, specific: Stomach, duodenum } "Mucosal Tissue Activated Oxygen-Producing Capacity in Endoscopic Redness of Gastric Mucosa by Chemiluminescence Assay"

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"P P 39 0888" P 39 0888 **Long-Term Outcome of Enteral Nutrition by Percutaneous Endoscopic Gastrostomy (PEG)** A. Jordan, A. Emde, A. Markus, W.F. Caspary, H. Seifert, J. Stein

II Department of Internal Medicine, Div. of Gastroenterology, J.W. Goethe-University, 60590 Frankfurt/Main, Germany Since percutaneous endoscopic gastrostomy (PEG) was first described in 1980 it has gained wide acceptance and is now the preferred method for providing long-term enteral nutrition. However, most published studies describe only short-term outcome follow-up in any detail. The objective of this retrospective study was to evaluate the complications and course of long-term enteral nutrition by percutaneous endoscopic gastrostomy.

**Subjects and methods** A retrospective analysis was performed on 80 patients (21 F, 59 M; mean age 57.9 – 11.5 years, range 21–86) treated by PEG between 1992 and 1995. Complications has been devised into minor (requiring local care) and major (requiring laparotomy or life threatening).

**Results** PEG insertion was technically successful in all cases, no procedure related mortality was observed. Mean duration of PEG was 132 – 121 days (12–731). Severe complications occurred in 5% (1 aspiration induced pneumonia, 2 PEG tube-dislocation, 1 ileus). Most common minor complications were peristomal wound infection (31.3%) and brief periods of abdominal pain (37.5%). Typical side effects specific to nutrition were gastrointestinal symptoms (45%) like diarrhoea (12%), vomiting (13%), obstipation (11%).

**Conclusion** Long-term enteral feeding by PEG was safe, cost-effective, and had a low complication rate. Our patients were managed by a specialist nutrition team, which may reduce the complication rate and hospital visits for patients being fed at home. } "Long-Term Outcome of Enteral Nutrition by Percutaneous Endoscopic Gastrostomy (PEG)"

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## "P P 39 0889" P 39 0889 Gastric Volvulus Managed by Endoscopic Decompression and Nonsurgical Gastropexia Via a Percutaneous Endoscopic Gastrostomy (PEG)

\*A. Schulte-Bockholt, U. Rosenstock, S. Clemens, A. Hofmann, B. Pleger, M. Keymling

II. Med. Klinik, Klinikum Meiningen, Germany Gastric volvulus, clinically characterized by Borchardts trias of pain, violent retching and inability to pass a nasogastric tube, occurs when the stomach twists on itself. We here describe a case of recurrent gastric Volvulus managed by endoscopic decompression and nonsurgical endoscopic gastropexia.

**Material and Methods** A 53 y male who was curatively treated with a resection of the cardia and fundus for an adenocarcinoma 6 years earlier, was hospitalized several times for pain and postprandial vomiting; a work up showed esophagitis grade III, but no obstruction. When admitted to our hospital with hematemesis, we again found esophagitis but this time were unable to visualize the pylorus and an organoaxial volvulus along the incisura was suspected. This condition resolved and reoccurred spontaneously twice over the next 5 days, and the patient was diagnosed endoscopically and radiologically of having a recurrent organoaxial gastric volvulus. When the volvulus reoccurred and a third time, we did a endoscopic decompression by advancing the scope past the point of torsion, turning and locking the tip and rotating the endoscope by 180 degrees, as described elsewhere. After decompression, as an alternative to a surgical gastropexia, the antrum of the stomach was attached to the abdominal wall by a 15 Fr. standard gastric pull through percutaneous endoscopic gastrostomy (PEG standard gastral; Fresenius, Germany). Our initial plan to attach the stomach to the abdominal wall by two PEG's instead of one, as described in the only other available case report, was not feasible. Because of resection of the cardia and fundus in our patient resulting in a small residual stomach, a second PEG could not be inserted.

**Results** After PEG placement the patients was without symptoms and the esophagitis resolved. The PEG was removed 4 month later, and after removal of the PEG the gastric volvulus did not reoccur within the last 6 month.

**Discussion** We describe here, to our knowledge, the second case of a gastric volvulus managed by endoscopic gastropexia via a percutaneous endoscopic gastrostomy. The assumed mechanism by which the stomach is fixed and stays attached to the abdominal wall are adhesions as seen with long standing PEG placement. While acute gastric volvulus with blood supply compromisation is often a dramatic illness, that requires fast surgical intervention, endoscopic gastropexia by PEG is a reasonable minimal invasive alternative treatment for recurrent and chronic volvulus. Endoscopy, specific: Stomach, duodenum Endoscopy, general: Instrumentation, therapy Clinical practice: Management strategy } "Gastric Volvulus Managed by Endoscopic Decompression and Nonsurgical Gastropexia Via a Percutaneous Endoscopic Gastrostomy (PEG)"

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## "P P 39 0890" P 39 0890 **Transnasal Percutaneous Endoscopic Gastrostomy in Head and Neck Cancer Patients**

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Uzsoki Teaching Hospital, Budapest, Hungary

<sup>1</sup> 1st Dept. of Surgery, Semmelweis Med. Univ., Budapest, Hungary

**The purpose of the study** Percutaneous endoscopic gastrostomy (PEG) feeding tubes are widely used for enteral feeding of undernourished cancer patients. PEG is frequently unsuccessful in head and neck malignancies. The purpose of the present study was to develop new endoscopic techniques for enhancing the success rate.

**The methods used** 32 consecutive patients with head and neck malignancies underwent 33 PEG placements between 01. 07. 95.–01. 05. 96. The "pull-through" method was used. There were three patients with partial trismus who were unable to open their mouths in a satisfactory degree for the introduction of the gastroscope. The gastroscope (Fujinon EG7–FP3) was inserted through the nostril and the esophagus was reached via the naso- and oropharynx. After carrying out the upper gastro-intestinal endoscopy a PEG was placed on the anterior wall of the stomach.

**Summary of the results** Transnasal introduction of the gastroscope and the placement of a PEG was successful in all patients. The procedure was well tolerated and was accomplished without any complications.

**Conclusions** Transnasal upper gastrointestinal tract endoscopy can be used for diagnostic and therapeutic reasons. This modification of the standard technique could be used in those cases when the oral route is inaccessible. The method is presented on video film. Clinical practice: Management strategy Nutrition: Techniques of nutrition Endoscopy, general: Instrumentation, therapy } "Transnasal Percutaneous Endoscopic Gastrostomy in Head and Neck Cancer Patients"

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"P P 39 0891" P 39 0891 **A Prospective Study of Enteral Long-Term Nutrition Via Percutaneous Endoscopic Gastrostomy (PEG) in 220 Patients** Chr. L'f6ser, S. Wolters, U.R. F'f6lsch

I. Medical Department, Christian-Albrechts-University of Kiel, Germany Aim of the present prospective study was to evaluate over a four-year observation period the long-term results, complication rates, subjective and general behaviour and nutritional problems in 220 patients with PEG.

**Methods** Between 1991 and 1995 a PEG was placed in 220 patients (130 ♂, 74 ♀; age 61.4 – 15.5 years) and the patients were prospectively controlled and followed up for an average of 134 – 182 (1–1498) days. 41% had malignant, 59% benign diseases. All patients received a single antibiotic prophylaxis (2 g cephalosporine i.v.). Indication, early and late complications, mortality, nutritional status, course of body weight and disease, individual behaviour and management as well as nutritional long-term problems were prospectively studied.

**Results** Indication: internal medicine 30%, ENT 28%, neurological diseases 42%. Duration of PEG procedure: 13.3 – 4.2 min. Mortality: 0%. Early complications (< 30 days): perforation = 0.5%, peritonitis 0.5%, aspiration 0.5%, mild local wound infection 10.3%. Late complications (> 30 days): local wound infections 1.5%, tube fracture 0.5%. In 6 patients the PEG had to be removed due to severe complications. In 39 patients with benign diseases the PEG could be removed without complication after sufficient oral food intake was reached. Concomitant patients' care: special hospitals 17%, nursing home 20%, at home by relatives 29%, by themselves 6%, by home-care services 21%. Drop of body weight in 3 months before PEG ( $\bar{x}$  = { - } 11.4 – 1.5 kg); gain of body weight during 1 year after PEG placement (all: +3.5 – 1.7 kg; malignant: +2.3 – 2.2 kg). Subjective acceptance: well 83%; sufficient 15%; bad 2%. Nutritional status was obviously improved.

**Conclusions** In this prospective study long-term enteral feeding via PEG proved to be a safe, effective, easy to practise and highly acceptable method with few complications and excellent long-term results. Early PEG placement significantly improves nutritional status and increases quality of life in all patients studied. Nutrition: Techniques of nutrition Endoscopy, general: Instrumentation, therapy Clinical practice: Management strategy } "A Prospective Study of Enteral Long-Term Nutrition Via Percutaneous Endoscopic Gastrostomy (PEG) in 220 Patients"

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## "P P 39 0892" P 39 0892 Percutaneous Endoscopic Gastrostomy — Experiences of 775 Procedures

\*M. Gawenda, B. Wolfgarten, H. Sch\`e4fer, M. Walter

Department of Surgery, Medical Center, University of Cologne, D-50924 Cologne, Germany Percutaneous endoscopic gastrostomy (PEG) was introduced in 1980 as an alternative to traditional operative methods for creation of a feeding gastrostomy. The simple procedure involves a shorter hospitalization, lower risk and reduced costs. The aim of this retrospective study was to determine the indications, success rate, the procedure-related mortality, and major and minor complication rates.

**Results** In our experience from 1st January 1987 to 15 March 1996 775 patients underwent placement of a percutaneous endoscopic gastrostomy (PEG) tube using a single endoscopic technique and a polyurethane gastrostomy tube; material costs amount below 100,— DM. Most patients (95%) received intravenous sedatives with topical anesthesia. 575 males and 200 females with mean age of 57.8 years (SEM – 0.5, range: 2–96) were supplied with PEG tubes for the purpose of enteral feeding. In 67.3% carcinoma disease indicated PEG tube. The most common indications for placement of the gastrostomy tube were otorhino-laryngeal disorders (52%) and carcinoma of the maxillo-facial region (15.9%). Neurologically based dysphagia indicated PEG-tube placement in 12.6%. The overall complication rate was 10.0%, with a major complication rate of 1.2%. Three method correlated death occurred.

**Conclusion** We conclude that PEG is the procedure of choice to achieve long-term enteral nutrition. Furthermore PEG is an efficient, rapid method with minimal morbidity, low costs and insignificant mortality that made placement possible without general anesthesia. Nutrition: Techniques of nutrition Endoscopy, specific: Stomach, duodenum Endoscopy, general: Instrumentation, therapy } "Percutaneous Endoscopic Gastrostomy / Experiences of 775 Procedures"

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## "P P 39 0893" P 39 0893 **Single Shot Antibiotics in Percutaneous Endoscopic Gastrostomy (PEG) — A Prospective Randomized Study**

\*M. Gawenda, H. Sch'4fer, B. Wolfgarten, M. Walter

Department of Surgery, Medical Center, University of Cologne, D-50924 Cologne, Germany Percutaneous endoscopic gastrostomy (PEG) was introduced in 1980 as an alternative to traditional operative methods for creation of a feeding gastrostomy. The simple procedure involves a shorter hospitalization, lower risk and reduced costs. To literature tube infection is the most common complication with a frequency of 10 to 30%. In a prospective randomized study we want to find out if single shot antibiotic at the time of tube insertion can reduce the rate of early local infections.

**Method** All patients that receive percutaneous endoscopic gastrostomy were randomized to two groups. Group I receive Cefazolin (2 gr.) as single shot antibiotic before starting the endoscopic procedure. The other patients (Group II) received PEG tube without antibiotics.

**Results** 100 patients underwent placement of a percutaneous endoscopic gastrostomy (PEG) tube using a single endoscopic technique and a polyurethane gastrostomy tube; material costs amount below 100,— DM. Most patients (97%) received intravenous sedatives with topical anesthesia. The procedure was technically successful in all patients. The mean age was 57.8 years (SEM – 0.5, range: 2–96). In both groups 5 patients developed local skin infections at the tube insertion. Therefore the overall complication rate was 10.0%, without major complications. No method correlated death occurred.

**Conclusion** We conclude that PEG is the procedure of choice to achieve long-term enteral nutrition. Furthermore PEG is an efficient, rapid method with minimal morbidity, low costs and insignificant mortality that made placement possible without general anesthesia. Single shot antibiotic cannot reduced the early skin infection rate. Endoscopy, general: Complications Endoscopy, specific: Stomach, duodenum Nutrition: Techniques of nutrition } "Single Shot Antibiotics in Percutaneous Endoscopic Gastrostomy (PEG) / A Prospective Randomized Study"

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## "P P 39 0894" P 39 0894 Percutaneous Endoscopic Gastrostomy Feeding: Scintigraphic Detection of Gastroesophageal Reflux

\*K.K. Balan, J. Bennett<sup>1</sup>, P. Maltby, S. Woods, S. Vinjamuri, J.R. Playfer<sup>2</sup>, M. Critchley

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<sup>1</sup> Department of Gastroenterology, Royal Liverpool & Broadgreen University Hospital Trust, Liverpool, L7 8XP, England

<sup>2</sup> Department of Geriatrics, Royal Liverpool & Broadgreen University Hospital Trust, Liverpool, L7 8XP, England Percutaneous endoscopic gastrostomy (PEG) is the method of choice for feeding patients who are unable to eat adequately and yet have a functional GI tract. PEG eliminates the need for surgery or nasogastric tubes, is easily performed with few demands on health service resources. Aspiration pneumonia may complicate PEG insertion but there are few studies on gastroesophageal reflux (GOR) in PEG patients.

**Methods** 19 patients (12 M, 7 F, age 43–83 years, median 72) with PEG underwent radionuclide GOR studies. 12 patients had neurological and 7 had mechanical dysphagia. They received 100 ml of orange juice containing 25 MBq of Tc<sup>99m</sup>-tin colloid followed by 250 ml of normal saline, through the PEG tube. Patients lay supine under the gamma camera linked to a digital computer system. 4 minute and 4 hour images over stomach, oesophagus and lungs were examined for GOR and lung aspiration.

**Results** 8 patients, 6 of whom with neurological dysphagia and 2 of whom with mechanical dysphagia, had severe GOR. 2 other patients with neurological dysphagia had mild GOR. One patient with severe GOR also had lung aspiration at 4 hours. 9 patients had normal studies.

**Conclusions** 1) Radionuclide imaging can assess GOR in PEG patients 2) GOR appears to be a significant problem in patients with PEG and 3) PEG patients with neurological dysphagia appear to be at greater risk for GOR than those with mechanical dysphagia. Further studies are in progress. Nutrition: Nutrients and gut function } "Percutaneous Endoscopic Gastrostomy Feeding: Scintigraphic Detection of Gastroesophageal Reflux"

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"P P 39 0895" P 39 0895 **Differences in Endoscopic and Clinico-Pathological Features of Primary and Secondary Gastric Non-Hodgkin's Lymphoma** M.-E. Kolve<sup>1</sup>, W. Fischbach<sup>2</sup>, Multicenter Study Group "Gastrointestinal Lymphoma"

<sup>1</sup> Medizinische Poliklinik, Univ. Würzburg, FRG

<sup>2</sup> Dept. of Internal Medicine, Aschaffenburg, FRG Lymphomatous neoplasia of the stomach may present as primary extranodal gastric B-cell lymphoma of the MALT (pgNHL) or as disseminated Non-Hodgkin's lymphoma secondarily involving the upper GI-tract (sgNHL). Considering the different pathogenesis of pgNHL and sgNHL differences in their clinical presentation and endoscopic appearance may be assumed. Tumor size, localization and macroscopic growth pattern were analysed in 146 patients with newly diagnosed pgNHL (low grade = 42, high grade = 104) and compared with the findings of 28 histologically verified sgNHL (low grade = 16, high grade = 12). PgNHL usually revealed a more extended tumor size and unifocal growth pattern as compared to sgNHL. PgNHL predominantly presented as ulcerative lesions (tab. 1). Table 1 Size Localization Growth pattern < 5 cm > 5 cm F C A D uni-multi- nor- polyp. ulcera- diff. fokal fokal mal tiv infiltrp NHL 33 98 10 74 82 3 123 23 0 47 84 33 23% 67% 7% 51% 56% 2% 84% 16% 0% 32% 58% 23% sNHL 7 10 14 21 11 7 9 11 10 14 13 2 41% 59% 26% 40% 21% 13% 45% 55% 25% 36% 33% 6% Tab. 1 F = Fundus, C = Corpus, A = Antrum, D = Duodenum Within the group of pgNHL bulky disease (tumor size > 5 cm) was detected more frequently in high grade NHL (hgNHL) than in low grade NHL (lgNHL), (tab. 2). Ulcerative and diffuse infiltrating lesions were detected predominantly in lgNHL. Table 2 lgNHL hgNHL Tumor size < 5 cm 18 (43%) 15 (14%) > 5 cm 23 (55%) 75 (72%) Unknown 1 14 (14%) Endoscopic appearance polypoid 11 (26%) 36 (34%) exulcerative 12 (29%) 35 (33%) ulcerative infiltrating 18 (43%) 29 (28%) diffuse infiltrating 17 (40%) 16 (15%) Although there are some differences in the endoscopic findings of pgNHL and sgNHL no characteristics could be elaborated being helpful to reliably differentiate these tumor entities on the basis of their macroscopic appearance. Supported by Deutsche Krebshilfe. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Echoendosonography: Echoendoscopy } "Differences in Endoscopic and Clinico-Pathological Features of Primary and Secondary Gastric Non-Hodgkin's Lymphoma"

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"P P 39 0896" P 39 0896 **Efficacy of Endoscopic Resection of Intramucosal Gastric Cancer after Five Pointed Laser Marking**

\*K. Fukase, T. Matsuda, M. Terashita, I. Aoyama, Y. Okuyama, J. Sakai, H. Saito, S. Sato

Dept. of Internal Medicine, Yamagata Prefectural Central Hospital, Yamagata-city, Japan

**Purpose** The result of endoscopic resection (ER) of intramucosal gastric cancer without marking was not satisfactory. For the purpose of accomplishing higher rate of complete resection (CR), ER was performed after marking.

**Patients and methods** From July 1978 to April 1996, 384 cases, 410 lesions of intramucosal gastric cancer were resected endoscopically. The laser marking was started in August 1990 and 86 cases, 89 lesions were treated with this method. Firstly 5 points (2 points in the oral and 1 point in the anal, anterior and posterior side) are marked endoscopically, about 2 mm distant from the border of the lesion, using a Nd-YAG laser. Secondly the lesions were resected including these markings. If 5 markings are detected, the lesion is considered to be completely resected. If the 2 oral markings are detected in the resected specimen, it is possible to find the orientation. And if there is a remnant lesion, the remaining markings make it easier to perform re-ER or additional laser treatment.

**Result** Out of 321 lesions without marking, 134 lesions were resected completely and the rate of CR was 41.7%. Out of 89 lesions with markings, 63 lesions were resected completely and the rate of CR was 70.8%. The rate of CR using laser markings was higher than the one without ( $p < 0.01$ ).

**Conclusion** This method is effective because it improves the rate of CR, it enables recognition of the orientation and greater ease of additional endoscopic treatment. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Stomach, duodenum } "Efficacy of Endoscopic Resection of Intramucosal Gastric Cancer after Five Pointed Laser Marking"

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"P P 39 0897" P 39 0897 **The Value of Endoscopic Ultrasonography (EUS) in Diagnosis and Staging of Primary Gastric Lymphoma** S. Tarazis,

\*C. Markoglou, E. Tsohataridis, M.Z. Trivizakis, N. Kalantzis

Department of Gastroenterology, NIMTS Hospital; Athens, Greece

**Purpose** The diagnosis of primary gastric lymphoma cannot always be established by endoscopic biopsies, because the lesion arises from the lymphatic tissue, which may not be reached with a biopsy forceps. Moreover, the lack of specific gross abnormalities does not allow the establishment of diagnosis during endoscopy. In our study we report our experience concerning the value of EUS in detecting and staging gastric Non-Hodgkin's lymphoma.

**Materials and methods** Between 1993 and 1996 EUS was performed in 550 patients in our department. Among the patients with non specific gross abnormalities, abnormal EUS findings, which would be compatible with primary gastric lymphoma, were shown in 55 patients. In 18 of them the final diagnosis established by surgery was primary gastric lymphoma. T<sub>1</sub>–T<sub>3</sub> patients were subjected to total or subtotal gastrectomy, while T<sub>4</sub> patients were followed-up by means of EUS after chemotherapy. In 13/18 patients the diagnosis was revealed by endoscopic biopsies. The other 5 patients required exploratory laparotomy to prove the diagnosis.

**Results** The results of EUS were compared with those obtained by endoscopy, CT scan, surgical exploration and the detailed histological examination of the resected specimens. One T<sub>3</sub> patient according to the EUS findings was finally T<sub>2</sub>. In 4 patients EUS failed in the N staging. One patient was overstaged and three were understaged. We *conclude* that EUS can clearly visualize the abnormalities of the layer structure of the gastric wall, and could be used together with other diagnostic procedures such as US and CT to determine the extent of a tumor and to decide whether to operate or to administer chemotherapy. Echoendosonography: Echoendoscopy Endoscopy, specific: Stomach, duodenum } "The Value of Endoscopic Ultrasonography (EUS) in Diagnosis and Staging of Primary Gastric Lymphoma"

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"P P 39 0898" P 39 0898 **Diagnosis of Early Gastric Cancers by an Endoscopic Autofluorescence Imaging System**

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<sup>1</sup> Yukawa Gastrointestinal Hosp., Osaka, Japan

<sup>2</sup> Dept. of Gastrointestinal Oncology Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan  
Cancer and precancerous lesions in many organs generates attenuated autofluorescence in green spectrum band compared to that from normal tissues when irradiated by blue light. In the present study, we examined the clinical value of a new endoscopic autofluorescence imaging system for diagnosis of early gastric cancers. This endoscopic system, LIFE-GI (Light Induced Fluorescence Endoscopy), was jointly developed by Olympus (Japan) and Xillix (Canada). LIFE-GI consists of a mercury light source with blue light pass filter, a camera equipped with two high sensitivity image sensors for detection of green and red autofluorescence, and imaging processor for displaying autofluorescence image. We applied this system to 30 patients with gastric cancer or suspicious of gastric cancer. In 23 of 25 early gastric cancers the lesions could be observed as a dark reddish-colored area by this system. Histological examinations of the resected specimens showed that the tumors corresponded well with the dark reddish-colored area. By this autofluorescence endoscopy, we could detect a small early gastric cancer which could not be observed by conventional endoscopy. Neither hyperplastic polyps nor gastric ulcer scars showed autofluorescence. In conclusion, autofluorescence endoscopy is useful for diagnosis of early gastric cancers. Oncology, specific: Stomach Endoscopy, specific: Stomach, duodenum } "Diagnosis of Early Gastric Cancers by an Endoscopic Autofluorescence Imaging System"

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"P P 39 0899" P 39 0899 **Endoscopic Ultrasonography (EUS) for Evaluating Early Gastric Cancer before Endoscopic Mucosal Resection (EMR)** M. Kida, Y. Yamada, T. Sakaguchi, H. Imaizumi, S. Tanabe, W. Koizumi, K. Saigenji, H. Shimao<sup>1</sup>

Dept. of Internal Medicine, Kitasato Univ. East Hospital, Sagamihara, Kanagawa, 228 Japan

<sup>1</sup> Dept. of Surgery, Kitasato Univ. East Hospital, Sagamihara, Kanagawa, 228 Japan

**Introduction** Endoscopic mucosal resection (EMR) has been attempted in patient with small cancer (<math>\leq 2\text{ cm}</math>) suspected to be mucosal invasion. We have already reported that EUS is the most accurate method presently available to determine the depth of cancer invasion and report the role of EUS for evaluating the indication of EMR.

**Method** We have already performed EUS in over 1300 patients with gastric cancer, and 1135 lesion were resected and studied histologically. And 56 lesions were removed by EMR in this group. EUS examination were performed with conventional EUS (GF-UM3, UM20, 34 lesions) and ultrasonic probe (USP, UM-3R, 2R, 22 lesions).

**Result** The diagnostic accuracy of USP vs EUS is 94.8% (93/98) vs 89.5% (274/306) in m-cancer, 68.1% (32/47) vs 69.3% (151/218) in sm-cancer, 54.5% (6/11) vs 72.8% (67/92) in pm-cancer, 75.0% (15/20) vs 89.8% (308/343) in ss-s-cancer, respectively. And totally 83.0% (146/176) vs 83.4% (800/959). Furthermore the accuracy of USP vs EUS for small lesion (<math>\leq 2\text{ cm}</math>) is 85.7% (54/63) vs 86.1% (180/209). In the group of lesions resected by EMR, the accuracy is 90.9% (20/22) vs 94.1% (32/34). It is sometimes difficult to detect the small and flat lesion by conventional EUS, however there was no cases that could not be detected by USP.

**Conclusions** EUS is useful for evaluating the indication of EMR and USP is helpful to evaluate the cases with small and flat lesions. } "Endoscopic Ultrasonography (EUS) for Evaluating Early Gastric Cancer before Endoscopic Mucosal Resection (EMR)"

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"P P 39 0900" P 39 0900 **A Role of Endoscopic Mucosal Resection (EMR) and Laser Irradiation for Early Gastric Cancer**

\*M. Morise, H. Shima, Y. Arai, S. Kikuchi, N. Kobayashi, H. Mieno, Y. Sakakibara, Y. Hiki, A. Kakita, Y. Yokoyama, H. Imaizumi, S. Tanabe

Department of Surgery and Gastroenterology, Kitasato University, Sagami-hara, Japan  
Endoscopic therapy, laparoscopic surgery, and minimally invasive surgery have been developed to as therapeutic procedures in patients with early gastric cancer. Presently, the procedure of choice for the endoscopic therapy of early gastric cancer is EMR because it permits histopathological evaluation. At our hospital we have performed EMR in 161 cases and laser therapy in 131 cases (total 292 cases) of early gastric cancer during 1981 to March 1995. The success rate for EMR, including absolute and relative indications, is about 50%. Various techniques are employed to treat remnant lesions. In inoperable cases, we use laser irradiation since there is no other satisfactory therapy. In operable cases, laser irradiation is performed in a limited number of indications because surgery has been established as radical therapy. Laser irradiation for remnant tumor after EMR in cases absolute indicated has been shown to be effective, with a cancer eradication rate of 93.1%. In cases relatively indicated for EMR, the rate for laser irradiation was 83.3%, which is rather good compared with that of 5.6% for EMR. Laser irradiation can thus be expected to provide a good outcome in the treatment of early gastric cancer, provided it is performed for the proper indications and objectives. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Stomach, duodenum } "A Role of Endoscopic Mucosal Resection (EMR) and Laser Irradiation for Early Gastric Cancer"

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"P P 39 0902" P 39 0902 **Endoscopic Opening of Totally Laparoscopic Gastrointestinal Anastomosis with Previous Suture (EA)**

\*K. Hashiba, A.L. Paula, S. Wada, W.R. Freitas, J.A. Delai, D. Moribe, A.F. Silva, D. Birolini

D. Dept. of Surgery, S. Paulo University Medical School, Dept. of Surgery Hospital and Mat. Atibaia, S. Paulo Brazil This study introduces a new idea for the performance of totally laparoscopic gastrointestinal anastomosis in which the lumen is opened after the suture to prevent contact of gastrointestinal contents with the peritoneal cavity. The opening was done through endoscopic procedure. A metal stitch is introduced through the walls of the organs to bring them together as in a "U" suture. The ends of this metal stitch are taken by an endoscope and pulled to the mouth. Then a suture with non-absorbable stitch is made around the area that was brought together in order to tie the walls. Next, the ends of metal stitch were pulled against a plastic tube and, like a polypectomy snare, the walls were cut with a cautery under endoscopic control. The anastomosis is thus opened. Under general anesthesia, 4 pigs underwent gastrojejunal derivation and another 4 pigs, gastrectomy. There were no complications in any procedures. Histology of the anastomoses did not reveal significant changes on the fifteenth day. One patient with small advanced gastric cancer underwent gastrectomy with EA. In the postoperative course this patient showed an abdominal wall hematoma. The results suggest that EA is a safe, easy and cheap procedure which opens a new path in the field of endoscopic procedures. Endoscopy, specific: Stomach, duodenum Laparoscopic surgery: Therapy }  
"Endoscopic Opening of Totally Laparoscopic Gastrointestinal Anastomosis with Previous Suture (EA)"

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## "P P 39 0903" P 39 0903 New Endoscopic Evaluation of the Healing Process of Gastric Ulcer

\*H. Imaizumi, M. Ohida, S. Noguchi, K. Hibi, S. Sugano, I. Kondou, Y. Kida, S. Tanabe, M. Kida, W. Koizumi, T. Mitsuhashi, K. Saigenji

Department of Gastroenterology, Kitasato University East Hospital, Sagamihara, Kanagawa, Japan To clarify the healing process of gastric ulcers, we studied the usefulness of the pharmacoscopy (PE) method using epinephrine (Ep) spray.

**Patient and Method** Sixty five scar lesions were selected for this purpose. After color of scar lesions were classified red and white by conventional endoscopy, 0.02% Ep (10 ml) were sprayed endoscopically. After 3 minits spraying, the changes in color of scar lesions were classified to P<sub>R</sub> (persistent reddish) and P<sub>W</sub> (whitish). We also investigated the blood volume of the ulcer scar lesions using computer image analysis both before and after Ep spray. Then, cumulative recurrent rates in each group was calculated.

**Result** The mean blood volume of the P<sub>R</sub> scar group was about 1.5 times higher than that of the surrounding normal mucosa. In contrast, the mean blood volume of the P<sub>W</sub> scar group was almost same as that of normal mucosa. Cumulative recurrent rate in each 4 groups was studied dualing 24 months. Twenty four months cumulative recurrent rate in red scar group was 45%, while 35% in white scar group. These rates in P<sub>R</sub> and P<sub>W</sub> scar group were 43% and 10% respectively. P<sub>W</sub> group showed the lowest 24 month cumulative recurrent rate among all groups. Biopsied specimens were examined histologically. The P<sub>W</sub> scar group was showed more matured regenerating epithelium than the P<sub>R</sub> scar group.

**Conclusion** These findings suggested that PE is useful for estimating the grade of ulcer healing especially for in scar stage. From the viewpoint of intra mucosal vessel function, ulcer scar showing P<sub>W</sub> seemed to be healed completely. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: Preparation, management Endoscopy, specific: Stomach, duodenum } "New Endoscopic Evaluation of the Healing Process of Gastric Ulcer"

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## "P P 39 0905" P 39 0905 **Diagnostic Accuracy of Salivary IgG Anti-Helicobacter Pylori in Dyspeptic Patients Referred to First Upper Digestive Endoscopy**

\*F. Costa, S. Marchi, M.R. Romano, G. Amato, C. Belcari, E. Tumino, M. Bellini, M. Manghetti, M. Spataro, G. Maltinti

U.O. Gastroenterologia, I Clinica Medica, Universit'e0 di Pisa, Pisa, Italia

**Introduction and aim** Salivary specific IgG anti-Helicobacter pylori (Hp) could be a simple and suitable tool for the diagnosis of Hp infection particularly in paediatric patients. The aim of the study was to evaluate the diagnostic accuracy of salivary IgG anti-Hp measurement by a new commercially available kit (Helisal-Cortecs Ltd. UK).

**Patients and Methods** Thirty consecutive dyspeptic patients (17 females, mean age 41 years) referred to first upper digestive endoscopy (UDE) entered the study. No patient had been treated before for Hp infection and had assumed non steroidal anti-inflammatory drugs, antisecretory drugs, antibiotics or bismuth compounds in the previous 3 months. Hp status was assessed by Cp-test, histology and serology (IgG Helori test Eurospital, Italy). Patients were defined as Hp positive if Cp-test and histology gave a positive result and negative if both tests resulted negative. Serum and unstimulated saliva were collected before UDE and stored at { - }20 \b0C and 4\b0C respectively until assayed.

**Results** UDE revealed duodenal ulcer (DU) in 5 patients and no gastroduodenal lesions (NUD) in 25 patients. Sixteen (53%) patients were diagnosed as Hp positive (5/5 DU and 11/25 NUD). Serum IgG anti-Hp gave 3 false positive and 0 false negative results; the sensitivity was 100%, the specificity 79%, the positive and negative predictive value (PPV and NPV) 84% and 100% respectively. Salivary IgG anti-Hp gave 5 false positive and 4 false negative results with a diagnostic sensitivity of 75%, a specificity of 64% and a PPV and a NPV of 71% and 44% respectively, the accuracy rate as a whole resulted of 70%. Salivary and serum IgG anti-Hp showed concordant results in 24 out of 30 patients.

**Conclusion** IgG anti-Hp are present in the saliva of Hp infected patients and their measurement can represent a simple and rapid method for the diagnosis of Hp infection. Our preliminary results, nevertheless, show a lower sensitivity, specificity and diagnostic accuracy if compared with serology and require further investigation. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Diagnostic Accuracy of Salivary IgG Anti-Helicobacter Pylori in Dyspeptic Patients Referred to First Upper Digestive Endoscopy"

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## "P P 39 0907" P 39 0907 **Prediction of Diagnosis of Dyspepsia in the Era of Open Access Endoscopy**

\*C.R. Ramsay, M.K. Campbell, M. Lopez<sup>1</sup>, S.A. Naji, F.E. Murray<sup>1</sup>

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<sup>1</sup> Dept of Clinical Pharmacology, Ninewells Hospital, Dundee DD1 9SY The investigation of dyspepsia has altered in much of the UK consequent to the wide spread of open access endoscopy. The benefit of a normal diagnosis remains to be confirmed.

**Aim** To evaluate factors which may be predictive of an endoscopy (1) in terms of impact on patient management and (2) in terms of patients with important clinical diagnoses, at a newly established open access endoscopy service.

**Methods** During a 1-year period, 1028 patients endoscoped within this service were evaluated. All patients were asked to complete a dyspepsia questionnaire, and referring doctors also completed a referral questionnaire for each patient. Follow-up questionnaires were sent to the referring doctors and patients one month after the endoscopy. The dataset was randomly split into two groups, one group (the Model group) was used to develop predictive models using logistic discriminant analysis and the second group (the Test group) to test the robustness of the developed models.

**Results** The accuracy of the referring doctor's provisional diagnosis ranged from 1% for ulcers and 5% for cancers to 39% for reflux oesophagitis. Two factors were predictive of 57% of significant diagnosis — smoking and sex of patient and six factors were found to be predictive of 57% of the reflux oesophagitis cases. No factors were identified which could predict a change in the patients management following endoscopy. The Test group patients showed a similar prediction level.

**Conclusion** Clinical diagnosis of dyspepsia based on symptoms alone remains imprecise and emphasises the need in clinical practice for access to diagnostic facilities in such patients. }"  
"Prediction of Diagnosis of Dyspepsia in the Era of Open Access Endoscopy"

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"P P 40 0908" P 40 0908 **Gastric Mass Survey by Photofluorography on 122,666 Subjects**

\*T. Kanai, A. Kashiwagi, T. Idesawa, I. Takayama, F. Kitahara, Y. Yoda, K. Kobayashi, M.A. Fujino

Health Care Center, Yamanashi, Prefectural Welfare Federation of Agricultural Cooperatives and Dept. Medicine, Yamanashi Medical University, Yamanashi, Japan Gastric carcinoma has been a frequent form of cancer in Japan. Mass survey has been widely performed to detect this cancer since 1960s. It has succeeded in detecting gastric cancers at an early stage. Furthermore, it has contributed to a remarkable improvement in the postoperative 5-year survival rate of gastric carcinoma. Our gastric mass survey, performed as a part of the general medical check-up, has been done for the past 6 years. In an itinerant check-up program for rural participants, we have used modified buses installed with photofluorographic apparatus. Among 122,666 subjects (50,659 males and 72,007 females) 21,883 (17.8%) were pointed out to have abnormal findings on photofluorography, requiring further diagnostic procedures. Two-hundred forty-five cases (0.20%) were ultimately diagnosed as gastric carcinoma. The expense for screening photofluorography was 3,500 Japanese yen per person and diagnostic endoscopy 22,000 Japanese yen per examination. The participants paid only 10 to 30% of the expense and the rest was covered by the governmental aid, however. As for the detected gastric cancer, 160 cases were detected at an early stage (65.0%) and 85 were advanced; early cancer ratio has been increasing year by year, from 59.0% in 1989 to 69.2% in 1994. Thirteen cases were curable by endoscopic resection in total. Itinerant mass survey by photofluorography is quite useful for early detection of gastric carcinoma. Oncology, general: Screening, prevention Oncology, specific: Stomach Radiology and ultrasound: Diagnosis } "Gastric Mass Survey by Photofluorography on 122,666 Subjects"

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"P P 42 0939" P 42 0939 **Endoscopic Healing with cA2 Anti-TNF Antibodies in Crohn's Disease: A European Multicenter Trial**

\*G.R. D'Haens, S.J.H. van Deventer, R. Van Hogezaand, D.M. Chalmers, T.A.J. Braakman, H. Bijl, P.J. Rutgeerts

The European cA2 study group in Leuven, Belgium; Amsterdam, Leiden, The Netherlands; Leeds, UK Several trials have demonstrated clinical efficacy of chimeric monoclonal anti-TNF- $\alpha$  antibody (cA2) therapy for active Crohn's disease (CD). Initial open-label experience revealed that this effect was accompanied by a fast endoscopic healing of colonic lesions. Endoscopic response to cA2 was further investigated in a multicenter randomized double-blind, placebo controlled trial including 108 pts with active CD (CDAI 220–400), 30 of whom were enrolled in Europe and underwent an ileocolonoscopy before and 4 weeks after IV administration of 5 mg/kg (n = 8), 10 mg/kg (n = 7), 20 mg/kg (n = 7) of cA2 or placebo (n = 8) as a single 2 hour IV infusion. Concomitant therapy was kept stable throughout the trial. Video-endoscopic examination was performed at baseline and 4 week later after standard bowel preparation by the same endoscopist. Lesions were scored by means of the CD Endoscopic Index of Severity (CDEIS), which was previously validated by the French GETAID. This score includes the presence of deep/superficial ulceration, ulcerated/non-ulcerated stenosis, and the segments and the proportion of mucosal surface involved by CD. Significant endoscopic improvement was observed in all cA2-treated patients, with a drop in mean CDEIS from 15.1 – 6.9 to 6.4 – 5.1 in the 5 mg/kg group (p = 0.006), from 10.6 – 7.8 to 4.3 – 5.4 in the 10 mg/kg group (p = 0.009), and from 13.3 – 6.9 to 5.2 – 2.8 in the 20 mg/kg group (p = 0.006). For all cA2-treated pts, the CDEIS dropped from 13.0 – 7.1 to 5.3 – 4.4 (p < 0.001), without a significant dose-response. There was no endoscopic improvement in the placebo group (CDEIS from 8.4 – 6.3 to 7.5 – 5.4). The changes in the endoscopic index CDEIS correlated highly with those in the clinical index CDAI (r = 0.56, p = 0.002). We conclude that the clinical improvement after cA2-therapy in active CD is accompanied by significant healing of endoscopically viewed ileocolonic lesions.

Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation Endoscopy, specific: Colon, rectum } "Endoscopic Healing with cA2 Anti-TNF Antibodies in Crohn's Disease: A European Multicenter Trial"

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"P P 43 0974" P 43 0974 **The Role of Small Bowel Biopsy in the Endoscopic Evaluation of Adults with Iron Deficiency Anemia**

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Department of Medicine, Hadassah University Hospital, Mount Scopus, Jerusalem, Israel  
The recommended evaluation of adult patients presenting with iron deficiency anemia (IDA) includes the performance of colonoscopy and esophagogastroduodenoscopy (EGD). IDA is a common feature in patients with celiac disease and, in several, may be the only presenting sign. The performance of small bowel biopsy (SBB) for the evaluation of celiac disease as the cause of IDA is not routinely recommended. The aim of the present study was to determine the yield of SBB performed during routine endoscopy of adults with IDA. We prospectively studied 93 patient with IDA. Three control groups were included: 23 patients with steatorrhea, 37 patients with idiopathic diarrhea and nine patients in whom SBB was performed for miscellaneous indications. Eleven patients with IDA and two patients with steatorrhea had SBB compatible with celiac disease. None of the patients from the other two groups had similar findings. Two patients with IDA, who were later diagnosed to suffer from celiac disease, presented — one with occult blood in the stool and the other with rectal bleeding. Subgroup analysis of patients with IDA revealed that patients with celiac disease were younger, had significantly more episodes of diarrhea, lower mean hemoglobin level and longer duration of anemia than those without celiac disease. Other mucosal abnormalities were found in a substantial number of patients with celiac disease: esophagitis, gastritis, duodenitis, hemorrhoids and colitis. A substantial number of adult Israeli patients who present with IDA are found, on SBB, to have mucosal abnormalities compatible with the diagnosis of celiac disease. The presence of esophagitis, gastritis or duodenitis on EGD, or other abnormalities on colonoscopy, do not exclude the coexistence of celiac disease. Celiac disease should be included and routinely looked for in the differential diagnosis of adult patients with IDA. Clinical practice: Management strategy Intestinal disorders, absorption: Gluten enteropathy Endoscopy, general: Instrumentation, diagnosis } "The Role of Small Bowel Biopsy in the Endoscopic Evaluation of Adults with Iron Deficiency Anemia"

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"P P 45 0997" P 45 0997 **Pancreatitis Associated Protein in Patients with Coeliac Disease. Serum Levels and Immunocytochemical Localization in Small Intestine** A. Carroccio, J. Iovanna, G. Iacono, M. Li Pani,

\*G. Montalto, F. Cavataio, L. Maras\ 'e0, S. Barthell\ 'e9my-Bialas, M. Soresi, S. Ippolito, J.C. Dagorn

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INSERM U315 Marsiglia, Italy and France PAP is a stress protein expressed in human pancreas during pancreatitis but also in the small intestine. We evaluated its expression in patients with celiac disease (CD). Serum PAP concentration were determined in 54 patients with CD on a free-diet (Group A), in 47 patients with CD on a gluten-free diet (Group B) and in 22 patients with other intestinal pathologies but with normal intestinal mucosa (Group C). Serum PAP levels (ng/ml) were significantly higher in Group A (127 – 57) than in the other groups (B: 47 – 20; C: 51 – 32). In Group A a positive correlation was observed between serum PAP values and anti-gluten antibody levels (vs AGA IgG  $r = 0.58$ ,  $p < 0.001$ ; vs AGA IgA  $r = 0.66$   $p < 0.001$ ). In addition 12 patients were followed before and after 10–12 months of gluten-free diet and in all serum PAP values decreased after the diet (mean – SD before the diet: 122 – 36, after the diet: 49 – 13 ng/ml,  $p < 0.001$ ). An immunocytochemical study localized PAP in the intestinal mucosa to the Paneth cells and to goblet cells, in patients with mucosal atrophy as well as in those with normal mucosa with no obvious quantitative difference. We concluded that in patients with CD the active phase of the disease was accompanied by an increased serum concentration of PAP, and PAP levels could be a marker of histological damage of the intestinal mucosa. Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption: children } "Pancreatitis Associated Protein in Patients with Coeliac Disease. Serum Levels and Immunocytochemical Localization in Small Intestine"

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"P P 45 1010" P 45 1010 **Long-Term Ultrasound Observation of Pancreatic Pseudocysts Spontaneous Course and Influence of Interventional Sonography** W. Johanns, J. Janssen, S. Kahl,

\*L. Greiner

Medical Clinic A, Municipal Hospital Wuppertal, University of Witten-Herdecke, Germany

**Introduction** Performance of repeated ultrasound scans at short intervals can provide a detailed insight into the natural history of pancreatic pseudocysts. This information is an important prerequisite for assessment of the prognostic significance of these cysts and for the decision as to whether and what form of treatment is indicated. We therefore conducted a retrospective study of the spontaneous course of pancreatic pseudocysts and the influence of interventional sonography.

**Patients/Methods** 69 patients (13 women, 56 men; average age 48.9 years) with pancreatic pseudocysts were monitored by ultrasound without operative intervention. The length of follow-up was between 3 and 136 months. The aetiologies were alcoholic (47), biliary (10), idiopathic (8), and malignant (4). There were 44 pseudocysts measuring  $\leq 4$  cm, 15 measuring  $\leq 6$  cm and 10 measuring  $> 6$  cm. Diagnostic aspiration was performed in 32 patients, therapeutic aspiration in 7 patients and percutaneous drainage in 3 patients.

**Results** 49 pseudocysts (71%) disappeared spontaneously, 2 became smaller spontaneously, 6 remained unchanged. The age and size of the pseudocysts and the aetiology of the pancreatitis had no influence on the rate of spontaneous regression. The success rate of therapeutic aspiration was 57.1%, that of drainage 100%.

**Conclusion** The study refutes the conventional wisdom that spontaneous regression only occurs during the first 6–12 weeks after development of the pseudocysts, is rare in patients with chronic pancreatitis and occurs mainly in small pseudocysts. The high success rate of interventional sonography reported in other studies is confirmed. In the light of these findings the recommendation of elective surgery for pseudocysts which show no signs of spontaneous regression after 6–12 weeks should be questioned. On the contrary, if there are no complications, pancreatic pseudocysts should be monitored by ultrasound in anticipation of their spontaneous regression. Pancreas: Pancreatitis, acute Pancreas: Pancreatitis, chronic } "Long-Term Ultrasound Observation of Pancreatic Pseudocysts Spontaneous Course and Influence of Interventional Sonography"

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"P P 45 1027" P 45 1027 **Endoscopic Pancreatic Sphincterotomy (EPS): Results of 150 Procedures**  
G. Costamagna, M. Mutignani,

\*A. Gabbrielli, V. Perri, M. Pandolfi, G.M. Colombo, A. Bruni, F. Crucitti

Istituto di Clinica Chirurgica, Catholic University of Rome, Italy Few published reports have deemed with indications, technical issues and results of EPS. This endoscopic procedure has gained popularity only recently, because of the increasing interest in the non-surgical approach to chronic pancreatitis (CP). Aim of this work is to report our clinical experience with EPS performed according to a standardized technique. *Patients and Technique.* Between June '88 and April '96, 150 EPS (132 at major papilla, 18 minor papilla) were attempted in 147 patients (112 M, 35 F, mean age 51.9 years, range 3–89 years). Indications included primary CP (n = 114), neoplastic obstructive CP (n = 19), benign obstructive CP (n = 6), external pancreatic fistula (n = 3), post-necrotic pseudocyst (n = 3), diagnostic aim (n = 1) and attempt at deep cannulation of the bile duct (n = 1). Technically a biliary sphincterotomy (EBS) is performed as the first step to get an easier access to the pancreatic office. After deep cannulation of the pancreatic duct with a guide wire, EPS is performed over the wire with a long-nose proximal papillotome having a 20 mm. cutting wire. Eighty watts of pure cut current are generally applied. EPS is accomplished under direct visual control with the sphincterotome oriented along the axis of the pancreatic duct at 12–2 o'clock direction. The length of the cut is mostly depending on the anatomy of the individual patient, averaging 5 to 10 mm. Minor papilla EPS is performed according to the same technique. In case of incomplete EPS, edema or obstruction of the distal pancreatic duct, it is always advisable to obtain a good drainage of the main pancreatic duct (naso-pancreatic drainage, extraction of stones, insertion of large bore 10 Fr pancreatic stent) to avoid septic complications or duct hypertension. *Results:* EPS was successful in all but 3 patients (2%). In 3 cases (2%) a needle-knife pre-cut was utilized. One 73 years old patient with fluid collection after acute pancreatitis, died within 30 days from septic complications. Specific complications of EPS in patients with primary CP, included one patient with a severe acute pancreatitis and pancreatic abscess who underwent surgery and one patient with overt bleeding who underwent endoscopic hemostasis (1.7%). Both patients eventually recovered. *Conclusions:* EPS is a safe and effective procedure. It is often the first step in the pancreatic operative endoscopy like EBS in the biliary tract. The technique deserves more critical review and prospective studies about his efficacy in various disease states. Pancreas: Pancreatitis, chronic Endoscopy, specific: Pancreatic } "Endoscopic Pancreatic Sphincterotomy (EPS): Results of 150 Procedures"

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## "P P 45 1028" P 45 1028 Painful Chronic Pancreatitis without Dilated Duct: Effect of Endoscopic Treatment

\*C. Renou, R. Laugier

Service d'Hépatogastro-entérologie et Inserm U-260, Hospital de la Conception, Marseille, France Surgery might be necessary to treat severe pain during chronic pancreatitis when medical attitudes have failed. Decompressive surgery is only feasible when the main pancreatic duct (MPD) is dilated over sufficient length; in other cases, resection becomes mandatory. Our aim was to evaluate in such special cases the results of endoscopic stent drainage. *Methods:* Out of our chronic pancreatitis (CP) patients, 16 were included in this study: 13 men, 3 women, 46.3 – 4.2 years. They presented a mean of 5.3 episodes of pain in the 6 months before treatment. Decompressive surgery was not possible because of a mean MPD diameter of 5.8 mm. CP was alcoholic in 11 cases, hereditary in one and idiopathic in 4 cases. Four patients had a pancreas divisum and 7 were also complicated by a cyst. Stents were 7 F in diameter in 8 patients and 12 F in the 8 others. They were left in the duct after endoscopic dilatation for 9.5 – 1.0 months (6 to 17), each stent being systematically changed every 4 months. In 5 patients, cysto gastrostomy (3) or duodenostomy (2) was associated. *Results:* During stenting we observed 2 early obstructions (one month) and 7 episodes of pain in 6 patients. Three episodes of mild acute pancreatitis were noted after stenting in one patient. At the end of treatment, all cysts disappeared and stenosis of MPD disappeared anatomically in 5 cases while it persisted in 4. Endoscopic treatment was stopped after 8 months in one patient. During follow up (22.2 months – 5.7) only 2 episodes of mild pain were noted (treated in outpatients). No cyst reappeared. Finally the mean diameter of MPD did not change after treatment. Complete disappearance of stenosis was only observed with 12 F stents and not with 7 F one ( $p < 0.05$ ). *Conclusion:* Endoscopic stenting treatment in selected cases of CP unsuitable for decompressive surgery appears to be safe efficient on clinical stand point. Perfect anatomical results are only obtained if large stents are used. Pancreas: Pancreatitis, chronic } "Painful Chronic Pancreatitis without Dilated Duct: Effect of Endoscopic Treatment"

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"P P 45 1029" P 45 1029 **Ultrasonographic Imaging of the Pancreatic Duct before and after Secretin Stimulation**

\*R. Alekse, J. Pokrotnieks

P. Stradins Clinical Hospital Riga, Latvia We have measured the caliber of the ultrasonographically visualized pancreatic duct in 42 patients with chronic pancreatitis and 20 practically healthy persons before and after secretin stimulation. The patients with marked duct dilatation and intraductal stones were excluded. The pancreatic duct diameter was measured in the region of corpus before and several times during the first 30 min. after intravenous injection of 1 CU secretin per kilogram body weight. In the group of 20 healthy persons we found an average duct diameter of 1.3 – 0.3 mm. After intravenous injection of secretin a duct enlargement was observed in all healthy persons to a mean of 3.1 – 0.3 mm. The maximal diameter was measured around 4–5 min. after injection. In the group of 42 patients with chronic pancreatitis the average duct diameter before secretin injection was 2.9 – 0.4 mm. In 33 of these patients no duct dilatation was observed after secretin injection. Only 9 patients showed a small duct dilatation on average only 0.8 mm. We conclude the use of ultrasonographic secretin test may be helpful in the diagnosis of chronic pancreatitis. Pancreas: Pancreatitis, chronic Radiology and ultrasound: Diagnosis } "Ultrasonographic Imaging of the Pancreatic Duct before and after Secretin Stimulation"

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"P P 45 1030" P 45 1030 **Endoscopic Pancreatic Stenting in Patients with Pain Due to Chronic Pancreatitis**

\*J.F. Pellicer, J.F. Fernandez, J.M. Mart'edn, H. Pallar'e9s, R. Romero, M. Hassan, R. Sa'e9nz, P. Hergueta, J.M. Herrer'edas

Servicio de Aparato Digestivo Hospital Universitario Virgen Macarena, Sevilla 41008

Espa'f1a *Introduction:* Chronic pancreatitis is a progressive disease that implies loss of acinar parenchyma and fibrosis of the gland. Consequences are exocrine and endocrine dysfunction and chronic pain. Pain is supposed to depend on two different mechanisms: A) intraglandular neural affection and B) pancreatic duct drainage obstruction with an increase in intraductal pressure. To achieve pain relief surgical and endoscopic stenting have been used. *Aim:* The aim of the study was to evaluate the efficacy of pancreatic duct stenting in patients with a narcotic-dependent pain due to chronic pancreatitis. *Patients and Methods:* From May 1994 to May 1996 we treated six male patients. Age ranged from 39 to 59 (mean: 47.5). Etiology of chronic pancreatitis was alcohol abuse in all cases. ERCP showed single or multiple strictures in Wirsung's duct. When intraductal lithiasis was present Fogarty-type balloon or Dormia's basket was used to remove them. Pancreatic duct strictures were negotiated with a 0.025-inch guide wire advancing a 7-F dilating catheter over the guide to dilate the stricture. Prothesis calibre was 7-F in all cases and variable length (5–10 cm) depending on the anatomical location of the stricture. Stents were removed when patients complained pain again. Stent survival time was defined as the patient's pain-free time. *Results:* Patient Wirsung's ERCP image Stents # Prothesis length Stent survival time (cm) (days) 1 Proximal stenosis 1 10 902 Proximal stenosis 2 5; 5 45; 873 Multiple stenosis without lithiasis 3 10; 5; 10 300; 30; 404 Proximal stenosis 1 5 1805 Multiple stenosis and lithiasis 2 10; 10 105; 2706 Multiple stenosis and lithiasis 1 10 95 Mean time to achieve pain relief was 3 days (mean: 1–5). No complications due to the procedure were observed. Mean stent survival was 136 days (first stent) and 197 days (second stent). *Conclusions:* 1. Endoscopic pancreatic stent drainage seems to be effective in pain relief due to chronic pancreatitis with ductal stenosis. 2. It is a safe procedure without complications in our series. 3. When the stent is placed through the stricture pain relief is achieved. **Pancreas: Pancreatitis, chronic Endoscopy, specific: Pancreatic }** "Endoscopic Pancreatic Stenting in Patients with Pain Due to Chronic Pancreatitis"

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## "P P 45 1033" P 45 1033 **Thirteen-Year Experience with Ultrasound-Guided Drainage of Pancreatic Pseudocysts**

\*G. Di Candio, U. Boggi, P.C. Giulianotti, F. Sbrana, R. Bellini, F. Mosca

Istituto di Chirurgia Generale e Sperimentale, Università di Pisa, Italy

The purpose of this retrospective study is the evaluation of our 13-year experience with ultrasound-guided (US-G) percutaneous drainage (PD) of pancreatic pseudocysts (PSCs). A statistical analysis of the factors influencing therapeutic outcome is also provided. The records of 70 pts (48 m. and 22 f., mean age: 56.4 years, range: 26–80) were reviewed. Based on D'Egidio's classification and on recommendations from the Consensus Conference on acute pancreatitis held in Atlanta in 1992, PSCs were classified into six groups: immature acute PSCs (n = 3) mature acute PSCs (n = 29), post-necrotic chronic PSCs (n = 9), retention chronic PSCs (n = 5), postoperative abscesses (n = 10) and pancreatic abscesses of infected PSCs (n = 14). After removal of the catheter, all pts were entered into a combined clinico-ultrasonographic follow-up. A total of 15 variables, potentially conditioning the therapeutic outcome, were statistically evaluated. In all pts PD achieved PSC detention with evident pain relief and sharp reduction of serum amylase. Sepsis promptly resolved in all infected collections. Four pts died: 3 from sequelae of severe pancreatitis and 1 from acute myocardial infarction. Procedure related morbidity was 17.6%. High amylase concentration in the cystic fluid (p = 0.02) and delayed removal of the catheter (p = 0.02) were statistically related to morbidity. Sixty-six pts were followed-up for a mean of 41 months (range 12–132). Eleven pts (15.7%) required repeated PDs. Long-term PD success rate was 85.7%. Factors influencing therapeutic outcome were: age (p = 0.01), type of PSC (0.04) and dilation of the main pancreatic duct (0.002). In conclusion, US-G PD of PSCs seems to be a safe and effective alternative to surgical management. In acute PSCs and postoperative abscesses PD this treatment should be considered as the initial therapy. In selected instances, after careful imaging of the pancreas, a small subset of chronic PSCs may also benefit from a PD.

Pancreas: Pancreatitis, acute  
Pancreas: Pancreatitis, chronic } "Thirteen-Year Experience with Ultrasound-Guided Drainage of Pancreatic Pseudocysts"

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**OT40 1037Nd:YAG Laser Combined with Omeprazole as a Treatment of Barrett's Esophagus. Preliminary Results of a Prospective Multicenter Study V. Meyer, J. Boyer, S. Naveau, G. Cadiot, A. Rotenberg, O. Bouché, M. Robaszkiewicz, M. Le Rhun, Barrett's Esophagus Study Group**

Angers, Paris, Dreux, Reims, Brest, Nantes, INSERM Clinical Research Network *Aim:* to determine whether Nd:YAG laser therapy combined with omeprazole is able to destroy Barrett's mucosa and to regenerate normal esophageal squamous cell mucosa. *Methods:* 19 patients with Barrett's esophagus (BE), mean age 55 years, were included by 6 centers in the study; the initial mean surface area was 1679 mm<sup>2</sup> (range 50–4900 mm<sup>2</sup>). Nd:YAG laser therapy was applied in combination with omeprazole 40 mg/day. On average, laser treatment was repeated every 2 weeks until endoscopic ablation of at least 80% of the initial BE surface (maximum 6 sessions). Endoscopic and histopathologic assessment was realized at 1 and 3 months. After 6 sessions of laser therapy, the persistence of more than 20% of the initial BE surface area was considered as a failure. The response was complete (CR) if no Barrett's mucosa was found on biopsies. If the response was incomplete at 1 or 3 months, supplementary Nd:YAG laser session was applied on the macroscopic or histological remnants. *Results:* More than 80% of BE was replaced with squamous cell mucosa in 18 of the 19 cases, after 1 to 6 sessions. In one patient who presented extensive phlebitis requiring anti-thrombotic treatment, laser therapy was stopped and he was considered as failure. At 1 month, 8 patients had a CR (42%) and 10 patients an incomplete response (mean remaining surface area 4.7%). At 3 months, the rate of CR was 53%. The tolerance of the treatment was good and no severe complication was noted. *Conclusion:* Nd:YAG laser photoablation combined with omeprazole is able to make BE to be replaced with a squamous cell mucosa. These results justify pursuing the study up to the inclusion of final number of patients. Oesophageal gastric duodenal disorders: EG Reflux Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus }" "Nd:YAG Laser Combined with Omeprazole as a Treatment of Barrett's Esophagus. Preliminary Results of a Prospective Multicenter Study"

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## OT40 1038 Does the Macroscopic Disappearance of Barrett's Oesophagus after Endoscopic Thermal Ablation Preclude Its Dysplastic Potential?

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<sup>1</sup> Pathology Unit, "Alexandra" University Hospital, Athens, Greece Barrett's esophagus is considered as a premalignant condition. The possibility of eradicating the metaplastic epithelium by application of thermal methods combined with antisecretory agents has been recently reported. Islets of residual specialised type glandular tissue beneath regenerative squamous epithelium is rarely mentioned after Barrett ablation. The *aim of our study* was to evaluate the possibility of Barrett's ablation by means of heater probe and examine if residual glandular mucosa remains beneath the restored epithelium. *Patients and Methods:* 10 patients (6 men, 4 women) with Barrett esophagus (length: 2.5–6 cm) and type III enteric metaplasia were enrolled in the study. Endoscopic application of thermal energy was applied by means of Heater Probe (Shirakawa Olympus Co. LTD Japan). All sessions started from the upper limit of Barrett mucosa progressing distally and causing injury by delivering pulses of 5–10 joules. They were repeated monthly until complete ablation was considered. Four-quadrant biopsies were obtained at one cm intervals, 1–3 months after the last session and stained with Alcian blue (AB) pH 2.5/PAS and AB pH1/HID. All patients were on 40 mg/day of omeprazole continuously. *Results:* Macroscopic ablation of Barrett mucosa, endoscopically evaluated, was achieved in all patients after 1–4 sessions. No complication was observed. Histological examination did not reveal superficial islet of enteric metaplasia in any of the biopsies obtained, but in 2 out of 10 patients, 3 specimens (3/24 biopsies in those 2 patients) showed residual enteric metaplasia beneath the restored mucosa. *Conclusions:* 1) Heater probe is an effective method for macroscopic Barrett's mucosa ablation but in some patients, islets of residual intestinal metaplasia were found beneath restored mucosa. 2) The malignant potential of this "covered" residual intestinal metaplasia has to be evaluated by prospective studies but until a final report comes out, a surveillance of ablated Barrett mucosa (possibly marked before) in our opinion should be continued. *Clinical practice:* Management strategy Oesophageal gastric duodenal disorders: EG Reflux Endoscopy, specific: Oesophagus } "Does the Macroscopic Disappearance of Barrett's Oesophagus after Endoscopic Thermal Ablation Preclude Its Dysplastic Potential?"

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## OT44 1043 Impact of Lymph Nodes Endoscopic Ultrasound-Guided Biopsy in the Decision Making for Esophageal Carcinoma

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*The aim* of this study was to evaluate the impact of EUS guided biopsy of lymph nodes in the therapeutic decision making for patients with esophageal carcinoma. *Patients and methods:* From January 1994 to April 1996, 150 patients (132 men and 17 women) with a mean age of 66 years (range: 42–76 years) underwent EUS for the local staging of a squamous cell carcinoma of the esophagus in 113 cases and an adenocarcinoma of the esophagus in 37 cases before treatment. 23/150 patients (15.3%) underwent EUS-lymph node guided biopsy. The indication of the EUS guided biopsy of lymph node were: tumor localized in the middle or inferior part of the mediastinum with cervical lymph nodes (16 cases), tumor localized in the superior part of the mediastinum with celiac lymph nodes (7 cases). The EUS endoscopes used are the FG 32UA and the EG 36-30U manufactured by Pentax. *Results.* Patient tolerance was excellent and the insertion of the needle into the lesion to be biopsied was always successful. An adequate specimen could not be obtained in 1 case. The sensitivity and specificity of the diagnosis of lymph node malignancy were 95.4% and 100%. The results of EUS guided biopsy of lymph nodes modified the stage of the tumor in 21/23 cases, these esophageal tumors with cervical or celiac lymph node involvement were considered like metastatic. The therapeutic decision making was modified by the results of the lymph node EUS guided biopsy in 15/23 patients (65%). These 15 patients were treated by a concomitant radiotherapy and chemotherapy and surgery was not indicated. *Conclusion:* in this prospective study of EUS for esophageal carcinoma, a EUS guided biopsy of lymph node was indicated in 15% of cases and the results of this biopsy modified the stage and the decision making in 91% and 65% of cases respectively.

Echoendosonography: Echoendoscopy Oncology, specific: Oesophagus } " Impact of Lymph Nodes Endoscopic Ultrasound-Guided Biopsy in the Decision Making for Esophageal Carcinoma"

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## OT44 1045 Villous Adenomatous Tissue in Colorectal Polyps

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Gastrointestinal Unit, Inselspital, Univ. of Berne, Switzerland *Background:* > 95% of colon cancers seem to develop from adenomatous polyps especially if villous adenomatous tissue is present. However, most (> 80%) polyps have been reported to be of the tubular type. *Methods:* Epidemiologic data from all patients (pts) in whom a lower endoscopy has been performed during 1980–1994, were analyzed. Pts with familial adenomatous polyposis or inflammatory bowel disease were excluded from the study. 61 pts with multiple (> 10) polyps were analyzed separately. *Results:* During the 15 years time period, lower endoscopy was performed in 12{a}565 pts (mean age: 66; range: 4–97; m:f = 1.7:1). Non-malignant adenomatous and malignant polyps were detected in 13% and 0.9%, respectively. In pts with polyps, synchronous or previous resected colon cancer were found in 8.5% and 4.9%, respectively. Polyp localization: Rectum: 19%; sigmoid colon: 46%; descending colon: 10%; transverse colon: 9%; ascending colon: 10%; caecum: 6%. Histological data in relation to size (1689 polyps). Size N Tubular Tubulo-villous Villous < 0.5 cm 22% 16% 5% 0.6% < 1 cm 37% 21% 16% 0.5% 1–2 cm 23% 8% 15% 0.6% > 2 cm 17% 6% 11% 2.3% Total 100% 49% 47% 4% Multiple colon polyps: 4% of pts had multiple (> 10) polyps. Polyp size: 51% < 0.5 cm, 44% = 0.5–1 cm, 5% > 1 cm. Localization: Rectum: 17%, sigmoid c.: 31%, descending c.: 13%, transverse c.: 16%, ascending c.: 13%, caecum: 9%. *Conclusion:* Careful histological analysis showed villous adenomatous tissue in approximately 50% of all polyps. Presence of villous tissue in polyps was closely correlated with polyp size. Approximately 2/3 of all polyps were in the rectum or sigma. Oncology, specific: Colon, rectum Oncology, general: Screening, prevention } "Villous Adenomatous Tissue in Colorectal Polyps"

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## OT45 1048 Effectiveness of Long-Term Colonoscopic Screening in Families with Hereditary Nonpolyposis Colorectal Cancer

\*M. Jablonsk\ 'e1, A. Chlumsk\ 'e1

IVth Medical Clinic, Charles University, Prague, Czech Republic *Background.* Identification of families with hereditary nonpolyposis colorectal cancer (HNPCC-Lynch-syndrome) provides an opportunity of early detection or even prevention of colorectal cancer (CRC). *The aim of this study* was to evaluate the effectiveness of long-term screening of such cases during a 15 year period. *Methods:* 364 asymptomatic HNPCC family members entered periodic colonoscopic surveillance at 1–1.5 year intervals; results and survival rates were compared with 237 symptomatic unscreened HNPCC members. *Results:* In the first group initial total colonoscopy revealed CRC in 16.7% and adenomas in 33.5%; on the whole — periodic colonoscopies included — CRC in 21% and adenomas in 43.5%. In the second group CRC was found in 61.5% and adenomas in 30.5%. In the first group CRC was classified as DUKES A in 53%, B in 29%, C in 18% and D in 0%; in the second group A in 21%, B in 46%, C in 18% and D in 15%. In the first group no death from CRC occurred during the follow-up; in the second group survival rates were 65% after 5, 52% after 10 and 30% after 15 years. *Summary:* Colonoscopic results and survival rates in CRC in HNPCC were clearly more favorable in an asymptomatic screened than in a symptomatic unscreened group. *Conclusions:* As long as genetic testing is not available colonoscopic surveillance of HNPCC members appears fully justified to achieve improved CRC control including longer survival rates. Oncology, general: Screening, prevention Oncology, specific: Colon, rectum } "Effectiveness of Long-Term Colonoscopic Screening in Families with Hereditary Nonpolyposis Colorectal Cancer"

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## OT45 1050 Incidence and Recurrence Rates of Colorectal Adenomas in First-Degree Relatives of Colon Cancer Patients

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Cattedra di Gastroenterologia, Universit'e0 di Bologna, Italy *Background:* we have shown that asymptomatic patients with one first-degree relative with colorectal cancer have an increased risk of developing adenomatous polyps, a significantly higher frequency of a proximal polyp location and a greater frequency of severely dysplastic lesions (Gastroenterology 1995; 109: 783–788). *Purpose:* the aim of the study was to compare the recurrence rate and the incidence rate of colorectal adenomas in patients with only one first-degree relative with colorectal cancer, and patients without such a family history. *Methods:* we evaluated 157 patients who underwent follow-up colonoscopy 3 years after the first examination. Patients were grouped on having either a positive family history defined by the presence of only one first-degree relative with colon cancer (no. 68; 42 males; mean age – SE: 59.7 – 1.4) or on having completely negative cancer family history (no. 89; 58 males; mean age – SE: 57.5 – 1.2). Both groups were composed of subjects with one or more adenomatous polyps at the first examination (evaluable for the recurrence rate) and subjects with a normal first examination (evaluable for the incidence rate). *Results:* three year follow-up colonoscopy showed no difference in the recurrence rate of adenomas, 28.6% (12/42) in the group with positive family history and 33.8% (26/77) in the group without family history (Chi-square test:  $p = ns$ ). As regarding the incidence rate, 26.9% (7/26) of patients with positive family history who had no adenomas at the first examination developed a new lesion, while in the group with no family history, the incidence rate was 0% (0/12) (Fisher exact test 1 tail:  $p = 0.05$ ). *Conclusions:* over a three year period, the recurrence rate of adenomatous polyps is similar in persons with and without positive family history of colorectal cancer; differently, the presence of such a history determines a significant increase in the incidence of new adenomas. Oncology, general: Screening, prevention Oncology, specific: Colon, rectum Endoscopy, specific: Colon, rectum } "Incidence and Recurrence Rates of Colorectal Adenomas in First-Degree Relatives of Colon Cancer Patients"

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## OT46 1052 Photodynamic Therapy of Stage IV Cholangiocellular Carcinoma

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<sup>1</sup> Lasercenter Steglitz, Berlin, Germany *Background:* Short term prognosis for palliative interventions in advanced cholangiocellular carcinoma (CCC) is very poor. The *Aim* of this study was to evaluate the efficacy of photodynamic therapy in stage IV, Bismuth III–IV CCC. Primary outcome parameter was reduction of cholestasis, secondary parameters were Quality of Life (Karnofsky index) and survival time. *Methods:* Thirteen patients (age: median 54 (40–74), 8 female, 5 male) with stage IV CCC (Bismuth III–IV) underwent biliary drainage by endoscopic double-endoprosthesis (left/right hepatic biliary duct). If cholestasis was not reduced effectively (bilirubin decrease > 50% within 7 days), patients underwent photodynamic therapy (PDT). Photofrin<sup>®</sup> (Quadra-Logica, Amsterdam, Holland) was infused intravenously (2 mg/kg bodyweight) and intraluminal photoactivation was performed by Argon dye laser via cholangioscopy (wavelength 630 nm, 400–500 mWatt/cm<sup>2</sup>). 3 Patients with remaining macroscopic tumor by control-cholangioscopy (after 8 weeks) received retreatment. *Results:* Endoprosthesis were implanted in all patients without technical problems. Bilirubin decreased sufficiently in 4 patients (31%) after stenting (from 433 – 99 to 144 – 42, p = 0.03), however Karnofsky index remained unchanged (52.5 – 2.5 and 42.5 – 11, p = 0.69). In these patients 30 day survival was 25% and 11 month survival 0%. In the remaining 9 patients with unsuccessful biliary drainage, PDT reduced bilirubin serum levels (Table) with no significant increase during monthly follow ups. Before stent After stent After PDT PBilirubin (mmol/l) 313 – 66.6 317 – 72.1 108 – 34.5 0.004 Karnofsky index 41.1 – 8.4 32.2 – 8.1 68.8 – 6.1 0.008 In contrast to stenting Karnofsky index improved significantly after PDT (Table). The 30 day survival after PDT was 100% and 11 month survival 78%. *Conclusion:* In patients with unsuccessful endoscopic biliary drainage due to disseminated CCC, photodynamic therapy results in a dramatic reduction of cholestasis and an increase in life quality. Survival in patients treated with photodynamic therapy appears to be prolonged in comparison with patients successfully stented. Oncology, specific: Liver, biliary Endoscopy, general: Instrumentation, therapy }" "Photodynamic Therapy of Stage IV Cholangiocellular Carcinoma"

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## OT46 1053 Is the Preoperative Diagnosis of a Benign Ampulloma Safe?

\*A. Sauvanet, O. Chapuis, Ph. Ponsot, P. Hammel, P. Bernades, J. Belghiti

Fédération d'Hépatogastroentérologie Médico-Chirurgicale, Hospital Beaujon, University Paris VII, Clichy, France. Malignant ampullomas can be curatively treated by pancreaticoduodenectomy (PD). A local excision can be proposed in case of benign ampulloma. The aim of this study was to evaluate the value of side-viewing duodenoscopy (SVD) with biopsies, endoscopic sphincterotomy (ES), and endoscopic ultrasonography (EUS) for preoperative diagnosis of benign and malignant ampullomas. *Material et methods:* From October 1989 to September 1995, 26 patients with ampulloma were explored preoperatively by SVD — including ES in 9 cases — and EUS. The papilla of Vater was always explored at SVD and forceps biopsies were performed in all patients except one with a typical malignant tumour. EUS evaluated the T stage of the TNM classification in all patients except six because of a previous ES (n = 5) and difficulty to localize the papilla (n = 1). The N stage of the TNM classification was evaluated by EUS in all cases. A curative resection was always performed: 2 local excisions of the ampulla (one adenoma with low-grade dysplasia and one xanthoma), and 24 PD for 20 carcinomas (including 9 (45%) N1) and 4 benign lesions. *Results:* At SVD, papilla was both ulcerated and protruding into the duodenal lumen in 10 cases, prominent and smooth in 15 cases, and normal in one case. Histologic examination of the 25 biopsies revealed malignancy in 10 cases (always confirmed by pathological examination of the resected specimen) and a benign lesion in 15 cases (resected specimen: 6 benign lesions and 9 carcinomas), among the 9 biopsies performed after ES, two only revealed a carcinoma (resected specimen: 4 benign lesions and 5 carcinomas) with an accuracy rate of 64% globally and 66% after ES. At EUS, 13 lesions were presumed limited to ampulla (benign lesion or stages T in situ and T1) but 4 out of these 13 were classified T2 or more histologically; among the 7 tumours classified T2 or more by EUS, one was histologically limited to ampulla. The accuracy rate of EUS for the T stage was 75%. At EUS, lymph nodes were presumed benign (N0) in 21 cases (histology: N0 in 15 cases and N1 in 6 cases) and metastatic (N1) in 5 cases (histology: N0 in 2 cases and N1 in 3 cases), with an accuracy rate of 69%. All endoscopic explorations were compatible with a benign lesion in 11 patients; histologically, 6 patients out of these 11 had a carcinoma including one with a T1N1 and two with a T2N0 tumour. *Conclusions:* In patients with ampulloma tumour, SVD with biopsies even after ES, and EUS are not accurate enough to make sure preoperatively that the tumour is benign. Therefore a local resection cannot be safely indicated. Oncology, specific: Liver, biliary } "Is the Preoperative Diagnosis of a Benign Ampulloma Safe?"

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## OT47 1060 Expression of Bombesin/Gastrin Releasing Peptide (BBS/GRP) Receptor in Lovo Clones with Different Metastasising Capacities

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<sup>2</sup> Molecular Biology Laboratory, Hospital Edouard Herriot, Lyon, France Gastrin releasing peptide is expressed in about 30% of cell lines established from colon carcinoma and is potentially involved in the stimulation of neoplastic growth. *Aim:* To compare the expression of the bombesin/GRP-receptor (GRP-R) in clone E2, with low metastatic potential, and clone C5, rapidly metastasising in new-born immunodeficient rats [1], from the human colon adenocarcinoma Lovo cell line, and in Caco-2 cells. *Methods:* Pharmacological characterisation of cell surface receptors was achieved by measuring the specific binding of <sup>125</sup>I-Tyr<sup>4</sup> bombesin (BBS). Activation of Phospholipase C by BBS was checked by (H3) inositol phosphate production. The level of GRP-R mRNA was compared by competitive amplification of a 570 bp sequence of the GRP-R cDNA (30 cycles, annealing temp. 53°C). A competitive template consisting of this PCR product with a 110 bp deletion was constructed after cloning in Bluescript vector. After reverse-transcription, the GRP-R cDNA was co-amplified with several dilutions of the competitive template. The PCR product was analysed on agarose gel and after Southern blotting. Whether BBS at least at high concentration (10 nM) stimulated cell proliferation was tested by cell count and <sup>3</sup>H-Thymidine incorporation. *Results:* Binding studies showed a single high affinity receptor (Kd = 0.45 nM) on clones E2 and C5 of the Lovo cell line, that however differed as to the estimated number of receptors (E2: 2600, C5: 560 per cell). As tested on E2 cells this receptor was a GRP-preferring (Ki = 0.49 nM for BBS, versus 250 nM for neuromedin B), and BBS had a weak but significant effect on (H3) inositol phosphate production (30% at 10 nM BBS). Caco-2 cells, whether undifferentiated or differentiated, did not bind <sup>125</sup>I-Tyr<sup>4</sup> BBS to any detectable extent. At competitive RT-PCR, the GRP-R mRNA levels in E2 cells were more than 10 fold higher than in C5 cells, and 100 times higher than in Caco 2 cells. The tested dose of BBS did not increase the growth rate of clone E2 nor of clone C5. *Conclusion:* The present study confirms that the bombesin receptor is expressed in Lovo cell line. We showed that this receptor is a GRP-preferring one. There is a fair consistency in Lovo and Caco-2 cells between GRP-R mRNA levels and the number of receptors per cell. However, the signification of a different GRP-R expression in the two Lovo clones in regard to their respective metastasising capacities remains to be elucidated.

Reference: Remy et al. Differentiation. 1993. 5. 191–200. Oncology, general: Molecular biology, genetics Hormones and receptors: Receptor characterization Hormones and receptors: Molecular biology } "Expression of Bombesin/Gastrin Releasing Peptide (BBS/GRP) Receptor in Lovo Clones with Different Metastasising Capacities"

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## OT51 1066 Octereotide Infusion Plus Emergency Sclerotherapy Versus Sclerotherapy Alone for the Control of Bleeding Oesophageal Varices: A Prospective Randomized Clinical Trial

\*G. Shiha, S. Sayed, M. Hamid, M. Farag, F> Azzam, H. Assalany

Internal Medicine Department, Almansoura Faculty of Medicine, Egypt Sclerotherapy is the gold standard for treatment of bleeding varices. Octereotide infusion is found to be effective in control of actively bleeding oesophageal varices. *The aim* of this work is to evaluate the use of the combination of emergent sclerotherapy and octereotide infusion in the control of bleeding from oesophageal varices in comparison to sclerotherapy alone. *Methods*: Cirrhotic patients presented to our unit with acute variceal bleeding for a period of six months (189 patients) were randomly allocated to receive either emergency sclerotherapy alone (Group I; 96 patients) or emergency sclerotherapy plus continuous infusion of octereotide 257 \b5g/hr for 48 hrs (Group II; 93 patients). *Results*: No statistically significant difference between the 2 groups as regard age, sex, etiology of cirrhosis and modified Child's scoring. Rebleeding was significantly less in group II (4.1%) when compared to group I (25%)  $P < 0.001$ ; and the transfusion requirements was significantly less in group II ( $P < 0.001$ ); but there was no significant difference in mortality due to bleeding ( $P > 0.05$ ). No major side effects were reported due to octereotide infusion. *Conclusion*: This study provides a support for the use of a continuous infusion of octereotide (25 \b5g/hr) in combination with emergency sclerotherapy for a better control of bleeding oesophageal varices. Endoscopy, general: GI bleeding Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Octereotide Infusion Plus Emergency Sclerotherapy Versus Sclerotherapy Alone for the Control of Bleeding Oesophageal Varices: A Prospective Randomized Clinical Trial"

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## OT51 1067 Comparison of Ring Elasticity and Ligation Volume of Different Variceal Single and Multiple Band Ligators Using a Multicylindrical Stretching Apparatus in a Porcine Esophagus Model in vitro

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<sup>2</sup> Inst. of Biomed, Statistics, Friedrich-Alexander-University, Erlangen, Germany Recently a new multiple-band ligator ("Speedband"; SpB; Microvasive, USA) was introduced which allows the consecutive application of up to 5 bands. In our first clinical experiences many of the Speedband bands were lost within 24 hours despite correct initial positioning (DDW'96#186). We therefore compared band elasticity and ligation volume of three esophageal and one hemorrhoidal ligator in material tests and on specially prepared porcine esophagi in vitro. *Mat & Meth:* The Bard Stiegman & Goff set (BA; USA), the Pauldrach OVL set (PD; Germany), the SpB Multiligator and a conventional hemorrhoidal set (R. Wolf, Germany) plus standard O-bands (HE; Hemolastic, Switzerland) were investigated. For elasticity measurements the different bands were mounted on a special apparatus composed of two hemi-cylinder shells with an o.a transversal diam. of 3/4/5/6/7/8/9/10 mm. The min. force [N] required to widen the bands at the chosen diameter was determined electronically for 5 bands/setting. To simulate the ligation situation "in vivo" 8 slaughterhouse-fresh porcine esophagi (1–2.5 h sacr. time) were opened longitudinally and submucosal depots of 2–3 ml saline were injected in order to lift the mucosa layer. This permitted suction of the mucosa and underlying fluid into the ligation cylinder (0.6 bars evac.). The volume of the thus created "ligation mushrooms" (n = 5/set) was determ. by means of water displacement (princ. of Archimedes; – 0.05 ml). *Results:* The vol. achieved with PD (m 0.61 – 0.07 ml) were sign. smaller (p < 0.01) than those of HE, SpB and BA (m HE = 0.88 – 0.03 ml; SpB = 0.94 – 0.07, BA = 0.91 – 0.07). The vol. for HE, SpB and BA were not sign. different. The mean inner \f8 of the unstretched bands were 1.81 mm (PD), 1.82 mm (BA), 2.50 mm (SpB) and 2.35 mm (HE), respectively, dir. after release. The radial force of the bands was: HE > PD > BA {\b3} SpB. ANOVA variance analysis showed sign. differences for HE and PA bands (p > 0.001; p < 0.05) compared to the SpB and BA bands (SpB to BA overall n.s.). The median stretching force [N] determined for a 3/6/9 mm inner band \d8 was: PD 1.40/3.62/5.05; HE 2.38/5.34/7.5; SpB 0.57/2.38/3.71; BA 0.86/2.43/3.56). The ligation volume of PD (m 0.60 – 0.07 ml) was sign. smaller (p < 0.01) to HE, SpB and BA (median HE 0.90, SpB 0.95, BA 0.95 ml; n.s.) *Conclusions:* Ligation devices can differ substantially in band characteristics and cylinder vol.. A larger inner \d8 plus a low radial retraction force may be the cause of an early loss of part of the SpB bands. However to date no negative influence of this phenomenon on acute complications or eradication rate could be observed. To optimize band and cylinder characteristics systematic investigations in animal models appear desirable and are presently in prep. Endoscopy, specific: Oesophagus/Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy } "Comparison of Ring Elasticity and Ligation Volume of Different Variceal Single and Multiple Band Ligators Using a Multicylindrical Stretching Apparatus in a Porcine Esophagus Model in vitro"

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## OT51 1069 Randomized, Prospective Comparison of Sclerotherapy Vs. Cyanoacrylate for Esophageal Variceal Bleeding in Child-Pugh C Cirrhotic Patients

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**Purpose:** Variceal bleeding is a high-mortality condition in Child-Pugh C, non-alcoholic cirrhotic patients. The tissue adhesive, n-butyl-2-cyanoacrylate, promotes immediate obliteration of esophageal varix, independently of coagulation or healing capabilities. Its higher performance when compared to sclerotherapy could decrease in-hospital mortality.

**Method:** Thirty non-alcoholic cirrhotic Child-Pugh C patients were admitted with a first episode of variceal hemorrhage. They were randomized to receive sclerotherapy with 3% ethanolamin oleate (Group I-16 pts) or injection with n-butyl-2-cyanoacrylate (Group II-14 pts). After bleeding interruption, all patients were submitted to weekly sessions of conventional sclerotherapy until variceal eradication. The recidives of variceal bleeding were managed following the randomization: sclerotherapy for Group I and cyanoacrylate for Group II pts. Pts were managed by ICU MDs who were blinded to endoscopic therapy.

**Results:** The groups were homogeneous in entry criteria: mean age of 49.4 years, 67% viral liver disease, mean Child-Pugh score of 11.4. 83.3% of the pts. presented with moderate or severe hemorrhage and received a mean of 3.1 URBC.

Group I	Group II	p value	
Rebleeding (%)	50	14.3	0.047
Rebleeding (episode/pt)	0.81	– 1.11	0.14
Esophageal ulcer (%)	37.5	0	0.02
Balloon tamponade (%)	31.2	0	0.04
In-hospital mortality (%)	75	35.7	0.040

**Conclusions:** The treatment with tissue adhesive changed the in-hospital course of variceal bleeding in Child-Pugh C non-alcoholic Cirrhotic patients when compared to conventional sclerotherapy. Liver and bile ducts, 1: Cirrhosis: portal hypertension

Endoscopy, general: GI bleeding } "Randomized, Prospective Comparison of Sclerotherapy Vs. Cyanoacrylate for Esophageal Variceal Bleeding in Child-Pugh C Cirrhotic Patients"

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## OT56 1081 Post-Operative Bile Duct Strictures (BDS): Long-Term Results after Endoscopic Treatment

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The endoscopic treatment of BDS is safe and can provide good immediate drainage. *Aim:* To assess long-term results after endoscopic treatment of post operative BDS. *Patients and methods:* Follow-up data (biliary symptoms, Alk Phosphatases and bilirubin serum levels) were obtained in all of 35 consecutive cases of post operative BDS (male: 20, age: 57 – 16 years) where the absence of further endoscopic treatment had been recommended because of a calibration of the BDS estimated to be sufficient. BDS, mainly attributable to cholecystectomy (N = 22) and OLTX (N = 6) were located in the main bile duct (N = 32), hilum (N = 1), left bile duct (N = 1) and hepaticojejunostomy (N = 1). The management had consisted of dilation, alone (N = 2), as well as associated with insertion of Wallstent (N = 6) or plastic stents (N = 29, for a period of 6.9 – 5.1 months). All patients with abnormal follow-up data underwent ERCP in order to confirm a recurrent BDS. *Results:* Probability of remaining free of BDS (%)

Compared to plastic stents, Wallstents were associated with a higher incidence of BDS recurrence 6 months after insertion of Wallstent or plastic stent removal ( $p < 0.01$ ). In this group, stenoses eventually recurred in all but 1 patient (83% of cases) and required hepaticojejunostomy (N = 2), continuous plastic stenting (N = 2) or repeated diathermic cleaning (N = 1). In contrast, recurrences after treatment with dilation alone or plastic stents were detected in 5 cases (17%) only and were successfully managed by a repeated calibration with plastic stents. *Conclusion:* These results show that dilation and plastic stenting are safe and efficient treatments of BDS on a long-term basis. Wallstents are followed by rapid restenosis and should be considered as contraindicated in this indication. If a stricture recurs after a first calibration procedure with plastic stents, a second similar procedure is indicated. } "Post-Operative Bile Duct Strictures (BDS): Long-Term Results after Endoscopic Treatment"

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## OT56 1082 Endoscopic Palliation of Malignant Biliary Strictures: Results of a Prospective Randomized Study

\*F. Prat, O. Chapat, T. Ponchon, J. Fritsch, A.D. Choury, G. Pelletier, C. Buffet

Bicêtre and Lyon, France The endoscopic approach to palliation of inoperable malignant biliary strictures has proven to be the option of choice. Although self-expanding metallic stents remain patent for a longer period than plastic stents, the optimal strategy is still controversial because of the high cost of metallic stents and the short life expectancy of candidates to palliation. 101 patients (mean age 72.5 – 12.9), OMS > 3, with a common bile duct stricture were included (pancreatic head cancer = 65 cases, cholangiocarcinoma = 21, ampulloma = 3, metastatic lymph nodes = 12). After randomization, patients received either an 11.5 F polyethylene stent, to be exchanged only in case of dysfunction (group 1, 33 patients), an 11.5 F stent to be exchanged every 3 months (group 2, 34 patients) or a metallic Wallstent® prosthesis (group 3, 34 patients). The three groups were comparable. Endoscopic procedures succeeded in 100% of cases. Procedure-related morbidity was 11.9% and mortality 2.9%. Complete relief of jaundice was obtained in all cases. Bilirubinemia after 48 hours (37.2 – 21.7% decrease) did not differ between groups. The patients were followed for a mean of 166 days (median 143; range 0–596 days); at the present time, 80 patients (80.2%) are dead. The global survivals were not different between groups 1, 2 and 3. However, the complication-free survival of groups 2 (systematic exchange) and 3 (metallic stents) was longer than that of group 1 ( $p = 0.07$  and  $0.06$  respectively), but groups 2 and 3 were not different ( $p = 0.61$ ). Cumulated hospital stays were 7.5 – 1.7, 13.1 – 3, and 6.4 – 1.7 days (groups 1, 2 and 3 respectively) —  $p = 0.05$  —. The cost-effectiveness analysis shows that metallic stents are cost-effective in patients surviving more than 6 months. In patients surviving 6 months or less, a plastic stent with one systematic exchange is cost-effective. *Conclusions:* The systematic quarterly exchange of plastic stents and the insertion of self-expandable metallic stents are two valuable alternatives to increase the complication-free survival of patients with inoperable malignant biliary strictures. The latter is cost-effective only in patients with the longest life expectancy. Oncology, specific: Liver, biliary Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary } "Endoscopic Palliation of Malignant Biliary Strictures: Results of a Prospective Randomized Study"

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## OT56 1083 Placement of Stents above or across the Sphincter of Oddi — A Randomised Controlled Trial

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The Department of Medical Gastroenterology, S, Odense University Hospital, Denmark

**Background:** Stents placed above the sphincter of Oddi (SO) in dogs seem to have a longer patency than stents placed across (ref. 1). **Aim:** To compare stent survival time in human patients with malignant biliary obstruction for stents placed across versus above the SO. **Methods:** 36 patients (13 male) with malignant biliary obstruction were randomised to have the stent placed endoscopically either across the SO (group A) or above the SO (group B). No sphincterotomy was performed. Straight 10 FG stents were used. In group B 9 patients had the distal flap of the stent removed before placement. The patients were evaluated clinically and biochemically every month till malfunction of the stent or death. **Results:** Across SO (A) Above SO (B) Total number (male) 20 (5) 16 (8) 50% patient survival, Kaplan-Meier. 88 days 139 days (25–75% percentiles) (41–283) (71–347) 50% stent survival, Kaplan-Meier. 89 days 139 days (25–75% percentiles) (53–126) (61–320) Number of patients with stent exchange 8 9 (dislocated/occluded) (5/3) (8/1) Median time for stent exchange 71 days 91 days (25–75% percentiles) (21–119) (27–230) **Conclusion:** We found no significant differences in survival time or complication rate between the groups. Stents placed above the SO might survive longer than stents placed across the SO, if the tendency of stent dislocation could be resolved.

Reference: 1: GUT 1991: A1232. Goghegan JG, Branch MS et al. Endoscopy, specific: Biliary }" "Placement of Stents above or across the Sphincter of Oddi / A Randomised Controlled Trial"

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## OT56 1084 Clinical Laserlithotripsy of Difficult Bile Duct Stones by Means of a Rhodamin-6 G Dye Laser with an Automatic Optical Stone/Tissue Detection System (oSTDS) — Results in 49 Patients

\*J. Hochberger, A. May, J. Bayer, S. M\fhldorfer, R. Stein, W.E. Fleig, E.G. Hahn, C. Ell

Department of Medicine I, Friedrich-Alexander-University, Erlangen, Germany Laserlithotripsy of difficult common bile duct stones (CBDS) has become a commonly accepted endoscopic treatment modality. The procedure is usually carried out under direct endoscopic vision due to the potential risk of bile duct injury in "blind" RX-guided laser application. In the following we report on our clinical results using a new laser triptor with integrated optical automat. stone/tissue detection system (oSTDS). *Patients, Mat. & Methods:* From 1st Sept. 1991 to 1st Jan. 1996 49 pts [33 = f, 16 = m; age: 71 – 13 y (39–96 y)] with giant or impacted CBDS [n stones > 1 cm: 3.0 – 1.0 (1–5 stones) with a size 2.2 – 1.0 cm (1.0–6.0 cm);] were treated on the endoscopic retrograde route using a rhodamine (Rh-6G) dye laser (595 nm, 2.5 \b5s, 250 \b5m fiber, Telemet Corp./C. Baasel Lasertech., D) with integrated oSTDS. In case of tissue contact oSTDS cuts off the laser pulse 190 ns after its beginning (8% of the total pulse energy delivered). The first 10 pts. (20%) were treated under cholangioscopic vision (M&B-scope), 28 pts. (57%) merely under oSTDS/intermitt. RX control via standard duodenoscopes and 7F catheters, 8 pts. (16%) using both techniques. *Results:* Laser-induced fragmentation could be achieved in all pts. (100%). 42/49 pts. (86%) became completely free of stones at the end of the treatment. 1.8 – 1.0 (1–4) laserlithotripsy sessions per pat. were performed. In one fully anticoagulated pat. a relevant hemobilia (Hb 13.5 g% {} 11.0 g%) and transient cholangitis occurred as well as 2 episodes of cholangitis in two further pats. as only relevant complications. They were successfully treated conservatively. *Conclusion:* Laserlithotripsy using the described Rh-6G dye laser with automatic optical stone/tissue detection system appears safe and effective and allows "blind" fragmentation of difficult CBDS via standard duodenoscopes and catheters. Endoscopy, specific: Biliary Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, general: Instrumentation, therapy } "Clinical Laserlithotripsy of Difficult Bile Duct Stones by Means of a Rhodamin-6 G Dye Laser with an Automatic Optical Stone/Tissue Detection System (oSTDS) / Results in 49 Patients"

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**OT66 1096A New Technic for Endoscopic Ultrasound-Guided Biopsy Using the Biopsy Needle – Vilmann Type. Results in 115 Patients M. Giovannini, G. Monges, J.F. Seitz**

Digestiv Oncology Unit, Paoli-Calmettes Institute, 232 bd St-Marguerite, 13273 Marseilles Cedex 9-France

*The aim* of this study was to evaluate 1) a new type of needle (Vilmann type) for endoscopic ultrasound (EUS) guided biopsy, 2) a new technic of EUS biopsy using a continuous vacuum applied to the needle using a 20 ml syringe with an auto-locked system and to compare the results of cytology and micro-histology performed for each lesion punctured. *Patients and Methods:* From august 1994 to april 1996, 115 patients (88 men and 27 women) with a mean age of 62 years (range: 24–82 years) underwent EUS with guided biopsy at our institution. The indications were: diagnosis of a pancreatic mass in 40 cases, mediastinal lymph nodes or masses in 23 cases, cervical lymph nodes in 14 cases, celiac lymph nodes in 17 cases, retropancreatic lymph nodes in 11 cases and peri-rectal lymph nodes in 10 cases. The EUS endoscop used are the FG 32UA and the EG 36-30U manufactured by Pentax. The biopsy needle (GIP-Medizin) consist of a biopsy handle with a needle with stilet and spiral sheath. The needle is a 170 cm long steel needle and 0.8 mm outer diameter. Two needle pass were necessary to obtain 1 adequate specimen for cytology and 1 adequate specimen for histologic examination. For the cytology, the material was smared onto a glass slide and stained according the MGG method. For the histologic examination, the core was placed in formaldehyde and fixed in paraffin. *Results.* Neither hemmorrhage nor any other complication was observed during this study. Patient tolerance was excellent and the insertion of the needle into the lesion to be biopsed was always successful. An adequate specimen could not be obtained in 6 cases (5.1%). The sensitivity and specificity of the diagnosis of malignancy were for the cytology 70.0% and 100%, for the micro-histology 81.4% ( $p < 0.05$ ) and 100% and for the combination cytology + histology 87.6% and 100%. For the pancreatic tumor, the sensitivity and specificity of the diagnosis of cancer were for the cytology 65.0% and 100%, for the micro-histology 77.5%) and 100% and for the combination cytology + histology 82.5% ( $p < 0.05$ ) and 100%. For the lymph nodes, the sensitivity and specificity of the diagnosis of malignancy were for the cytology 72.6% and 100%, for the micro-histology 83.5%) and 100% and for the combination cytology + histology 90.4% ( $p < 0.05$ ) and 100%. *Conclusion:* the results of EUS biopsy using the new Vilmann-needle with continuous vacuum system are superior than these obtained with the first prototype of needle. The results of this study suggest that it was necessary to combine cytologic and histologic examination for obtain a sensitivity about 87%. Echoendosonography: Echoendoscopy }" "A New Technic for Endoscopic Ultrasound-Guided Biopsy Using the Biopsy Needle – Vilmann Type. Results in 115 Patients"

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## OT66 1097 Accuracy of Endoscopic Ultrasonography (EUS) in the Staging of Gastric Malt Lymphoma

\*Ph. Jacob, B. Pujol, B. Napoleon, O. Keriven-Souquet, J.C. Souquet

Department of Digestive Diseases, Hospital E. Herriot, Lyon, France EUS has been considered as an useful investigation for the preoperative staging of gastric lymphoma. Primary gastric lymphoma of the Mucosa-Associated-Lymphoid-Tissue (MALT), when associated with *Helicobacter pylori* (Hp) could be treated with anti-Hp therapy. However, this treatment is often limited to low grade lymphoma and its efficacy is unknown in case of transmural gastric invasion and/or lymph node extension. Therefore, the aim of this study was to compare the results of EUS to the pathology of resection specimens after gastrectomy in the specific subgroup of gastric MALT lymphoma. *Methods:* From 1990 to 1995, EUS was performed with an Olympus echoendoscope in 16 patients (8 men, 8 women; mean age, 54 years; range, 37–86 years) with confirmed gastric MALT lymphoma. In 15 cases, the diagnosis was made by endoscopic biopsies with immunohistopathologic studies before EUS. In the last case, lymphoma was only suspected before EUS. The findings at endoscopy showed large or multiple small ulcers in 10 cases and enlarged gastric folds in 6 cases. Gastrectomy was total in 10 patients and subtotal in 6. The mean interval between EUS and surgery was 32 days (range: 2–137 days). *Results:* EUS in evaluating the gastric wall was normal in 4 cases, found a thickening of the second layer and the third submucosal layer respectively in 8 and 3 cases, a transmural infiltration with complete disappearance of the layer structure in 1 case. Histopathologic examination of resection specimens showed: 4 cases with serosal involvement by MALT lymphoma with low (n = 3) and high grade malignancy (n = 1) and 12 cases with only mucosa and submucosa involvement. The depth of tumor infiltration was correctly assessed by EUS in 81.3% of cases. EUS underestimated tumor infiltration in 3 patients with serosal involvement by low grade gastric lymphoma but its staging was accurate for the high grade lymphoma. Histopathologic examination showed involved lymph nodes located in the perigastric area in 5 cases. EUS was 85% accurate in detecting lymph nodes invasion, but 2 false negatives were encountered. *Conclusions:* EUS had a good efficacy in staging gastric MALT lymphoma (more than 80% for parietal invasion and lymph node involvement). However, patients with low grade gastric MALT lymphoma, can present a transmural gastric infiltration with lymph nodes involvement. In this form, EUS can understage the lymphoma. Thus, EUS improves lymphoma evaluation, but careful follow-up will remain mandatory. Echoendosonography: Echoendoscopy Oncology, specific: Stomach } "Accuracy of Endoscopic Ultrasonography (EUS) in the Staging of Gastric Malt Lymphoma"

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## OT66 1098 Transrectal Ultrasound in the Diagnosis and Management of Inflammatory Bowel Disease

\*\dc. Dagi, H. \d6ver, A. Tezel, \c7. Baysal, A. \dclker, G. Temu\`e7in

Y\`fcksek Ihtisas Hospital, Ankara-Turkey The value of transrectal ultrasonography (TRUS) in the assessment of IBD was determined. TRUS was found to be useful for estimation of the histological changes of IBD. TRUS examinations were performed to study 30 healthy individual and 84 patients with IBD, including 60 ulcerative colitis (UC), 24 Crohn's disease (CD). A rigid linear endorectal probe was used to examine the rectal wall. In healthy individuals, the rectal wall showed five layers with a total diameter of maximum 3 mm (mean: 2.6, range: 2.2–3). The patients with quiescent UC, active UC and healthy control subjects revealed significant differences in total rectal wall thickness, submucosal and mucosal thicknesses. In active UC, the average rectal wall thickness was found 6.17 mm (range 5.1–7.5). In quiescent UC, it was 4.02 mm (range 2.4–5.5). Besides these findings in cases with active UC irregularity of the submucosa and an increase in the vascularity diagnosed by doppler US, was observed. The cases with CD localized to ileum revealed normal TRUS findings. But all our cases with ileocolitis and colitis (including the cases with normal rectoscopic findings) showed transmural inflammation findings. 5 of these cases during the follow-up period had undergone colectomy. Mucosal inflammation was noticed in 4 cases and transmural inflammation in 1 case. The histological examination of the colectomy specimens was in accordance with our TRUS findings. As a conclusion; TRUS can be used as an additional method in the differential diagnosis of UC and CD as well as the evaluation of the active UC. Intestinal disorders: IBD diagnosis, monitoring Echoendosonography: Therapy } "Transrectal Ultrasound in the Diagnosis and Management of Inflammatory Bowel Disease"

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**OT66 10993-Dimensional Endoscopic Ultrasonography (3D-EUS) for Upper Gastrointestinal Diseases**M. Kida, M. Watanabe, S. Sugano, Y. Yamada, T. Sakaguchi, M. Noto, M. Oh-Ida, K. Saigenji

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Japan  
*Introduction:* EUS has opened up a new era and played an important role in gastroenterological imaging diagnosis. Now we have performed new prototype 3D-EUS made by Olympus in evaluating UGI diseases and report the usefulness of 3D-EUS.  
*Methods:* From November 1994 to now, we have performed 3D-EUS in 33 patients with 13 early gastric cancer, 8 advanced gastric cancer, 5 submucosal tumor (SMT), 4 post endoscopic resection (EMR), 2 esophageal cancer, and others respectively. The specification of 3D-EUS (UM-3R3D, 2R3D) are as follows; the maximum size is 3.4 mm in diameter, the frequency is 20 (3R3D) or 12 (2R3D) MHz, automatic mechanical spiral scanning is longitudinally carried out within 40 or 20 or 8 mm like helical CT.  
*Result:* After scanning, both radial and linear cross sectional image can be obtained at the same time by computer. The image quality of 3D-EUS is nearly of the same to ultrasonic probe (UM-3R, 2R). Three dimensional presentation that is reconstructed by the optimal radial and linear cross sectional image with the surface image of GI tract like normal endoscopy can be possible. It is also possible to calculate the volume of lesion by tracing the lesion on each radial image. The diagnostic accuracy of 3D-EUS for evaluating the depth of gastric cancer invasion is 86.7% (13/15 resected cases).  
*Conclusions:* Using 3D-EUS, the most important image can be evaluated after scanning, therefore it seems that 3D-EUS can become more accurate and easy, compare to EUS. And 3D-EUS will become the interface between endoscopist and endosonographer. Echoendosonography: Echoendoscopy  
Endoscopy, specific: Stomach, duodenum  
Endoscopy, specific: Oesophagus } "3-Dimensional Endoscopic Ultrasonography (3D-EUS) for Upper Gastrointestinal Diseases"

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## OT66 1100 Modalities for Three-Dimensional Endoscopic and Laparoscopic Ultrasonography: In vitro and in vivo Evaluation

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<sup>1</sup> Dep. of Surgery, Eastern Hospital, University of Gothenburg, Gothenburg, Sweden

Dep. of Medicine A, Haukeland Hospital, University of Bergen, Bergen, Norway *Purpose:* To evaluate different modalities for three-dimensional (3D) reconstructions based on ultrasound (US) images obtained during endoscopic (EUS) or laparoscopic (LUS) ultrasonography. *Methods:* We used cardiac transesophageal multiplane (MP) or biplane (BP) echo-probes (Vingmed, Acuson), radial scanning 7.5/12 MHz echo-endoscopes, (Olympus EU-M20/M30), 8 Fr miniature 12 MHz (UM-2R) and 20 MHz (UM-3R) US probes (Olympus) and a guidewire-fitted 8 Fr 20 Mhz US catheter (CVIS) for volume estimation (0–12 ml) and tissue visualisation (0.5–2 cm in size) in vitro, as well as for investigation of healthy subjects and patients with upper GI lesions. MP, BP, UM-2R, UM-3R and CVIS were also adopted for laparoscopic examinations. A computer-controlled stepping motor device was used for the acquisition of 2D-images, and 3D image processing was performed with a Tomtec Echo-scan work-station or locally developed PC-based prototype system (CMR – Chr. Michelsen Research, Bergen, Norway). *Results:* UM-2/3R, EU-M20/M30 and BP were most accurate for visualization and volume estimation in vitro, error 0.6–7 percent. In vivo 3D reconstructions was best done with EU-M20/M30. Post processing with Tomtec or CMR were equal for volume estimations, error 2.3 percent. Inter observer error was low. Post-processed images could be edited for optimized performance, and orthogonal slicing helped visualizing reconstructed volumes. *Conclusions:* 3D images can easily and accurately be obtained from EUS or LUS recordings, facilitating the visualization and volume estimation of lesions. Better guidance for interventions may also be achieved. Echoendosonography: EchoendoscopyLaparoscopic surgery: DiagnosisRadiology and ultrasound: Diagnosis }" "Modalities for Three-Dimensional Endoscopic and Laparoscopic Ultrasonography: In vitro and in vivo Evaluation"

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## OT66 1101 EUS-Guided Injection of Botulinum Toxin for Achalasia

\*B. Hoffman, W. Knapple, M. Bhutani, L. Aabakken, N. Verne, R. Hawes

Digestive Disease Center, Medical University of South Carolina

*Purpose:* Preliminary data has suggested that EUS-guided injection of Botox for treatment of achalasia may have an improved long term success rate compared to blind endoscopic injection. Here, we update our results from a previous report with a larger number of patients (pts) and longer follow-up.

*Methods:* The study population consists of 7 pts with manometrically confirmed achalasia. All patients underwent questioning in regard to symptoms of regurgitation, chest pain, and dysphagia before treatment and every 3 months after. They were scored based upon the following scale: 0, none; 1, occasionally; 2, daily; 3, with every meal. The maximum possible symptom score was nine; failure of treatment was considered a score of 3 or more. EUS was performed using the Pentax FG32UA linear array echoendoscope. A 4 cm long, 23 gauge needle was passed through the echoendoscope and advanced into the muscularis propria at the level of the LES under real-time EUS guidance. Four injections of Botox (20 u/cc) were made into the LES in different quadrants. An enlarging hypoechoic zone around the needle was seen as the Botox was injected.

*Results:* Six of seven patients were tolerating a regular diet within 48 hours. Follow-up has ranged from 1 to 13 months with six of seven patients reporting no dysphagia, chest pain, or regurgitation (symptoms scores of 0 of 9). Two of the seven patients had prior balloon dilatation. The seventh patient had undergone two prior Botox injections with blind endoscopic injection that failed; he also did not respond to EUS-guided injection.

*Conclusion:* EUS-guided Botox injection may have a better long term success (87% versus 66%) than endoscopic blind injection. In patients who have received two prior endoscopic injections of Botox, antibodies may form thus making EUS-guidance of no further benefit. Botox injection is recommended in those who have failed balloon dilatation.

Echoendosonography: Echoendoscopy  
Oesophageal gastric duodenal disorders:  
Oesophageal disorders, non reflux  
Endoscopy, specific: Oesophagus }

"EUS-Guided Injection of Botulinum Toxin for Achalasia"

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## "P P 46 1106" P 46 1106 **Esophageal Clearance and Gastro-Esophageal Reflux Examined by Ultrasound**

\*L. M\edi-Szab\3, Gy. Kocsis, J. Penyige

Dept. of Gastro., Budagy\6ngye k\3rh\1z, Budapest, Hungary *Purpose of the study:*

Ultrasound is able to visualize the upper and lower quarters of the esophagus: it is without any interference with the normal conditions and displays the events in motion. *Method:* 25 patients were selected on the endoscopic signs of esophagitis (Group I) and 25 ones on initial abdominal ultrasonography (Group II). The patients starved for 3–6 hours prior to ultrasonography.

Ultrasonography was performed for 15–20 minutes, in that the patients drank 1–2 mouthful of water, or tea. The events were recorded on VTR. Endoscopy was carried out in all cases; in 46 cases (21 and 25) gastric acidity was subsequently examined (test meal). Manometry was not carried out, pH measurements were done in 12 patients. *Results:* In 32 patients of 46 GERD (gastro-esophageal reflux disease) a special kind of reflux was demonstrated by ultrasonography: a slow, trickling reflux of the gastric content was seen. Several episodes were followed by a fast clearing movement only after 1–2 minutes. On the opposite, in healthy people only a fast reflux and immediate clearance were observed. Ultrasound Endoscopy pH-monitoring GERD Trickling form Esophagitis in Slow decrease(46) of reflux 70% in 9 No GERD Only fast reflux Esophagitis in No events(4) 25% in 3 *Conclusion:* The observation above seems to refer to a special form of gastro-esophageal reflux, a slow, trickling form, that can be responsible for the development of GERD. This special form was observed only in GERD patients. This can explain a number of often contradictory measurements and the effect of cisapride. Acidic form requires aggressive treatment (omeprazol). Oesophageal gastric duodenal disorders: EG Reflux } "Esophageal Clearance and Gastro-Esophageal Reflux Examined by Ultrasound"

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## "P P 46 1120" P 46 1120 Transcutaneous Ultrasonography of the Esophagogastric Junction

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Medical Clinic A, Municipal Hospital Wuppertal, University of Witten, Herdecke

*Purpose.* We performed a prospective trial in order to evaluate the diagnostic facilities of transcutaneous ultrasonography (TUS) of the esophagogastric junction in comparison with endoscopic results.

*Methods.* 211 patients without prior endoscopy or X-ray of the upper gastrointestinal tract were consecutively examined by TUS and endoscopy. Examinations were independently done by two experienced investigators who always inquired the patient's history. Diagnostic findings and values for length and width of the terminal esophagus were registered.

*Results.* In all 211 patients the terminal esophagus or hiatal hernia could be seen by TUS. 27 times examination conditions were impaired by ascites, meteorism, enlarged liver or thoracic abnormalities. 78 patients with normal results in TUS and endoscopy showed a mean length of 3.4 cm (1.7–5.4 cm) and a mean width of 4.5 mm (2.3–6.6 mm) of the abdominal esophagus. Eight patients had a hypoechoic thickening of the wall (8–27 mm) with underlying carcinoma (n = 6, T2–T4), lymphoma (n = 1) or Crohn's disease (n = 1). There were no malignant lesions missed by TUS. 64 out of 77 hiatal hernias (85.3%) and three out of eight cases with esophageal varices were correctly diagnosed by TUS. In one patient achalasia was found in TUS and endoscopy as well. Four times normal status was misinterpreted as hiatal hernia.

*Conclusion.* TUS of the esophagogastric junction can successfully be done in nearly every patient. Our data show that it is a confident means in detecting hiatal hernia and malignant lesions of the terminal esophagus or cardia at least in advanced stages. Differentiation between benign and malignant disease is not possible by TUS. Decompensated achalasia presents with a characteristic calyx like ultrasonographic pattern. We suggest that TUS of the esophagogastric junction should be used as screening method more often, because TUS is the first technical examination applied to most patients with gastroenterologic problems. Further diagnostic procedures can be selected more precisely, but may seldom become avoidable by TUS.

Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux

Radiology and ultrasound: Diagnosis }

"Transcutaneous Ultrasonography of the Esophagogastric Junction"

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"P P 47 1130" P 47 1130 **Assessment of Esophageal Wall in Patients with the Nutcracker Esophagus (NE) by Endoscopic Ultrasonography (EUS)**

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Dept. Gastroenterology, Sackler School of Medicine, Tel Aviv University *Purpose:* The NE is diagnosed when high pressure is recorded in the esophagus. It may be assumed that in NE patients the muscularis propria (MP) may be wider than normal. *Methods:* Eighteen patients with manometric features of NE and six controls were examined for assessment of the esophageal width of muscularis propria by EUS (360° Rotatable Echoendoscope JF-UM20, Olympus, Japan). Total and MP diameters were measured at the gastroesophageal junction (GEJ), 5 cm (lower esophagus), 10 cm (middle) and 15 cm (upper) above the GEJ. In patients with NE the width of MP was correlated with symptoms and esophageal pressure. *Results:* Mean MP diameter – SD (mm) at various levels of the esophagus are presented in the table. GEJ LE ME UE Patients 1.8 – 1.4\* 1.5 – 1.2 1.5 – 0.8 1.2 – 0.4\* Control 1.2 – 0.3 1.2 – 0.3 1.1 – 0.3 0.9 – 0.1 \*p < 0.05 A wide MP was found in six NE patients (33%). The width of the MP was 3, 4, and 6 mm in 3, 2 and 1 patients, respectively. The site of the wide MP had no correlation with the esophageal segment where high pressure was recorded, except for one patient in whom an extraordinarily high pressure (> 800 mm Hg) was recorded in the same segment in which a 6 mm MP was measured by EUS. There was no correlation of MP width and factors, such as length of disease, frequency of symptoms and the length of each symptomatic period. *Conclusion:* Hypertrophy of MP is demonstrated by EUS in one third of patients with the NE. This anatomic finding is in no correlation with the site of manometric abnormality or with the clinical presentation. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus Echoendosonography: Echoendoscopy } "Assessment of Esophageal Wall in Patients with the Nutcracker Esophagus (NE) by Endoscopic Ultrasonography (EUS)"

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## "P P 47 1143" P 47 1143 Risk Factors of Early Complication after Progressive Pneumatic Dilation for Achalasia

\*E.H. Metman, J.P. Lagasse, L. Picon, L. d'Alteroche, B. Scotto, J.P. Barbieux

Gastroenterology CHU Trousseau Tours-France Esophageal perforation is the most serious complication after dilation for achalasia. The aim of this study was to determine factors associated with increased risk of perforation or other immediate complications after progressive pneumatic dilation (PPD) for achalasia. *Methods:* Between 1979 to 1994, 504 dilations with our own design Sippy balloons until 1989 then Rigiflex balloons (3 to 4 cm), were performed in 237 achalasic patients (pts). The first dilation was usually performed with a balloon of 30 or 35 mm diameter for women and 35 mm for men, inflated at 6 psi. X-ray esophageal transit were performed 24 h after each dilation. We observed 15 complications (6% of pts): 7 perforations (3% of pts), 3 asymptomatic esophageal mucosal tears, 4 esophageal hematomas and 1 fever. We compared the clinical, radiographic, endoscopic, manometric and technical data of the 15 pts with complications and the 7 pts with perforation to the data of pts without complications. *Results:* six of 7 perforations occurred in women (NS). There were no perforations in pts with hiatal hernia (27 pts), epiphrenic diverticulum (13 pts), vigorous achalasia (21 pts). Esophagitis did not increase the risk of perforation (4.6% vs 2.6%, NS). Six of 7 perforations occurred during the first dilation. In women, the use of a balloon larger than 3 cm during the first dilation tended to increase the risk of perforation (8.5% vs 1.7%, NS). Difficulty to keep the balloon in the correct position during dilation significantly increased the risk of early complications (12.7% vs 4.3%,  $p < 0.05$ ). *Conclusion:* Pts with hiatal hernia, esophageal diverticulum or vigorous achalasia may safely undergo PPD. There was no predictive pre-therapeutic factor of perforation, but the role of the gender remains questionable. Difficulty to keep the balloon in the correct position increased the risk of early complications. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus }  
"Risk Factors of Early Complication after Progressive Pneumatic Dilation for Achalasia"

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## "P P 47 1144" P 47 1144 Endoscopic Balloon Dilation of Vigorous Achalasia

\*F.J. Jimenez, A. Arin, I. Martedn-Granizo, F. Borda

Hospital de Navarra, Pamplona, Spain Vigorous achalasia is a variant of idiopathic achalasia characterized by the appearance of both simultaneous and high amplitude contractions in the oesophageal body. From a therapeutic viewpoint vigorous achalasia has been thought to have a poorer response to dilation than the classical variety and it has been considered an indication for surgery. The aim of this study is to analyse both clinical and manometric results after endoscopic dilation. *Material and Methods:* From January 1.990 to December 1.995, 46 patients were diagnosed of achalasia in our Motility Unit. 17 out of them (36.9%) were considered to have vigorous achalasia (8 males/9 females; mean age 51.2 – 17.3). Endoscopic treatment was proposed and 16 of them accepted to undergo balloon dilation. 35 mm Rigiflex balloon dilators were used. The balloon was inflated to generate a pressure of 250 mmHg and kept in place during one minute for three times under endoscopic control. Post-dilation endoscopic examination was performed to discharge complications. X-ray films were taken 4 hours after the procedure for identical reasons. Follow up (6–62 months) was both manometric and clinical. *Results:* Successful dilation was achieved in all patients and no major complications were observed. Patients initiated a virtually normal diet 48 hours after dilation. LOS resting pressure dropped after dilation (35.7 – 14.8 vs 10.3 – 6.5 mmHg) with statistical significance ( $p < 0.01$ ). 3 patients required a second dilation 29/36/26 months after the first procedure. *Conclusions:* 1. Endoscopic balloon dilation is an effective treatment for vigorous achalasia. 2. Motor disorders of the oesophageal body seem to play a secondary role in this entity. 3. Surgery might be questioned as first choice therapy. Motility, specific: Oesophagus Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } "Endoscopic Balloon Dilation of Vigorous Achalasia"

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"P P 47 1146" P 47 1146 **Progressive Pneumatic Dilation in Achalasia. Long Term Results in 237 Patients**

\*E.H. Metman, L. d'Alteroché, J.P. Lagasse, L. Picon, J.P. Barbieux, E.D. Dorval

Gastroenterology CHU Trousseau, Tours-France Single dilation with large balloon and high pressure in achalasia are associated with high rate of perforation. Progressive pneumatic dilation (PPD) minimize this risk. The aim of our study was to evaluate the long term results of PPD. *Methods:* Between 1979–1994, 237 consecutive achalasic patients (pts) (124 males; mean age at time of PPD 57 years) were treated by PPD using our own designed balloons until 1989 then Rigiflex balloons. A serie of PPD was composed of 1 to 4 dilations performed every other day with balloons of progressively increasing diameter, according to radiological and manometric controls performed the day after each dilation. The serie could be repeated some months later according to the clinical evolution. After the first serie, 227 pts were evaluated (4 lost to follow up, 6 died before 6 months). Forty six pts had 2 or more series and 43 of them were evaluated (3 lost to follow up). After the final treatment, 222 pts were evaluated. Long term results were assessed according to Vantrappen's classification (fair and poor results: relapses; good and excellent results: remissions). The probability of remission was calculated using the Kaplan Meier estimator. *Results:* The probability of remission after the first serie (64%) was constant over 3 years. Repetition of series increased the probability of remission from 64% to 75%. 1<sup>st</sup> serie 2<sup>nd</sup> serie Final treatment Mean follow up (months) 44 39 50 Remission probability (3 years) 64% 47% 75% *Conclusion:* PPD was an efficient treatment of achalasia in 2 of 3 pts after 1 serie and again in 1 of 2 pts after a second serie. Final long term probability of remission was 75%. Relapses were rarely observed after 3 years (after 1 as well more series). Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus } "Progressive Pneumatic Dilation in Achalasia. Long Term Results in 237 Patients"

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"P P 47 1147" P 47 1147 **Polyethylene Balloons for Pneumatic Dilation in Achalasia**

\*V. Balatsos, V. Delis, K. Kastanas, A. Goundopoulos, A. Pantes, N. Skandalis

Gastroenterology Department, District General Hospital of Athens "George Gennimatas". Athens, Greece The purpose of the present study was to evaluate the efficacy and safety of the Microvasive Rigiflex Balloon Dilator in patients with achalasia. Twenty one patients, 13 men and 8 women, age 20–85 years, were included in this prospective study. Their symptoms were: dysphagia 21, regurgitation 14, weight loss 9 and chest pain 2. Barium esophagograms were compatible with achalasia and manometry revealed absent or incomplete relaxation of the lower esophageal sphincter. Pre-treatment endoscopy revealed dilated and/or tortuous esophagus, aperistalsis or minimal peristalsis. In all patients this was the first dilation therapy for achalasia. A floppy-tipped guide wire was passed through the biopsy channel of the gastroscopy into the stomach. The Microvasive Rigiflex Balloon Dilator was inserted over the guide wire under fluoroscopic control and was positioned across the distal segment of the esophagus. The balloon was inflated to pressure ranging from 10 to 15 psi for 60 sec. Chest x-rays and gastrografin esophagogram was performed after dilation's. The patients hospitalized for a day. A total of 21 patients underwent 26 procedures (1–2 procedures per patient) with 30, 35 or 40 mm balloons. Patients in 4 of 26 procedures complained of post-dilation chest pain which disappeared in ten minutes. There was not any complication. The patients were followed up for 6–46 months. 17/21 (81%) patients are ingesting liquid and solid food with no difficulty and 3/21 (14%) with mild difficulty. One patient (5%) did not have any improvement. We conclude that pneumatic balloon dilation for achalasia is highly efficacious, safe and cost effective. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Endoscopy, general: Instrumentation, therapy } "Polyethylene Balloons for Pneumatic Dilation in Achalasia"

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## "P P 47 1150" P 47 1150 Botulinum Toxin (Botox) for Achalasia

\*P. Souto, D. Gomes, J. Baranda, H. Lopes, C. Gregório, H. Gouveia, Diniz de Freitas

Dept. of Gastroenterology, Coimbra University Hospital, Coimbra, Portugal  
*Aim:* To determine the efficacy and adverse effects of intrasphincteric Botox injection in patients with achalasia.  
*Methods:* Prospectively, 16 symptomatic patients with achalasia, underwent endoscopy with Botox injection (20 U/ml, 4 × 1 ml) at the lower esophageal sphincter (LES). Manometry was done pre-treatment and after treatment (at 1 and 6 months). Symptoms were assessed by scores: dysphagia (D), chest pain (CP), regurgitation (R), each on a 0–3 scale (occasional = 1, daily = 2, every meal = 3), and total symptoms, on a 9 point scale total (TS = D + CP + R). Weight loss score (W) was also assessed (1–5 kg = 1, 5–10 kg = 2, > 10 kg = 3). Stages (St II or St III) were used either as inclusion criteria or as failure criteria (St = TS + W; I = 2–3, II = 4–5 and III = > 6). Statistical analysis was done by t-Student, Wilcoxon and correlation tests.  
*Results:* From the 16 patients (age: 18–85 years; 9 female and 7 male), half had symptoms for more than 2 years and only 5 had never received prior treatment. A mild transient chest pain, immediately after injection, was frequent (10 of 16). The mean follow-up was 5 – 1.4 (3–7) months. At the first month, there was only 1 failure (1 of 16). TS (from "5.9 – 1.6" to "2.4 – 2.2";  $p < 0.003$ ) and individual scores improved, except for chest pain. LES pressure decreased from 29 – 10.5 to 16.5 – 9 mmHg ( $p < 0.001$ ). After initial improvement, 3 of 5 patients return to St II at the 6 month examination, and other 2, of the remaining 10, relapsed 3 and 5 month after treatment. Good response was not related to age, sex, duration of illness, previous treatments, prior LES pressure or initial symptomatic scores ( $p = \text{NS}$ ). A better response was seen in patients with higher esophageal body wave mean amplitude.  
*Conclusion:* Botox injection is safe, simple and effective at short-term, even in patients with prior balloon dilation.  
Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus  
Clinical practice: Management strategy } " Botulinum Toxin (Botox) for Achalasia"

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"P P 48 1153" P 48 1153 **Sedation Is Not Needed for Diagnostic Upper Gastrointestinal Endoscopy** G. Gatto, V. Peri<sup>1</sup>, M. Amuso,

\*M. Traina

Divisione di Medicina Interna, Az. Ospedaliera V. Cervello

<sup>1</sup> Istituto di Clinica Medica R, Università degli Studi, Palermo, Italy *Aim:* Cardiopulmonary complications of upper gastrointestinal (GI) endoscopy have been related to sedation. Pharyngeal anaesthesia reduces patient's discomfort during the procedure. Aim of the present study was to assess safety, efficiency and acceptability of upper GI endoscopy performed without conscious sedation in patients presenting for their first examination. *Methods:* Retrospective review of all new endoscopies performed in a 100 days-period, in a regional hospital in Palermo, Italy. Main measures were: number of upper GI endoscopies performed without sedation in a diagnostic or emergency/operative setting; number of endoscopies interrupted because of patient's intolerance or judged unsatisfactory for diagnosis by endoscopist; number of procedure-related adverse outcomes. *Results:* Four hundreds records of all new endoscopies performed in a 100-days period were reviewed: 312 diagnostic, 75 emergency/operative, 13 jejunoscopies. A total of 52 (13%) endoscopies were performed under sedation: 15/312 diagnostic (5%), 31/75 emergency/operative (41%) and 6/13 jejunoscopies (50%). The use of sedation was not related to sex, age and to the indication to procedure. Seven procedures were interrupted: 3 among sedated (6%) and 4 among non sedated patients (1%). Eight procedures were judged unsatisfactory by the endoscopist, 3 among sedated (4%) and 5 among non sedated patients (1.4%). No adverse outcome occurred. *Conclusions:* Up to 95% diagnostic and up to 60% emergency/operative procedures in this series were successfully performed without sedation. Avoidance of sedation did not increase the number of procedures interrupted or judged technically unsatisfactory. Upper GI endoscopy can be safely and efficiently performed without sedation. Endoscopy, general: Preparation, management Endoscopy, general: Complications } "Sedation Is Not Needed for Diagnostic Upper Gastrointestinal Endoscopy"

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## "P P 48 1154" P 48 1154 **Changes in Haemodynamic Parameters during Upper Endoscopy**

\*P. P\'e9rez-Rojo, M. Mu\'f1oz-Navas, M.T. Bet\'e9s, J.C. Subtil

University Clinic of Navarra, Pamplona, Spain Knowledge of changes in vital variables during upper endoscopy, according to different medication, can help to improve nursing and medical care of patients undergoing upper endoscopy. We present the preliminary results of an on-going prospective study to assess the influence of medication, supplemental oxygen and maneuvering the endoscope on oxygen saturation, heart rate and blood pressure controlled by monitoring system. All endoscopic procedures and data collection (recorded at 1–2 minutes intervals before, during and after the endoscopy) were performed by the same doctor and nurse. One hundred and twelve unselected patients were randomly divided into three groups receive to different medication: without medication (group I); with midazolam-pethidine (group II) and with propofol-atropine administered by an anesthetist (group III). Continuous supplemental oxygen via nasal or oral route was provided in a predetermined number of cases. No significant differences between groups were recorded with regard to age, sex, body mass index, smoking, previous endoscopy, procedure duration and basal data. An increase in heart rate was recorded during upper endoscopy in all groups. Changes were significantly greater in group I or II, than in group III (patients with propofol-atropine) ( $p < 0.001$ ). No significant differences were observed between groups I and II. Mean arterial pressure significantly increased in group I and II but not in group III ( $p < 0.001$ ). No significant differences were observed between groups I and II. After endoscopic procedure no significant differences in haemodynamic parameters were recorded according to different medication or without medication ( $p > 0.05$ ). No patient with oxygen supplementation via nasal route presented desaturation episodes ( $\text{SatO}_2 < 90\%$ ). When no oxygen supplementation was provided, 2 patients in group I and 3 patients in group II presented desaturation episodes. Endoscopy, general: Preparation, management Endoscopy, specific: Stomach, duodenum } "Changes in Haemodynamic Parameters during Upper Endoscopy"

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**"P P 48 1156" P 48 1156A Randomized, Double-Blind Study Comparing Intravenous and Oral Administrated Sedatives for Diagnostic Upper Gastrointestinal Endoscopy — Preliminary Results**

\*R.R.O. Castro, A.P. Ferrari, A.N. Atallah, S. Geocze, M.R.S. Rohr, C.Q. Brant, E.D. Libera

Digestive Endoscopy Section of the UNIFESP, São Paulo, Brazil Evidence is needed regarding the degree of improvement in patient satisfaction and comfort when intravenous (IV) as opposed to oral (PO) sedation is used during endoscopic procedures. Diazepam, one of the standardly-used drugs, requires a sedation period that largely exceeds the duration of the examination. In addition to the desired effects, significant respiratory depression and localized effects due to IV administration may occur. For this study, we assessed patient satisfaction when undergoing diagnostic upper gastrointestinal endoscopy (UGE) using diazepam IV as compared to midazolam, PO, and analyzed the cost/benefit relationship of each administration route and working conditions after the examination. We conducted a randomized, double-blind study comprised of 143 patients (ages 18–65) submitted to UGE. Sixty eight patients received midazolam, 7.5 mg, PO and 75 received diazepam, 10 mg, IV. The endoscopist evaluated the satisfaction of the patients immediately after the procedures; and 24 hours later the patients answered a telephone survey. There was no statistically significant difference between IV and PO groups degree of satisfaction ( $\chi^2 = 1.92$ ,  $p = 0.16$ ) and same day working conditions ( $\chi^2 = 0.30$ ,  $p = 0.55$ ). However, the variables amnesia ( $\chi^2 = 13.03$ ,  $p = 0.0003$ ) and afternoon drowsiness ( $\chi^2 = 14.76$ ,  $p = 0.0001$ ) yielded results showing statistical significance with the IV group predominating. The IV group costs were twice as high as the PO group. To be able to have 90% statistical power, with 95% confidence interval is necessary to double the sample size. Endoscopy, general: Preparation, management Endoscopy, specific: Oesophagus Endoscopy, specific: Stomach, duodenum } "A Randomized, Double-Blind Study Comparing Intravenous and Oral Administrated Sedatives for Diagnostic Upper Gastrointestinal Endoscopy / Preliminary Results"

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"P P 48 1157" P 48 1157 **Patient Stress and Patient Satisfaction When Allowed Presence of an Accompanying Person during Endoscopy**

\*J. Lachter, H. Wiseman, Y. Lavee

Seker Medical Center and Faculties of Education and of Social Work, Haifa University, Haifa, Israel  
*Introduction:* We hypothesized that it may be possible to decrease patient stress and anxiety, thereby possibly making procedures safer, and also possibly increasing patient satisfaction, by allowing an accompanying person (AP) to be present in the endoscopy suite during gastroscopy (EGD).  
*Patients and methods:* Forty one patients were randomly divided into two groups who would either be offered to have an AP with them during endoscopy, or not to be so offered. Spielberg's well-validated state anxiety evaluation was administered before and after EGD. The benefit was significant for persons with higher levels of state anxiety before the EGD ( $p < 0.04$ ). APs completed questionnaires as to their reactions after EGD.  
*Results:* 58.8% of patients so offered chose to have APs in the endoscopy suite with them. After the procedures, 83% of the APs recommended the accompaniment of patients. The patients who underwent EGD with an AP showed a trend ( $p < 0.06$ ) to have a lessening in measurable anxiety compared to the patients to whom having an AP was not offered. Patients undergoing EGD for the first time had more anxiety than those with previous EGD experience ( $p < 0.034$ ). The benefit of having an AP was significant for persons with higher levels of state anxiety before the EGD ( $p < 0.04$ ).  
*Discussion and Conclusions:* Offering to permit the presence of an accompanying person during EGD was shown to often have such benefits as improving patient satisfaction and reducing anxiety. Clinical practice: Psychosomatics Endoscopy, general: Preparation, management }

"Patient Stress and Patient Satisfaction When Allowed Presence of an Accompanying Person during Endoscopy"

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## "P P 48 1158" P 48 1158 Evaluation of Bacteriological Contamination of Gastrointestinal and Pulmonary Endoscopes after Cleaning and Disinfection Procedures

\*D. Luu Duc, J. Shum Cheong Sing, M.R. Mallaret, H. Soule, C. Arnaud, J. Croiz'e9, J. Calop

University Hospital, Grenoble, France The increasing number of endoscopic interventions as well as the risk of patient transfer of microorganisms contributed to put maintenance procedures of endoscopic instruments forward. We evaluated the quality of the procedures applied in our hospital during 2 years: a manual and an automated disinfection with Olympus ETD, 14 bronchoscopes, 20 colonoscopes and 22 gastroscopes were studied. The manual procedure included channels brushing and cleaning with a detergent and a disinfection for 15 min in glutaraldehyde 2%. The internal channels were sampled by injecting a mixture inhibiting the glutaraldehyde effect containing 3% (v/v) tween 80, 0.3% (w/v) lecithin, 0.1% (w/v) L-histidin. They were shown to be more contaminated than the other sampled sites (moving extremity part, valves). The operator channel was shown to be more often contaminated in case of colonoscopes (85%) in comparison with the results for the gastroscopes (72.3%) and bronchoscopes (57.1%); however the contamination was lower after an automated maintenance instead of a manual maintenance ( $p = 0.05$ ). Concerning storage, a period superior to 12 hours was shown to increase the level of contamination of the operator channel, and it was all the more contaminated since the drying was not well performed. The most encountered bacteria are: negative coagulase *Staphylococcus*, *Pseudomonas aeruginosa*, *Bacillus* and *Pseudomonas species*. Clinical practice: Quality assurance } "Evaluation of Bacteriological Contamination of Gastrointestinal and Pulmonary Endoscopes after Cleaning and Disinfection Procedures"

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"P P 48 1159" P 48 1159 **Systematic Hepatitis C Virus (HCV) Screening in Patients Submitted to Ambulatory Endoscopic Procedures**

\*J.L. Gaudin, R. Bobichon, O. Dumont, J.C. Souquet

Hepatogastroenterology, Hospital de la Croix-Rousse, Lyon, France HCV transmission is usually due to blood transfusions or intravenous drug injections. Such an etiology can not be found in about 30% of contaminated patients. Endoscopy has been considered as a potential contamination source, although no definite case has been reported in the literature. The aim of our study was to determine systematically the VHC status of patients admitted to our ambulatory unit and to compare the frequency of positive tests in patients with and without previous endoscopic examinations. *Methods:* From December 95 and on, all patients admitted for endoscopic examinations in the ambulatory unit, had an Elisa III test for HCV with their agreement. They were asked about their past history of GI diseases and their files were searched for previous endoscopy. Most patients with previous examinations had their procedures performed in our division. All examinations under sedation are performed in the same endoscopic room. All liver diseases, including chronic hepatitis C, are treated. Moreover the hospital includes a large liver surgery unit (with liver transplantation) and an infectious diseases unit with HIV patients (drug abusers). So HCV positive patients are regularly referred for endoscopy but usually seen as non-ambulatory patients. Disinfection protocols have evolved with time according to the scientific recommendations. So far all procedures have been performed by the nurses without washing-machine. Autoclave for endoscopic material has been systematically used since 1995. *Results:* So far 302 patients have been included. Mean age was 50 yrs (range 17–85), with a slight male predominance (54.4%). Most examinations (91%) consisted in gastroscopy and colonoscopy. 172 patients (57%) had no previous endoscopic procedures, while 130 (43%) had at least one procedure more than 6 months before inclusion. In this last group, median year for the 1st endoscopic examination was 1993 (range 1983–1995) and median number of procedures was 3 (range 1–15). Only 8 patients had no biopsy or polypectomy during these previous examinations. Results of VHC screening was available in 289 patients (95.7%). Missing data were observed respectively in 3% and 8% of patients with and without previous examinations. Only 2 patients had a positive test for HCV, one in each group. The patient with previous endoscopic examinations, was referred for HCV cirrhosis before his 1st endoscopic procedure. Thus of the 130 patients with previous endoscopy studied so far, none had hepatitis C related to endoscopy. *Conclusions:* this ongoing study does not show a high risk of HCV transmission by endoscopic procedure, even with the previous less careful decontamination procedures. Endoscopy, general: Preparation, management Endoscopy, general: Complications Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Systematic Hepatitis C Virus (HCV) Screening in Patients Submitted to Ambulatory Endoscopic Procedures"

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"P P 48 1160" P 48 1160 **Development of a Filing System for Endoscopy Fullfilling the Guidelines of the Minimal Standards Committee of Esge**

\*A. Grassi, V. Casale, M. Crespi

National Cancer Institute Regina Elena, Rome, Italy A multimedia filing system for endoscopic reports, enabling the management of the clinical and research activities has recently been developed for our Endoscopy Units. This system, called ELENA, is built on a database including clinical records of patients and endoscopic pictures taken directly from the videoendoscopes during the procedure. Considering the importance that computerized systems be homogenous, we considered the guidelines of the "Minimal Standards Committee" of the ESGE, introducing in our filing system the full recommendations for the structure of the endoscopic record, the "reasons for performing endoscopy", as well as the terms for describing the endoscopic findings and the diagnosis. Considering that this new multimedia system will be the third edition of the existing software for the management of our Endoscopy Service, we didn't find substantial problems to fullfill the Minimal Standards recommendations. We are convinced that the possibility to equalise the clinical records in endoscopy must be taken today into consideration for the development of new softwares and the updating of the old ones. Clinical practice: Management strategy Clinical practice: Quality assurance } "Development of a Filing System for Endoscopy Fullfilling the Guidelines of the Minimal Standards Committee of Esge"

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## "P P 48 1161" P 48 1161 How Long Does It Takes to Form a Good Biliary Endoscopist?

\*M. Tantau, M. Prelipceanu, O. Pascu, M. Chiorean

University of Medicine and Pharmacy Cluj-Napoca, Romania There is no agreement about the duration of the training period for endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES), and there are few endoscopists publishing their early results. *Objectives:* To study prospectively the impact of the accumulating experience on the results of diagnostic and therapeutic biliary endoscopy in an attempt to define the minimum required to perform competitively ERCP and ES. *Methods:* We studied prospectively the results of the first 271 ERCPs and 100 ESs performed by a young endoscopist between December 1994 and May 1996, in the university medical center of Cluj-Napoca, Romania, after having a one year biliary endoscopy training in a good gastroenterological center in France. Two groups of patients were formed: one group included the first 50 ES and the other group the remaining 50 ES both with the period corresponding diagnostic ERCPs. Success rate of diagnostic ERCP, ES and stone extraction, the number of sessions per procedure and the rate of complications in the two groups of patients were followed. *Results:* ERCP was successful in 89% of patients in the first group, compared with 94% in the second group; we noted 3 and respectively one failure of ES, 7 and respectively 2 impossibilities of removing choledocal stones after sphincterotomy in the both groups. Overall success of treatment was 80% in the first group and 92% in the second group. 5 (10%) complications were noted for the first 50 sphincterotomies: 3 hemorrhages, and 2 acute pancreatitis; in the second group only one (2%) acute pancreatitis was noted. Mortality was null in both groups. 1.38 sessions were needed per procedure in the first group, versus 1.12 in the second group. *Conclusions:* Although one year of education for diagnostic and therapeutic biliary endoscopy could be enough, two years, in which minimum 300 diagnostic ERCPs and 50 ESs are needed to form a competitive biliary endoscopist. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, general: Instrumentation, therapy } "How Long Does It Takes to Form a Good Biliary Endoscopist?"

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**"P P 48 1162" P 48 1162 Effect of Different Upper Gastrointestinal Tract Diseases (UGITD) and Endoscopy on Quality of Life (QOL): Results from the Hercules Project**

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University of Plymouth, UK QoL has become widely accepted as a major outcome in the healthcare process, particularly in pharmacological therapy. QoL in UGITD has been assessed with different general questionnaires, while experience with specific instrument for peptic ulcer and/or GORD is limited. A specific questionnaire for UGITD, called QPD32 (Quality of life in Patients with Dyspepsia-32 items) has been developed and validated in Italy and now it is submitted to validation in some countries. It consists of 32 items exploring pain, symptoms and physical domains. To detect differences in individual QoL due to psychological characteristics a Personality Inventory Scale is included. In order to verify if different UGITD have different impact on QoL and if administration of a questionnaire before or after endoscopy may result in different score, a transversal, observational survey was performed with the three major Italian gastroenterological societies. QPD32 and the general tool SF36 were administered to patients (pts) suffering from gastric (GU) or duodenal (DU) ulcer, oesophagitis (OE), other upper gastrointestinal complaints (O). 32 gastroenterologists administered both questionnaires to 305 pts (61.1% males, mean age 45.9 y) who suffered from GU (8%), DU (46%), OE (29%) and O (15%). The mean total scores of QPD32 in GU, DU, OE and O were respectively 62.9, 61.9, 62.8 and 61.6; score was similar when QPD32 was administered before (61.25), just after (60.0) or few days after endoscopy (60.5). SF36 scores showed a not significant better QoL in OE and DU pts and after endoscopy. In conclusion, pts with different UGITD have the same perception of their illness when QoL is measured with a specific tool. Moreover, thanks to its specificity, QPD32 could be administered indifferently before or after an UGIT endoscopy. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, specific: Stomach, duodenum } "Effect of Different Upper Gastrointestinal Tract Diseases (UGITD) and Endoscopy on Quality of Life (QOL): Results from the Hercules Project"

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"P P 48 1163" P 48 1163 **Diagnostic Jejunoscopy with the Pentax VSB-P2900 Endoscope** N. Skandalis,

\*K. Paraskeva, A. Dalianas, A. Konstantinidis, V. Balatsos, V. Ntelis

Gastroenterology department, General Hospital of Athens, Greece *Objective:* To evaluate the efficacy of the VSB-P2900 endoscope in small bowel diseases. *Patients:* 84 patients, 43 female and 41 male, mean age of 51.5 years range 14–83, underwent small bowel enteroscopy during the last 3 years, in our department. Indications for the examination included: occult GI bleeding (37 patients), diarrhea (30 patients), abdominal pain (6 patients), abnormal barium studies of the small bowel (4 patients) secondary malignancy (2 patients), possible upper involvement of Crohn's disease (5 patients). Previous diagnostic studies included gastroscopy (79 patients), colonoscopy (80 patients) and radiographic barium studies (10 patients). *Method:* The Pentax VSB-P 2900 endoscope, which has a working length of 250 cm was used. Midazolam (1–5 mg) was given as sedation. The instrument passed through the oesophagus towards the second part of the duodenum (as in routine upper endoscopy) and was then inserted to maximum depth. Final depth of small bowel intubation was estimated by straightening the instrument to remove the gastric loop and subtracting 80, cm from the ligament of Treitz. Forcep biopsies were obtained when necessary. *Results:* Visualization of the small bowel was excellent in all patients. Mean depth of insertion was 50 cm past the ligament of Treitz (range 5–100 cm) Duration of the examination was 15–40 min. Tolerance of the procedure was good (similar to the upper endoscopy) for all patients. There were no complications or post procedure symptom complaints. Findings included: Arteriovenous Malformations (7 patients), adenocarcinoma (2 patients), leiomyoma (2 patients), hamartomas (1 patient), celiac sprue (3 patients), eosinophilic gastroenteritis (1 patient), Crohn's disease (5 patients) and long efferent loop in BILL II (1 patient). Findings proximal to the ligament of Treitz included duodenal ulcer (3 patients), Mallory-Weiss tear (1 patient) and polyp of Vater papilla (1 patient). *Conclusion:* Enteroscopy using the VSB-P2900 is simple, safe and efficacious in the diagnosis of small bowel diseases. Endoscopy, specific: Enteroscopy Endoscopy, general: Instrumentation, diagnosis } "Diagnostic Jejunoscopy with the Pentax VSB-P2900 Endoscope"

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## "P P 48 1164" P 48 1164 Diagnostic Efficiency of Push Type Enteroscopy

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Department of Gastroenterology, La\`ebnec Hospital, Paris, France

Department of Gastroenterology, Cochin Hospital, Paris, France Push-type enteroscopy (PE) is still being assessed. The aim of this study was to report the diagnostic efficiency of this procedure according to the indication. *Patients and Methods:* From march 1994 to march 1996, 173 patients (mean age: 34 years) underwent PE using an Olympus SIF 100 videoenteroscope (upper GI tract PE: n = 105, lower GI tract PE: n = 17; double way PE: n = 51). The indications were: unexplained iron-deficiency anemia (n = 41) or gastro-intestinal macroscopic bleeding (n = 45), radiological suspicion of small bowel lesion (small bowel follow through: n = 23; CT scan: n = 2), unexplained diarrhea and/or malabsorption (n = 15), abdominal pain of obscure origin (n = 13), various indications (n = 34). Each patient had negative upper and lower GI tract endoscopies prior to PE. *Results:* The mean length of jejunal and ileal insertion was respectively 120 cm (30–160) and 60 cm (20–120) (failure of ileoscopy: 15/68). A small bowel lesion potentially responsible for bleeding was detected in 2 patients (5%) with iron-deficiency anemia and in 8 patients (18%) with macroscopic gastrointestinal bleeding. An upper or lower GI tract lesion previously not shown by gastroscopy or colonoscopy was found in 12 of these patients (14%). PE provided a diagnosis or modified the radiological interpretation in 19 cases out of 25 (76%) of suspected small bowel lesion. In the exploration of unexplained diarrhea and/or malabsorption, PE provided a diagnosis in 4 cases (26%). PE was normal in all patients with abdominal pain. *Conclusion:* PE was very efficient for the diagnosis of small bowel radiological abnormalities. It provided a diagnosis in 26% of patients with unexplained chronic diarrhea, in 15% of patients with macroscopic gastrointestinal bleeding, in 5% only of those with iron-deficiency anemia and was negative in all cases of abdominal pain. Endoscopy, specific: Enteroscopy Endoscopy, general: GI bleeding } "Diagnostic Efficiency of Push Type Enteroscopy"

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"P P 48 1165" P 48 1165 **Comparison between Push Type Enteroscopy and Radiological Examination of the Small Bowel in Patients with Gastrointestinal Bleeding of Obscure Origin**

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A radiological examination of the small bowel is often performed in case of gastrointestinal bleeding of obscure origin. More recently, push type enteroscopy (PE) has been reported as a valuable tool in this indication. The purpose of this study was to compare the diagnosis efficiency of this two procedures. *Methods:* From February 1994 to June 1995, 34 patients (mean age: 51 years) with obscure gastrointestinal bleeding (iron-deficiency anemia without obvious cause of blood loss or malabsorption: n = 15; macroscopic gastrointestinal bleeding: n = 19) were examined by small bowel follow through (SBFT) and PE (jejunoscopy n = 17; double way examination n = 17). An Olympus SIF 100 videoenteroscope was used. Each patient had negative upper and lower GI tract endoscopies prior to small bowel examinations. *Results:* SBFT revealed only one lesion potentially responsible for blood loss, corresponding to a jejunal leiomyoma. PE detected small bowel lesions potentially responsible for blood loss in 5 patients (15%). The lesions were always located in the jejunum (arteriovenous malformations: n = 3; metastasis: n = 1; leiomyoma: n = 1). The efficiency of PE for the detection of a small bowel lesion was of 21% in case of macroscopic bleeding and of 6% in case of iron-deficiency anemia. PE also revealed lesions previously not detected by gastroscopy or colonoscopy in 6 patients (18%). *Conclusion:* PE was more effective than SBFT to detect the origin of obscure gastrointestinal bleeding. Nevertheless, its efficiency for the diagnosis of a small bowel lesion was limited, in particular in case of iron-deficiency anemia without macroscopic bleeding. Endoscopy, specific: Enteroscopy Endoscopy, general: GI bleeding } "Comparison between Push Type Enteroscopy and Radiological Examination of the Small Bowel in Patients with Gastrointestinal Bleeding of Obscure Origin"

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"P P 48 1166" P 48 1166 **Evaluation of a Near-Infrared Electronic Endoscope in the Alcoholics with and without Cirrhosis**

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New vascular signs identified only with a near-infrared electronic endoscopy would be predictive of esophageal varices (EV) bleeding. *The aim of the study* was to describe vascular signs with a near-infrared light in alcoholics. *Method.* Twelve alcoholics without cirrhosis and 16 alcoholics with histologically proven cirrhosis were included prospectively. The patients (pts) were examined with a near-infrared electronic endoscope (Scop Olympus, Rungis) in white light and in near-infrared light – injection of 2 mg/kg of indocyanine green (ICG) which absorbed this infrared light. With near-infrared light and injection of ICG, a dark lines on pink background was interpreted as the opacification of a vessel. *Results.* 1. The near-infrared endoscopy without injection of ICG was less performant than the white light endoscopy. 2. With near-infrared light and injection of ICG: esophageal non variceal vessels invisible in white light were observed in 4/16 pts with cirrhosis and in 1/12 pts without cirrhosis (p = NS). Ten pts with cirrhosis had EV. Opacification of EV was observed in 2 pts and had not bled. Conversely, 2 other pts had bled and had large varices with red signs predictive of EV bleeding in white light. Gastric vessels invisible in white light were observed in 7/12 pts without cirrhosis and in 4/16 pts with cirrhosis (p = NS). In the pts with cirrhosis, gastric vessels were observed in 2/11 pts with congestive gastropathy and in 2/5 pts without congestive gastropathy (p = NS). *Conclusion.* Vascular signs invisible in white light are identified both in the pts with and without cirrhosis. Further studies are needed to know the significance and the interest of these signs. Moreover, the improvement of the picture contrast is necessary. Liver and bile ducts, 1: Cirrhosis: portal hypertension  
Endoscopy, general: Instrumentation, diagnosis } "Evaluation of a Near-Infrared Electronic Endoscope in the Alcoholics with and without Cirrhosis"

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"P P 48 1167" P 48 1167 **In vivo Observation with a Near-Infrared Camera of Fluorescent Gastrointestinal Vessels in Rats**

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<sup>3</sup> service de Physiologie, UFR Paris XI, Kremlin Bicêtre, France Indocyanine green (ICG) is fluorescent in the near-infrared light. This property is used for high resolution choroidal fluorescence angiography. The observation of fluorescent gastrointestinal vessels by an endoscope could be useful in case of portal hypertension or bleeding ulcer. *The aim of the study* was to observe fluorescent gastrointestinal vessels with a near-infrared camera. *Method.* The near-infrared source was a 100 mW, 808 nm laser diode. The fluorescence was selected by two 830 nm band-pass filters. A computer allowed image capture and treatment. Eleven Wistar rats were anesthetized and a catheter was inserted in the femoral vein. A laparotomy was performed. Before and after injection of ICG and both with white and near-infrared lights, we made pictures of the vessels of the stomach, the small intestine or the colon. *Results.* Some serous vessels larger than one mm were visible with white light. None vessels were observable with near-infrared light without injection of ICG. Conversely, with near-infrared light and after injection of ICG, we observed numerous white lines on dark background corresponding to a transient and bright fluorescence of vessels larger than 1/10 mm. Thanks to high resolution, we could distinguish arterial and venous fluorescence. The fluorescence reappeared after each new injection of ICG but a background white noise from the parenchymatous grewed. *Conclusion.* This animal pattern allows to display gastrointestinal vessels flow. It could help to develop a near-infrared endoscope and be useful in surgery to test the vitality of the gut. Endoscopy, general: Instrumentation, diagnosis } "In vivo Observation with a Near-Infrared Camera of Fluorescent Gastrointestinal Vessels in Rats"

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"P P 48 1168" P 48 1168 **Laser Induced Fluorescence Spectroscopy at Endoscopy** L. Lilge<sup>1</sup>, R. DaCosta<sup>1</sup>, D. Scheider<sup>2</sup>, G.A. Duvall<sup>2</sup>, J. Kost<sup>1</sup>, S. Hassaram<sup>2</sup>, M. Cirocco<sup>2</sup>, T. Mang<sup>1</sup>, B.C. Wilson<sup>1</sup>,

\*N. Marcon<sup>2</sup>

<sup>1</sup> The Ontario Cancer Institute, Toronto, Canada

<sup>2</sup> The Wellesley Hospital, Toronto, Canada *Purpose:* Demonstrate the effect of different light delivery-detector geometries on Laser Induced Fluorescence Spectroscopy (LIFS) in the gastrointestinal tract following 437 nm excitation. *Methods:* 122 patients (61 colonoscopies and 61 esophagogastroduodenoscopies, EGD) undergoing endoscopy consented to LIFS examination. Abnormalities, identified during white light endoscopy, and their surrounding normal appearing mucosa were additionally examined by LIFS, using 437 nm as excitation wavelength and optical fibers for light delivery and detection. The fluorescence light detection fiber was in contact with the mucosa for all patients, while the excitation light delivery was either via a fiber adjacent to the detector fiber (50 patients), or via the endoscope illumination bundle (72 patients). Fluorescence spectra were collected with an optical multi channel analyzer. Tissue samples of the abnormalities and the surrounding normal tissue were retrieved. In a blinded fashion, all samples were assessed by a single pathologist. A specific numerical diagnostic code (1–4 denoting non-neoplastic changes, 6 to 9 neoplastic, and 5 atypia of undetermined significance) was assigned to each sample. *Results:* A total of 158/347 colonoscopies and 124/275 EGD evaluable spectra were obtained for excitation light delivery via fiber/endoscope illumination channel respectively. Spectra were normalized and grouped according to their anatomical site and the observed pathological state. The average spectra with the corresponding standard deviation were derived for each group. Using MVLR either two or three spectral bandwidth providing maximum sensitivity to differentiate non-neoplastic from neoplastic mucosa were identified. For both excitation light delivery geometries 510 and 670 nm proved most effective for 2 spectral bandwidth, while 510, 600 and 670 nm proved best for 3 spectral bandwidth. Sensitivity and specificity of the differentiation was in the 75% to 88% range for both excitation light delivery modalities and all investigated sites. Theoretical modeling of the data indicates that macroscopic morphological changes in the mucosa causes most of the spectral differences observed. *Conclusion:* LIFS for the gastrointestinal tract is a feasible tool to identify histologically significant lesions from histologically insignificant lesions with an acceptable sensitivity and specificity if a repetitive light delivery detection geometry is selected. Oncology, general: Screening, prevention Endoscopy, general: Instrumentation, diagnosis } "Laser Induced Fluorescence Spectroscopy at Endoscopy"

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"P P 48 1169" P 48 1169 **Detection of Dysplasia Using Fluorescence in vivo Using the XILLIX-Life-GE-System**

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There is increasing interest in the exploration of the usefulness of tissue autofluorescence (FL) in the detection of dysplasia and malignancy. In a pilot study 38 patients (pts) were screened between february and may 1996 for dysplasia using the XILLIX-life gastrointestinal FL system in "in vivo" endoscopy. Olympus Tokyo and the XILLIX Technologies corp. developed an endoscope in which the use of regular endoscopy and FL, using a blue light source and a sensitive camera to detect an FL pattern were combined. All pts were screened with regular endoscopy and with FL. FL of normal mucosa is seen as a blue image on the screen. If however dysplasia is present either as mild, moderate, severe or (in situ) carcinoma (ca) the reflected light is altered and a reddish brown to red FL pattern is seen. Thus a distinction can be made which could lead to better targeted biopsies of suspicious lesions using FL. For the analysis all lesions were judged to be either normal or suspicious using both techniques, the diagnosis was appropriately confirmed with histology. Colonoscopy was performed in 23 pts, gastroscopy in 15 pts. In the colon 17 pts were screened for polyps or earlier ca, three for ulcerative colitis (UC), one had a pneumatosis coli in the past, one mucosal prolaps and one ileo-anal pouch for UC. In 15 gastroscopies: 6 Barrett's oesophagus, 3 oesophagusca, 1 hiatal hernia, one Billroth-II stomach resection, three prior stomach cancers and one duodenal villous adenoma were examined. Three FL investigations failed, two because of a blue light source failure during colonoscopy, one because of poor visualisation in the stomach. Matching FL images and histology, the sensitivity and specificity of FL could be calculated, as shown in the table:

	Colonoscopy	Gastroscopy	Total
True positive	5	7	12
True negative	13	6	19
False positive	3	1	4
False negative	0	0	0
Failed	2	1	3
Sensitivity	100%	100%	100%
Specificity	76.9%	83.3%	78.9%

*Conclusions:* in this pilot study no false negative results were obtained, leading to a high sensitivity. The false positive results may be due to biopsy sampling error in this early learning stage with the new technique, because visualisation of the biopsy forceps using blue light is occasionally difficult. The false positive results can also occur due to interference of mucus, stool or blood, which all give an intense FL signal. In two pts a carcinoma in a Barrett's segment, which was not clearly identified during regular endoscopy, was diagnosed using FL. Both pts had a curative oesophageal resection in this early stage of their disease. The technique of in vivo FL for earlier dysplasia detection in combination with a regular endoscopy looks promising, especially in diseases known to predispose for malignancy. }

"Detection of Dysplasia Using Fluorescence in vivo Using the XILLIX-Life-GE-System"

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"P P 48 1170" P 48 1170 **Laser Induced Fluorescence (LIF) Endoscopy (E): A Pilot Study of a Real-Time (RT) Autofluorescence Imaging System for Early Detection of Dysplasia and Carcinoma in the Gastrointestinal (GI) Tract**

G.A. DuVall<sup>1</sup>, J. Kost<sup>2</sup>, D. Scheider<sup>1</sup>, L. Lilge<sup>2</sup>, M. Cirocco<sup>1</sup>, S. Hassaram<sup>1</sup>, G. Kandel<sup>1</sup>, P. Kortan<sup>1</sup>, G. Haber<sup>1</sup>, T. Mang<sup>2</sup>, R. DaCosta<sup>2</sup>, B. Wilson<sup>2</sup>,

\*N. Marcon<sup>1</sup>

<sup>1</sup> The Wellesley Hospital, Toronto, Canada

<sup>2</sup> The Ontario Cancer Institute, Toronto, Canada *Purpose:* RT LIF bronchoscopy (Xillix, Vancouver) has been established as a sensitive screening tool for dysplasia/carcinoma in the bronchial tree. The purpose of this study was to demonstrate the feasibility of RT LIFE in the GI tract for differentiating normal mucosa from dysplasia/carcinoma. *Methods:* 102 patients (59 male, mean age 65) consented to have RT LIFE imaging performed during routine colonoscopy, 59; esophagogastroduodenoscopies (EGD), 43. All procedures were documented with video and still images. In addition to routine white light endoscopy, all mucosal abnormalities were examined with RT LIFE using an excitation wavelength of 437 nm. Tissue from the lesions and adjacent normal mucosa was obtained. In a blinded fashion, all samples were assessed by a single pathologist. A specific numerical diagnostic code (1 to 4 denoting non-neoplastic changes, 6 to 9 neoplastic, and 5 atypia of undetermined significance) was assigned to each sample. *Results:* All lesions noted on routine endoscopy were seen on RT LIFE. The still LIFE images were reviewed by a single gastroenterologist familiar with the RT LIFE system. The lesions were classified as LIFE positive ("red" fluorescence) or LIFE negative ("no red" fluorescence) when compared with normal ("green" fluorescence) mucosa. The sensitivity and specificity of the LIFE system was calculated by correlating the positive and negative LIFE findings to the pathology codes. The sensitivity and specificity for colonic disease were 89.6% and 86.8%. In esophageal disease, excluding Barrett's without obvious carcinoma (as it universally produced false positive LIF findings) the sensitivity and specificity were 93.3% and 86.9%, respectively. *Conclusion:* The RT LIFE imaging system in the GI tract can differentiate normal mucosa from dysplasia/carcinoma with a combined sensitivity and specificity of 90.5% and 86.8%, if Barrett's esophagus is excluded. Given that Barrett's esophagus produces a false positive fluorescent signal (due to intrinsic differences in fluorescent properties of gastric and squamous mucosa), it is difficult to identify dysplasia/carcinoma within the gastric metaplasia, as compared to identifying dysplasia/carcinoma in the setting of squamous epithelium. Further investigation is needed to better define the role of RT LIFE imaging in the surveillance of Barrett's esophagus. *Oncology, general: Screening, prevention Endoscopy, general: Instrumentation, diagnosis }* "Laser Induced Fluorescence (LIF) Endoscopy (E): A Pilot Study of a Real-Time (RT) Autofluorescence Imaging System for Early Detection of Dysplasia and Carcinoma in the Gastrointestinal (GI) Tract"

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"P P 48 1171" P 48 1171 **Endo-Loop in the Prevention of Post-Polypectomy Bleeding — Preliminary Results** J.-F. Rey<sup>1</sup>, T.A. Marek<sup>2</sup>

<sup>1</sup> Institut Arnault Tzanck, Saint-Laurent-du-Var, France

<sup>2</sup> Silesian Medical Academy, Katowice, Poland *Introduction:* Bleeding is the most frequent complication of endoscopic polypectomy, occurring in up to 4% of cases. The risk of post-polypectomy bleeding is especially increased in large, thick-stalked polyps. The risk of bleeding is also higher in patients on anti-coagulant/NSAID treatment. The injection of adrenaline or adrenaline and sclerosant is recommended for such cases, but the injection of adrenaline alone may not prevent the delayed bleeding, while sclerosant injection may increase the risk of bowel perforation. The development of mechanical devices, i.e. endo-loop, and clips, opened the new possibility in the prevention of post-polypectomy hemorrhage. Both tools could be placed on polyp's stalk before snaring, compressing mechanically stalk's vessels and preventing early, as well as, by being left on the stalk remnant, delayed bleeding. We herein report our preliminary results of use of endo-loop in the prevention of bleeding after colonic polypectomy. *Methods and patients:* The prototype endo-loop (Olympus Optical Co.) is made from teflon, with length of 50 mm and width of 35 mm when completely opened. The closing of the loop is performed by sliding the stopper. After visualization of the polyp endo-loop is placed on the stalk and closed. The polypectomy is then performed in the standard manner, cutting the stalk between endo-loop and polyp's head. After the polypectomy the loop is left on place to spontaneous fall off, what occurs about 7 days after the procedure. During the period between July 1994 and November 1995, endo-loops were used prophylactically in 15 patients with colonic polyps. *Results:* Endo-loops were placed correctly in 14 out 15 attempts. In one patient the placement failed, due to size of the polyp (> 25 mm). The significant change of the color of the polyp's head caused by ischaemia was noted. In all 14 patients with correctly placed endo-loop it was possible to perform cutting between endo-loop and the head of the polyp. No blood flow from the stalk was observed after polypectomy. No delayed bleeding occurred in one month after the procedure. *Conclusions:* 1. Endo-loop seems to be efficient tool in the prevention of post-polypectomy bleeding. 2. The placement of endo-loop before polypectomy is technically easy. 3. The endo-loop prevention may be of value in patients with increased risk of bleeding, i.e. patients with big, thick-stalked polyps, clotting disorders, low platelet count and being on anti-coagulant/NSAID treatment. } "Endo-Loop in the Prevention of Post-Polypectomy Bleeding / Preliminary Results"

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"P P 48 1172" P 48 1172 **Use of Argon Beamer Electrocoagulation in a UK Endoscopy Unit**

S. Elhasani, R.M. Hodson, H.H. Tsai, G.S. Duthie

\*K.R. Wedgwood

Castle Hill Hospital, Cottingham, East Yorkshire, England, HU16 5JQ The argon beamer is a new device that delivers controlled electrocoagulation. This device can be introduced via an endoscope and may aid in haemostasis and tumour debulking in the GI tract. We have evaluated its usefulness in a GI endoscopy unit. *Methods:* A prospective audit of the use of the argon beamer (ERBE ICC200) over an 8 month period (1.10.95–21.5.96) in a busy endoscopy unit. *Results:* A total of 28 therapeutic procedures were carried out using the argon beamer in 18 patients. The therapeutic procedures were for haemostasis (11), tumour debulking (8), angiodysplasia (6), inflammatory polyps (2) and tumour ablation (1). Of those patients whom underwent argon beam coagulation for haemostasis, 2 were for bleeding from oesophageal ulcers (1 malignant), 6 patients had coagulation of the polyp base after snare polypectomy, 1 patient was treated for bleeding after biopsy of a gastric ulcer, 1 patient for bleeding after a papillotomy and 1 patient had a bleeding ampullary cancer. All patients had a successful arrest of bleeding after 1 treatment. 4 patients had treatment for tumour debulking (1 previously stented oesophageal cancer, 1 cardia lesion, 1 rectal, 1 ampullary), requiring a mean of 2 sessions to achieve adequate tumour debulking. 3 patients were successfully treated for angiodysplastic lesions (2 stomach, 1 colonic) after a mean of 2 sessions. 1 patient had a villous tumour of the caecum which was successfully ablated after 1 treatment and 1 patient underwent 2 treatments to successfully eradicate inflammatory polyps in the oesophagus. All operators found the argon beamer easy to use and there were no complications. *Conclusions:* Argon beamer electrocoagulation therapy appears to be a safe, effective and versatile tool for the endoscopist. It is valuable as a therapeutic modality for bleeding, tumour debulking and obliteration of angiodysplasia. Endoscopy, general: Instrumentation, therapy Endoscopy, general: GI bleeding } "  
"Use of Argon Beamer Electrocoagulation in a UK Endoscopy Unit"

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"P P 48 1173" P 48 1173 **Argon Plasma Coagulation (APC) in Flexible Endoscopy of the Gastrointestinal Tract: In vitro Studies** W. Johanns, J. Janssen, C. Jakobeit,

\*L Greiner

Medical Clinic A, Municipal Hospital Wuppertal, University of Witten Herdecke, Germany

*Introduction:* Diathermy procedures are indispensable in interventional endoscopy. Argon plasma coagulation (APC) is an innovative no-touch electrocoagulation technique in which high-frequency alternating current is delivered to the tissue by ionised argon gas without contact. Before clinical application of the technique, we studied the effect of APC to the tissue under defined in-vitro conditions in order to obtain data on the diameter and depth of necrosis and thus assess the risk of perforation. *Methods:* The coagulation current was applied to a total of 20 fresh operative specimens, 4 from the stomach, 6 from the small intestine and 10 from the colon. Five different power/gas flow settings between 40 and 155 W and 2 and 7 l/min were used. The impact time (1 s–10 s) and the incident angle of the probe (45° and 90°) were also varied. The treated specimens were fixed in 4% formalin solution and examined microscopically. *Results:* We evaluated a total of 640 lesions. The histological examinations showed an onion-skin-type pattern with a layer of vesicular necrosis (desiccation zone), followed by a dense homogenised layer (coagulation zone), then by increasing occurrence of fibrous structures and pyknotic nuclei (devitalisation zone). The depth and diameter of the coagulation zone increased with increasing impact times and energy settings. Depending on the energy setting and impact time the diameter of the coagulation zone was 0.1–1.1 cm and the depth of penetration 0.1–2.4 mm. Variation of the incident angle of the probe only produced a more oval-shaped coagulation zone but did not reduce the depth of penetration. No perforation of the intestinal wall occurred in any of the constellations investigated. *Conclusion:* APC is an effective and relatively low-cost alternative to laser therapy in gastrointestinal endoscopy. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Instrumentation, therapy } "Argon Plasma Coagulation (APC) in Flexible Endoscopy of the Gastrointestinal Tract: In vitro Studies"

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"P P 48 1174" P 48 1174 **Argon Plasma Coagulation (APC) in Flexible Endoscopy of the Gastrointestinal Tract: Initial Clinical Experiences** W. Johanns, J. Janssen, C. Jakobeit,

\*L. Greiner

Medical Clinic A, Municipal Hospital Wuppertal, University of Witten Herdecke,

Germany *Introduction:* Interventional endoscopy would be inconceivable without the use of high-frequency diathermy techniques, e.g. for polypectomy and papillotomy. In addition to the conventional unipolar and bipolar coagulation techniques, the argon plasma coagulation (APC) provides us with a new method of electrocoagulation in which high-frequency alternating current can be delivered to the tissue by a no-touch technique. *Patients/Methods:* APC was used in the upper and lower gastrointestinal tract in 66 consecutive patients with a mean age of 68 (47–86) years. The indications for treatment were bleeding from angiodysplastic lesions or polypectomy sites, oozing of blood from erosions or ulcers, bleeding due to vascular penetration by tumours, residual sessile adenoma tissue after snare adenomectomy and palliative treatment of stenosing tumours to restore patency before stent implantation. The maximum intensity of bleeding was Forrest Ib. The treatment was performed under combined sedation and analgesia. Two power/gas flow settings of 40 and 70 W and 2 and 3 l/min, respectively, were used. The impact time and incident angle were varied individually. *Results:* In 49 of the 50 patients with gastrointestinal hemorrhage definitive haemostasis was achieved in one to two sessions. In all of the 11 patients with residual sessile adenoma tissue complete removal was possible. Oesophageal patency was restored in all 5 patients with stenosing tumours. In one patient with angiodysplasia of the caecal pole an asymptomatic accumulation of gas in the submucosa was observed which resolved spontaneously. In two patients with extensive oesophageal carcinoma there was a transitory — also asymptomatic — accumulation of gas in the mediastinum and peritoneal cavity but no evidence of perforation. *Conclusion:* APC is an useful and non expensive alternative to laser therapy in the endoscopic management of gastrointestinal hemorrhage and flat or stenosing tumors. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Instrumentation, therapy } "Argon Plasma Coagulation (APC) in Flexible Endoscopy of the Gastrointestinal Tract: Initial Clinical Experiences"

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"P P 48 1175" P 48 1175 **Endoscopic Infusion of Ethanol in Inoperable Tumours of the Upper and Lower Gastrointestinal Tract**

\*G. Alexandrakis, P. Skordilis, S. Potamianos, I. Mouzas, S. Spanoudakis, N. Fragiadakis, E. Kouroumalis, O.N. Manousos

Dept. of Gastroenterology, University Hospital of Crete, Heraklion, Greece Laser palliative treatment of inoperable tumours of oesophagus and large bowel is an accepted, well established but very expensive treatment. *Aim of the Study:* To assess the efficacy of endoscopic infusion of absolute ethanol for the palliative treatment of inoperable gastrointestinal tumours. *Patients and Methods:* 15 patients were studied (age 66–88 years, median 71 years) 11 patients with obstructive inoperable tumours of the large bowel, (8 men and 3 women), and 4 patients (1 man and 3 women) with extensive inoperable oesophageal carcinomas. Through a sclerotherapy needle absolute ethanol was injected in dosage from 5 to 40 ml according to the mass volume. *Results:* After 4–6 sessions of ethanol injection, obstruction of large bowel was considerably diminished with easy passage of the endoscope and no more problems for a 6 month follow-up period in 8 of the 11 patients. In only one patient a palliative surgical procedure was necessary. No complications were noted. In 3 of the 4 patients with oesophageal carcinoma, dysphagia was significantly reduced. However one patient died from cerebrovascular accident one month later. *Conclusions:* Ethanol infusion is a cheap and effective palliative alternative to Laser treatment for inoperable oesophageal and large bowel tumours. Oncology, general: Therapy Oncology, specific: Oesophagus Oncology, specific: Colon, rectum } "Endoscopic Infusion of Ethanol in Inoperable Tumours of the Upper and Lower Gastrointestinal Tract"

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## "P P 48 1177" P 48 1177 Virtual CT-Gastroscopy — A New Technique

\*P. Springer, A. Dessel, S.M. Giacomuzzi, W. Buchberger, A. Stöfger, M. Oberwalder, W. Jaschke

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The purpose was to evaluate different techniques of virtual CT-gastroscopy in correlation to fiberoptic endoscopy. 3 mm helical CT-scans of a pig stomach were obtained with air insufflation, instillation of diluted contrast (amidotrizoat) and with double contrast. Afterwards virtual endoscopy images were calculated on a Sun Sparc 20 workstation (128 MB RAM, 4 GB Festplatte) by using dedicated Software (Navigator, General Electrics Medical Systems Company). The endoscopy sequences were compared to fiberoptic endoscopy. Virtual endoscopy with diluted contrast and with double contrast showed artifacts simulating polyps, erosions or flat ulcers. Monocontrast air insufflation sequences showed excellent correlation to real endoscopy and anatomical specimen with no artifacts except slice artifacts (partial voluming). As our preliminary results show virtual CT-gastroscopy is able to produce insights into the upper gastrointestinal tract similar to fiberoptic endoscopy, but it is, as spatial resolution of CT is limited, not competitive to fiberoptic gastroscopy. Radiology and ultrasound: Diagnosis Endoscopy, specific: Stomach, duodenum Endoscopy, general: Instrumentation, diagnosis }

"Virtual CT-Gastroscopy / A New Technique"

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## "P P 48 1178" P 48 1178 Virtual Reality in Surgical Practice

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<sup>1</sup> Dep. of Medicine A, Haukeland Hospital, University of Bergen, Bergen, Norway *Purpose:* To evaluate whether a new software technology for exploring spatial environment could be applied during gastrointestinal endoscopic and laparoscopic surgery in order to improve the three-dimensional impression of the surgical field. *Material and methods:* The new software was applied during examinations on phantoms *in vitro* and in patients during endoscopy or laparoscopic surgery. A stereotactic frame was attached to the phantom or the operating table, and a system for position and orientation registration was interfaced to the endoscopic or laparoscopic instruments. The optical devices were manipulated by a stepping motor device. Images were captured, digitized and processed using a WindowsNT work-station with commercially available software. *Results:* *In vitro* studies demonstrated good correlation between the actual object and the computer based spatial scene. The technique could be applied for endoscopic and laparoscopic image reconstructions. A correct perspective was maintained, giving the user the sense of being there and looking around. *Conclusions:* This imaging modality enables interactive manipulation and realistic 360\ 'b0 simulation of endoscopic and laparoscopic scenes. Virtual reality images can be produced for surgical planning and education, and the technique may impact surgical approaches, especially during minimal invasive procedures. Endoscopy, general: Instrumentation, diagnosis Laparoscopic surgery: Diagnosis } "Virtual Reality in Surgical Practice"

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## "P P 48 1179" P 48 1179 Endoscopic Ultrasound-Guided Histologic Needle Biopsy

\*N. Harada, T. Kouzu, M. Arima, K. Isono

Department of Surgery (II), Chiba University School of Medicine, Chiba, Japan Endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) is recently under evaluation. However, histologic biopsy may have advantage rather than aspiration cytology in diagnosing e.g., myogenic tumors. We evaluated the role of EUS-guided histologic needle biopsy in those patients with submucosal tumors and extrinsic lesions of UGI tract. *Methods:* From August 1994 to January 1996, 20 consecutive patients (10 M, 10 F; mean age 61.4 years, range 42–87 years) underwent EUS-guided histologic needle biopsy. Of the 20 lesions, 14 were submucosal (3 esophageal, 11 gastric) and 6 were extrinsic (3 pancreas, 1 retroperitoneal, 1 mediastinal and 1 paraaortic lymph node). EUS-guided histologic needle biopsy was performed using a phased array endoscopic ultrasound transducer Toshiba PEF-703FA. The needle used was the EUS-guided histologic biopsy needle Endo-Sonopsy Needle (21-gauge, 25-mm needle, 1600-mm Teflon catheter embedded stainless steel wire mesh with stylet; Hakko Shoji, Tokyo, Japan). *Results:* In 17 of 20 patients, adequate tissue specimens were obtained (85%). EUS-guided histologic needle biopsy was diagnostic in 15 of 17 patients in whom surgical confirmation was available or confirmed by clinical follow-up (88.2%). In the subgroup of patients with myogenic tumors, EUS-guided histologic needle biopsy was diagnostic in 7 of 9 patient (77.8%). There were no complications in this series. *Summary:* 1) EUS-guided histologic needle biopsy is a sensitive technique for establishing a histologic diagnosis. 2) EUS guided histologic needle biopsy permits histologic confirmation of myogenic lesions. *Conclusion:* EUS-guided histologic needle biopsy should be considered in the evaluation of gastrointestinal and extrinsic lesions. Endoscopy, general: Instrumentation, diagnosis Echoendosonography: Echoendoscopy } "Endoscopic Ultrasound-Guided Histologic Needle Biopsy"

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## "P P 48 1180" P 48 1180 Endoscopic Ultrasound-Guided Fine Needle Aspiration in the Evaluation of Extrarectal Pelvic Masses

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Division of Gastroenterology and Section of Surgical Oncology, Medical University of South Carolina, Charleston, South Carolina

<sup>1</sup> Digestive Disease Center, Medical University of South Carolina, Charleston, South Carolina  
*Introduction:* The role of endoscopic ultrasound (EUS) in staging rectal cancer is well established but its role in the evaluation of peri-rectal processes is less well defined. The development of the linear array echoendoscope (EE) now allows guided fine needle aspiration (FNA) cytology. We performed this study to determine the role of EUS-guided FNA in the evaluation of pelvic masses. *Patients/Methods:* Between June 1994 and October 1995, 8 patients were referred for EUS evaluation of pelvic masses. A 360° radial scanning EE was first used to identify the abnormality and establish overall orientation. Next, the linear array EE (Pentax FG 32-UA) was used to perform guided FNA. Pulsed and/or color Doppler were used to distinguish vascular structures. A Teflon catheter with a 23 gauge needle was advanced thru the working channel of the EE and the needle guided into the mass using real time ultrasound imaging. *Results:* In 5/8 (63%), a definitive diagnosis of malignancy was made. These included adenocarcinoma (2), ovarian carcinoma (1), cervical carcinoma (1), and lymphoma (1). In two patients the EUS image and FNA were consistent with abscesses; both were treated accordingly with resolution of symptoms. The EUS images and FNA from the sample of the remaining patient suggested an inflammatory reaction felt to be related to prior radiation therapy. The total cost excluding cytopathology ranged from \$1046–1252 for EUS compared to \$1323–1823 for a CT-guided aspiration. The diagnostic yield of EUS + FNA was 100% as determined by positive FNA and/or clinical follow-up. The procedures were completed in 45 minutes on average, required no sedation, and there were no biopsy related complications. *Conclusions:* EUS is able to detect pelvic abnormalities; fine needle aspiration is a useful adjunct for suspected neoplasms and EUS-guided FNA may be a cost-saving diagnostic method in these pts.  
Echoendosonography: Echoendoscopy Oncology, general: Screening, prevention } "Endoscopic Ultrasound-Guided Fine Needle Aspiration in the Evaluation of Extrarectal Pelvic Masses"

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"P P 48 1181" P 48 1181 **Ultrasonically Guided Percutaneous Therapy of Postoperative Complications in Gastrointestinal Surgery**

\*M. Opacic, N. Rustemovic, R. Pulanic, B. Vucelic, R. Ostojic, Z. Krznaric, T. Brkic

Division of Gastroenterology, Department of Internal Medicine, University Hospital Rebro, Zagreb, Croatia *Purpose:* To evaluate percutaneous drainage as a method of choice in therapy of intraperitoneal collections after abdominal surgery. *Method:* 31 intraperitoneal fluid collections with different intraperitoneal localisation (22 abscesses, 6 hematomas and 3 bilomas) in 30 patients with recent intraabdominal surgical intervention were found and verified by aspiration under ultrasonographic guidance. Some of the patients had high risk for surgical therapy of complications. Modified Seldinger and trocar technique were used in drainage procedure. Drainage was performed with various "Angiomed" and "Cook" catheters, 10 to 16 Fr in diameter and "Aloka 680 SSD" ultrasound unit with 3.5 MHz convex probe. Puncture was guided by free hand technique. Therapeutic procedure was effective in 28 collections (90%). Average duration of drainage was 14 days. There were no serious complications during the drainage procedure. In three patients additional surgical procedure was necessary to complete the evacuation of collections. *Conclusion:* Drainage was successful in 90% of our patients, without serious complications. Our experience confirmed the value of ultrasonically guided percutaneous drainage in previously surgically treated patients with intraperitoneal abscesses and liquid collections, especially in patients with high risk for surgical treatment of such complications. Radiology and ultrasound: Therapy } "Ultrasonically Guided Percutaneous Therapy of Postoperative Complications in Gastrointestinal Surgery"

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"P P 48 1182" P 48 1182 **Development of a High Intensity Focused Ultrasound (HIFU) Transducer Suitable for Endoscopic Applications**

\*F. Prat, J.Y. Chapelon, A. Arefiev, Y. Theillière, D. Cathignol

INSERM U281, Lyon, France The potentialities of HIFU for selective and non-invasive tissue destruction have been demonstrated experimentally and clinically. Until now, only large transducers for extracorporeal applications had been evaluated. We have developed small HIFU transducers for endoscopic (GI and laparoscopic) purposes. The therapeutic element used was a semi-spherical piezocomposite transducer, 50 × 22 mm, mounted on a handpiece, with a focal distance of 45 mm and a working frequency of 3 MHz. Targeting was achieved with a 2-dimensional ultrasound sector scan probe. 16 new Zealand hybrid rabbits were used for preliminary experiments designed for therapeutic parameter determination. The beam was directed transcutaneously to the liver parenchyma at depths of 20–25 mm from the abdominal wall. Pulses were adjusted to respiratory motion in order to achieve destruction of 1 cm<sup>3</sup> tissue volumes. In a second series of 3 animals bearing a percutaneous gastrostomy, volumes of liver parenchyma were targeted through the gastric wall. Autopsies were performed 24 hours after treatment. 1.2 – 0.2 cm<sup>3</sup> volumes of coagulation necrosis were reproducibly obtained in the liver at the desired site with twenty, 4 sec pulses delivered at a power output of 13 W.cm<sup>-2</sup>. The mean treatment duration required to generate one such lesion in the liver was 17 – 3 minutes. In the rabbits treated through the gastric wall, 1.1 – 0.2 cm<sup>3</sup> lesion volumes were obtained. Neither skin nor gastric wall burns were observed with the treatment parameters defined. HIFU can be applied successfully with small transducers readily adaptable to the tip of an endoscope, thus opening a new perspective for endotherapy. Endoscopy, general: Instrumentation, therapy Oncology, general: Therapy Radiology and ultrasound: Therapy } "Development of a High Intensity Focused Ultrasound (HIFU) Transducer Suitable for Endoscopic Applications"

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"P P 48 1184" P 48 1184 **The 3D Surface Image of the Ultrasonic Probe; Comparison of the Reconstructed Image with the Macroscopic Findings of Gastrointestinal Lesions**

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2nd Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan

*Purpose:* The aim of this study is to clarify the usefulness of three-dimensional (3D) ultrasonic surface images obtained with the endoscopic ultrasonic probe. *Methods:* Eighteen formalin-fixed resected specimens of gastrointestinal (GI) lesions (2 esophageal cancers, 11 gastric cancers, 2 gastric ulcers, 1 duodenal ulcer, and 2 colonic cancers) and 20 patients with GI tract lesions (6 esophageal lesions, 3 gastric lesions, and 11 rectal lesions) were examined with the ultrasonic probe. The probe was passed over the specimens in vitro and withdrawn via the biopsy channel in vitro at a constant speed. The images were recorded on video and, following the examination, 3D displays of the lesions were reconstructed by computer (DEC station 3000/300) and compared with the gross pathological findings. We used the ultrasound probe (MP-PN series, 15 MHz, SSD-550, Aloka Co. Ltd.) to obtain ultrasound images. We compared 3D surface images with the macroscopic findings of the resected specimens and the lesions in vivo. We evaluated quality in three grades: good, fair, and poor. *Results:* In vitro study, the reconstructed surface image was consistent with the macroscopic findings. According to our evaluation, 13 cases were judged good, 4 fair, and 1 poor. In vivo study, 2 cases in the upper GI were evaluated good, 6 fair, and 1 poor. On the other hand, 7 cases of rectal lesions were evaluated good, 3 fair, and 1 poor. The surface image of flat and non-demarcated lesions didn't correlate well with the macroscopic findings. We could not obtain good images of upper GI lesions compared with rectal lesions because of breathing and circulatory pulsations. However, we could obtain the reconstructed surface image of lesions behind a fold or from the view opposite that of the conventional viewpoint by scanning with the probe. *Conclusions:* Using the endoscopic ultrasound probe, we can obtain both cross-sectional images and surface image of GI lesions. Endoscopy, general: Instrumentation, diagnosis Radiology and ultrasound: Diagnosis } "The 3D Surface Image of the Ultrasonic Probe; Comparison of the Reconstructed Image with the Macroscopic Findings of Gastrointestinal Lesions"

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## "P P 48 1185" P 48 1185 Identification and Histologic Correlation of Gastrointestinal Wall Layers Imaged with a MR-Endoscope

\*D. Kulling, D. Bohning, C. Kay, K. Spicer, R. Hawes

Digestive Disease Center, Medical University of South Carolina, Charleston, SC *Purpose:* To define the anatomic correlates to the gastrointestinal wall layers imaged in vitro with the new magnetic resonance (MR) endoscope. *Methods:* Using a MR-endoscope (XGIF MR30, Olympus, Tokyo, Japan) in a 1.5 Tesla scanner, 22 porcine tissue specimens (4 esophageal, 6 gastric, 6 duodenal, 6 rectal) were imaged. We performed T1- and T2-weighted spin echo, T2-weighted fast spin echo and FSPGR sequences. Serving as a marker, 0.1 ml cyanoacrylate was injected into the tissue strips. 18 specimens were imaged in a fresh state, 6 were reexamined after fixation in 10% formalin and 4 specimens were scanned in a fixed state only. Tissue sections representing the area previously scanned were stained with hematoxylin and eosin. *Results:* T1-weighted spin echo images (TR 600, TE 30, FOV 4 {\'b4} 4 cm, 256 {\'b4} 224 matrix, 3 mm slice, 1.5 mm spacing, 2 NEX) revealed the best layer discrimination. The use of a cyanoacrylate drop injected into the tissue strip provided an accurate mechanism to correlate histologic layers with the MR images. In T1 images, in general, the mucosa shows high signal intensity, the submucosa shows low intensity and the muscularis propria has an intermediate signal intensity. In the proximal duodenum and distal rectum however, the submucosa is densely infiltrated by glands, resulting in high signal intensity of the submucosa. In the esophagus and rectum the muscularis propria can be visualized as 3 layers consisting of circular and longitudinal muscle and intervening connective tissue, which appears with low signal intensity. Imaging after fixation of the tissue showed significantly reduced contrast between different layers. *Conclusions:* In vitro imaging with the new MR-endoscope shows 3 to 5 wall layers of the porcine gastrointestinal tract depending on the segment scanned. This detail in gut wall imaging opens promising prospects for T-staging of gastrointestinal tumors. Endoscopy, general: Instrumentation, diagnosis }" "Identification and Histologic Correlation of Gastrointestinal Wall Layers Imaged with a MR-Endoscope"

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## "P P 50 1197" P 50 1197 Efficacy and Longterm Follow-Up of Endoscopic Variceal Ligation in Esophageal Varix Bleeding

\*D.H. Lee, K.K. Lee, H.C. Jung, H.S. Lee, Y.B. Yoon, I.S. Song, C.Y. Kim

Department of Internal Medicine and Liver Research Institute, Seoul National University, College of Medicine, Seoul, Korea Hemorrhage from esophageal varices is a catastrophic complication of portal hypertension. Endoscopic variceal ligation (EVL) has been proven to be a viable substitute for endoscopic injection sclerotherapy (EIS). But rebleeding after EVL treatment is not infrequent and has been a problem of longterm management of esophageal varix bleeding. *Aim:* The aim of this study was to evaluate longterm outcome of EVL, rebleeding rate of esophageal varices and longterm survival rate. *Methods:* Total 52 patients who had received EVL because of esophageal varix bleeding were followed-up and analysed during three years period. *Results:* Total 689 ligations were performed during 117 separate EVL sessions. Control rate of acute bleeding was 90.5% (38 of 42 patients). Four patient who were failed in control of bleeding were taken EIS with successful bleeding control. The eradication rate of esophageal varix was 76.2% (32 of 42 patients) and the mean session for eradication of varix was 3.0 (2–6), the mean number of bands per person was 16.0 (5–41), and the mean number of bands per session was 6.0 (4–11). Rebleeding after initiation of EVL occurred in 11 of 42 patient (26.2%); Rebleeding occurred after 1–27 months (mean 11.7 months) since EVL was done. 81.8% of rebleeding occurred after 6 months since EVL was done. The mortality rate and survival rate after varix eradication during follow-up period (6–45 months, mean: 15.5 months) was each 14.3% (6/42) and 85.7% (36/42). The causes of death were hepatic failure (3/6), esophageal variceal bleeding (2/6) and hepatic encephalopathy (1/6). After EVL, there were no serious treatment-related complications; except mild complications of mild chest pain in 5 patient (12.0%) and mild substernal pain in 7 patients (16.6%). *Conclusion:* 1) These results suggested that although EVL is a safe and effective method for treatment of variceal bleeding control and eradication of esophageal varices with least serious complication, rebleeding of varices after EVL treatment occurred in about one forth and about 80% of rebleeding occurred after 6 months since EVL was done. 2) Regular periodic examination for early detection of recurrence of esophageal varix (esophagogastrosocopy) and repeat EVL should be required because of high risk of rebleeding especially after 6 months since EVL was done. Endoscopy, general: GI bleeding Endoscopy, specific: Oesophagus } "Efficacy and Longterm Follow-Up of Endoscopic Variceal Ligation in Esophageal Varix Bleeding"

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## "P P 50 1198" P 50 1198 Endoscopic Ligation in Acute Esophageal Variceal Bleeding Will Exacerbate Concomitant Gastric Variceal Bleeding?

\*C.Y. Chen<sup>1</sup>, C.Y. Chen, T.T. Chang, X.Z. Lin

<sup>1</sup> Department of Internal Medicine, Chia-Yi Christian Hospital, Taiwan

National Cheng Kung University Hospital, Taiwan Endoscopic variceal ligation (EVL) has been developed to provide a safe and effective alternative for treatment of bleeding esophageal varices. However, in bleeding esophageal varices (EV) with concomitant gastric varices (GV), EVL may be relatively contraindicated for fear of the exacerbation of GV bleeding. Histoacryl injection of gastric varices had shown excellent effect. *Material and Method:* We initiate this randomized, controlled study to evaluate the hemostatic effect of EVL and the GV status. Forty-five patients were included because of bleeding EV with concomitant GV at index endoscopy. Twenty-two patients were treated with histoacryl injection of GV followed with EVL for bleeding EV (Group A), and 23 patients with EVL for bleeding EV alone (Group B). EVL was according to Stiegmann method. Histoacryl was injected intra-variceally into concomitant nonbleeding gastric varices only during the first session in patients of the Group A with lipiodol (1:1). *Result:* Active EV bleeding at the first treatment was controlled in 40 of 45 patients (88.8%): 19/22 (86.3%) in Group A and 21/23 (91.3%) in Group B,  $P > 0.05$ . Five episodes of early EV rebleeding were controlled by the second EVL. No evidence of early GV bleeding was found in both group. Variceal eradication was achieved in 35 of 45 patients (77.7%): 18/22 (81.8%) in Group A and 17/23 (73.9%) in Group B,  $P > 0.05$ . Recurrent bleeding occurred in 22.7% (5/22) in Group A compared to 30.4% (4/23) in Group B ( $P > 0.05$ ). However, one fatal rebleeding from GV in Group B was found 183 days after initial treatment. *Conclusion:* EVL can be safely performed in bleeding EV with concomitant GV. There was no significant benefit in variceal eradication and prevention of second gastric variceal bleeding if further histoacryl injection of concomitant gastric varix was done. However, prophylactic histoacryl injection of GV may prevent further fatal GV bleeding after esophageal variceal eradication. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, specific: Oesophagus Endoscopy, general: GI bleeding } "Endoscopic Ligation in Acute Esophageal Variceal Bleeding Will Exacerbate Concomitant Gastric Variceal Bleeding?"

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## "P P 50 1199" P 50 1199 The "Six-Shooter" — A New Technique for Endoscopic Variceal Ligation

\*U. Seitz, S. Bohnacker, K.F. Binmoeller, F. Thonke, B. Brand, N. Soehendra

Department of Endoscopic Surgery, University Hospital Eppendorf, Hamburg, Germany Ligation therapy of varices is an established procedure. The major drawback is the multiple introduction of the endoscope, that necessitates an overtube. We report our experience with the new Multishooter-Rubberband-Ligation-Set "Six-Shooter" (Wilson-Cook Co.). Six ligations can be placed before the endoscope has to be reloaded. There is no need for an overtube. *Methods:* Time for application, misshooting rate, and efficacy of treatment were determined. 45 patients (Child A: 26 pts/B: 15 pts/C: 4 pts) with non-bleeding varices (I 6 pts/II 21 pts/III 18 pts) were treated in 122 sessions with 132 "Six-shooter"-sets. Patients were divided in 2 groups: untreated varices (UTR, 19 pts) and prior treated with sclerotherapy and/or Histoacryl'-obliteration (SKL, 26 pts). Hemostasis of acute variceal bleedings was achieved by Histoacryl'-injection before ligation was started. When ligation showed no further effect on the size of varices in 2 subsequent sessions treatment was changed to sclerotherapy. *Results:* Median follow-up was 7 weeks (1–39). Median 6 rubberbands/session (2–14) were applied in median 2 minutes (0.5–9.0). Eradication of the varices was possible in 94% of the UTR-pts (median 2 sessions; 1–4) and in 70% of the SKL-patients (median 2 sessions; 1–4). Recurrence of varices had to be noted 58% of the UTR-pts within 4 weeks. There was no severe complication like perforation, stricture or procedure related bleeding. *Conclusions:* The handling of the Six-Shooter is safe. Application of rubberbands is easy and fast. Eradication of prior untreated varices is possible within few sessions, but recurrence of varices occurs frequently. A majority of recurrent varices after sclerotherapy may be successfully treated by the "Six-shooter". Endoscopy, specific: Oesophagus Endoscopy, general: Instrumentation, therapy } "The "Six-Shooter" / A New Technique for Endoscopic Variceal Ligation"

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"P P 50 1200" P 50 1200 **Combination of Ligation and Sclerotherapy Versus Ligation Alone in Eradication of Bleeding Esophageal Varices** B.D. Djurdjevic

Zvezdara University Hospital, Belgrade, Dimitrija Tucovica 161 *Aim:* A prospective, randomized trial was performed in order to assess whether faster eradication of bleeding esophageal varices was achieved with a combination of ligation and sclerotherapy than with ligation alone. *Patients and methods:* Thirty-six patients with esophageal varices that were actively bleeding or had bled recently were randomly assigned to a combination of ligation and sclerotherapy with a smaller volume of sclerosing agent (1 ml of 1% Aethoxysclerol). Ligation was done as described by Stiegmann. Endoscopic treatment was repeated a week later after initial procedure and then at 14-day intervals until variceal obliteration was achieved or varices were reduced to grade I. Thereafter, endoscopic examination was done at three-month intervals or whenever rebleeding occurred. Mean follow-up was 5.5 months. *Results:* No significant differences were found between combined therapy and ligation alone in respect to the number of sessions, required for achieving of variceal eradication (2.3 – 0.2 vs. 2.5 – 0.3), rebleeding (8% vs 9%) complications (11% vs 8.5%), or deaths (10% vs 12%). *Conclusions:* We conclude that a combination of ligation and sclerotherapy is not superior to ligation alone in regard to rapidity of eradication of esophageal varices and decreasing the rate of complications and therefore we do not recommend this combining therapy for the treatment of esophageal varices. Endoscopy, general: GI bleeding Endoscopy, specific: Oesophagus } "Combination of Ligation and Sclerotherapy Versus Ligation Alone in Eradication of Bleeding Esophageal Varices"

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**"P P 50 1201" P 50 1201 Audit of Combined Band Ligation and Injection Sclerotherapy Following Octreotide Infusion in Grade IV Bleeding Esophageal Varices Gun Tayyab**

Cons. Gastroenterologist, Jinnah Hospital, Lahore, Pakistan Bleeding varices is one of the common emergencies in our hospitals due to high prevalence of the post infectious chronic liver disease. Hemostasis is in particularly difficult to achieve when the varices are big and tortuous with the hemocystic areas on the overlying mucosa. Band ligation alone may not be sufficient in these patients. In February 1996 a policy was adopted to keep all the patients with the h/o upper GI bleed on octreotide infusion (50 ug stat and 50 ug/h) till endoscopic intervention. At the time of endoscopy patients with grade IV varices were separated out and dealt by band ligation followed by injection sclerotherapy with absolute. alcohol at the O.G jn and 5 cm proximal. Octreotide infusion was continued for another 48 hr. following the sclerotherapy. An upper GI endoscopy was repeated in all these patients every week till the time of complete obliteration of varices. Till 15th May, 70 patients had presented to us with variceal bleeding and 25 of these patients were found to have grade IV varices at the time of endoscopy. Their subsequent management was carried out according to the above mentioned routine. Mean age of these patients is 37 yrs (range 17–65 yr.) with a male to female ratio of 15:10, 7, 13 and 5 patients were in Child–Pugh stage A, B, and C respectively. One patient in first 24 hr. (4%) and two patients in the first 48 hr rebled (8%) which were managed successfully with esophageal transaction and stapling. None of the other patients rebled. A marked reduction of variceal size was observed in all the patients except for two on the endoscopy carried out on 7th day (21/23) and all the patients received another set of sclerosant injections on 14th day. The varices were well settled by third week. Two patients complained of transient dysphagia and pleuritic type of chest pain each. This audit is strongly in favor of using a combined approach (band ligation + injection sclerotherapy) along with octreotide infusion and there is a need of running a controlled trial to confirm these observations. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding Endoscopy, general: Instrumentation, therapy }  
"Audit of Combined Band Ligation and Injection Sclerotherapy Following Octreotide Infusion in Grade IV Bleeding Esophageal Varices"

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"P P 50 1202" P 50 1202 **Multiple-Fire Versus One-Shot Ligator in Endoscopic Elastic Band Ligation of Esophageal Varices** F. Garc\'eda Dur\'e1n, P. Mench\'e9n, C. Senent, R. Alvarez, P. Jimenez, J.A. Carneros, R. Ba\'flares<sup>1</sup>, M. Romero, J.L. Velo, E. Cos

<sup>1</sup> Gastrointestinal Department, Endoscopic Unit, Haemorrhagic Unit

General University Hospital "Gregorio Mara\'f1\'f3n" *Introduction:* The endoscopic elastic band ligation is a technique that it has been demonstrated efficient in the treatment of the esophageal varices. The appearance of multiple-fire ligators is permitting a better variceal management. *Aim:* Compare the endoscopic elastic band ligation with multiple-fire ligator versus one-shot ligator in two groups of patients, analyzing eradication rate, number of sessions for the variceal disappearance and cost of the treatment. *Methods:* Endoscopic elastic band ligation was used to prevent recurrence of variceal hemorrhage in 26 cirrhotic patients who had previously bled from esophageal varices. 13 patients were treated with one-shot ligator (Bard) and 13 with multiple-fire ligator (SpeedBand). There were no difference between the two groups concerning Child-Pugh score or variceal size at the beginning of the treatment. *Results:* The variceal eradication rate was similar in the two groups (0.92 vs 0.85 (p = 0.5), multiple-fire vs one-shot ligator, respectively). Also, the number of strips applied by patient, was similar in the two groups (8.07 vs 10.15, p = 0.2). The better patient tolerance permitted to apply more strips by session in the multiple-fire ligator group (5.01) than in the one-shot group (2.8). On the other hand, less sessions by patient were needed in the multiple-fire ligator group for variceal eradication (1.6 vs 3.6 (p < 0.001)). The cost medium of the treatment by patient to achieve the variceal eradication was similar in both groups. *Conclusions:* 1. Both treatments have a similar efficiency for variceal eradication. 2. The multiple-shot ligator permits to put more strips by session than one-shot ligator, due to a better patient allowance. 3. The multiple-fire ligator permits the variceal eradication in a minor number of sessions and with a similar cost than one-shot ligator. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy Endoscopy, general: GI bleeding } "Multiple-Fire Versus One-Shot Ligator in Endoscopic Elastic Band Ligation of Esophageal Varices"

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"P P 50 1203" P 50 1203 **Ligation of Esophageal Varices with Endo-Loop — an Alternative for Rubber Banding** J.F. REY<sup>1</sup>, T. MAREK<sup>2</sup>

<sup>1</sup> Institut Arnault Tzanck, St. Laurent-Du-Var, France

<sup>2</sup> Silesian Medical Academy, Katowice, Poland *Background and aim:* The results of treatment of esophageal varices by rubber banding are comparable to sclerotherapy, with significantly fewer complications. Variceal ligation with endo-loop is, like rubber banding, a new method based on mechanical compression of the varix. Study was undertaken to assess the safety and efficiency of endo-loop ligation in the treatment of esophageal varices. *Material and methods:* 34 patients with either recent history (22) or acute variceal bleeding (12) were treated by endo-loop ligation. Endo-loops were placed in sessions in ten days intervals, with average number of 2.7 loops per session and 4.2 sessions per patient. *Results:* Hemostasis was obtained in 11 out of 12 patients with acute bleeding; the remaining patient died. Early rebleeding was observed in additional 2 patients (6%); both underwent successful repeated treatment. The only early complication was fever observed in in 2 (6%) cases. Complete eradication of varices was obtained in 27 (79%) patients; in 7 cases ligation was supported with sclerotherapy and in 2 with the placement of clips. After average 6 months of follow-up 27 patients are still alive, 5 died from hepatic encephalopathy and 1 from the next episode of bleeding. *Conclusions:* 1. Ligation of esophageal varices with endo-loop appears to be safe and easy method. 2. The eradication rate after endo-loop placement does not differ significantly from results obtained by sclerotherapy or rubber banding. Endoscopy, general: GI bleeding } "Ligation of Esophageal Varices with Endo-Loop / an Alternative for Rubber Banding"

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## "P P 50 1204" P 50 1204 **Role of Endoscopic Ligation in Active Variceal Bleeding under Emergency Conditions**

\*W. Veltzke, A. Adler, R.E. Hintze

Depts. of Gastroenterology, Central Interdisciplinary Endoscopy, Virchow-Klinikum, Humboldt-University of Berlin

**Introduction:** Ligation of esophageal varices was introduced by Stiegmann and Goff as method of choice for eradication of esophageal varices. The role of banding therapy in the management of active variceal hemorrhage remains controversial. We conducted a prospective trial to assess the use of endoscopic banding (EB) under emergency conditions.

**Patients and methods:** From 7/94–10/95 we tried to control active variceal bleeding in n = 54 patients (male n = 38, female n = 16, average age 49.2) in the first line with banding therapy.

**Results:** In only n = 13 patients (24.1%) out of n = 54 patients EB was successful in stopping haemorrhage. In n = 41 patients (75.1%) we had to treat by sclerotherapy (ST) in the same endoscopic course. This procedure was efficient in n = 34 patients (82.9%). Only n = 7 (13%) patients underwent Sengstacken-Blackmore tube.

**Discussion:** In comparison to sclerotherapy EB is less effective in active variceal hemorrhage under emergency conditions. Main reason for failure is the reduced endoscopic view caused by the commercial ligation instrument. Only 30% of the video screen is available in a situation where also blood reduces sight. Definition of the bleeding source and placement of the ligation is therefore difficult. We are looking forward to better results with a new constructed ligation instrument for emergency conditions.

Endoscopy, specific: Oesophagus  
Endoscopy, general: Instrumentation, therapy  
Endoscopy, general: Preparation, management }

"Role of Endoscopic Ligation in Active Variceal Bleeding under Emergency Conditions"

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## "P P 50 1205" P 50 1205 Emergency Sclerotherapy Vs. Banding Ligation for Arresting of Actively Bleeding Esophageal Varices

\*G.H. Lo, K.H. Lai, J.S. Huang

Division of Gastroenterology, Department of Medicine, Veterans General Hospital-Kaohsiung, Kaohsiung, Taiwan

**Purpose:** The efficacy of endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) in the management of actively bleeding esophageal varices is still undetermined. This study was conducted to compare the efficacy and complications of both methods in the arresting of actively bleeding esophageal varices.

**Methods:** Patients with actively bleeding esophageal varices on endoscopy, without malignancy, or gastric varices, were enrolled. Seventy-one eligible patients were randomized to receive EVL (37 patients) or EIS (34 patients) immediately after endoscopic examinations.

**Results:** Initial success rate (bleeding stopped for 48 hours) was 95% in the EVL group and 76% in the EIS ( $p = 0.009$ ). The efficacy of EVL was similar to EIS in the control of oozing varices (100% vs. 89%,  $p > 0.05$ ), whereas EVL was superior to EIS in the control of spurting varices (94% vs. 62%,  $p = 0.012$ ). Definite control of hemorrhage at one month was 92% in the EVL group vs. 70% in the EIS group ( $p = 0.02$ ). Blood transfusion requirement was significantly lower in the EVL group than in the EIS group (3.2 – 1.2 vs. 4.5 – 1.8 units,  $p < 0.01$ ). Rebleeding rate at one month was 17% in the EVL group and 33% in the EIS group ( $p = 0.09$ ). Significant complications were encountered in 5% of the EVL group and 29% of the EIS group ( $p < 0.03$ ). Mortality rates at one month was 19% in the EVL group and 38% in the EIS group ( $p > 0.05$ ).

**Conclusions:** EVL was superior to EIS in the control of actively bleeding esophageal varices, with greater effectiveness, lower requirement of blood transfusion and less complications. Liver and bile ducts, 1: Cirrhosis: portal hypertension

Endoscopy, general: Instrumentation, therapy  
Endoscopy, general: GI bleeding }

"Emergency Sclerotherapy Vs. Banding Ligation for Arresting of Actively Bleeding Esophageal Varices"

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"P P 50 1206" P 50 1206 **Injection Sclerotherapy for Non-Variceal Bleeding of Stomach and Duodenum** M. Bulajic,

\*N. Popovic, M. Glisic, P. Popovic, T. Milosavljevic, M. Ugljesic, L. Pandey, R. Krstic, D. Popovic, P. Dugalic, D. Tomic, S. \d0Ouranovic, N. Mijalkovic, O. Matejic, K. Todorovic

Clinic for Gastroenterology and Hepatology, Clinical Center, Belgrade, Yugoslavia In the period between 1992–96, 645 (44 males, 205 females, age 17–91) consecutively admitted patients with active non-variceal upper GI bleeding were treated by endoscopic injection sclerotherapy of combined epinephrine/polydocanol, within 1–6 hours of admission. Control endoscopy was performed in 24–72 hours. Bleeding lesions were graded according to Forrest classification: active arterial bleeding – F Ia 57 (8.83%), active venous or capillary bleeding – F Ib 381 (59.06%), visible blood vessel – F IIa, 107 (16.58%) and adhering clot – F IIb 100 (15.50%). Initial hemostasis was achieved in 638 (98.91%), and definitive hemostasis in 600 (93.02%), respectively: in F Ia – 51 (89.47%), in F Ib – 361 (94.75%), in F IIa – 95 (88.78%), in F IIb – 96 (96.00%). Definitive hemostasis was achieved in 88.92% of gastric and in 94.86% of duodenal ulcers. The gastric ulcers had 12.24% of recidives and duodenal ulcers had 5.50% of recidives. Thirty six (5.58%) patients underwent surgery, and 1 (0.15%) patient underwent arterial embolization. There were 7 (1.08%) lethal outcomes, in patients with additional heart and renal diseases. There were three cases of perforation (0.46%) of resclerozated duodenal ulcers. *Conclusion:* Injection endoscopic sclerotherapy is an efficient and safe procedure for definitive hemostasis of non-variceal bleeding in stomach and duodenum, with minimal complications. Clinical practice: Management strategy Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Injection Sclerotherapy for Non-Variceal Bleeding of Stomach and Duodenum"

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## "P P 50 1208" P 50 1208 **Results of Injection Sclerotherapy for Esophageal Varices in Noncirrhotic Portal Hypertension**

\*G. Boztas, Z. Mungan, S. \d6zdil, O. Yegins\fc, Y. \c7akaloglu, S. Kaymakoglu, F. Besisik, A. \d6kten, N. Erol, R. Sezer

Dept. of Gastroenterohepatology, Istanbul Medical Faculty, Istanbul T\fc rkiye Porto-systemic shunts and non-shunting procedures have been used for the management of bleeding esophageal varices (EV) in noncirrhotic portal hypertensive (NCPH) patients. Endoscopic injection sclerotherapy (EIS) may be an effective alternative procedure in these patients. From January 1988 to December 1995, 32 consecutive NCPH patients (20 males; mean age 39 – 15) with a history of EV bleeding were admitted for EIS. The mean number of bleeding episodes before admission to EIS were 3.48 – 2.93/patient. The underlying causes of portal hypertension were portal vein thrombosis (37.5%), congenital hepatic fibrosis (12.5%), splenic vein thrombosis (6.25%), portal vein hypoplasia (6.25%) and idiopathic portal hypertension (37.5%). Earlier surgical procedures were done in 20 patients (splenectomy alone in 12 patients, shunt operation in 6 patients, devascularization in 2 patients). Six patients were excluded from study because of they refused further therapy so 26 patients were evaluated at the end of study. EIS was unsuccessful in two patients (7.7%), in these patients surgical procedures were done successfully. We were able to obliterate EV in 24 patients (92.3%). The mean therapy session number were 4.87 – 2.09/patient. The mean total volume of sclerosant solution (sodium tetradecyl sulfate, 2%) used until complete variceal obliteration were 45 – 17.4 ml/patient. Complications related to the EIS were developed in 21 patients (superficial ulcers 62.5%, deep ulcers 16.7%, esophageal stenosis 8.3%) and all of them were resolved by medical therapy. The average follow-up period of 24 patients after variceal obliteration were 38.88 – 20.37 months (7–66 months); during this period recurrent EV was noted in 41.7% and rebleeding in 8.3%. EIS was performed in all these patients. There was no bleeding related mortality. *Conclusion:* EIS may be an alternative to surgical therapeutic approaches for the secondary prophylaxis of variceal bleeding in NCPH patients. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Endoscopy, general: Instrumentation, therapy Endoscopy, general: GI bleeding } "Results of Injection Sclerotherapy for Esophageal Varices in Noncirrhotic Portal Hypertension"

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"P P 50 1209" P 50 1209 **Endosonographic Evaluation of the Venous Changes Around the Gastro-Esophageal Junction during Band Ligation and Injection Sclerotherapy of Varices**

\*G. Choudhuri, A. Srivastava, D.K. Agarwal, R.K. Dhiman

Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India In this prospective longitudinal study using endoscopic ultrasound (EUS) we tried to see if the changes in the venous anatomy around the GE junction that accompany successful variceal ligation (EVL) of large esophageal varices differ from those that follow injection sclerotherapy (EST). Eleven cirrhotic portal hypertensive patients (m: B, age 38.2 yrs) with large esophageal varices on endoscopy were found on initial evaluation with EUS to have  $3.45 \pm 1.21$  submucosal veins/varices (SMV) measuring  $4.27 \pm 1.00$  mm in diameter and  $4.63 \pm 1.20$  paraesophageal veins (PEV) measuring  $3.90 \pm 1.64$  mm in diameter lying adjacent to the esophageal wall before starting therapy. EUS was repeated after variceal obliteration. In 4 of the 6 patients (6 men, mean age 45 years) who achieved variceal sclerosis after EST (mean of 6.8 sessions), obliteration of SMV was accompanied by a reduction in number (3.5 vs 1.25) and size (5.0 mm vs 2.75 mm) of PEVs. However in all the 5 patients (5 men, mean age 28.6 years) who achieved immediate collapse and thrombosis of varices following EVL, there was no change in the number (3.8 vs 3.2) and size (4.2 vs 4.6 mm) of PEVs. Our initial observations show that successful obliteration of esophageal varices by injection sclerotherapy is accompanied by obliteration of paraesophageal collateral veins. These PEVs seems to remain unaffected after EVL. Persistence of dilated paraesophageal veins after successful initial EVL could lead to early recurrence of varices. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding Echoendosonography: Echoendoscopy } "Endosonographic Evaluation of the Venous Changes Around the Gastro-Esophageal Junction during Band Ligation and Injection Sclerotherapy of Varices"

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"P P 50 1210" P 50 1210 **Long-Term Follow-Up of Gastric Variceal Sclerotherapy: An 11 Year Experience** S.K. Sarin

Department of Gastroenterology, G.B. Pant Hospital, New Delhi, India *Background:* Bleeding from gastric varices (GV) is often a serious medical emergency. The role of endoscopy in the management of GV bleeding is still controversial. The type of GV and the management strategies for different types of GV have not been identified. *Materials and Methods:* GV were observed in 209 of the 939 (22.3%) patients with portal hypertension. Seventy one patients (mean age 33.9 – 18.2 yr, M:F::46:25) underwent GV sclerotherapy; 53 (75%) for a GV bleed. Portal hypertension was due to cirrhosis in 33 (46.5%) and non-cirrhotic causes in the remaining. Using a previously described classification (Hepatology 1992: 102: 994), GV were divided into Gastroesophageal varices type 1 (GOV1) (n = 21) and type II (GOV2) (n = 34); and Isolated GV (IGV1) (n = 16). GV sclerotherapy was done every week, using a combination of para- and intravariceal technique and absolute alcohol as a sclerosant. *Results:* GV sclerotherapy could arrest acute bleed in 12 (66.7%) of 18 patients. Variceal obliteration could be achieved in 45 of the 60 (75%) patients. While the success of GV sclerotherapy in different types of GV was comparable in acute bleed, variceal obliteration was higher in patients with GOV1 (94.4%) than GOV2 (70.4%) and IGV1 (41%). Rebleed after elective GV sclerotherapy was 5.5%, 19% and 40% respectively in the three types of GV. There was no recurrence as GV during a mean follow-up of 24.2 – 22.9 mo. Seventeen (24%) patients died; nearly equally due to rebleeding and liver failure. *Conclusions:* (i) GV sclerotherapy can successfully arrest acute GV bleed (66%) and achieve GV obliteration (75%) (ii) GV sclerotherapy is more effective in patients with gastroesophageal varices. (iii) Alternative therapies need to be evaluated for patients with IGV1. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Long-Term Follow-Up of Gastric Variceal Sclerotherapy: An 11 Year Experience"

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## "P P 50 1214" P 50 1214 **Emergency Medical Treatment of Bleeding Esophageal Varices**

\*S.S. Elsyed, M.F. Farag, F. Azzam, M. Hamid, G. Shiha, H. Askalani, A. Meneesy

Mansoura Faculty of Medicine, Mansoura, Egypt  
The aim of this study is a trial to find the most effective emergency medical modality treatment of bleeding esophageal varices which provide acute hemostasis and prevent early rebleeding with less side effects and complications. This research comprised 2442 patients presented with upper gastrointestinal bleeding. Patients with variceal bleeding (70%) were divided into groups according to the line of therapy (drugs eg. sandostatin and glypressin, balloon tamponade, band ligation, and sclerotherapy either alone or in combination), besides conservative treatment. They followed up for 12 months after treatment. Evaluation of treatment depending on: Overall control of bleeding, early rebleeding, units of blood transfused, mortality and number of sclerotherapy needed on follow up. From the results it was found that: The best line of treatment was sandostatin plus sclerotherapy. Sandostatin was effective as sclerotherapy. Sandostatin was more effective than glypressin. Band ligation was effective as sclerotherapy with less side effects. Adding sandostatin infusion to balloon tamponade markedly decrease the mortality and morbidity. Sandostatin infusion decrease the number of blood units transfused and the number of sclerotherapy on follow up. In a conclusion: For medical treatment of acute variceal bleeding, sandostatin infusion must be given to all patients for the first 48 hours. Sandostatin infusion plus sclerotherapy is the ideal medical modality treatment. Combined sandostatin infusion and balloon tamponade is advisable in hospitals not equipped with endoscopic services. Sandostatin infusion decrease the number of blood units needed and also decrease the numbers of sclerotherapy needed on follow up. Clinical practice: Management strategy Endoscopy, general: GI bleeding Endoscopy, specific: Oesophagus } "Emergency Medical Treatment of Bleeding Esophageal Varices"

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## "P P 50 1215" P 50 1215 Octreotide Use in Acute Variceal Haemorrhage: A Prospective Randomized Study

\*S.H.A. Shah, S.M.W. Jafri, A. Ahmed, S.S. Hamid, A.H. Khan

Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan Sclerotherapy of bleeding oesophageal varices is considered the most effective treatment to arrest haemorrhage. However, the risk of rebleeding and mortality is high. There is a need to have adjunctive treatment to prevent early rebleeding and risk of death. In a prospective study we evaluated the role of octreotide (50 µg/hr for 36 hrs) along with sclerotherapy in 105 adult cirrhotic patients who were actively bleeding from varices or had a recent bleed. Patients were assigned to receive octreotide plus sclerotherapy or sclerotherapy alone. Initial control of bleeding was achieved in 46/51 (90.2%) patients who received combined treatment compared to 41/51 (80.4%) patients ( $p = 0.05$ ) in sclerotherapy alone group. Rebleeding after the first 24 hrs was less in the octreotide treated patients, 2/46 vs 8/41 patients ( $p = 0.003$ ). The octreotide treated patients had a better short term (5 days) survival 44/51 vs 33/54 ( $p = 0.003$ ) and shorter hospital stay, 5.314 – 3.87 days vs 6.63 – 3.86,  $p = 0.008$  as compared to sclerotherapy alone group. The blood transfusion requirement was also less in the combined treatment group 3.882 – 2.805 vs 5.37 – 3.152 ( $p = 0.002$ ). We conclude, 1) The combination of sclerotherapy and octreotide is more effective than sclerotherapy alone in the treatment of acute variceal bleeding. 2) Although early mortality is improved, there is no difference in the overall inpatient mortality between the two treatment modalities. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Octreotide Use in Acute Variceal Haemorrhage: A Prospective Randomized Study"

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"P P 50 1218" P 50 1218 **Portal Haemodynamic Effect of Octreotide Subcutaneously Twice Daily Post Endoscopic Sclerotherapy for Oesophageal Varices Bleeding and Portal Hypertensive Gastropathy Caused by Liver Cirrhosis**

\*Soemarno<sup>1</sup>, Daldijono<sup>2</sup>, Sjaifoellah Noer<sup>2</sup>

<sup>1</sup> Endoscopic Unit of Sint Carolus Hospital

<sup>2</sup> Depart. of Internal Medicine University of Indonesia Upper gastrointestinal bleeding sources has mostly caused by oesophageal varices ruptured and portal hypertensive gastropathy. In this study we have investigated effect of 0.1 mg octreotide subcutaneously twice daily for 5 days after sclerotherapy oesophageal varices on portal blood flow. *Materials and methods* From April 1994 until April 1996 we have 125 patients 92 males and 33 females, aged range from 42 years until 68 years, mean aged 55 years, was entered to emergency ward as upper gastrointestinal bleeding caused by portal hypertension, immediately measured of portal blood flow by echo Doppler and than endoscopic sclerotherapy followed by 0.1 mg octreotide twice daily for 5 days and than follow up by echo Doppler. *Result* \* 62% (77 patients) had portal blood flow 9–15 cm per second, bleeding from oesophageal varices, after 5 days the portal blood flow decrease until 7–11 cm per second and the bleeding has been controlled. \* 28% (35 patients) had portal blood flow 15–20 cm per second, bleeding from oesophageal varices and portal gastropathy, after 5 days the portal blood flow became 8–11 cm per second and able to control the bleeding. \* 10% (13 patients) had portal blood flow 18–22 cm per second, the bleeding only from portal gastropathy, after 5 days the portal blood flow reduced until 9–10 cm per second, the active bleeding has been stopped. *Conclusion* Octreotide is first line treatment of choice after endoscopic sclerotherapy, will act immediately to reduced the portal hypertension, very effective to controlled the active bleeding and prevent the rebleeding and also reduced the blood transfusion. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Portal Haemodynamic Effect of Octreotide Subcutaneously Twice Daily Post Endoscopic Sclerotherapy for Oesophageal Varices Bleeding and Portal Hypertensive Gastropathy Caused by Liver Cirrhosis"

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## "P P 51 1226" P 51 1226 Conventional Surgical Treatment for Cholecystolithiasis and Choledocholithiasis with and without Preoperative Endoscopic Papillotomy

\*A. Figueira, E.J. Lobo, L.F.R. Gatto, A.N. Dias, NETO R. Colleoni, F.º B. Herani, J.R. Ferraro, A. Goldenberg, T. Trivi\`f1o

Universidade Federal De S\`e3o Paulo, Brasil

Escola Paulista De Medicina, S\`e3o Paulo, Brasil To study the risks of postoperative complications and death and technical failure to remove stones from common bile duct, 101 patients with symptomatic cholecystolithiasis and choledocholithiasis and papillary obstruction due to stone or inflammatory process were considered in two groups: Group I (n = 50) underwent preoperative endoscopic papillotomy and open cholecystectomy in the same hospitalization; Group II (n = 51) underwent open cholecystectomy, common bile duct exploration, T-tube drainage and transduodenal papillotomy. Patients with intermediate operative risk (ASA III – American Society of Anesthesiology) were present in 33.3% (Group I) and 36.0% (Group II). Patients with poor risk (ASA IV and V) were excluded. The common bile duct was free of stones in 75% (Group I) and 90% (Group II). Multivariate analysis showed that surgical team (p = 0.032) was related to postoperative complications and greater hospitalization in the conventional surgery (Group II); surgical risk (p = 0.53) was related to systemic postoperative complications in the conventional surgery (Group II); distal choledochal stenosis (p = 0.014) was related to technical failure, complications and death in the preoperative endoscopic procedures (Group I); choledochal stenosis was found to be more influent factor for complications than the number and size of stones. The conclusion is that the preoperative endoscopic papillotomy should remain the procedure of choice for common bile duct stones in patients with comorbid illnesses and cholecystectomy and common bile duct exploration is the procedure of choice in no risk patients. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary }" "Conventional Surgical Treatment for Cholecystolithiasis and Choledocholithiasis with and without Preoperative Endoscopic Papillotomy"

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"P P 51 1227" P 51 1227 **The Application of Endoscopic Papillosphinctero-Manometry (EPSM) for Prevention of the Retro-Duodenal Perforation (RDP) on Papillary Stenosis**

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The purpose: is to determine the frequency of the development of RDP and the opportunities of its prevention on the patients (pts.) with isolated papillary stenosis (PS). The pts. to the trial were selected according to 11 criteria: the absence of peripapillary diverticula, operations on PDM, bilio-digestive anastomoses, gastric resections, acute pancreato-biliary diseases at the moment of investigation, etc. Such a selection was necessary for the objective evaluation of the complications, depending only on the character and volume of operation. Firstly the retrospective analysis of the results of EPST was made out on 38 pts. with CBD stones less than 15 mm – control group – without pathological changes of PDM (m-4, f-34; mean age 66.4 yrs.) and on 36 pts. with isolated PS (m-3, f-33; mean age 63.3 yrs.). The length of EPST was defined on the basis of the preoperative ERCP and endoscopic landmarks. There was no RDP after EPST on the control group of pts. with CBD stones. Opposite to it there was 3 (8.3%) cases of RDP in pts. with PS. Thus, we came to the conclusion, that after EPST, carried out for PS, the frequency of RDP is higher, than on choledocholithiasis ( $p < 0.025$ ). Then 37 pts. with isolated PS (m-1, f-36; mean age 58.4 yrs.) were examined prospectively. They underwent EPSM, – modified in our clinic method of standard sphincter of Oddi (SO) manometry, – before EPST. This method allowed us in each case to define precisely the length of SO, the localization and the stretch of stenotic segment of Oddi zone, on the basis of pathologically high pressure borders in SO (the major sign of PS – the basal pressure in SO is more than 35 mm Hg). The optimal length of EPST in all the cases was defined on the basis of EPSM, as the middle of the distance between the proximal margin of stenosis and the total length of SO. There was no RDP in this group of pts. Consequently EPSM gives the opportunity to estimate objectively the optimal volume of EPST in pts. with PS and to avoid RDP during this endoscopic intervention.

Motility, specific: Small bowel  
Endoscopy, general:  
Complications  
Endoscopy, specific: Biliary } "The Application of Endoscopic Papillosphinctero-Manometry (EPSM) for Prevention of the Retro-Duodenal Perforation (RDP) on Papillary Stenosis"

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"P P 51 1228" P 51 1228 **Endoscopic Sphincterotomy for Common Bile Duct Stones in Patients under 60 Years of Age**

\*F.M. Pedersen, A.T. Lassen, O.B. Schaffalitzky de Muckadell

Department of medical gastroenterology S, Odense University Hospital, Denmark *Background:* In the era of LC and the absence of prospective controlled studies concerning treatment of young patients with CBD, considerable controversy exists about the management of these patients. *Methods:* This study reports the results of a medium-term follow-up study of 86 (68 women) consecutive patients under 60 years of age who underwent endoscopic sphincterotomy (ES) for common bile duct stones. The median observation time after ES was 27.1 months. Complete follow-up was accomplished in 80 patients. *Results:* Sixty-one patients were discharged after ES with gallbladder left in situ. At the time of ES subsequent cholecystectomy was planned in 18 patients. Acute cholecystectomy was undertaken in seven patients due to acute cholecystitis (n = 4) or biliary colic (n = 3). Recurrent attacks of biliary colic required elective cholecystectomy in another nine patients. Cholecystectomy was not needed in 27 patients, of which 23 had gallbladder stones. One hundred ninety days after ES the probability of still having a gallbladder in situ was 50%. Most surgery was undertaken within half a year after ES. *Conclusion:* Young patients manage well without any need of cholecystectomy after ES for common bile duct stones. This group represented nearly half of those discharged after ES with gallbladder left in situ. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Endoscopic Sphincterotomy for Common Bile Duct Stones in Patients under 60 Years of Age"

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"P P 51 1229" P 51 1229 **Endoscopic Sphincteroclasia for Choledocholithiasis**

\*F. Prat, J. Boyer, G. Pelletier, J. Fritsch, A.D. Choury, B. Person, J.F. Bretagne, C. Buffet

Hepatogastroenterology, Bic\atre, Angers and Rennes hospitals, France The hydrostatic dilatation of the sphincter of Oddi (endoscopic sphincteroclasia – ESpl –) is a recently proposed alternative to sphincterotomy for common bile duct stones (CBDL). Our aim was to assess the results and feasibility of the technique. 30 patients (12 men, 18 women, mean age 64.2 – 16.4 years) with suspected CBDL were enrolled with the following criteria: signs and symptoms of biliary obstruction, presence on retrograde opacification of not more than 4 stones, not exceeding 10 mm in diameter. Two patients had an impaired coagulation; 6 had a gastrojejunal anastomosis duodenal diverticulae. Cannulation was performed with an indwelling guidewire, the papilla was dilated with a 2 cm-long Maxforce' balloon catheter (diameter 8 mm) inflated at 12 atmospheres during 60 seconds. Patients were followed prospectively during one month. In 3 patients, cannulation with a guidewire failed and a papillotomy was needed. Of the other 27, 24 had CBDL (1.4 – 0.8 stones; range 0–3; largest stone diameter: 5.1 – 2.9 mm) and no stone was found in 3 patients. Complete stone extraction was possible in 100% of the cases after ESpl. Mechanical lithotripsy was never required. A naso-biliary drainage was used in 3 patients. There was no conversion to sphincterotomy. Bile duct clearance was achieved after one session in 22/24 cases (91.6%). Success rate was therefore 90% (27/30). Immediate and 1-month morbidity was 6.6% (one mild pancreatitis; one asymptomatic case of tears of the lower part of the bile duct). ESpl is feasible and suitable for the endoscopic therapy of CBDL when stones are neither too large nor too many; its morbidity seems to be low. Its long term results and effects on the sphincter of Oddi require evaluation. Endoscopy, specific: Biliary Endoscopy, general: Instrumentation, therapy Liver and bile ducts, 2: Gallstones, formation, treatment } "Endoscopic Sphincteroclasia for Choledocholithiasis"

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"P P 51 1230" P 51 1230 **Severe Stenosis Following Endoscopic Sphincterotomy** F. Dos Santos,

\*T. Ponchon, R. Lambert, A. Chavaillon, R. Bory, B. Napol'eon, F. Hedelius, S. Sidi

Department of Digestive Diseases Hospital E. Herriot, Lyon, France Long-term complications following endoscopic sphincterotomy (ES) have still to be classified and analyzed. Recent publications pointed out to a particular complication which consists in a stricture of the biliopancreatic orifice. We reviewed the follow-up of a series of 3.138 consecutive ES done for choledocholithiasis and sphincter of Oddi dysfunction from January 1985 to December 1994 in our unit, to look for such a complication. We found 4 cases of ES stricture and we present here the clinical, fluoroscopic and endoscopic features of these cases and the management we used. *Patients:* Four patients (female: 4, age: 33–50, previous cholecystectomy in all) underwent an endoscopic sphincterotomy for bile duct lithiasis in 2 and for papillary stenosis in 2. No immediate complication was observed. One to 4 months later (mean: 80 days), the patients (pts) presented with acute mild pancreatitis (1 case), cholangitis in (2 cases), and abdominal pain and cholestasis (1 case). Endoscopy showed a punctiform sphincterotomy orifice with retraction of the peripapillary duodenal folds. The orifice was difficult to catheterize and cholangiography revealed a long stricture extending up to 7–15 mm beyond the biliary orifice and a common bile duct dilation. Pancreatic ducts were found normal. *Treatment:* Repeated endoscopic sphincterotomy was attempted in 2 pts but could not relieve the stricture. Plastic stents (Three 10 french stent side to side) were inserted in 2 pts during 6 months and a metallic stent in one. Stenoses recurred when removing the plastic stent, and the metallic stent rapidly occluded due to inflammatory processes. Finally the 4 pts were submitted to a choledochojejunostomy. Two pts then presented 2 and 6 months later a stenosis of the anastomosis and are now treated by a percutaneous prolonged silicone drainage. *Conclusions:* Endoscopic sphincterotomy stricture has a low prevalence of 1 for 1.000 ES. The endoscopic and cholangiographic features are impressive and the management, endoscopic or surgical, is difficult. Papillary stenosis and constitutional problems of scarring could be etiological factors. Endoscopy, specific: Biliary } "Severe Stenosis Following Endoscopic Sphincterotomy"

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"P P 51 1231" P 51 1231 **Endoscopic Therapy of Choledocholithiasis 1973-1995: A Meta-Analysis** W. Sandschin, P. Born, K. Ulm<sup>1</sup>, M. Classen

<sup>1</sup> 2nd Medical Department, Institute for Medical Statistics and Epidemiology, Germany

Klinikum rechts der Isar, Technical University of Munich, Germany *Introduction:* Since its introduction in 1973 endoscopic papillotomy has gained a broad acceptance in the therapy of choledocholithiasis. The continuous improvement of the technical equipment enables endoscopists now to treat nearly all kind of biliary stones. In a Meta-Analysis this development as to success rates and complication rates was evaluated. *Material and Methods:* 31 papers published since 1979 including a total of 10335 patients were evaluated using a meta-analytical approach. Test on homogeneity (95% CI) were performed using the Yussuf-Peto method. Success rates (short and long term) as well as complication rates were investigated. The results of three different periods of time (I = 1973–1980, II = 1980–1990, 1990–1996) were compared. *Results:* Shortterm success rates were in I: 87.2% in II: 90.4% and in III: 94.6%. Complications were seen in 6.5% (I), 9.4% (II) and 6.8% (III) respectively. The increase of the complications (I-II) was significant (CI 95%). Longterm outcome was beneficial in 90% for pat. with gallbladder in situ and 87.4% for cholecystomized pat. respectively. The in situ of the gallbladder shows no influence with respect to the long term outcome. In pat. with gallbladder in situ success rates were 86.4% compared to 86.5% in pat. after cholecystectomy (95% CI). *Conclusion:* Endoscopic therapy in the treatment of choledocholithiasis is highly effective. Likely due to the development of additional therapeutic systems such as ESWL or laser success rates significantly increased from 1973 to 1995. Despite of growing experience short term complication rates did not significantly improve, a consequence, as we think of the growing proportion of high risk patients. Thus in a time of laparoscopic cholecystectomy with splitting the therapeutic modalities between surgery and endoscopy endoscopic therapy is an important partner of surgery. Clinical practice: Epidemiology (non cancer) Liver, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Endoscopic Therapy of Choledocholithiasis 1973-1995: A Meta-Analysis"

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"P P 51 1232" P 51 1232 **The Safety Sphincterotome: An Effective Design to Minimise Risk**

\*D.F. Martin, R.E. England

Department of Radiology, South Manchester University Hospitals, Manchester, UK Endoscopic sphincterotomy has become increasingly safe because of an appreciation of technical and clinical factors which lead to complication. There has been little attention to factors in the design of the sphincterotome, which may be associated with risk. We have designed a wire-guided tapered tip long nosed sphincterome, with a partly insulated 3 cm cutting wire. Each component of the design is incorporated specifically to reduce risk of complication based upon previous experience with commercially available devices. The long nose maintains access during sphincterotomy. Wire guidance ensures bile duct placement after deep cannulation with a standard cannula. A long cutting wire maintains axial orientation. Partial insulation of the cutting wire guards against inadvertent contact with endoscope or duodenum when the cutting wire is fully withdrawn from the papilla, in order to maintain high current density for sphincterotomy. We have used two similar devices, one with a mono filament cutting wire and another with a braided cutting wire, whilst assessing the power requirements for sphincterotomy by measuring total cutting time for each sphincterotomy. 75 patients with bile duct stones have undergone sphincterotomy with these devices. A complication of sphincterotomy (bleeding requiring transfusion) has occurred in only one patient. No other complication has occurred and sphincterotomy has been successful in all cases. There is no difference in the crudely measured power requirement between mono filament and braided wire sphincterotomes. This device appears to enable safe, certain endoscopic sphincterotomy. Endoscopy, specific: Biliary Endoscopy, general: Instrumentation, therapy Liver and bile ducts, 2: Gallstones, formation, treatment } "The Safety Sphincterotome: An Effective Design to Minimise Risk"

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## "P P 51 1233" P 51 1233 Endoscopic Retrograde Cholangiographic Patterns of Biliary Fascioliasis

\*M.Y.T. Rashed, T.A. El-Sefi, I. Boghdadi

HPB Unit Alexandria University, Surg. Dept. Liver Institute, and Medical Dept., Faculty of Medicine Menoufiya University, Egypt The cholangiographic patterns of 14 patients with biliary fascioliasis were reviewed to define its characteristics; The diagnosis was confirmed by retrieval of Fasciola flukes from the biliary tree either endoscopically or/and surgically. In all patients, bile ducts were dilated with one or more of the following cholangiographic patterns (ERC). Endoscopic retrograde cholangiographic patterns: 1) Single or multiple leaf shaped filling defects 2) whip-worm like filling defects (7/14). 3) Irregular changing filling defects on serial films (3/14). 4) Jagged irregular bile duct wall (5/14). 5) Segmental main bile duct stricture (2/14). In three patients, there were associated bile duct stones. In 9 patients (64 m/m), the gallbladder was infested. The gallbladder filling patterns included: 1) Dry cracked earth appearance (4/9). 2) Numerous whip worm like filling defects in the fundus or at the neck with beaded cystic duct (2/9). 3) Vague ill defined filling defects with jagged irregular wall (2/9). 4) Contracted small sized gallbladder (1/9). In two patients, there were associated small gallbladder stones. In conclusions, these endoscopic cholangiographic patterns should be considered as specific for the diagnosis of biliary Fascioliasis. } "Endoscopic Retrograde Cholangiographic Patterns of Biliary Fascioliasis"

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## "P P 51 1234" P 51 1234 Endoscopic Treatment of Biliary Fistula: Papillotomy or Stenting?

\*Z. Wajda, M. Dobosz, A. Babicki

II Department of Surgery, Medical University of Gdansk, Gdansk, Poland Authors present 21 patients with postoperative biliary fistula. The biliary fistula was a consequence of laparoscopic cholecystectomy in 6 patients, open cholecystectomy in 6 patients, T-tube drainage failure in 4 patients. In 3 patients the biliary leakage was recognized after right hemihepatectomy, and in 2 patients following stab or blunt hepatic wound. ERCP examination revealed intrahepatic bile duct leakage in 5 patients, while in 16 patients the bile duct injury involved extrahepatic biliary tree. The patients were divided into three groups. Group A comprised 10 patients in whom endoscopic papillotomy was performed only, and was sufficient for fistulas healing. Group B consisted of 6 patients in whom endoscopic papillotomy did not diminished biliary leakage, and consecutive endoprosthesis impacement was performed. Group C included 5 patients In these patients endoscopic papillotomy and endoprosthesis placement were carried out simultaneously. There were no differences concerning the amount of biliary leakage and the site of the bile duct injury. In all the patients the biliary fistula was healed. No complications were observed following endoscopic treatment. The mean time of fistulas healing was in group A 8.3 days, in group B 14.6 days, and in group C 3.9 days. Since it is difficult to predict in which cases endoscopic papillotomy might be sufficient in biliary fistulas healing, authors suggest than in patients with postoperative biliary leakage primary biliary stenting shorten hospital stay period and should be considered as a procedure of choice. Liver and bile ducts, 2: Bile formation, cholestasis Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic } " Endoscopic Treatment of Biliary Fistula: Papillotomy or Stenting?"

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## "P P 51 1235" P 51 1235 Peroral Cholangioscopy Using a Dissolving Top Chip without Endoscopic Sphincterotomy

\*Y. Shinohara, K. Takeda, K. Takei, T. Itoi, K. Nakamura, S. Fukuda, S. Ogiwara, T. Horibe, H. Kakutani, T. Saitoh

Department of 4th Internal Medicine, Tokyo Medical College Hospital, Tokyo, Japan *Purpose:* Peroral Cholangioscope with forceps channel and angulation system has been known to require endoscopic sphincterotomy (EST) in order to intubate of biliary duct. We developed a dissolving top chip (DTP) for the purpose of introducing cholangioscope into the bile duct without EST. *Patients and Methods:* Sixteen patients who were examined by the peroral cholangioscopy with DTP were studied. DTP has the shape of cone and is made from polyvinyl alcohol for medical use. DTP can be easily dissolved and disappeared within several hours in the bile duct because of its characteristics. The cholangioscope (FCP-9BP, Pentax) is 3.1 mm in external diameter at the rigid portion of the tip, has a working channel 1.2 mm in diameter and two directional angulation system (up and down). At first step, catheter was inserted into the CBD without EST using standard therapeutic duodenoscope and endoscopic retrograde cholangiography was performed. Each patient was administered with preparation of isosorbide dinitrate in the biliary duct in order to relax papillary sphincter. Then, guide-wire was inserted into CBD through the catheter. Cone-shaped DTP was passed over the guide-wire and followed by cholangioscope. Combination of DTP and cholangioscope made it possible to get insertion quite reliably. *Results:* With the help of DTP, the insertion of cholangioscope into CBD without EST was successful in fourteen cases (87.5%). DTP did not prevent us from viewing the bile duct. Observation of papilla immediately after examination showed no bleeding or edema. Complications such as cholangitis and acute pancreatitis did not occur after this examination. *Conclusion:* Using DTP, cholangioscope with forceps channel and angulation system can be readily inserted into CBD without EST. We are convinced that this method would be very useful in improving the diagnostic and therapeutic ability of cholangioscope and could be applied even in the case of youth or the patient who has hemorrhagic diathesis. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Biliary } "Peroral Cholangioscopy Using a Dissolving Top Chip without Endoscopic Sphincterotomy"

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## "P P 51 1236" P 51 1236 Correlation between the Location of Juxtapapillary Diverticula and Choledocholithiasis

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<sup>1</sup> Division of Gastroenterology and Nuclear medicine, Taiwan

Veterans General Hospital-Kaohsiung, Taiwan

*Purpose* To evaluate the distribution of Juxtapapillary diverticulum (JPD) and its relationship with choledocholithiasis. *Methods* 1128 consecutive cases underwent ERCP between October 1990 and October 1994. The location of JPD and the papilla of Vater was subdivided into six types: type A: the papilla was located at inferior border of JPD, 6 o'clock; type B: the papilla was located at inferior border of JPD, 7 to 9 o'clock; type C: the papilla was located at inferior border of JPD, 3 to 5 o'clock; type D: the papilla was located inside the JPD; type E: the papilla was located at > 1 cm distal to JPD; type F: the papilla was located at the proximal portion of JPD. 141 patients (76 cases with JPD, 65 cases without JPD) with prior cholecystectomy and endoscopic sphincterotomy had received quantitative cholescintigraphy (QC) after complete clearance of stones and normalization of liver function test. *Result* The incidence of JPD in our series was 30% (334/1128) and the incidence increased with age. The incidence of common bile duct (CBD) stones in patients with JPD is higher than patients without JPD (53.5% Vs 27%  $P < 0.01$ ). The incidence of CBD stones in different types of JPD are as followings: type A: 75/152 (49%); type B: 54/84 (64%); type C: 19/26 (73%); type D: 2/9 (22%); type E: 26/54 (48%); type F: 3/9 (33%). (type B Vs A, D, E, F,  $P < 0.01$ , type C Vs A, D, E, F,  $P < 0.01$ ). In QC, there was no significant difference in time-activity curves between the patients with JPD and without JPD, but the patients with type B and C JPD had delayed hepatic clearance of isotopes compared with other types and patients without JPD. *Conclusion:* The incidence of choledocholithiasis was higher in patients with JPD, especially type B and C probably due to slower hepatic clearance or biliary emptying. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Biliary } "Correlation between the Location of Juxtapapillary Diverticula and Choledocholithiasis"

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"P P 51 1237" P 51 1237 **Duodenal Diverticula: Relationship with the Function of Sphincter Oddi, Biliary and Pancreatic Disease** B. Vladimirov

Clinical Center of Gastroenterology, University Hospital "Tz. Joanna", Sofia, Bulgaria In this study we assessed the clinical significance of duodenal diverticula (DD) and function of sphincter Oddi (SO) in patients with biliary and pancreatic diseases. Diverticula were found in 196 of the patients (12.3%), underwent ERCP. The mean age of these patients was 64.9 – 13.9 years. The most frequent diverticula were singles (87%) and with periampullary localization (60%). Selective cannulation of the papilla Vateri in these patients was not more difficult than in nondiverticulum patients – 98.4% and 99% respectively. The significant changes in this group compared to the patients without DD were: 1. The incidence of common bile duct stones after cholecystectomy – 59%; 2. The incidence of pancreatitis was 37%; 3. Fecal type bacterial overgrowth in duodenum and biliary juice; 4. Abnormal SO manometric findings: SO stenosis (elevated basal SO pressure > 40 mmHg) – 16%, SO insufficiency – 8% and SO dysfunction (amplitude > 240 mmHg, frequency > 10 p/min and retrograde sequence > 50%) – 76%. Endoscopic sphincterotomy with/without stone extraction and lithotripsy was performed in 119 patients with DD. The endoscopic methods for treatment were more difficult. The complications (pancreatitis and hemorrhage) were significantly higher, but most of them were not severe and treated nonsurgically. Success rate was the same as in the patients without duodenal diverticula. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary } "Duodenal Diverticula: Relationship with the Function of Sphincter Oddi, Biliary and Pancreatic Disease"

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"P P 51 1238" P 51 1238 **Endoscopic Brush Cytology for Cancer Diagnosis in Obstructive Jaundice** R. Colleoni,

\*A. Figueira, J.N. St'evale, Filho O. Giannotti, A. Castelo

Federal University of S'eo Paulo, Brazil

Escola Paulista de Medicina, S'eo Paulo, Brazil To study the efficacy of endoscopic transpapillary brushing for the diagnosis of neoplasms in patients with obstructive jaundice we selected 34 patients, 17 with benign diseases and 17 with malignant tumors. Samples were stained by Papanicolaou method and analysed by two pathologists who had no clinical informations. Results were classified as negative, positive and suspect. The results showed: Observer 1 Observer 2 Sensibility 73.3% 80.0% Specificity 94.1% 88.2% Accuracy 84.3% 84.3% Positive predictive value 91.6% 85.7% Negative predictive value 80.0% 83.3% Positive likelihood ratio 12.2 6.8 Negative likelihood ratio 0.3 0.2 Endoscopic brushing cytology is an appropriate method for diagnostic confirmation of previously suspected neoplasms leading to obstructive jaundice. However, a negative result doesn't allow to exclude neoplasms and should be considered in association with other diagnostic results. Interobserver agreement beyond chance (kappa) was good (77.5%) when the results positive and suspect were considered together and moderate (60.0%) when analysed separately, suggesting that the method as far as valid is reproducible. Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic } "Endoscopic Brush Cytology for Cancer Diagnosis in Obstructive Jaundice"

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"P P 51 1240" P 51 1240 **Endoscopic Drainage Treatment of Biliary Fistulas Caused by Gunshot Wounds**

\*M. Bulajic, V. Korneti, M. Markovic, M. Ugljesic, R. Krstic, T. Milosavljevic

Institute for Digestive Diseases, University Clinical Center, Belgrade, Yugoslavia  
The gunshot biliary fistulas may be very common, especially if obtained in war. Their surgical treatment is very difficult because they are frequently associated with shock and blast injuries of the liver and the adjacent organs. Consequently, complicated biliary fistulas require endoscopic drainage as a preoperative or definite therapeutical procedure. During the period from 1993–1995 we treated endoscopically six patients with war injuries. Three of them had bilio-bronchial fistulas. In those cases, EST was performed, and biliary stents applied. The nasobiliary catheter (NBC) was inserted, also after EST, in two wounded patients with bilio-pancreatico-colic fistulas. The remaining two patients with bilio-biliary fistulas underwent a combination of endoprosthesis-NBC drainage. The endoscopic drainage has been applied as a definite treatment procedure in 3 patients, while 4 patients, after significant recovery, due to endoscopy, underwent surgery. One patients died 1 month after surgery. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary } "Endoscopic Drainage Treatment of Biliary Fistulas Caused by Gunshot Wounds"

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"P P 51 1241" P 51 1241 **Post-ERCP Pancreatitis: Comparison of Two Different Approaches in Patients with Choledocholithiasis**. Wojtun, W. Gietka,

\*M. Gil, J. Gil

Digestive Endoscopy Unit, Central Clinical Hospital, Armed Forces Medical Academy, Warsaw, Poland *Aim:* Diagnostic and therapeutic ERCP are complicated by pancreatitis in 1 to 10% of patients, and evidence suggest that the type of procedure may be here of importance. Our aim was to compare two different ERCP procedures in patients with choledocholithiasis concerning the frequency of pancreatitis after the procedure. *Methods:* 535 patients were retrospectively analysed. Cases where biliary tree cannulation was easily obtained during first approach were excluded from final analysis. The rest of the patients were divided into two groups: A (n = 135), where cannulation finally succeeded using standard fashion ERCP, and B (n = 112) where selective biliary tree visualisation was obtained using wire-guided technique. Following parameters were analysed: blood and serum amylase, transaminases, bilirubin, WBC. *Results:* Among patients in group A 1 case of perforation, 3 cases of bleeding, 4 cases of pancreatitis were noted. In group B these figures were 0, 0, 1, respectively. Statistically significant differences were seen ( $p < 0.05$ ), in the incidence of perforations, bleeding and pancreatitis. Serum amylase elevation in group A was seen 50% more often and lasted longer than in group B. *Conclusions:* In order to decrease the number of post-ERCP pancreatitis wire-guided procedure should in our view be recommended as a standard approach, when biliary tree visualisation cannot be obtained without difficulty. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: Complications Clinical practice: Management strategy } "Post-ERCP Pancreatitis: Comparison of Two Different Approaches in Patients with Choledocholithiasis"

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"P P 51 1242" P 51 1242 **Tazobactam-Piperacillin Effectively Prevents Post-ERCP Infections**

\*R. Fried, C. Beglinger, G. Stalder

Dept. of Gastroenterology, Univ. of Basel, Switzerland *Introduction:* In patients with cholestasis, post-procedure cholangitis is one of the major complications of therapeutic ERCP. Because of its excellent penetration into bile we used a combination of the broad-spectrum antibiotic piperacillin with the beta-lactamase inhibitor tazobactam (TAZ; Lederle AG, Switzerland) as prophylaxis in patients with cholestasis undergoing ERCP. *Methods:* 84 patients (37 f, 47 m; mean age 64.7 y [22–92]) with elevated parameters of cholestasis or dilatation of bile ducts at risk for procedure-related cholangitis were included in this open-label multicenter study and had antibiotic prophylaxis with TAZ (4.5 g iv) before, and 8 h and 16 h after ERCP. Patients already receiving antibiotics or with an allergy to penicillins were excluded. Patients were followed after ERCP for 1 week. *Results:* Cholangiography was achieved in 79/84 (94%). ERC was normal in 5 cases. Drainage was established during primary ERCP in 66 of the remaining 79 patients (84%). The etiology of cholestasis was choledocholithiasis in 36, a pancreatic tumor or cholangiocarcinoma in 34, and a stricture in 4. Cholangitis after ERCP was suspected in 8 cases. In one of these, endoscopic drainage had not been possible. After three courses of TAZ, antibiotics were continued in 5 cases because of repeat ERCP/PTC, preoperatively in 3, and for other reasons in 2. No side effects of TAZ were noted. *Summary:* Tazobactam-piperacillin (4.5 g iv) before and 8 h and 16 h after ERCP prevented post-procedural infections in 91% of patients at high risk for cholangitis. *Conclusions:* Because of its efficacy and excellent tolerance, tazobactam-piperacillin appears to be a very cost-effective drug for prophylaxis of post-ERCP cholangitis in patients with cholestasis in whom therapeutic ERCP is planned. Endoscopy, general: Complications Endoscopy, specific: Biliary } "Tazobactam-Piperacillin Effectively Prevents Post-ERCP Infections"

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"P P 51 1243" P 51 1243 **Bile Leaks: Minimally Invasive Management?** R.E. England, J.P. McLindon, D.F. Martin

Departments of Radiology & Gastroenterology South Manchester University Hospitals NHS Trust Bile leaks are relatively uncommon but associated with significant morbidity and mortality. Early diagnosis is essential and close collaboration between endoscopist, interventional radiologist and surgeon is necessary to optimise patient care. *Aim:* To review our experience of bile leaks — their cause, management and outcome. *Method:* Retrospective review of notes and imaging of all patients with bile leaks between January 1991 and December 1995. *Results:* 27 patients, 11 M 16 F, median age 54.5 (range 28–83). Aetiologies include: post cholecystectomy (16), post-intervention (ERCP + PTC) (9), trauma (1) and spontaneous leak associated with distal bile duct stricture (1). Leaks post cholecystectomy were post laparoscopic surgery in 10 and sites of leak were cystic duct stump (9), ducts of Luschka (2) and along T-tube tracks (5). 15 were managed endoscopically with sphincterotomy (ES) in 9, stents in 5 and ES and stent in 1. 1 patient was managed percutaneously with extraction of retained stones. Post-intervention leaks were clinically significant in 3 of 9 and managed with percutaneous metal stents (2) and endoscopic stenting (1). The spontaneous leak occurred from the GB in the presence of a distal bile duct stricture, and post operatively a persistent leak from the GB fossa was managed with endoscopic stenting. The trauma induced leak was a self-inflicted knife wound transecting the CBD and PD. Although the CBD could be stented the patient succumbed to multi-organ failure. 20 of 27 leaks responded to percutaneous or endoscopic techniques, 6 resolved spontaneously and only one failed to respond. *Conclusion:* The majority of bile leaks can be managed safely and effectively using a variety of endoscopic and percutaneous techniques. Endoscopy, specific: Biliary Radiology and ultrasound: Therapy Endoscopy, general: Instrumentation, therapy } "Bile Leaks: Minimally Invasive Management?"

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"P P 51 1245" P 51 1245 **Acute Cholecystitis Treated by Transpapillary Endoscopic Retrograde Cholecystostomy** R. Dumas, J.F. Demarquay, P. Hastier, B. Maes, J.P. Delmont

Department of Gastroenterology, Cimiez Hospital, Nice, France A new approach of the gallbladder is now possible due to recent advances in endoscopic techniques and instruments, allowing selective cannulation of the cystic duct during ERCP. From October 1993, to March 1996, 15 unoperable patients were referred with the diagnosis of acute cholecystitis (male: 9, female: 6, mean age: 72.6, ext.: 34–92). Contraindications for surgery were: recent severe polytraumatism 1, subarachno\`efdal hemorrhage 1, cardiac failure 4, poor general status, in elderly patients 7, cirrhosis with liver failure 1, therapeutic aplasia after chemotherapy for leukemia 1. Indications for endoscopic drainage were: lithiasic acute cholecystitis 14, associated with acute cholangitis in 5 pts, with acute pancreatitis in 2 pts; acalculus cholecystitis (with perforated gallbladder) in 1 pt. Selective cannulation of the cystic duct and gallbladder endoscopic drainage were successfully achieved in 13 (86.6%). Endoscopic procedures were carried out under sedation by pethidine or propofol. An endoscopic sphincterotomy was performed in 13 pts. An hydrophilic atraumatic terumo' guide was used in 12 cases, being driven into the cystic duct through a specific preshaped catheter ("retrogall" Schneider) in 4 patients. In one patient a miniscope (Pentax FCP9P) appeared to be helpful. Gallbladder drainage was carried out through standard naso biliary catheters (10 cases) or specific "intragall" Schneider catheters (3 cases) in association with irrigations, infusion of mucolytic agents, and intravenous antibiotherapy during 7 to 14 days. No complication was observed. In 12 of the 13 patients with successful endoscopic drainage emergency cholecystectomy could be avoided. Absence of clinical and ultrasonographic improvement lead to surgical cholecystectomy in one patient. In the 12 other patients (92.3%) evolution was favorable including the patient with perforated gallbladder. ESWL allowed gallbladder stones clearance in two patients. Cystic duct was stented with a double pig tail endoprosthesis in 4 cases during 6 weeks. The leukemic patient could be cholecystectomised 2 months later, after therapeutic aplasia had disappeared. The follow up of the other patients doesn't suggest high risk of relapse until now. *Conclusion:* our results suggest that in unoperable patients with acute cholecystitis endoscopic transpapillary drainage should be considered as an alternative to emergency cholecystectomy. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary } "Acute Cholecystitis Treated by Transpapillary Endoscopic Retrograde Cholecystostomy"

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"P P 51 1246" P 51 1246 **Basic Investigations Concerning a New Low-Cost Piezo-Acoustic Stone-Tissue-Discrimination-System (paSTDS) for "Smart" Laserlithotriptors and "Blind" Fragmentation of Gallstones** J. Hochberger, J. Tschepe<sup>1</sup>,

\*S. Tex, J. Bayer, R. Stein, C. Ell, J. Helfmann<sup>1</sup>, P. Martus<sup>2</sup>, E.G. Hahn

Dept. of Medicine I, Friedr.-Alexander-University, Erlangen

<sup>2</sup> I. Biom. Statist., Friedr.-Alexander-University, Erlangen

<sup>1</sup> Laser Medical Technologies Berlin, Berlin, FRG In animal experiments and clinically we were able to prove the effectiveness of an optical stone-tissue-discrimination-system (oSTDS) in combination with a Rhodamine-6 dye laser ("Lithognost", Baasel Lasertechnik, FRG). The system provides the possibility of disintegrating biliary concretions in a reliable and safe manner using standard duodenoscopes and catheters without cholangioscopic control. However, the dye laser and the oSTD system represent two expensive components of this sophisticated technology, thus restricting the use of this "smart laser" to selected gastroenterologic centers at present. In the following we report on our preliminary results concerning a new low cost piezo acoustic STDS (paSTDS), which is currently integrated in a frequency-doubled double-pulse Nd:YAG-laser (FREDDY). *Mat. & Methods:* The paSTDS was used in combination with FREDDY (laser double pulse at 532 nm/1064 nm wavelength, 16/79 mJ, 1.4 us, "Lithon", Clyxon Corp. Berlin, FRG) and a 280 μm quartz-fiber system. The fundamental concept of paSTDS is the good conductance of quartz for mechanical waves as generated e.g. during plasma expansion, pseudo-cavitation and "bubble collapse" in laserlithotripsy. 20 human gallstones, porcine gall bladder "in vitro" and 6 rabbit gallbladders in acute animal experiment were exposed to laser pulses at different energy settings (35–95 mJ; 0–16 mJ at 532 nm) in direct stone/tissue contact. The time interval between plasma expansion (1st signal) and collapse of the plasma induced bubble (2nd signal) were detected by a needle-hydrophone as well as by a piezosensor attached to the fiber surface and analyzed optically and electronically (storage oscilloscope/paSTDS). *Results:* Concerning the stones, paSTDS using a 280 μm quartz fiber proved dependable detection of the acquired signals in comparison to the hydrophone measurements (300–700 us). On the porcine gallbladder in vitro no plasma signals were detected even after 10.000 FREDDY laser pulses. In preliminary animal experiments plasma formation on tissue was rare with the lack of plasma formation in up to 1,000 pulses on the gallbladder of the rabbit. Further testings in the animal and first clin. applications are currently under investigation. *Conclusions:* According to our preliminary results paSTDS appears to offer a very promising low-cost alternative stone-tissue-discrimination-system for "blind" laserlithotripsy of gallstones allowing the use of standard duodenoscopes and catheters. However, the clinical outcome, realized in FREDDY + paSTDS as a first alternative "low cost smart laserlithotripter" at 1/3 of the prize of established systems has to be awaited. Endoscopy, specific: Biliary/Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, general: Instrumentation, therapy } "Basic Investigations Concerning a New Low-Cost Piezo-Acoustic Stone-Tissue-Discrimination-System (paSTDS) for "Smart" Laserlithotriptors and "Blind" Fragmentation of Gallstones"

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"P P 51 1248" P 51 1248 **Intra-Corporeal Lithotripsy in Complex Biliary Stones** B. Behjou, F. Prat, J. Fritsch, A.D. Choury, G. Pelletier, C. Buffet

Hepatogastroentérologie, CHU de Bicêtre, le Kremlin-Bicêtre In 2 to 5% of cases of biliary lithiasis, the usual endoscopic techniques fail to make bile ducts free. Intracorporeal lithotripsy (ICL) is a recognized method for the treatment of such cases. Our aims were to compare two different techniques, laser (L-ICL) and electrohydraulic (EH-ICL) lithotripsy, and to assess the long term results of these methods. 40 patients (27 women, 13 men, mean age 76 – 14 years) were treated by L-ICL (22 patients), EH-ICL (10 patients) or both techniques successively (8 patients). Stones (mean diameter 23 – 12 mm) were intra-hepatic in 4 cases, choledochal in 31 cases and both intra- and extra-hepatic in 5 cases. Stones were approached via the trans-hepatic route in 3 cases, the endoscopic retrograde route in 35 cases and both routes in 2 cases. The 3 groups were statistically identical. The mean number of ICL sessions was 1.6 – 0.8; complete fragmentation and free bile ducts were obtained in 95% of cases (2 failures: Roux-en-Y anastomosis = 1; conservative treatment = 1). The mean hospital stay was 10.8 – 9.5 days. The global morbidity at 30 days was 32.5% (mostly transitory bouts of hyperthermia) but only one case of major morbidity was noted (bleeding sphincterotomy: 2.5%) and was not directly related to ICL, there was no procedure-related mortality. There was no difference between groups for all of these criteria. Long term information was obtained in 36 patients (90%) with a median follow-up of 17 months (range 4–52). Ten patients died from non-biliary diseases. Two patients developed biliary symptoms 24 and 34 months after ICL (5%), one of whom after a failed ICL. ICL is an effective method for the treatment of the most complex cases of biliary lithiasis. Its morbidity is acceptable. Both techniques (L-ICL and EH-ICL) yield similar results. The long term symptomatic complications of ICL seem to be rare. Endoscopy, specific: Biliary Endoscopy, general: Instrumentation, therapy Liver and bile ducts, 2: Gallstones, formation, treatment } "Intra-Corporeal Lithotripsy in Complex Biliary Stones"

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## "P P 51 1249" P 51 1249 Usefulness of Electro Hydrouric Lithotripsy for Common Bile Duct and Intraheptic Bile Duct Stone

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<sup>1</sup> Division of Int. Med. of Gastroenterology Iwate Prefectural Central Hospital, Morioka Iwate, Japan

<sup>2</sup> Division of Int. Med. of Gastroenterology Iwate Red Cross Hospital, Morioka Iwate, Japan

<sup>3</sup> Division of Int. Med. of Gastroenterology Iwate Prefectural Miyako Hospital, Morioka Iwate, Japan  
*Introduction:* Although, Electro Hydrouric Lithotripsy (EHL) is an effective treatment for common bile duct (CBD) stone, EHL is difficult to perform in patients with huge stone or confluence stone. Laser or extracorporeal shock wave lithotripsy (ESWL) would not be cost-effective. *Aim and Method:* We evaluated the usefulness of EHL with peri oral cholangio scopy (POCS) in the treatment of CBD stone. We also examined the effect of EHL on intraheptic bile duct stone after choledochojejunostomy. EHL was performed using the 4.5 or 3 Fr. probe under POCS with mother scope (TJF M20) and babyscope (CHF B20). *Patients:* EHL with POCS was done in 11 patients (male 6, female 5, mean age 68) and EHL with percutaneous transhepatic cholangioscopy (PTCS) in 4 (male 3, female 1, mean age 61). *Results:* Mean diameter of CBD stones in treated by EHL with POCS was 22 mm (range 18 – 30 mm). Seven demonstrated Bilirubin stone and four demonstrated cholesterol stones. Four patients had confluence stones. EHL was successful in all patients. Lithotriptic time for bilirubin stones was less than one hour in 6 of 7 patients, (mean time 48 min, range 35 – 70 min). While lithotriptic time for cholesterol stones required more than one hour in all four patients, presumably due to the increased hardness (mean time 62 min, range 60 – 70 min). In patients undergoing EHL with POCS, CBD was examined following removal of the stones to investigate the effect of EHL on the mucosa and determine the presence of CBD residual stones. EHL with PTCS was performed for bilirubin stones in patients with stenosis after choledochojejunostomy. Stenosis was successfully dilated by balloon following EHL removal of stones. *Conclusion:* EHL with POCS is an effective treatment for huge CBD stones and confluence stones, although the time required for the procedure is longer. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary Oncology, general: Therapy } "Usefulness of Electro Hydrouric Lithotripsy for Common Bile Duct and Intraheptic Bile Duct Stone"

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## "P P 51 1250" P 51 1250 Transhepatic Cholangioscopy in the Treatment Difficult Choledocholithiasis

\*J. Petrt<sup>1</sup>, V. Dufek, R. Brůha, Z. Marecek

Ist Medical Department, Charles University, Prague, Czech Republic  
Choledocholithiasis (CDL) is the most common biliary tree disturbance, affecting more than 50% of population in Central and Eastern Europe in the elderly. Endoscopic solution of CDL is, in general, a method of choice, nowadays. However, in about 12% of patients (pts) the endoscopy fails and such a stones are mentioned as difficult ones (DCDL). *Aim:* This study was performed to assess the feasibility of transhepatic cholangioscopy (THCS) in the treatment of DCDL. *Patients and Methods:* Since May 93 to May 96, 20 consecutive pts with DCDL (7 females, 13 males, mean age 66.7 years) were entered into the study. In six of them, gastric resections, periampullary diverticula or CBD stenoses were present, in 14 cases, hepaticolithiasis or large CBD stones were found during ERCP. THCS was performed using a flexible scopes. For the stones removal, an intracorporeal shock waves lithotrypsi (ISWL) was used. *Results:* In all pts, the crushing and removal of DCDL was achieved in 1.5 sessions (range 1–3). Analgosedation by fentanyl and midazolam was the only treatment modality in THCS. CBD strictures of benign origine in 2 cases were treated by metallic endoprostheses before ISWL. The toleration of both THCS and ISWL was excellent. We were not able to demonstrate any weighty side effect, either local or systemic. *Conclusions:* On the basis of the results mentioned is possible to conclude, that THCS in combination with ISWL is, nowadays, the method of choice in the nonsurgical treatment of DCDL. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Transhepatic Cholangioscopy in the Treatment Difficult Choledocholithiasis"

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P P 51 1251"P 51 1251**Percutaneous Cholecystostomy in Elderly Patients with Acute Calculous Cholecystitis**T. Noro, H. Hashimoto, K. Kino, M. Naito, Y. Tanaka, K. Yoshiura, K. Katsuragawa

Tokyo Metropolitan Geriatric Hospital, Department of Surgery and Internal Medicine, Tokyo, Japan*Purpose:* Efficacy of percutaneous cholecystostostomy as a therapeutic maneuver was evaluated in 70 patients of advanced age with acute cholecystitis.*Method:* 60 patients consisting of 40 men and 30 Women, 61–94 years old (mean age; 78.7 years) with acute cholecystitis underwent percutaneous cholecystostomy. All patients were with one or more medical problems, including respiratory failure, congestive heart failure, renal failure, and cerebrovascular accident. etc. and had a high fever ( $> 38^{\circ}\text{C}$ ), elevated WBC counts, and evidence of abdominal pain or tenderness in the right upper quadrant on clinical examination. Percutaneous cholecystostomy was performed by using a transhepatic approach with sonographic guidance. Under local anesthesia, the gallbladder was punctuated with a 22-gauge needle. Catheters were then placed in tandem to the needle into the gallbladder.*Results:* In all of 70 patients, significant improvement was shown in the clinical condition within 24 to 48 hr, including disappearance of abdominal pain or tenderness, defervescence, WBC count returning to normal. No complications related to catheter in sertion occurred.*Conclusion:* Percutaneous cholecystostomy is an effective temporary measwe in elderly patints with acnte cholecystitis and, under close clinical supervision, a safe alternative to surgical intervention Liver and bile ducts, 2: Gallstones, formation, treatmentClinical practice: Management strategy }" "Percutaneous Cholecystostomy in Elderly Patients with Acute Calculous Cholecystitis"

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"P P 51 1252" P 51 1252 **Are Expandable Metal Stents an Improvement over Plastic Stents in the Palliative Management of Malignant Stenosis of the Common Bile Duct?** J.M. Canard, H. Fontaine<sup>1</sup>, R. Chollet<sup>2</sup>

<sup>1</sup> C.M.C du Trocad\ 'e9ro 62, rue de la Tour 75016 Paris

<sup>2</sup> Groupe Hospitalier Piti\ 'e9 Salp\ 'e9tri\ 'e9re 75013 Paris The aim of the study is to demonstrate whether there is a difference between plastic and metallic stents in terms of complications, stent patency, and patient survival rate. *Patients:* from January 1992 to May 1995 endoscopic biliary decompression using metal stents (group 1, 20 Strecker, 11 Wallstent and 4 endocoil prostheses, n = 35) or plastic stents (group 2, n = 31) was performed in 62 patients (29 men and 33 women) whose mean age was 71 – 15 years. They had malignant stenosis of the common bile duct: pancreatic cancer (n = 35), vaterian tumors (n = 7), cholangiocarcinoma (n = 9), metastasis (n = 11). *Methods:* the first question is: are the two groups comparable? 1 – Is the distribution between metal and plastic stents appropriate? The chi 2 test found p = 0.33 (NS). 2 – Are the disease criteria between the two groups matched? A student's test was made for age, infection, cholestasis, and confirmed lock of significant difference. A chi 2 test was made for malignancy stenosis and there was no difference between groups. *Results:* Stent insertion was a failure in 10 cases (15.2%) There appeared to be no significant difference in early or late complications between the two groups. Early complications < 30 days Plastic Metal Angiocholitis 7 2 Bleeding 1 1 Cholecystitis 1 0 Migration 0 1 9 (29%) 4 (11.5%) NS Late complications > 30 days Obstructions 9 6 (NS) Cancer – 6 Sedimentation 9 – The stent patency at 6 months was 80% – 10% for metal stents versus 45% – 13% for plastic stents (p = 0.02). There was no significant difference in term of patient survival (15 – 8% for metal stent, versus 13 – 7% for plastic stent). *Conclusions:* There was no significant difference between early and late complications due to either of the stents. The patency of the metal stents was greater than that of the plastic stent but there was no final difference in terms of survival rates. The metal stent needs to be improved and a study on cost efficiency ratios must be carried out. Endoscopy, specific: Biliary Endoscopy, general: Instrumentation, therapy Oncology, specific: Liver, biliary } "Are Expandable Metal Stents an Improvement over Plastic Stents in the Palliative Management of Malignant Stenosis of the Common Bile Duct?"

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## "P P 51 1253" P 51 1253 Endoscopic Stent Placement without Sphincterotomy in Malignant Biliary Tract Obstruction

\*F.J. Jimenez, R. Aznarez, I. Martedn-Granizo, F. Borda

Hospital de Navarra, Pamplona, Spain Endoscopic stent placement has become accepted therapy for malignant biliary tract obstruction. Endoscopic stenting has less morbidity and mortality in malignant jaundice than surgery or percutaneous stenting. Sphincterotomy is usually performed to facilitate insertion of the stent and to prevent possible occlusion of the pancreatic orifice by the stent and secondary pancreatitis. However, stenting morbidity and mortality rates might be influenced by sphincterotomy complications. We report our experience in endoscopic stenting without previous sphincterotomy in malignant jaundice. *Material and Methods:* 41 patients (22 women/19 men) with ages between 57 and 91 years (mean 74.2) were treated because of malignant jaundice by means of endoscopic stenting without previous sphincterotomy. Diagnosis was pancreatic cancer in 23 patients, cholangiocarcinoma in 12 patients, ampullary cancer in 5 patients and metastatic cancer in 1 patient. Stents were 10 F (n = 35) or 11.5 F (n = 6) slightly curved polyethylene Cotton-Leung stents of different lengths and they were all positioned with an Oasis stent introducer set (Wilson Cook Medical Inc.). *Results:* All stents could be placed endoscopically. Previous dilation of the stenosis was necessary in only 3 patients. Cytologic specimens could be taken using Cytomax cytology brushes (Wilson Cook Medical Inc). Only one patient (2.4%) developed secondary pancreatitis which was managed conservatively. *Conclusions:* 1. Sphincterotomy performance is not necessary for endoscopic stenting. 2. Stenting alone avoids potential complications due to sphincterotomy. 3. Stenting without sphincterotomy does not increase the incidence of pancreatitis. Oncology, specific: Liver, biliary Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary }"  
"Endoscopic Stent Placement without Sphincterotomy in Malignant Biliary Tract Obstruction"

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"P P 51 1254" P 51 1254 **Post-Surgical Biliary Stricture. Clinical Outcome of Endoscopic Stenting** G. Viceconte, E. Di Giulio, F. Fiocca, G. D'Ambra, G. Delle Fave

Progetto Cooperativo per lo Studio delle Malattie Digestive Università degli Studi di Roma "La Sapienza" *Introduction:* benign strictures of the bile duct following surgery (cholecystectomy, choledochotomy, etc.) are reported in about 1% of operated patients. The criteria for their management remain to be solved. The therapeutic approach: by surgery, radiology or endoscopy has been reported to be successful in about 80% of patients but the small number of patients reported in very few series, still make the question open for studies with larger series of patients. Then we aimed a study to evaluate the clinical outcome of endoscopic biliary stenting in patients with post-surgical benign biliary stricture. *Materials and Methods:* 59 patients (54% male; 32–76 aged), previously operated for cholecystectomy 81% (43.7% laparotomy; 37.5% laparoscopy); 4.1% choledochotomy and 2.8% end to end anastomosis were attempted for endoscopic biliary stenting. *Study protocol:* during 1 year, 1 to 3 plastic prothesis were positioned per patient and changed every 3–6 months. After 1 year the prothesis were removed in all patients. *Results:* the procedure was successfully attempted in 48 of 59 patients (81%). A 28 months median follow-up were completed in 91% of all patients (4 lost at follow-up). Of the 48 treated patients 65.9 had excellent results (normal liver function and no cholangitis); 13.6% good (1 episode/year of cholangitis); 20.4% had poor results (2 or more episodes of cholangitis/year). The complications during the treatment year were 9.7% cholangitis and 2.4% acute pancreatitis. Finally the overall evaluation demonstrated that 59.3% (35 out of 59 patients) were successfully treated (excellent + good score) but when the stent/s were successfully positioned the positive results increase to 79.5%. *Conclusion:* the endoscopic biliary stenting appear to be a well tolerated, poorly invasive, a low rate of complication procedure and then may be considered as first choice for treatment of post-surgical biliary strictures. Endoscopy, specific: Biliary Endoscopy, general: Instrumentation, therapy } "Post-Surgical Biliary Stricture. Clinical Outcome of Endoscopic Stenting"

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## "P P 51 1255" P 51 1255 Temporary and Long Term Biliary Stenting for Retained Common Bile Duct Stones in an Irish Cohort

\*S. Pathmakanthan, J. Goh, E. Clarke, J. Lennon, P. MacMathuna, J. Crowe

Department of Gastroenterology, Mater Misericordiae Hospital, Dublin, Ireland

Common bile duct (CBD) stones that are not amenable to extraction at ERCP can be managed by temporary biliary stenting. In selected patients, repeated biliary stenting may be an alternative to definitive surgical procedures. The aim of the present study is to evaluate the safety and clinical outcome of temporary and long-term stenting.

337 patients underwent ERCP for CBD stones over a 4 year period (1991–1995). 295 (87%) had successful duct clearance after a single ERCP while the remaining 42 (12%; 19 M, 23 F mean age 77.5; range 56–95) underwent temporary biliary stenting for non-extractable stones. The last cohort was followed up for a mean period of 20 months. Of the 42 patients who underwent temporary biliary stenting initially, 4 underwent surgical CBD clearance; 17 patients (40%) underwent successful endoscopic CBD clearance after only one additional ERCP in 65% (range 1–4); the remaining 21 patients (Mean age 77, range 68–95) had unsuccessful stone clearance subsequently and were managed by long-term biliary stenting with stent change performed for stent blockage. In this long-term stenting group, 6 died from non-biliary causes and the remainder have not experienced any biliary-related complications during a mean follow-up period of 20 months. Early complications following stenting included pancreatitis (1), cholangitis (3), oesophageal laceration during stent removal (1) and stent migration (1). Late complications (> 72 hours post ERCP) occurred in 6 and comprised stent migration, cholangitis and hepatic abscess. No mortality was observed.

**Conclusion:** Biliary stenting for non-extractable CBD stones at the first attempt is safe and allows further attempts at duct clearance to be performed electively. Long-term biliary stenting with elective stent change is a safe management option in the frail and elderly. Liver and bile ducts, 2: Gallstones, formation, treatment

Endoscopy, specific: Biliary } "Temporary and Long Term Biliary Stenting for Retained Common Bile Duct Stones in an Irish Cohort"

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"P P 51 1256" P 51 1256 **Biliary Stenting with Self-Expandable Nitinol Spring Stent** J.F. Rey<sup>1</sup>,  
D. Duforest<sup>1</sup>, T.A. Marek<sup>2</sup>

<sup>1</sup> Institut Arnault Tzanck, Saint Laurent du Var, France

<sup>2</sup> Silesian Medical Academy, Katowice, Poland *Introduction:* Biliary stenting with self-expandable metal stents is gaining increasingly wider acceptance as a palliative treatment of pancreatic and bile duct cancer. Recently, a new kind of metal stent has been developed, which structure could better prevent tumor ingrowth. *Stent description:* The stent (EndoCoil, InStent, USA) is made from a nickel and titanium alloy, in shape of coil spring. The stent is introduced constricted over a 12F catheter, hold by a wire. During three-phase (proximal end, distal end, center) delivery stent shortens (closing spaces between spring coils) and widens rapidly, up to 24F. *Patients:* Between January 1994 and November 1995 stent insertion was attempted in 27 patients (11 M, 16 F; age range: 47–91) with obstructive jaundice due to non-resectable cancer. The tumor was located in the pancreatic head in 20 cases, in 4 cases in the upper CBD, and in 3 in the papilla of Vater. *Insertion:* Stents were correctly placed in 19/27 (70%) patients. In 6 cases we were not able to pass the introduction catheter through the stricture. In 2 cases stents initially did not expand completely, what resulted in the entrapment of the delivery catheter. In both cases stents had to be removed. *Occlusion* of the stent occurred in 12 (6 – overgrowth, 6 – sludge) cases after median time of 213 (range: 145–255) days. This was managed by cleaning with Dormia basket (6), additional stent placement (4) or stent replacement (2 cases). No tumor ingrowth into the tight stenting section was observed. *Removal:* We were able to withdraw the stent by pulling the distal end using Dormia basket/polypectomy snare in 4 cases (in 2 due to tumor overgrowth, in 2 due to inadequate expansion), with 1 complication. *Complications* occurred in 3 cases (14%) with one fatality (5%). The removal of the stent with entrapped delivery system resulted in perforation of the distal CBD and severe bleeding, leading to death. In additional 2 cases clinically asymptomatic perforation of the CBD occurred, as a consequence of CBD wall pinching between neighboring coils of the stent helix during delivery. *Conclusions:* The new self-expandable stent offers several advantages; the ingrowth prevention and the possibility of removal are the most important. However, the insertion system should be improved, to avoid CBD injury during stent's shortening and the possible entrapment of delivery catheter. The removal of the stent should be carefully monitored endoscopically and radiologically. Endoscopy, specific: Biliary } "Biliary Stenting with Self-Expandable Nitinol Spring Stent"

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"P P 51 1257" P 51 1257 **Importance of Hydraulic Dilatation (h.d.) before Biliary Stenting with Endocoil Instent (e.i.) Prostheses, Preliminary Results in 35 Patients** A. Verduron, O. de Loubens, F. Girault

Clinique Pereire, Levallois, France The new self expandable metallic biliary stent e. i. is supposed to prevent tumor ingrowth, owing to the tight loops of the coil. However when the stenosis is too hard, the radial force of the stent may not be strong enough to allow fast full expansion and therefore easy withdrawal of the delivery catheter and quick loops joining. We propose previous h.d. in order to give the stenosis the diameter of the fully expanded stent. We report our experience with this new prosthesis first without, then with, previous h.d. *Patients-methods:* Between November 1994 and April 1996, stent insertion was attempted in 35 patients (19 F-16 M,  $\bar{x}$  age 73 – 15 years) with obstructive jaundice due to non resectable malignant stenosis of the intra pancreatic common bile duct. The first 13 patients had no h.d. (Group 1), the next 22 (Group 2) had h.d. first with a biliary balloon (Maxforce-microvasive) able to reach a 24 FR diameter with a 12 ATM, pressure. Patients were comparable in term of age, stenosis and cholestasis. *Results:* Stent insertion was successful in all 35 patients. Withdrawal of the delivery catheter was laborious in all Group 1 patients, for 2 of them the catheter got caught in the stenosis during 3 and 4 days, withdrawal was easy and immediate in all Group 2 patients. The average time for full stent expansion was 5.3. days (range 1–12) in Group 1 vs 1.14 (range 0–5) in Group 2 ( $p < 0.05$ ). At the fourth post-operative day there was a total bilirubin decrease of 16% in Group 1 vs 42% in Group 2. Cholecystitis requiring cholecystectomy occurred in 3 Group 1 patients within 2 weeks of insertion, stent clogging by tumor ingrowth happened in 2 Group 1 patients respectively 1 and 2 months after the intervention. There was no complication in Group 2. Median follow up after insertion was 121 days (range 12–341). *Conclusion:* These preliminary results show that previous h.d. in biliary stenting with e.i. is essential to remove immediate technical difficulties. Moreover they suggest that it improves immediate successful drainage and prevents late clogging by tumour ingrowth. Oncology, specific: Pancreas Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary }" "Importance of Hydraulic Dilatation (h.d.) before Biliary Stenting with Endocoil Instent (e.i.) Prostheses, Preliminary Results in 35 Patients"

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## "P P 52 1260" P 52 1260 Outcome of Malignant Colo-Rectal Polyps

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<sup>1</sup> Gastrointestinal Unit, Kantonsspital St. Gallen

<sup>2</sup> Surgical Department, Kantonsspital St. Gallen *Background:* Malignant colo-rectal polyps are defined as endoscopically detected polyps which revealed cancer tissue in the histological examination. We studied epidemiologic data and outcome in our patients (pts) with malignant polyps. *Methods:* All pts in whom a endoscopy has been performed during 1986–1995, were analyzed. Outcome was assessed by interview with patients and general practitioners. *Results:* Lower endoscopy was performed in 6605 pts (mean-age: 68, range: 53–83; m: f = 2.5:1) and a malignant polyp was detected in 35 (0.5%) pts. Six pts were treated by primary segmental colonic resection (histological staging see table 1). Staging pT1N0M0 pT2N0M0 pT3N0M0 pT3N1M0 pT4NxMxN = 6 2 3 0 1 0 In 29 patients, local polyp resection was performed. In 11 of these 29 patients, a segmental colonic/rectal resection was performed because histological analysis suggested an incomplete tumor resection (histological staging see table 2). Histology Normal Adenoma pT1 pT2 pT3 pTN1 pTNM1N = 11 8 2 1 0 0 0 0 Pts who were adequately treated exclusively by polypectomy, showed no local or distance recurrence. Three pts (9%) had an unfavourable outcome. One patient after endoscopic polypectomy who refused surgical resection despite unfavourable histology (G3 and lymphatic vessels – infiltration) developed local recurrence. One patient died postoperatively and one patient died after segmental colon resection because of liver metastasis. *Conclusion:* Malignant polyps were detected in approximately 0.5% of all lower endoscopies or 4% of patients with polyps. Patients remained tumor-free in 91%. Endoscopic polypectomy is the treatment of choice for patients with favorable histology. Oncology, specific: Colon, rectum Oncology, general: Therapy Oncology, general: Epidemiology } "Outcome of Malignant Colo-Rectal Polyps"

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## "P P 52 1261" P 52 1261 What are the Optimal Intervals for the Survey of Patients with Adenomatous Colon Polyps?

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IJsselland Hospital, Capelle a/d IJssel, The Netherlands

<sup>1</sup> Comprehensive Cancer Centre, Rotterdam, The Netherlands *Aim.* The follow-up of patients with adenomatous colon polyps is an accepted strategy. The surveillance intervals however are subject of discussion. According to the Dutch consensus these are 1 year after polypectomy followed by an interval of 3 years (> 1 polyp) and 5 years (1 polyp). In this study we evaluated the yield of this schedule and tried to identify enrolment risk factors. *Method.* In 315 patients a colonoscopy was performed 1 year after removal of newly diagnosed adenomatous polyps and in 69 of these patients (no relapse after 1 year) again 3 years later. At enrolment and follow-up colonoscopy sex, age, polyp-location, -size, -number, sessile or pedunculated, histological type and grade of dysplasia were recorded. *Results.* After 1 year in 63 patients (20%) polyps were found. In 16 patients (5.1%) these polyps were classified as local relapse, mainly correlated with initial villous sessile (> 1 cm) polyps (15 sessile vs 1 pedunculated;  $p < 0.01$ ). In the remaining 47 patients (14.9%) the polyps were either newly formed or initially missed. Two risk factors were identified: multiple polyps (20% multiple vs 11% single;  $p < 0.05$ ) and age. The relapse rate after 1 year in 126 patients younger than 60 years was 8% against 21% in 189 older patients ( $p < 0.01$ ). Three patients (all > 60 years and > 1 polyp at enrolment) had high-grade dysplasia or invasive cancer. In the 69 patients four years after the initial polypectomy the relapse rate was 17%; no enrolment risk factors and no high-grade dysplasia or invasive cancer were detected in this group. *Conclusions.* The relapse rate after one year seems high, however we are dealing with newly formed polyps and polyps missed at the initial colonoscopy which can be up to 29% according to literature. Our results suggest that colonoscopy after 1 year should only be performed in patients older than 60 years with multiple or sessile (> 1 cm) polyps. Otherwise a three years interval seems acceptable. In this study the number of colonoscopies after 1 year would be reduced with 30%. Clinical practice: Management strategy Oncology, general: Screening, prevention Oncology, specific: Colon, rectum } "What are the Optimal Intervals for the Survey of Patients with Adenomatous Colon Polyps?"

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"P P 52 1263" P 52 1263 **Regression of Small Intestinal and Colonic Polyps after Non-Steroidal Antiinflammatory Drug-Tenoxicam Treatment in Patients with Adenomatous Polyposis**

\*M. Tuncer, A. Dobrucali, I. Yurdakul, S. Tuncer, A. \c7elik, K. Bal, H. Uzanismail, E. Oktay

Gastroenterology Department of Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey *Purpose:* Colonic cancer is the leading cause of death in patients with adenomatous polyposis. The aim of this study was to assess the effect of the non-steroidal antiinflammatory drug-Tenoxicam on duodenal and colonic polyps in patients with adenomatous polyposis. *Method:* Twenty-eight patients with advanced duodenal and colonic polyposis were randomly planned to receive a six months treatment of either 20 mg Tenoxicam (Tenoxicam group (TG) n = 14) or placebo [Placebo group (PG), n = 14] twice a day. Duodenoscopy and colonoscopy before and after 6 months was done and dimension and number of polyps in the duodenum and colon region were assessed by a blinded observer. The size of polyps was estimated by comparison with an opened biopsy forceps. *Results:* Both groups were comparable with regard to pretreatment polyp number (TG: 12 – 5, PG: 10 – 5) and dimension (TG: 4.5 – 1.5 mm; PG: 4.7 – 1.4 mm). After six month, more patients in the PG than in the TG have developed new polyps (p < 0.05). Polyps with less than 3 mm in size decreased or disappeared in 11 TG patients (79%) but only 3 PG patients (21%) (p < 0.05). Polyps with more than 5 mm in size were not significantly changed in both groups. *Conclusion:* These findings suggest that non-steroidal antiinflammatory drug-Tenoxicam induces regression of small intestinal and colonic polyps. Further studies will reveal if Adenomatous polyposis patients with early stage of intestinal and colonic disease could benefit from tenoxicam therapy. Oncology, general: Therapy Oncology, specific: Small bowel Oncology, specific: Colon, rectum } "Regression of Small Intestinal and Colonic Polyps after Non-Steroidal Antiinflammatory Drug-Tenoxicam Treatment in Patients with Adenomatous Polyposis"

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## "P P 52 1264" P 52 1264 Significance of Colorectal Polyps Found on Sigmoidoscopy in Asymptomatic Patients

\*J. Kim, H.J. Son, H.Y. Lee, P.L. Rhee, K.C. Koh, S.W. Paik, J.C. Rhee, Y.L. Oh<sup>1</sup>

Division of Gastroenterology, Samsung Medical Center, Seoul, Korea

<sup>1</sup> Department of Pathology, Samsung Medical Center, Seoul, Korea *Purpose:* There has been much controversy regarding the significance of the hyperplastic polyps found on sigmoidoscopy as markers for synchronous adenomatous polyps. Therefore, we prospectively performed colonoscopy in asymptomatic individuals with colorectal polyps found on screening sigmoidoscopy to determine the possible association between synchronous polyps with the size or histologic type of colorectal polyps. *Method:* We performed flexible sigmoidoscopy in 2895 persons who wanted sigmoidoscopy out of 10705 healthy persons who visited Samsung Medical Center for health check up from August 1994 to November 1995. Colorectal polyps were found in 590 of 2895 individuals and colonoscopy was performed in 280 of 590 subjects. The size and location of all polyps were noted and biopsied. *Result:* Of 280 subjects, 73 (26.1%) subjects had synchronous polyps and 55 subjects (19.6%) had synchronous adenomatous polyps. 134 polyps were found in colonoscopy including adenomatous polyps (61.3%), hyperplastic polyps (12.9%) and inflammatory polyps (16.1%). The proportion of subjects with adenomatous polyps who had synchronous adenomatous polyps (25%) was significantly greater than the proportion of those with hyperplastic polyps who had synchronous adenomatous polyps (6.8%) ( $p < 0.05$ ). The percentage of subjects with larger polyps ( $> 0.5$  cm) who had synchronous adenomatous polyps (43.2%) was significantly greater than the proportion of those with diminutive polyps ( $\leq 0.5$  cm) who had synchronous adenomatous polyps (16.0%) ( $p < 0.05$ ). *Conclusions:* Adenomatous polyps found during sigmoidoscopy justify colonoscopy for synchronous polyps. However, diminutive hyperplastic polyps are not significant indicators of risk for synchronous adenomatous polyps. Oncology, specific: Colon, rectum Endoscopy, specific: Colon, rectum }" "Significance of Colorectal Polyps Found on Sigmoidoscopy in Asymptomatic Patients"

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"P P 52 1267" P 52 1267 **Differences in the Risk of Severe Dysplasia between Endoscopically and Surgically Removed Colorectal Adenomas** G. Nusko, U. Mansmann, A. Altendorf-Hofmann, Kessler, Ch. Wittekind, C. Ell, E.G. Hahn

Depts. of Medicine I, Surgery & Pathology, Tumor Registry, University of Erlangen, Germany

Institute of Medical Statistics, Free University of Berlin, Germany Risk factors for severe dysplasia in colorectal adenomas have been studied in endoscopically removed specimens (Gastroenterology 1990, Scand J Gastroenterol 1993). The aim of this study is to detect differences in variables of risk between endoscopically or surgically removed adenomas. *Methods:* From 1978 to 1993, 6631 consecutive patients of the Medical & Surgical Depts. with colorectal polyps were prospectively documented at the Erlangen Registry of Polyps. A total number of 11380 adenomas were documented according to the WHO classification and statistically analysed by logistic regression. *Results:* At the initial examination 5972 adenomas were removed *endoscopically* in 3343 patients and 3820 adenomas were removed *surgically* in 1749 patients. 313 (9%) endoscopic and 260 (15%) surgical patients had adenomas with severe dysplasia. The strongest discrimination between these groups was given by the size (significant cutpoint at 32 mm). Size of adenomas was the most important risk factor (endoscopic OR 8.2; 95% CI: 5.6–11.9 and surgical OR 13.8; 95% CI: 6.8–28.2). Tubulovillous and villous adenomas were of a higher risk in endoscopic (OR 2.3; 95% CI: 1.7–3.0) and surgical (OR 4.3; 95% CI: 1.4–13.6) specimens. Adenomas located in the right colon showed a lower risk in endoscopic (OR 0.4; 95% CI: 0.3–0.7) and surgical (OR 0.4; 95% CI: 0.2–0.9) resections. The risk factors in *endoscopic* removed adenomas can be described by a model of independent variables. But the risk of severe dysplasia in *surgical* resected adenomas have to be described by an interactive model. Significant interactive effects were found for the size ( $\geq 10$  mm) and villous structure (OR 0.2; 95% CI: 0.1–0.7), size ( $\geq 20$  mm) and right colon location (OR 2.7; 95% CI: 1.1–6.7), and villous structure and colonic compared with rectal location (OR 2.7; 95% CI: 1.3–5.8). *Conclusions:* Size and villous structure are the most important risk factors for developing severe dysplasia whereas adenomas located in the right colon are of a lower risk in both groups. The difference between endoscopic and surgically removed adenomas is that size, villous structure and location are independent risk factors in endoscopically specimens. The risk of severe dysplasia in surgically removed adenomas has to be described by an interactive model with modifying interactive effects of size, villous component and location. Oncology, specific: Colon, rectum Endoscopy, specific: Colon, rectum } "Differences in the Risk of Severe Dysplasia between Endoscopically and Surgically Removed Colorectal Adenomas"

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**"P P 52 1268" P 52 1268 Polyps Found in Screening Colonoscopy: A Three Year Single Center Experience K. Lang,**

\*J. Hammer, Ch. Oesterreicher, R. Pöfötz, A. Gangl

General Hospital of Vienna, Abt. f. Gastroenterologie und Hepatologie, University of Vienna, Austria We evaluated frequency, site, and histologic characteristic of polyps found during colonoscopy of consecutive asymptomatic patients. Between January 1992 and December 1994 complete colonoscopies were performed on 2387 individuals who did not have a history of colonic polyps, inflammatory bowel disease, intestinal resection, or hematochezia, and did not have a contraindication against biopsies. All polyps found were either resected or, if polypectomy was not possible, biopsied. Polyps were found in 822 patients (34% of all individuals, 438 men, 384 women). The table shows number of patients with one or more than one polyps found in the colonic regions and histology of polyps. "Others" summarizes hyperplastic polyps, inflammatory polyps, carcinoids (2 cases) and leiomyomas (2 cases). 1 polyp {b3} 2 polyps Adenomas Carcinomas Others Rectum 256 96 201 17 134 Sigmoid 252 99 258 5 88 Descending 109 24 113 3 17 Transverse 93 23 94 3 19 Ascending 158 59 163 12 42 Cecum 78 19 69 5 23 As expected, most polyps were found in the distal colon. However, 34% of all polyps found were located in the proximal colon (i.e. transverse colon, ascending colon, and cecum) and 22% of patients only had polyps in the proximal colon. Moreover, the chance that a polyp was an adenoma (or carcinoma) increased proximally: in the rectum 62% of all polyps were adenomas (or carcinomas), 75% in the sigmoid colon, 87% (descending colon), 84% (transverse colon), 81% (ascending colon), and 76% (cecum), respectively. In summary, adenomas and carcinomas are often found in the proximal colon. Our data, we believe, argue for screening colonoscopy (instead of sigmoidoscopy) in primary work up of asymptomatic individuals. } "Polyps Found in Screening Colonoscopy: A Three Year Single Center Experience"

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"P P 53 1269" P 53 1269 **A New Technique for Endoscopic Crossing Lower Digestive Tract Stenoses**

\*L. De Salvo, F.E. Gianiorio, G. Borgonovo, C. Bianchi, A. Arezzo, F.P. Mattioli

Clinica Chirurgica R. University of Genoa, Genoa, Italy Endoscopic dilatation of the of rectal and sigmoid stenoses are performed more and more frequently, but, despite of the large diameter of the dilator used, it is often impossible to drive the endoscope through the stricture. *Aim of the study* is to test a new technique to pass through rectal and sigmoidal stenoses. *Material and methods:* We used a balloon dilator (Meditech Rigiflex Microvasive 18 mm.\d8) previously modified cutting off and blunting the thin tip of flexible plastic material in order to avoid perforation. This dilator inflated is kept near to the tip of the endoscope and becomes itself an ogival tip of the endoscopic tool. Strictures can be crossed by pushing the dilator and the instrument together. A partial view of the lumen is obtained through the balloon dilator made of transparent material. In this way from 1993 Jan. and 1996 Jan. 43 rectal strictures have been dilated with balloon or bougie dilators and then crossed with the endoscopic tool using the technique previously described. We also obtained by using this method an accurate description of the stenotic bowel and its carefully measurement. Moreover biopsy or brushing of the lesion was performed in almost all the cases. *Results:* In this group of 43 pts. (24 male and 19 female) with an age range from 42 to 86 years we were able to go through the stricture in 37 cases (86%). In six pts. this was not possible for a wide and fixed angulus formed by the bowel proximal to the stricture. Major complications such as perforation or rupture of the stricture was never seen. A mild or moderate pain during the dilatation time was present in 16 pts. and mild self limiting bleeding was observed during the manouvre in. We never used this procedure in pts. with known diverticular disease. *Conclusion:* We can conclude that this method is a safe and acceptable procedure to pass through rectal and lower sigmoid strictures. Endoscopy, specific: Colon, rectum Endoscopy, general: Instrumentation, therapy } "A New Technique for Endoscopic Crossing Lower Digestive Tract Stenoses"

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## "P P 53 1270" P 53 1270 Usefulness of a Specially Designed Grasping Forceps in Retrieving the Polypectomized Multiple Polyps of the Colon

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*Purpose:* Because the histopathological diagnosis of colonic polyps is an integral part of the polypectomy procedure, the resected specimens should be retrieved without destruction. However, in cases with multiple colonic polyps, several insertions of the colonoscope are necessary to retrieve all polypectomized polyps, then it usually becomes very time-consuming and troublesome for patients and also colonoscopists. Therefore, we developed a specially designed grasping forceps to retrieve multiple polyps in only one session.

*Methods:* A specially designed grasping forceps which we developed is essentially similar to the basket type grasping forceps FG-16L (Olympus Lab.). However, the tip basket part of our forceps can be detached by manipulating the operation part near at hand. One of different color strings 3–4 cm in length have been tied to each basket. Retrieving multiple polyps, after first polypectomy the specimen is grasped by the basket type forceps, and the basket part grasping the specimen is detached and left temporarily within the colon. Then other polyps are treated in the same way. When all polyps have been polypectomized and grasped, all strings are hold one after another by a standard biopsy forceps. When the entire instrument with some baskets just outside the tip of the scope is withdrawn, the multiple specimens can be retrieved. The identification of each polyp can be confirmed by the color of each string.

*Results:* We have used this forceps on 21 patients with multiple colonic polyps. Polyps less than 20 mm in diameter could be grasped with this forceps, and even three specimens could be easily retrieved in one session. We have never experienced any complications.

*Conclusion:* The use of a grasping forceps with detachable basket tip allows the colonoscopist to retrieve the polypectomized multiple polyps in one session, and this method is safe in practice.

Endoscopy, specific: Colon, rectum  
Endoscopy, general: Instrumentation, therapy }

"Usefulness of a Specially Designed Grasping Forceps in Retrieving the Polypectomized Multiple Polyps of the Colon"

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"P P 53 1271" P 53 1271 **Management of Ileus Caused by Cancer in the Left Colon-  
Colonoscopic Retrograde Bowel Drainage (CRBD)**

\*T. Ochiai, M. Sugitani, M. Moriwaki, K. Yasuda, T. Sakakibara, H. Noguchi, T. Okada, T. Toyoda, N. Sakakibara

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The First Department of Surgery, Juntendo University School of Medicine, Tokyo, Japan Since nasal tube insertion was not so effective for the management of ileus caused by cancer in the left colon, emergency operation often has been performed for the ileus. Recently a new preoperative colonoscopic procedure was invented to avoid the emergency operation. The method is colonoscopic retrograde bowel drainage (CRBD). The following is the procedure of CRBD. After confirming the lesion with colonoscopy, the drainage (decompression) tube is inserted beyond the obstructive lesion through the guide-wire and dilator. This method was applied to 12 patients (8 male and 4 female). Average age of the patients was 64.4 (44 – 81 years old). Ten cases were successful (1 case of the descending colon cancer, 5 cases of the sigmoid colon cancer, 2 cases of the rectal cancer and 2 cases of Schnitzler metastasis). It was the 10.5 days before the surgery. In this duration, preoperative examinations and complete preparation of the colon could be performed, and operations were performed satisfactorily. The most important point of CRBD is that obstructive lesion is observed in frontal view with colonoscope. This procedure prevents some complications. CRBD can avoid the emergency operation. We concluded that CRBD should be tried first. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Colon, rectum } "Management of Ileus Caused by Cancer in the Left Colon-Colonoscopy Retrograde Bowel Drainage (CRBD)"

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## "P P 53 1272" P 53 1272 Endoscopic Laser Therapy in Rectal Diseases

\*H. Schmidt, P. Pescatore, B.C. Manegold

Department of Surgical Endoscopy, Klinikum Mannheim, Germany  
The aim of our study was to evaluate the safety and efficacy of laser therapy in rectal diseases.  
*Methods:* Retrospective review of all 181 patients (100 men, 81 women; age 73 years; 32–97) treated by Nd-YAG laser (MEDILAS 2 MBB) from 01.01.88–31.12.1995. Indications were 137 inoperable rectal cancers, 18 anastomotic strictures, 17 villous adenomas and 9 others.  
*Results:* The symptoms leading to laser therapy of rectal cancer (obstipation n = 100, bleeding n = 33, mucous discharge n = 4) were successfully relieved in 94% of cases after 4 (1–9) sessions in intervals of 2 days. Restenosis had to be treated again every 4 weeks. All anastomotic strictures were effectively dilated in intervals of 2 days after 1.4 (1–2) sessions. In 55% of cases a supplementary balloon dilation was carried out. Long-term efficacy was obtained in 17/18 patients, 1 anastomosis resection was necessary. All adenomas were completely removed in 3 (1–7) sessions in intervals of 2 days without further recurrence. Complications were: 6 bleedings, 3 perforations and 1 perianal abscess, 3 of which had to be operated upon. The procedure related mortality was 1.1%.  
*Conclusions:* Laser therapy in rectal diseases is safe and effective. In palliative management of rectal carcinomas repeated sessions in 4 weeks intervals are necessary.  
Oncology, general: Therapy  
Oncology, specific: Colon, rectum  
Endoscopy, specific: Colon, rectum } "Endoscopic Laser Therapy in Rectal Diseases"

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"P P 53 1273" P 53 1273 **Long-Term Follow-Up of Patients Treated by Laser for Rectal Villous Adenoma Staged T1N0 at Endoscopic Ultrasound (EUS)**

\*M. Angels Gines, B. Napoleon, O. Keriven-Souquet, B. Pujol, F. Descos, J.C. Souquet

Department of Digestive Diseases, Hospital E Herriot, Lyon, France A major concern in laser treatment of rectal villous adenoma is the lack of pathologic study of the whole adenoma. Invasion of the muscularis propria, or metastatic nodes can be missed with a risk of cancer recurrence. EUS, while unable to detect mucosal cancer, has been shown accurate for the detection of muscularis propria invasion (T2). Its efficacy to detect malignant nodes is unknown, as the surgical series presented only a few number of N1 patients. This retrospective study aimed to define the long-term results of laser treatment in villous adenoma either large (> 3 cm) or with severe dysplasia/carcinoma, and staged uT1N0 before treatment. *Methods:* From 1982 to 1994, of the 411 patients treated by laser for villous adenoma of the rectum, 107 had a pretherapeutic EUS (Bruel & Kjaer rigid probe, Olympus echoendoscopes). Follow-up was always superior to 12 months. 93 were staged T1N0, while 2 were T2N0 and 12 were not staged (poor cleansing, artifacts). The present series deals with the 93 T1N0 patients. *Results:* In these 93 patients, initial biopsies showed carcinoma in 13, severe dysplasia in 21, and moderate dysplasia in 59. During follow-up (mean 49.2 months), 5 patients (5.4%) presented cancer evolution. 1 patient with cancer persistence, was operated on, 4 months after the start of treatment. The tumor was pT2N0 (slight invasion of the muscularis propria). The patient was well 4 yrs later. 3 patients developed cancer during treatment at 4, 12, and 24 months respectively. One was cured by laser (more than 2 yrs follow-up thereafter), 2 were operated on and were both pT1N0. The last patient with cancer initially was considered as cured, but extraparietal recurrence (node?) occurred more than 4 yrs after the diagnosis and the patient finally died from metastasis. Noteworthy, of the 13 patients with carcinoma at initial biopsies, 11 were cured by laser, while one was operated on after 4 months for persistent cancer. The last patient had a local recurrence and died from metastasis 57 m after the diagnosis. *Conclusions:* T1N0 staging of villous adenoma at EUS gave a high percentage of cure by laser. Cancer evolution occurred usually at the wall level and was controlled by careful follow-up and surgery. Node recurrence could be discussed in only one patient, the only death from cancer. As recurrence occurred more than 4 yrs after diagnosis, long-term follow-up is necessary to ensure cure and evaluate treatments. Echoendosonography: Echoendoscopy Oncology, specific: Colon, rectum } "Long-Term Follow-Up of Patients Treated by Laser for Rectal Villous Adenoma Staged T1N0 at Endoscopic Ultrasound (EUS)"

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## "P P 53 1274" P 53 1274 Argon Plasma Coagulation (APC) after Piecemeal Polypectomy for Colorectal Adenomas

\*J. Regula, E. Wronska, M. Polkowski, J. Pachlewski, E. Butruk

Dept of Gastroenterology, Institute of Oncology, Warsaw, Poland The purpose of this study was to assess prospectively the efficacy and safety of argon plasma coagulation (APC) as a method ensuring total ablation of neoplastic tissue after piecemeal polypectomy of large sessile colorectal adenomas. Of 309 snare polypectomies in 153 patients performed between March 95' and May 96' APC was employed to treat 31 sessile adenomas in 24 patients after piecemeal polypectomy. Patients' median age was 66 years (range 42–83). Adenomas were located in the rectum (21), sigmoid colon (7) or right colon (3). Ten adenomas were 1–1.9 cm, nine were 2–2.9 cm and twelve were 3–5 cm in diameter. The protocol included histopathology, endoscopic ultrasound, abdominal ultrasound, and serum CEA to exclude carcinoma. Median interval between polypectomy and APC was 3 weeks. After polypectomy and before APC biopsies were taken from polypectomy site to check whether the visible mucosal abnormality represents true remnant adenomatous tissue. Follow-up included endoscopies with biopsies from treated area 1, 3, 6, 9 and 12 months after treatment. To achieve complete destruction of adenomas 1–9 APC sessions at 2–7 days intervals were required. Two patients were excluded from efficacy analysis because biopsies taken before APC did not show dysplasia. One patient had an invasive carcinoma diagnosed after APC was started. He was referred for surgery. Remaining 28 adenomas in 21 patients were followed-up for median time of 6 months (range 1–12 months). Only one recurrence of adenoma was detected 3 months after treatment (3.5% of treated adenomas). Six patients (25%) reported mild and transient side effects following APC: abdominal pain (5 patients), diarrhea (2 patients) and blood in stools (3 patients). Argon plasma coagulation may be used as a safe and effective supplement to polypectomy of sessile colorectal adenomas. Complete destruction of remnant adenomatous tissue may require repeat treatment sessions. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Colon, rectum Oncology, specific: Colon, rectum } " Argon Plasma Coagulation (APC) after Piecemeal Polypectomy for Colorectal Adenomas "

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## "P P 53 1275" P 53 1275 Endoscopic Mucosal Resection for Large Flat or Sessile Colorectal Neoplasia

\*C.R. Teixeira, R.J.S. Torresini, N.H.V. Coelho, C. Saul<sup>1</sup>, S. Tanaka<sup>2</sup>

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<sup>2</sup> First Dept. Internal Medicine, Hiroshima University School of Medicine, Hiroshima, Japan Endoscopic treatment of colorectal polyps is essential for the secondary prevention of colorectal carcinoma. Large sessile or flat colorectal lesions are technically difficult to be resected by the standard snare polypectomy. We assessed the safety and usefulness of endoscopic mucosal resection (EMR) for large polypoid colorectal lesions. *Methods:* From July 1994 to March 1996 we have performed 11 EMR for flat or sessile colorectal lesions measuring 2 to 4 cm in diameter (mean 2.7 cm). Seven lesions were located in the right colon and 4 at the rectum. Following the injection of saline solution into the submucosa underneath the lesion, the procedure was done in a similar mode to the standard snare polipectomy. Indigo-carmin was sprayed on all lesions to have the margins demarcated. *Results:* Six lesions measuring 2 cm were resected by single EMR, whereas piece-meal resection was applied to 5 lesions greater than 2.5 cm. Histologic examination disclosed 6 adenomas with moderate atypia, 2 with severe atypia and 3 intramucosal carcinoma. Mild bleeding occurred in one case which was controlled endoscopically. Ten lesions showed biopsy proved normal scarring at follow up colonoscopy. At 6 month follow-up one lesion showed recurrence that was endoscopically managed. *Conclusions:* Endoscopic mucosal resection proved effective and safe for the management of large flat or sessile colorectal neoplasia. Close follow-up colonoscopy is mandatory to evaluate healing. Endoscopy, specific: Colon, rectum Endoscopy, general: Instrumentation, therapy }" "Endoscopic Mucosal Resection for Large Flat or Sessile Colorectal Neoplasia"

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"P P 53 1276" P 53 1276 **Results of Endoscopic Removal of Large Sessile Colorectal Villous Tumors (LCVT): Association of Snare Resection and Laser Therapy**

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Department of Gastroenterology, Hospital Nord C.H.U. de Saint-Etienne, 42055 Saint-Etienne Cedex 2, France

*Purpose:* Endoscopic removal of LCVT is considered as difficult and hazardous. We analyzed, in this retrospective study, the results and the one-year recurrence of 80 endoscopic removals of LCVT, using a combination of snare and laser therapy.

*Methods:* The Nd:YAG laser had a maximal power output of 80 Watts. The energy used in each session varied between 700 and 2500 Joules, and was applied with pulses of 1 to 3 seconds. In most cases, it was used after snare resection, during the same session. Patients were treated every 20 days until complete eradication of the tumor.

*Results:* The mean age was 72.6 years (range 45–90 years), for the 43 men and 37 women. Only one tumor was resected for each patient. Most of the lesions were located in the rectum (66.2%). All the tumors were villous and sessile. The size was ranged from 20 to 50 mm (mean: 28.5 mm). Complete resection was obtained in 62 cases (77.5%), with a mean of 1.9 sessions. Histologic examination revealed a grade ranged between mild and severe dysplasia. An invasive carcinoma was detected in 3 patients on biopsy specimens. The treatment was well-accepted by all the patients, without major complication. Only 5 patients (6.2%) experienced moderate hemorrhage. No perforation was observed. Six patients were excluded of the study (3 invasive carcinomas and 3 failures of the treatment). Follow-up evaluation over 1 year was possible in 66 out of the 74 remaining patients (89.2%). Seven patients (11.3%) had a local recurrence. All of them revealed lower size and dysplasia, compared to the original lesion.

*Conclusion:* The combination of snare resection and laser Nd:YAG for the treatment of LCVT presents a sure efficacy with a little or none risk. It seems also well-tolerated by the patients. So this method, subject to strict endoscopic survey, could be now considered before surgery for the treatment of benign LCVT.

Oncology, specific: Colon, rectum  
Endoscopy, general: Instrumentation, therapy  
Endoscopy, specific: Colon, rectum }

"Results of Endoscopic Removal of Large Sessile Colorectal Villous Tumors (LCVT): Association of Snare Resection and Laser Therapy"

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"P P 53 1277" P 53 1277 **Endoscopic Stent Implantation for Palliation of Obstructing Rectal Cancer**

\*M. H\fcnerbein, M. Dohmoto, P.M. Schlag

Virchow Hospital, Robert-R\fcssle Hospital and Tumor Institute, Humboldt University Berlin, Germany *Purpose:* The rationale of palliative endoscopic treatment is to avoid a colostomy in patients with advanced disease and limited life expectancy. This study was conducted to evaluate the role of endoscopic stent implantation for palliation of obstructing rectal cancer. *Methods:* Overall 11 patients with non-resectable or metastatic rectal cancer were treated by stent insertion after laser recanalization or dilation. Two types of stents self expanding mesh stents (n = 6) and endocoil stents (n = 5) were used to maintain luminal patency. *Results:* Endoscopic stent implantation was successfully performed in all 11 patients. Long term luminal patency and satisfactory bowel function was achieved in 10 of 11 patients. After a median follow up of 4 months 7 of the patients have died and 4 are still alive without evidence of recurrent obstruction. Dislocation of the endoprosthesis occurred in 1 patient. There was no evidence of treatment failure in 5 patients who received endocoil stents. None of the patients experienced serious complications related to the endoscopic procedure. *Conclusion:* Endoscopic stent implantation seems to be a safe and efficient palliative approach to selected patients with obstructing rectal cancer. Currently self expanding coil stents are superior to other devices because of lower risk of dislocation and tumor ingrowth. Oncology, specific: Colon, rectum Oncology, general: Therapy Endoscopy, specific: Colon, rectum } "Endoscopic Stent Implantation for Palliation of Obstructing Rectal Cancer"

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"P P 53 1278" P 53 1278 **Clinicopathological Study on Endoscopic Mucosal Resection of Superficial Early Colon Cancer** M. Hayakawa

Dept. of Gastroenterology, Meitetsu Hospital, Nagoya, Japan Over the last 4 years, total colonoscopy was performed in 4,898 patients and 435 colon cancers were detected. Among them 154 were found to be superficial early cancers. In the study with dissecting microscopy, early cancer showed irregular small-sized pit structure more often and disappearance of the pit structure was considered to be the feature of submucosal invasion. On histological examination, all mucosal cancer lesions were demonstrated to be well-differentiated adenocarcinoma. Interestingly, the bill like irregular glandular structure was found the mucosal cancer lesions, which correspond to the irregular small-sized pit structure observed in the dissecting microscopy. We studied the expression of p53 protein immunohistochemically in formal in-fixed paraffin-embedded resected specimens of 20 adenomas, 10 mucosal cancers and 10 submucosal cancers with a monoclonal antibody specific for the p53 protein. P53 protein expression localized in the nuclei was found in 16% of adenomas, 66% of mucosal cancers and 97% of submucosal cancers. When analyzed by plotting p53-positive point on the mucosal structure in the dissecting microscopy, p53 protein expression corresponded with the irregular small-sized pit structure and histologically proven bill like irregular glandular structure. The bill like irregular glandular structure can be regarded to be a characteristic feature of the superficial colon cancer. Oncology, general: Therapy Oncology, specific: Colon, rectum Endoscopy, specific: Colon, rectum } "Clinicopathological Study on Endoscopic Mucosal Resection of Superficial Early Colon Cancer"

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"P P 54 1290" P 54 1290 **Colonoscopic Follow-Up after Surgery for Colorectal Carcinoma R. Silva,**

\*H. Lombaviana, A. Correia, L. Dias, R. Lombaviana

Department of Gastroenterology, Oncology Portuguese Institute, Oporto, Portugal *Objective:* To determine postoperative endoluminal recurrence and metachronous carcinoma incidence and assess the role of colonoscopy in the follow-up of colorectal carcinoma. *Patients and Methods:* 317 patients (161 men and 156 women) submitted to a total of 779 post-surgical colonoscopies in our department during a period of 21 years (1975–95) were retrospectively studied. Mean age at surgery was 61 years. During a 5 years clinical follow-up, from the 317 patients, 114 were examined once, 85 twice, 58 three times and 60 had four or more colonoscopies. *Results:* Neoplastic lesions were found in 121 patients (38%). We observed 20 cases of anastomotic recurrence in 19 patients (6%) 15 – 8 months after surgery for rectal (13), sigmoid (6) and transverse (1) carcinoma. One synchronous carcinoma not detected pre-operatively was diagnosed in a patient. Eight patients (3%) developed a total of 9 metachronous carcinoma 95 – 63 months after the index tumour. Half of the patients with recurrence or metachronous carcinoma were asymptomatic and no increase of CEA had been detected. Seven of the 9 metachronous carcinoma were stage I or II (TNM). Those who developed metachronous carcinoma were in, average, 8 years younger. Adenomas with high grade dysplasia were detected in 13 patients (4%). *Conclusions:* Colonoscopic follow-up after resection for colorectal carcinoma gave a high yield of asymptomatic and initial stage neoplastic lesions and may be particularly useful in younger patients who have a higher risk of developing metachronous carcinoma. Oncology, specific: Colon, rectum Endoscopy, specific: Colon, rectum }"  
"Colonoscopic Follow-Up after Surgery for Colorectal Carcinoma"

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## "P P 55 1305" P 55 1305A Prospective Study of the Prognostic Value of Type IV Collagenase Activity in Colorectal Cancer Tissue

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The barrier for an invading epithelial tumor is the basement membrane, consisting of laminin and type IV collagen. The type IV collagenase (IV ase), which is a specific enzyme capable of degrading type IV collagen, has been demonstrated to play an important role in penetration through the basement membrane in the process of tumor invasion and metastasis. The purpose of this prospective study was to evaluate the prognostic value of the IV ase activity in colorectal cancer tissue in 31 colorectal cancer patients on disease-free and overall survival. The clinicopathologic factors studied for prognostic value were age, tumor location, tumor differentiation, preoperative serum levels of carcinoembryonic antigen, Dukes' stage, and IV ase activity in colorectal cancer tissue. Tissue IV ase activity was measured using purified radiolabeled [<sup>3</sup>H] human type IV collagen. IV ase activities in colorectal cancer tissue were significantly higher in the group of patients with recurrences than in the group without recurrences ( $P = 0.019$ ). Patients with high IV ase activity in colorectal cancer tissue had a significantly shorter disease-free survival ( $P = 0.0016$ ) and overall survival ( $P = 0.022$ ) time than those with low IV ase activity. Univariate and multivariate analyses showed that significant prognostic factors for disease-free survival were Dukes' stage ( $P = 0.029$ ,  $P = 0.046$ , respectively) and IV ase activity status ( $P = 0.0016$ ,  $P = 0.0026$ , respectively). With respect to overall survival, only IV ase activity status provided significant predictive value in multivariate analysis ( $P = 0.041$ ). This prospective study suggests that IV ase activity could be a valuable prognostic indicator in colorectal cancer patients.

Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum }

"A Prospective Study of the Prognostic Value of Type IV Collagenase Activity in Colorectal Cancer Tissue"

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"P P 58 1396" P 58 1396 **Non-Ulcer Dyspepsia in Children — Parallels of Endoscopy, Ultrasonography and Histology** A.A. Chernova, A.V. Kruglov,

\*P.L. Shcherbakov, V.V. Gangan, M.A. Kvirkvelia, G.D. Prokofiev

Russian State Medical University, Izmailovsky Children Hospital, Moscow, Russia *Aim:* ultrasonic diagnostics of gastritis in non-ulcer dyspepsia (NUD) in children. *Methods:* 38 children (mean age 11.7 years, range: 7–15 years) underwent by endoscopy with urease test and histological examination, and abdominal stomach ultrasonography. *Results:* on endoscopy 16 children showed normal gastric and duodenal mucosa (group 1), 22 – gastritis/gastroduodenitis (group 2). The results of the study were summarized as follows: Ultrasonic Urease biopsy Histologically Histologically stomach picture rest+ H. Pylori+ gastritis Group 1 Normal 5 0 0 0 Almost normal\* 5 0 1 3 (including 1 H. pylori+) Gastritis\*\* 6 2 4 6 Group 2 Normal 0 Almost 1 1 1 1 Normal\* Gastritis\*\* 21 14 19 21 \*volume of liquid on an empty stomach (VLES) > 30 ml, \*\*VLES > 30 ml, thickening and unclear layers of gastric wall, uneven intrinsic contour of gastric mucosa. Gastritis undetectable by endoscopy can be found by the stomach ultrasonography. *Conclusions.* Stomach ultrasonography can be used as an initial diagnostics of gastritis in NUD children: 1. If one determines or suspects gastritis by sonography, further specification by endoscopy with histological & H. pylori examination must be performed, 2. If normal ultrasonic picture is seen, the endoscopy is not needed. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Endoscopy, general: Endoscopy: children Radiology and ultrasound: Diagnosis } "Non-Ulcer Dyspepsia in Children / Parallels of Endoscopy, Ultrasonography and Histology"

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## "P P 58 1403" P 58 1403 Digital Image Processing Does Not Identifies Intestinal Metaplasia in Gastric Mucosa

\*L. Sosa Valencia, B. Beker, M. Guelrud

G.I. Unit, Hospital General del Oeste, Los Magallanes, Caracas, Venezuela Endoscopic images offer an additional domain (color) for tissue characterization. Because intestinal metaplasia (IM) is associated with gastric cancer, noninvasive markers of chronic atrophic gastritis have been suggested. IM is defined histologically but has some difficult endoscopic identification features that has led the examiner to used methylene blue staining in other to obtain guided biopsies. *Aim of the study:* we sought to determine if digital image analysis of endoscopic images allowed accurate identification of gastric (antral) IM. *Patients (pts) and methods:* Digital red, green, and blue signals were obtained directly from the processor of an electronic endoscope (Olympus, video gastroscope EVIS 100) using a 24 bit color frame grabber (Raster Ops Corporation, USA) and stored. Images were obtained from areas of gastric antral pre piloric mucosa with and without IM confirmed by histological samples taken at the same time and from the same area where the images were taken. The areas of interest were marked on the digital images by one of us (MG or BB) and analized separately by a doctor with computer skills (LS) who was unaware of the endoscopic appearance of the gastritis or the significance of the marked areas. Color analysis was performed using a color analysis program (Adobe Photoshop). This program measures intensity of red, green, and blue on a gray scale basis from 0–256. Thirty nine volunteer patients with gastritis were evaluated according to the Sydney modified 1991 classification, 9 patients had IM and 30 patients had gastritis without IM. One measurement was taken from the area of abnormal tissue. Results are mean – standard deviation and differences were determined non parametrically (Wilcoxon test). *Results:* Age ranged from 28–72 years. In patients with IM, color values were red = 207 – 30, green = 119 – 21, blue = 93 – 17 and gray = 142 – 22. In patients without IM, color values were red = 205 + { - } 29, green = 118 – 18, blue = 91 – 15 and gray = 141 – 20. There was no identifiable difference between antral gastritis images with or without IM ( $p > 0.05$ ). *Conclusions.* Image processing can not identify intestinal metaplasia in abnormal gastric mucosa. Color information does not provides information for diagnosis of gastric IM. Color reproductivity of endoscopic images should be reached before further evaluation. **Key words:** intestinal metaplasia, digital images, color Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Digital Image Processing Does Not Identifies Intestinal Metaplasia in Gastric Mucosa"

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## "P P 59 1409" P 59 1409 **Massive Arterial Bleeding of the Gastroduodenum and Two-Stage Sclerotherapy-Our Experience**

\*V. Vasilevski, M. Krstevski, R. Coleski, P. Mishevskaja, J. Mishevski, D. Trajanovski, V. Calovska

Clinic of Gastroenterology, Medical Faculty-Skopje, Republic of Macedonia

In this paper our results of the two-stage sclerotherapy in the treatment of the massive arterial bleeding are presented. In 543 patients, urgently performed endoscopy revealed massive arterial bleeding from the gastroduodenum, but in 32 (5.9%) the source of bleeding was not detectable because of the large quantity of blood in the stomach. Out of 511 detected bleeding lesions, 447 (87.5%) were gastroduodenal ulcers, 31 (6.0%) were Dieulafoye lesions and 33 (6.5%) Mallory-Weiss lesions. According to the classification of Forrest, 327 (64%) were Ia, 184 (36%) Forrest II. Mean age of the patients was 56.5 years. Two-stage sclerotherapy with Adrenaline and 1% Polydocanol was performed in all cases. Initial hemostasis was achieved in 472 (92.3%) of the patients, and of the remaining 39 (7.7%), in 11 hemostasis was achieved with medical therapy, while 28 are urgently operated, of whom 8 (28.5%) died because of postoperative complications or cardiac failure. During the same hospitalization re-bleeding appeared in 26 (5.5%) of primarily effectively sclerotherapy treated patients, so definitive healing was achieved in 446 (94.5%) of the patients treated with sclerotherapy. Out of the 26 rebled patients, 6 died because of hemorrhagic shock, and in five patients hemostasis was achieved with medical therapy. The remaining 15 patients had to be urgently operated, with positive outcome in nine patients. The mortality rate was 60% (surgical complications or cardiopulmonary failure). The rebled patients had lethality of 46%. Direct complications of the sclerotherapy occurred in two patients (duodenal wall necrosis), both in the rebleeding group, with a fatal outcome after the operation. The obtained results showed that in the hands of the experienced endoscopist sclerotherapy is safe and powerful method to control bleeding, and our results are in accordance with those reported in the literature. Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum }

"Massive Arterial Bleeding of the Gastroduodenum and Two-Stage Sclerotherapy-Our Experience"

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"P P 59 1413" P 59 1413 **Fibrin Sealing — New Method and Concept for Treatment of the Bleeding Peptic Ulcer** Olaf Friedrichs

Duisburg Institute of Endoscopy Duisburg, Germany The technique of fibrin gluing is a standard haemostatic procedure which uses a two-component adhesive consisting of fibrinogen and thrombin, which when mixed in the tissue, form a fibrin clot via the third phase of the blood coagulation cascade, thereby inducing the mechanisms of wound repair. In a new endoscopic procedure, the components are simultaneously injected into the tissue beneath the bleeding lesion close to the vessel. There they form a mechanically resilient and stable fibrin clot which is firmly anchored into the tissue. This "bioidentical" type of procedure can be safely repeated, in contrast to all other thermal and injection methods, thus allowing multiple injections to achieve increased stability and better control. Supported by a scheme of close follow-up endoscopies permitting any number of subsequent therapeutic and prophylactic injections to be given for persistent bleeding stigmata, the new treatment method proves to be not only suitable for initial haemostasis and preventing rebleeding, but — for the first time — enables the limited time interval after initial haemostasis to be used for genuine prophylactic therapy, called "early elective endoscopic therapy". We perform the first reendoscopy after 3 to 6 hours after initial haemostasis. Outstanding results can be achieved using this concept. We report about a series of 375 patients cared for as outpatients or day patients, at least (30 patients) with a definite reduction of hospital stay. Thus a clear clinical advantage for the patient could be achieved, in addition with a cost-to-benefit advantage. Using this technique, individual prediction of the outcome seems to be possible. Our results are favourable as compared with a recently published multicentre trial. At the present time this mild form of tissue-compatible therapy offers the only genuine prophylactic therapy. Endoscopy, general: Instrumentation, therapy Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Fibrin Sealing / New Method and Concept for Treatment of the Bleeding Peptic Ulcer"

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## "P P 59 1415" P 59 1415 Six Month Audit of a Management Protocol for Upper GI Haemorrhage

\*S.M. Everett, D.M. Chalmers, A.T.R. Axon

Centre for Digestive Diseases, The General Infirmary, Leeds, UK *Purpose:* In April 1995, a protocol for the management of upper GI haemorrhage was introduced at Leeds General Infirmary. All patients are categorised according to risk status, into shocked (pulse > 100 bpm or systolic bp < 100 mmHg), high risk (age > 60, Hb < 10 g/dl or coexistent cardiovascular disease), or low risk (all others). Depending on risk status, patients are admitted to either a surgical, specialised GI, or general medical ward, with early endoscopy and intensive monitoring. More conservative management is used in low risk cases. This audit was undertaken to monitor the success of the protocol. *Methods:* Details of all upper GI bleeds (including those occurring in in-patients) for the 6 months between April and September 1995 were collected prospectively from casualty records, endoscopy records and discharge diagnostic coding. Notes were reviewed retrospectively, and a standardised proforma completed. *Results:* 89.5% of all case records requested were reviewed. From these there were 256 cases of upper GI haemorrhage. Mean age was 59.0 years, with 19.5% of cases over 80 years. Endoscopy was performed in 81.6% of cases, 85.2% of which was within 24 hours of the bleed. Total rebleed rate was 5.9%, operative rate was 2.4%, and mortality rate was 10.5% (3.4% for new patients; 40.0% for existing inpatients). Results according to risk are tabulated below:

	Number	(%)	Rebleed rate (%)	Operative rate (%)	Mortality rate (%)
Low risk	31.2	0	0	0	0
High risk	45.8	6.1	0	13.8	Shocked
Shocked	22.9	13.8	8.9	15.5	

*Conclusions:* Favourable results in the management of upper GI haemorrhage can be achieved by intensifying management according to risk status, without the use of a specialised bleeding unit. Patients with low risk status can safely be managed in a more conservative fashion. Endoscopy, general: GI bleeding Clinical practice: Management strategy } "Six Month Audit of a Management Protocol for Upper GI Haemorrhage"

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## "P P 59 1420" P 59 1420 Endoscopic Hemostasis for GI Bleeding

\*K. Handa, H. Takahashi, K. Kirihara, R. Fujita

Department of Gastroenterology, Fujigaoka Hospital, Showa University Yokohama, Japan

The significance of emergency endoscopy and subsequent endoscopic hemostatic procedures at the onset of upper gastrointestinal hemorrhage is virtually established. The hemostatic effects of hemoclipping, the pure ethanol local injection method and the heater probe method on hemorrhagic gastric and duodenal ulcers associated with exposed blood vessels, were compared. The locations of the exposed blood vessels, as well as characteristics and severity of the hemorrhage were discussed. The hemoclipping method was used in 125 patients, the pure ethanol local injection in 52 patients, and the heater probe method in 63 patients. The hemoclipping and pure ethanol local injection method were effective in all the patients with exposed blood vessels around the margin of the ulcers. The efficacy rate was 95%, 100% and 100%, respectively, when exposed blood vessels at the base of the ulcer. The efficacy rate was 96%, 93% and 92% for the three hemostatic methods, respectively, when oozing hemorrhagic lesions was present. The three methods had an efficacy rate in spurting hemorrhagic lesions was 92%, 83% and 88% for the three methods, respectively. The hemoclipping and pure ethanol local injection were effective in 100% of slight and moderate hemorrhagic cases, while the heater probe method was effective in only 95% of moderate cases. The efficacy rate was 85%, 85% and 83% respectively, for severe cases. Overall, the efficacy rate was 88% for the hemoclipping method, 85% for the pure ethanol local injection and 83% for the heater probe method, and there was no significant difference between the three methods with regard of the overall efficacy rate. Rebleeding occurred in 23 of 240 cases of gastric ulcers (9.6%). The presence of exposed blood vessels at the base of the ulcer, spurting and oozing bleeding and severe hemorrhage were thought to be the most important risk factor for rebleeding.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic

Endoscopy, general: GI bleeding

Endoscopy, specific: Stomach, duodenum }

"Endoscopic Hemostasis for GI Bleeding"

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"P P 59 1421" P 59 1421 **Endoscopic Therapy for Bleeding Vascular Lesions of the Stomach and Duodenum**

\*K. Kirihara, H. Takahashi, K. Handa, R. Fujita

Department of Gastroenterology, Fujigaoka Hospital, Showa University Yokohama, Japan *Objective of the study:* To assess the effectiveness of endoscopic therapy in the management of bleeding vascular lesions of the stomach and duodenum. *Material and methods:* Our study consists of 39 patients, diagnosed as having gastric or duodenal bleeding from Dieulafoy ulcer (DU) (28 cases) or angiodysplasia (11 cases), treated at Fujigaoka Hosp. from May 1985 to December 1995. The patients were treated with either heater probe unit (HPU), ethanol injection (EI) or hemoclip, alone or in a combination of these methods if hemostasis was not achieved after using only one methods. Therapy was considered successful when hemostasis was maintained 48 hours after completion of the procedure. *Results:* In the case of Dieulafoy ulcer, hemoclip was used in 21 patients, EI in 1, HPU in 4, hemoclip plus EI in 1, and EI plus HPU in 1. Among those with angiodysplasia, hemoclip was used in 8 patients, HPU in 2 and hemoclip plus HPU in 1. Success was achieved in 38 patients (97%), and only one (3%), bleeding from DU, underwent surgery due to persistent bleeding. *Discussion:* DU and angiodysplasia are infrequent lesions in the stomach and duodenum, but they can cause severe bleeding which is difficult to manage medically, and many of these patients must finally be operated on. The effectiveness of endoscopic therapy, especially that of hemoclip, has not been fully established, but our results indicate that hemostasis can be achieved in most cases. *Conclusion:* We believe that therapeutic endoscopic methods (especially hemoclip) are highly effective in the management of bleeding from DU and angiodysplasia. Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Endoscopic Therapy for Bleeding Vascular Lesions of the Stomach and Duodenum"

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"P P 59 1422" P 59 1422 **Elastic Band Ligation for Gastric Angiodysplasias** V. Delis, V. Balatsos, V. Vamvakousis, A. Germenopoulos, N. Skandalis

Gastroenterology Department, District General Hospital of Athens G. "Gennimatas". Athens, Greece Elastic band ligation (E.B.L.) has become the treatment of choice for bleeding esophageal varices and is an alternative treatment for other U.G.I. lesions. Our experience concerning the treatment of gastric angiodysplasias with band ligation, is reported in this study. Nine patients, 5 men and 4 women, age 58–82 years, with a history of single or recurrent U.G.I. bleeding and gastric angiodysplasia being the only U.G.I. endoscopic finding, were included in the study. Four patients had single and five multiple (2–7) lesions, diameter up to 15 mm, located in the gastric antrum and/or body. In two patients a multiple shot band ligator (Speed-band, Microvasive) was used and in seven a single shot band ligator (Bard). Endoscopy was repeated in two, four and fifteen days. All patients were given omeprazole 20 mg b.d. for two weeks. All the elastic bands were properly positioned and dropped after 2–4 days. All the remained ulcers were healed in two weeks. There was not any complication and in a mean follow up of 6 months no patients experienced any recurrent bleeding. It is concluded then elastic band ligation is a simple, effective and safe treatment of symptomatic gastric angiodysplasias, sized less than 15 mm and should be considered as an alternative treatment for these lesions. Endoscopy, specific: Stomach, duodenum Clinical practice: Management strategy } "Elastic Band Ligation for Gastric Angiodysplasias"

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"P P 59 1424" P 59 1424 **NSAIDS Lesions and Non-Variceal Bleeding from Stomach and Duodenum: Endoscopic Findings in 1997 Patients Upper GI Bleeding**

\*N. Popovic, M. Bulajic, M. Glisic, P. Popovic, T. Milosavljevic, M. Ugljesic, R. Krstic, D. Popovic, P. Dugalic, D. Tomic, S. \d0Ouranovic, K. Todorovic, O. Matejic

Clinic for Gastroenterology and Hepatology, Clinical Center, Belgrade, Yugoslavia From Jan. 94 to Dec. 95, we analyzed 1997 patients (pts) – 1195 males (m) and 802 females (f) with upper GI bleeding. We studied the features and frequency of the mucosal changes in the pts with gastric and duodenal bleeding, divided into 2 groups: group I, with a history of NSAIDs intake, and group II, without contact with NSAIDs. All the pts underwent urgent endoscopy within 1–6 h. Pts with gastrectomy, liver cirrhosis, renal failure, gastric cancer or hematological diseases were excluded from the study. Group I presented, besides gastric and duodenal ulcers, multiple erosions of various forms, serpiginous and ulcer-like. EIH (epineph. + polydocanol, or 98% aethanol) was carried out in 239 pts (11.96%) suffering active bleeding from gastric ulcer and duodenal ulcer, of which 129 (12.42%) belonged to group I, and 110 (11.47%) belonged to group II. Group I (pts with Group II (pts with bleeding from melena/hematem., NSAIDs gastroduodenum, without 24–72 h. prior to bleeding) NSAIDs) Age 57.5 (17–91) 55.9 (20–89) Male Female Total Male Female Total Gastric ulcer 101 73 174 (16.76%) 98 60 158 (16.47%) Pyloric ulcer 42 23 65 (6.25%) 17 9 26 (2.71%) Duoden. ulcer 268 108 375 (36.13%) 270 138 408 (42.55%) Erosive gastritis 122 118 240 (23.12%) 94 89 183 (19.08%) Erosive duodenit. 93 90 183 (17.63%) 90 94 184 (19.18%) Total 626 412 1038 569 390 959 *Conclusion:* Regarding the results of this study 51.97% pts had NSAIDs intake 1–3 days prior to bleeding. In group I (with NSAIDs) there was a higher incidence of pyloric ulcer, gastric erosions of various forms were frequent in males and in females, and there was a high percentage of actively bleeding ulcers requiring endoscopic treatment. In group II (without NSAIDs) duodenal ulcer and erosive duodenitis were more frequent, while gastric ulcer was equivalently frequent in both groups. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "NSAIDS Lesions and Non-Variceal Bleeding from Stomach and Duodenum: Endoscopic Findings in 1997 Patients Upper GI Bleeding"

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"P P 59 1425" P 59 1425 **Ambulant Endoscopic Management of Forrest Ia or Ib Bleeding Duodenal Ulcers in Young Compliant Patients is Cost Effective and Safe**

\*P. Janetschek<sup>1</sup>, U. Bockmann<sup>1</sup>, B. Kaduk<sup>2</sup>

<sup>1</sup> Tagesklinik Muenchen-Nord, Bereich Gastroenterologie, Frauenlobstr., Muenchen, Germany

<sup>2</sup> Tagesklinik Muenchen, Institut fuer Pathologie, Frauenlobstr., Muenchen, Germany *Purpose:* Management of upper gastrointestinal bleeding is generally performed in-patient. Thus costs are high, unemployment is long. Therefore we checked safety, efficacy and cost effectiveness of ambulant endoscopic hemostasis and ambulant management of upper gastrointestinal bleeding. *Methods:* To avoid a hospitalisation and to reduce the overall costs for the management of upper gastrointestinal bleeding, we performed ambulant endoscopic hemostasis in 12 young healthy compliant patients with a partner at home with Forrest Ia or Ib bleeding duodenal ulcers. In order to lower the frequency of re-bleeding we used a combination of two different hemostatic therapy strategies (application of fibrin tissue sealant and/or hemostatic clipping of vessel and/or injection therapy with 1:10.000 epinephrine in water). The efficacy of hemostasis was controlled endoscopically all 12 hours for two days. For another two days controls were done daily; at this period patients were allowed to work again. *Results:* After ambulant endoscopy management of Forrest Ia or Ib duodenal ulcer bleeding under strict control neither re-bleeding has occurred, nor other complications related to the use of the medication have developed. *Conclusion:* We conclude that ambulant management of acute upper gastrointestinal bleeding in compliant young patients under strict control and by use of adapted hemostatic therapy strategy is cost effective, safe and prevents long unemployment. Endoscopy, general: GI bleeding } "Ambulant Endoscopic Management of Forrest Ia or Ib Bleeding Duodenal Ulcers in Young Compliant Patients is Cost Effective and Safe"

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"P P 59 1426" P 59 1426 **The Effect of Endoscopic Injection Therapy on the Clinical Outcome of Patients with Peptic Ulcer Bleeding. An Analysis of 1935 Cases**  
**K. Thomopoulos,**

\*V. Nikolopoulou, K. Mimidis, V. Margaritis, E. Katsakoulis, C. Vagianos

Department of Internal Medicine, Division of Gastroenterology and Department of Surgery, University Hospital, Patras, Greece

Acute bleeding is a life threatening complication of peptic ulcer disease. In recent years endoscopic hemostasis is used as the treatment of choice for these patients. In this study we have examined the effect of endoscopic injection therapy in the clinical outcome of patients with benign peptic ulcer bleeding.

*Patients-Methods:* In this study 1203 patients admitted with peptic ulcer bleeding over a 5-year period before endoscopic therapy and 732 patients admitted with peptic ulcer bleeding after introduction of endoscopic therapy in our department were assessed. Endoscopic treatment was performed in all patients with active bleeding or non bleeding visible vessel (NBVV) during emergency endoscopy with injection of adrenaline 1:10,000 in 0.9% saline (A/S).

*Results:* The introduction of injection therapy was associated with a reduction in transfusion needs, hospitalisation days, surgical interventions (from 15.7% to 9.4%) and mortality (from 4.5% to 2.2%) ( $p < 0.05$ ). Emergency surgical hemostasis and mortality were reduced in patients with active bleeding or NBVV while in the other patients remained unchanged. Patients with gastric ulcer had a more pronounced reduction concerning emergency surgical hemostasis (from 23.2% to 9%) and mortality (from 8.1% to 2.8%) ( $p < 0.05$ ) than patients with duodenal ulcer. There were no deaths or procedure-related complications.

*Conclusion:* These results suggest that endoscopic injection therapy with A/S is a simple, low cost and safe method which improves the clinical outcome and reduces mortality in patients with peptic ulcer bleeding.

Endoscopy, general: GI bleeding } "The Effect of Endoscopic Injection Therapy on the Clinical Outcome of Patients with Peptic Ulcer Bleeding. An Analysis of 1935 Cases"

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"P P 59 1427" P 59 1427 **Endoscopic Injection Hemostasis in the Treatment of Bleeding Upper GI Ulcers** E. Zdanytė, N.E. Samalavicius, G. Radžiūnas, A. Buinevičiūtė, J. Stanaitis

"Red Cross" Hospital of Vilnius University, Vilnius, Lithuania The purpose of our study was to evaluate the efficacy of endoscopic injection hemostasis (EIH) in the treatment of bleeding upper GI ulcers. Retrospective analysis of 50 patients who underwent EIH because of bleeding upper GI ulcer during 2 years period from January 1994 to December 1995 was performed. There were 35 males and 15 females, with a mean age of 55.82 years. Data collected included known risk factors, endoscopic findings and management, details of surgery, diagnosis, complications, and mortality. There were 40 (80%) peptic ulcers, 9 (18%) stress-induced and 1 (2%) drug-induced ulcer. The bleeding site was duodenal ulcer in 19 (38%), gastric ulcer in 30 (60%), esophageal ulcer in 1 (2%) cases. Bleeding lesions were graded according to the Forrest classification: arterial bleeding FIa – 4 (8%), oozing FIIf – 25 (50%), clot lying on ulcer base, nonbleeding visible vessel (NBVV) FII – 21 (42%). Techniques included: epinephrine injections around the lesion (0.5–1 mL per injection, up to 20 mL, 1:10,000, N = 15), ethanol injections around NBVV (0.3–0.5 mL per injection, up to 2.5 mL, 80% v/v, N = 15) and combination of them (N = 20). Hemostasis was achieved in all cases. The rebleeding rate 8% (4 cases). No major complication was observed. 9 (18%) patients underwent emergency surgery. There were 7 (14%) deaths exclusively because of severe comorbidity. *Conclusion:* epinephrine and/or ethanol injection is an effective, simple, and economical method of endoscopic hemostasis for bleeding upper GI ulcers. Endoscopy, general: GI bleeding Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Stomach, duodenum } "Endoscopic Injection Hemostasis in the Treatment of Bleeding Upper GI Ulcers"

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"P P 59 1428" P 59 1428 **Occult Recurrent Bleeding from Peptic Gastro-Duodenal Ulcers: The Importance of Active Dynamic Endoscopy (ADE)**

\*E.D. Fedorov, V.I. Sidorenko, T.M. Suchinina

Department of Abdominal Surgery, Gastroenterology & Digestive Endoscopy; Russia State Medical University, Moscow, Russia

The purpose of the study: is to reveal the role of AD ("second-look") endoscopy in making out early diagnosis and the prevention of rebleeding from peptic gastro-duodenal ulcers. Patients (pts.) (n = 40; m-33, f-7; mean age 45.6 + 3.4 yrs.; range 18–60 yrs.) with bleeding peptic ulcers (BPU) (gastric-12, duodenal-28) (Forrest 1a-8; Forrest 2a & 2b – 32) and high rebleeding risk, — according to clinical, endoscopic criteria and the results of computer-aided prediction — were included in a prospective controlled trial. They were randomized in 2 treatment groups: MH. Monopolar hydroelectro-coagulation (n = 20); AE. Absolute ethanol + 25% ethanol-novocain solution (n = 20). Both groups were clinically and endoscopically comparable and treated with anti-secretory drugs in high dose. Initial hemostasis was successful in both groups. ADE was carried out daily till the change of high prognostic index of rebleeding risk. In case of emergence of "new" vessels in the ulcer crater we performed additional hemostatic manipulations. Rebleeding occurred from 16 hours to 4 days in 10 (25%) pts.: MH-6 (30%) pts.; AE-4 (20%) pts. It did not show any clinical signs of bleeding (occult rebleeding) and was diagnosed only during ADE in 7 out of 10 pts. Nine pts. underwent emergency surgery, according to tactical approaches of our clinic and the conditions of randomized trial. In one case the bleeding was arrested endoscopically. No significant complications and mortality were reported. The analysis of the rebleeding causes revealed the statistically proved appropriateness between the expansion of an ulcer defect, the emergence of new vessels in the ulcer floor and following rebleeding. Thus the ADE is an important method of timely diagnostics of occult rebleeding and prophylactics of massive recurrent hemorrhage. For high risk patients who are thought unable to survive laparotomy, endoscopic treatment, including ADE is a preferable way to make out an early diagnosis and to attain definitive control of rebleeding.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic

Endoscopy, general: GI bleeding

Endoscopy, specific: Stomach, duodenum }

"Occult Recurrent Bleeding from Peptic Gastro-Duodenal Ulcers: The Importance of Active Dynamic Endoscopy (ADE)"

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## "P P 59 1429" P 59 1429 Endoscopic Hemostasis for GI Bleeding

\*K. Handa, H. Takahashi, K. Kirihara, R. Fujita

Department of Gastroenterology, Fujigaoka Hospital, Showa University Yokohama, Japan

The significance of emergency endoscopy and subsequent endoscopic hemostatic procedures at the onset of upper gastrointestinal hemorrhage is virtually established. The hemostatic effects of hemoclipping, the pure ethanol local injection method and the heater probe method on hemorrhagic gastric and duodenal ulcers associated with exposed blood vessels, were compared. The locations of the exposed blood vessels, as well as characteristics and severity of the hemorrhage were discussed. The hemoclipping method was used in 125 patients, the pure ethanol local injection in 52 patients, and the heater probe method in 63 patients. The hemoclipping and pure ethanol local injection method were effective in all the patients with exposed blood vessels around the margin of the ulcers. The efficacy rate was 95%, 100% and 100%, respectively, when exposed blood vessels at the base of the ulcer. The efficacy rate was 96%, 93% and 92% for the three hemostatic methods, respectively, when oozing hemorrhagic lesions was present. The three methods had an efficacy rate in spurting hemorrhagic lesions was 92%, 83% and 88% for the three methods, respectively. The hemoclipping and pure ethanol local injection were effective in 100% of slight and moderate hemorrhagic cases, while the heater probe method was effective in only 95% of moderate cases. The efficacy rate was 85%, 85% and 83% respectively, for severe cases. Overall, the efficacy rate was 88% for the hemoclipping method, 85% for the pure ethanol local injection and 83% for the heater probe method, and there was no significant difference between the three methods with regard of the overall efficacy rate. Rebleeding occurred in 23 of 240 cases of gastric ulcers (9.6%). The presence of exposed blood vessels at the base of the ulcer, spurting and oozing bleeding and severe hemorrhage were thought to be the most important risk factor for rebleeding. } "Endoscopic Hemostasis for GI Bleeding"

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"P P 59 1430" P 59 1430 **Endoscopic Therapy for Bleeding Vascular Lesions of the Stomach and Duodenum**

\*K. Kirihara, H. Takahashi, K. Handa, R. Fujita

Department of Gastroenterology, Fujigaoka Hospital, Showa University, Yokohama, Japan

*Objective of the study:* To assess the effectiveness of endoscopic therapy in the management of bleeding vascular lesions of the stomach and duodenum. *Material and methods:* Our study consists of 39 patients, diagnosed as having gastric or duodenal bleeding from Dieulafoy ulcer (DU) (28 cases) or angiodysplasia (11 cases), treated at Fujigaoka Hosp. from May 1985 to December 1995. The patients were treated with either heater probe unit (HPU), ethanol injection (EI) or hemoclip, alone or in a combination of these methods if hemostasis was not achieved after using only one methods. Therapy was considered successful when hemostasis was maintained 48 hours after completion of the procedure. *Results:* In the case of Dieulafoy ulcer, hemoclip was used in 21 patients, EI in 1, HPU in 4, hemoclip plus EI in 1, and EI plus HPU in 1. Among those with angiodysplasia, hemoclip was used in 8 patients, HPU in 2 and hemoclip plus HPU in 1. Success was achieved in 38 patients (97%), and only one (3%), bleeding from DU, underwent surgery due to persistent bleeding. *Discussion:* DU and angiodysplasia are infrequent lesions in the stomach and duodenum, but they can cause severe bleeding which is difficult to manage medically, and many of these patients must finally be operated on. The effectiveness of endoscopic therapy, especially that of hemoclip, has not been fully established, but our results indicate that hemostasis can be achieved in most cases. *Conclusion:* We believe that therapeutic endoscopic methods (especially hemoclip) are highly effective in the management of bleeding from DU and angiodysplasia. } "Endoscopic Therapy for Bleeding Vascular Lesions of the Stomach and Duodenum"

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"P P 59 1431" P 59 1431 **Endoscopic Band Ligation for Hemostasis of Non-Variceal Upper Gastrointestinal Bleeding**

\*S. Matsui, R. Inoue, K. Takahei, K. Araragi, N. Hirota, M. Sakamoto, M. Kinoshita, N. Aoki

Second Department of Internal Medicine, Kinki University School of Medicine, Osakasayama, Osaka, Japan Endoscopic band ligation (EBL) originally developed by Stiegmann has recently been performed in Japan as an effective treatment of bleeding esophageal varices. *Purpose:* This study was performed to evaluate the hemostasis effect of EBL in non-variceal upper gastrointestinal bleeding. *Patients:* Ten patients (5 males, 5 females) aged from 21 to 66 years were studied between September 1994 and April 1996. Underlying diseases consisted of 4 Dieulafoy's ulcers (Diu), 4 Mallory-Weiss syndromes (MWS), 1 gastric ulcer (GU) and 1 gastric angiodysplasia (GA). All patients showed active bleeding such as spurting and oozing on emergency endoscopy. *Methods:* At emergency endoscopy routinely employing the over tube for the EBL treatment, we determined the location of bleeding and applied there an O-ring of the EBL device for hemostasis. *Results:* Permanent hemostasis was obtained in 4/4 (100%) for MWS, 1/1 (100%) for GU, 1/1 (100%) for GA and 3/4 (75%) for Diu. Rebleeding occurred in one case of Diu. There was no other complication including perforation, fever and epigastric pain. *Conclusion:* EBL is effective and safe as a procedure for hemostasis in patients with Diu, MWS and other diseases which show no or only mild fibrosis. Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Endoscopic Band Ligation for Hemostasis of Non-Variceal Upper Gastrointestinal Bleeding"

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"P P 61 1489" P 61 1489 **Ultrasonographic (US) Assessment of Coeliac Disease (CD) in Children: Comparison with Antiendomysium Antibodies (EMA)**

\*D. Micetic-Turk, S. Umek-Bradac, M. Gorenjak

Depts of Pediatrics, Radiology and Biochemistry, Teaching Hospital Maribor, Slovenia Many attempts have been made to find precise screening tests for CD in order to reduce the need for biopsy or to achieve better selection criteria before intestinal biopsy. To facilitate the decision, we decided to evaluate the usefulness of screening for EMA in the diagnosis of CD in children in comparison with the US changes related to CD. *Patients:* we studied 35 children (1–15 years) with untreated CD (N = 15), treated CD (N = 10) and controls (N = 10) undergoing small bowel biopsy in diagnostic procedure. *Methods:* US of the small bowel was done using a 4 or 7 MHz transducer of an ATL HDI 3000 computed sonography device, before biopsy. The thickness of the intestinal wall and the motility of the bowel were carefully recorded. Simultaneously, all children had serum routinely sampled for IgA EMA. *Results:* All controls had a histologically normal small mucosa and the US showed a small bowel thickness of 1 mm with normal movements in 9 children and unspecific US changes in 1 child. In 1 control case EMA was weak positive, in others negative. In 15 children with untreated CD, severe enteropathy and strongly positive EMA was found in 10 cases, in 5 children moderate enteropathy and positive EMA was established. Severe US changes were found in all children (thickness of intestinal wall > 1.6 mm, hyperperistalsis and abundant fluid in bowel). Mild enteropathy was found in 10 children with treated CD (1–3 months gluten free diet). In 2 children EMA was positive and in 8, weak positive. Unspecific US changes were found in 6 children. The estimated sensitivity of the EMA tests is 100% and its estimated specificity is 90%. The estimated sensitivity for US changes is 84% and its specificity 90%. In conclusion, our results indicate that US can offer further information on small-bowel structure, which serves as additional data for the indication of small bowel biopsy. This study confirm stronger association between EMA and CD than between US and CD. Intestinal disorders, absorption: Gluten enteropathy Immunology and microbiology: GI infection, children Radiology and ultrasound: Diagnosis }

"Ultrasonographic (US) Assessment of Coeliac Disease (CD) in Children: Comparison with Antiendomysium Antibodies (EMA)"

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## "P P 64 1531" P 64 1531 Endoscopic Ultrasound (EUS) Can Effectively Diagnose and Predict Resectability of Pancreatic Cancers

\*B. Hoffman, L. Aabakken, D. Cole, L. Baron, D. Daniel, R. Hawes, P. Baron

Departments of Surgery, Radiology, Biometry, and Medicine, Medical University of South Carolina, Charleston, SC *Purpose:* Patients suspected of having cancer of the pancreas frequently undergo extensive testing to confirm malignancy and determine tumor resectability. Radial and linear array EUS systems can be used to identify pancreatic masses and guide fine needle aspiration (FNA) biopsy respectively. The purpose of this study was to determine the ability of EUS to diagnose cancer and judge resectability. *Methods:* Between 5/91–11/95, 54 patients were preoperatively evaluated by contrast-enhanced CT and radial array EUS prior to surgical exploration for potentially resectable cancers of the pancreas and periampullary region. From 6/94–11/95, masses in this region were also biopsied with a 23 gauge needle using the linear array EUS system with color Doppler to identify vascular structures. *Results:* There were 51 adenocarcinomas (42 pancreas, 6 ampulla, 3 distal bile duct) and 3 islet cell tumors. A mass was identified by CT in 36 (67%) cases and by EUS in 50 (93%) cases. In 18 patients, CT failed to visualize masses seen with EUS ( $p < 0.001$  by Sign Test). The 4 EUS negative results were during the first 2 years of study. EUS-guided biopsy confirmed cancer in 22 of 23 patients where it was attempted: 19 pancreatic adenocarcinoma (14 head, 3 body, 2 tail), and 3 pancreatic islet cell tumors (2 head, 1 tail). EUS was further analyzed for effectiveness at predicting resectability: EUS stage Total Resected T1 (localized) 18 12 (67%) T2 (outside pancreas) 14 12 (86%) T3 (invading large vessel) 18 3 (17%)<sup>1,21</sup> Both ""resected"" T3 tumors were removed by distal pancreatectomy; <sup>2</sup> $p < 0.001$  for T1 and T2 vs T3 by Fisher's Exact Test *Conclusion:* EUS is superior to CT for localizing pancreatic tumors and can direct the FNA of these lesions. Most patients in which EUS identifies vascular invasion (T3) have unresectable cancers, and may therefore be able to avoid the morbidity and expense of numerous preoperative radiologic and endoscopic tests. Echoendosonography: Echoendoscopy Oncology, specific: Pancreas }  
"Endoscopic Ultrasound (EUS) Can Effectively Diagnose and Predict Resectability of Pancreatic Cancers"

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## "P P 65 1538" P 65 1538 Value of Endoscopy and Computed Tomography in the Diagnosis of HIV-Associated Colonic Diseases

\*A. Adler, F. Knollmann, W. Veltzke, R. Felix, K.E. Hampel, R.E. Hintze

Depts. of Gastroenterology, Central Interdisciplinary Endoscopy and Radiology, Virchow-Klinikum, Humboldt-University of Berlin, Germany

**Introduction:** Patients with clinical manifest AIDS often show infections and AIDS-associated diseases of the gastrointestinal tract with watery to bloody diarrhoea. Aim of this study is the definition of the value of colonoscopy and computed tomography (CT) in those diseases.

**Methods and patients:** From 7/91 to 10/95 122 colonoscopies in 71 patients with suspicion of a HIV-associated colonic disease were performed. In 46 patients an abdominal CT in a maximum time interval of 6 months to the endoscopy was made. Only these patients were compared in our study (thereof 42 male, all homosexual, 4 female, 3x drug abuse, 1x partner contact, mean age: 31.5 years (min 26–max 62)). All had a value of less than 200 CD4-cells/<sup>l</sup>.

**Results:** Despite of 3 patients with a colonoscopy without pathological findings, the other 43 patients (100%) showed the following alterations: 36x inflammatory (83.7%) and 7x neoplastic (16.3%); 12x with ubiquitous (27.9%) and 31x with segmental or focal (72.1%) localisation. 18x histologically a HIV-associated unspecific colitis was found (41.9%), 10x a CMV-colitis (23.3%), 5x a Kaposi-sarcoma (11.6%), 4x an MAI-infection (9.3%), 2x a non-Hodgkin-lymphoma (4.7%), 1x Mycobacterium africanum (2.3%), 1x Cryptosporidium (2.3%), 1x Microsporidium with a HIV-coeliac-like enteropathy (2.3%), 1x enterotoxigenic E. coli (2.3%). The HIV associated unspecific colitis often showed histologically cytomegal-transformed cells but no CMV-typical cytopathologic effects in immunohistology resp. PCR-analysis. In the comparative CT in 33 patients (71.7%) thick intestinal walls, pathologic mesenteric lymph nodes, striated signs of the pericolic fat, target lesions and/or ascites could be found.

**Conclusions:** Endoscopy is for HIV-associated colonic mucosal alterations the probative method. A normal CT-finding implicates not a normal endoscopic finding. Kaposi's sarcoma and rectal findings can hardly be demonstrated with CT. In contrary in CT often endoscopically not identified small intestinal alterations are found as well as prognostic relevant pathologic entities as intraabdominal lymphoma, ascites or liver tumors.

**Immunology and microbiology:** GI infections in adults

**Radiology and ultrasound:** Diagnosis

**Endoscopy, specific: Colon, rectum }** "Value of Endoscopy and Computed Tomography in the Diagnosis of HIV-Associated Colonic Diseases"

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## "P P 65 1539" P 65 1539 Colonoscopic Findings in Patients with AIDS and Diarrhea

\*M. Averbach, R. Cutait, P. Correa, J.L. Borges

Hospital S\edrio Liban\ eas, S\ e3o Paulo, Brazil Diarrhea is a frequent symptom, affecting around 60% of patients with AIDS during the course of their illness. The recognition of the cause of this symptom is very important to permit the establishment of an specific treatment. This study was done to determine the most frequent causes of diarrhea in AIDS patients, verifying the colonoscopic manifestations of each condition. From November 1993 to March 1995, 86 patients with AIDS and diarrhea, for a minimum period of three weeks, were studied prospectively. According to the CDC classification, the majority (82.8%) of the patients were C2 and C3, showing an advanced disease. The patients were submitted to: stools exams, parasitologic culture and *Cryptosporidium sp.* and *Isospora sp.* surveillance and colonoscopy with biopsies. CMV colitis was the most frequent infection observed in 27.9% of the patients, followed by *Cryptosporidium sp.* diagnosed in 17.4%. The statistic analisis of these data showed the relation between the endoscopic findings and the pathogens identified. The predominant findings in patients with CMV colitis were ulcers (83.3%) mainly in the ascending colon ceacum. In the patients in whom *Cryptosporidim sp.* was the unic pathogen found the most frequent endoscopic alteration was colitis without ulcer. Colonoscopy with biopsies had an specific result in more than half of the patients identifying at least one pathogen. In 18.6% two or more pathogens were found. Therefore, colonoscopy with biopsies is an important tool to find the cause of diarrhea in AIDS patients. Endoscopy, specific: Colon, rectum Immunology and microbiology: GI infections in adults } " Colonoscopic Findings in Patients with AIDS and Diarrhea "

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## OT84 1588 Are Pediatric Endoscopes Adapted to Perform Transnasal Oesogastroduodenoscopy in Adults?

\*T. Ponchon, J. Dumortier, B. Moulinier, P. Paliard, F. Zarka, R. Lambert

Department of Digestive Diseases, Hospital E. Herriot, Lyon, France Recent literature suggests an improved tolerance to gastroscopy without sedation, when thin endoscopes are introduced by the transnasal route. We conducted a study to determine whether commercially available thin endoscopes adapted to pediatric indications are adapted to perform oesogastro-duodenoscopy in adults. *Method:* transnasal endoscopy was performed in 227 adult patients (115 female, 112 male) referred in the unit for upper digestive endoscopy. The nasal cavities were anesthetized with 4% lidocaine (plus naphazoline for vasoconstriction) on cotton pledgets. The thin endoscope was introduced if possible blindly, or if not, under visual control. Two models were used: – a fiberscope (OLYMPUS N 30, length 925 mm, outer diameter 5 mm) in 77 patients – a videoscope (OLYMPUS N 200, length 950 mm outer diameter 6 mm) in 150 patients. Efficacy in routine endoscopy was assessed on the following 4 criteria: successful passage in the nasal cavities, ability to reach the 2nd part of the duodenum, quality of vision, interpretation of biopsies with small forceps. *Results: Nasal passage:* The thin endoscope was introduced transnasally in 195 patients (86%). The 5 mm fiberscope (success: 90%) was easier to introduce than the 6 mm videoscope (success 82%). Transnasal introduction of the endoscope failed in 32 patients for the following reasons: – difficulty to advance in the nasal cavities in 17 – nasal pain in 6 – epistaxis in 5 – refusal in 4 patients. *Progression:* the endoscope was advanced to the second portion of the duodenum in 197 patients (87%); the respective rates with the fiberscope and the videoscope were 79% and 91%. *Vision:* its quality was judged good in 215 patients and poor in 12, because of lavage or aspiration. This is explained by the absence of a specific air-water channel on both endoscopes. *Pathology:* the interpretation of the biopsies was satisfactory in all cases. Finally, by taking into account the combined effect of all 4 parameters, the use of pediatric endoscopes was determined satisfactory in 161 patients (71%); the respective rates with the fiberscope and the videoscope being 67% and 72%. *Conclusion:* Pediatric endoscopes are adapted to perform transnasal oesophago-gastro-duodenoscopy in around 70% of cases. Technical improvements of the material (length, outer diameter, air-water channel) are required for routine use. Endoscopy, specific: Oesophagus Endoscopy, specific: Stomach, duodenum }" "Are Pediatric Endoscopes Adapted to Perform Transnasal Oesogastroduodenoscopy in Adults?"

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## OT84 1589 Usefulness of a New Auto-Fluorescence Endoscopic Imaging System for the Diagnosis of Gastric Neoplasm

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Gastrointestinal neoplastic tissue has been reported to show intrinsic auto-fluorescence which is different from the auto-fluorescence of normal tissue when excited by blue or violet light. For the imaging of the regions of dysplasia and carcinomas in gastrointestinal tract, auto-fluorescence endoscopic imaging system (LIFE-GI system; Xillix technology Corp., Canada and Olympus optical Co., Japan) was newly developed using mercury light for excitation. We investigated the usefulness of LIFE-GI system for the detection of gastric neoplasm. We also evaluated the possibility of the detection by applying LIFE-GI system to the small remnant of gastric neoplasm after endoscopic treatment of gastric cancer and adenoma. *Methods:* Auto-fluorescence was observed by LIFE-GI system in 36 patients with or without gastric cancer and the findings were compared with the findings obtained by conventional endoscopy. Moreover, we studied the small remnant of gastric neoplasm in followed-up patients after endoscopic treatment of gastric lesion. Biopsy specimens from abnormal region detected by conventional endoscopy or LIFE-GI system were examined histologically. *Results:* 1) Twenty-six lesions, including all 20 carcinomas, showed abnormal fluorescence images by LIFE-GI system; 6 lesions were benign tissues by histological examination. 2) Remaining of tumor after endoscopic treatment was suspected in 7 lesions by LIFE-GI system; 3 lesions were proven histologically as dysplasia or adenocarcinoma, other 4 lesions were regenerative or erosive change histologically. *Conclusion:* We applied the newly developed autofluorescence endoscopic imaging system (LIFE-GI) for gastric neoplastic lesions. LIFE-GI system made it possible to detect the gastric cancer or dysplasia as well as conventional endoscopy. Small neoplastic lesions such as the remnant after endoscopic resection, which were difficult to be diagnosed by conventional endoscopy, could be detected by the LIFE-GI system. This suggests that the LIFE-GI system may be useful in the detection of small malignant lesions. Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Stomach, duodenum Oncology, specific: Stomach } "Usefulness of a New Auto-Fluorescence Endoscopic Imaging System for the Diagnosis of Gastric Neoplasm"

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OT84 1590 **Hepatitis C Virus RNA on Digestive Endoscopes** D. Smith<sup>1</sup>, J.M. Raymond<sup>1</sup>, P. Trimoulet<sup>2</sup>, V. De Ledinghen<sup>1</sup>, H. Fleury<sup>2</sup>, M. Amouretti<sup>1</sup>, P. Couzigou<sup>1</sup>

<sup>1</sup> CHU du Haut L'e9veque, Bordeaux, France

<sup>2</sup> University de Bordeaux II, France In 20 to 40% of cases, routes of contamination by hepatitis C virus (HCV) remain unknown, and digestive endoscopy has been suspected to be one of them. The aim of this study was to detect HCV viral nucleic acid on endoscopes and biopsy-forceps used in patients with known chronic HCV infection. *Methods:* First, to assess the method of sampling, a biopsy-forceps was artificially immersed in an HCV-positive serum sample and this serum was aspirated into the suction-biopsy channel of a gastrointestinal endoscope. Then, an oesogastroscopy with biopsy was performed in patients with known chronic HCV infection (RIBA 2+) and ASAT > 2N. All patients had a positive HCV viraemia on the day of the endoscopic procedure. Samples were obtained after pushing 10 ml of sterile water through the suction-biopsy channel and after immersion of the biopsy-forceps in 2 ml of sterile water. This sampling technique was used three times: immediately after endoscopic procedure (t0), after washing with detergent (t1) and after an immersion for 20 minutes in 2% glutaraldehyde solution (t2). Samples were stored immediately at { - }20\b0C. A polymerase chain reaction (PCR) was subsequently used to detect HCV RNA presence. *Results:* The suction-biopsy channel and the biopsy-forceps of the control endoscope were positive at t0 and negative at t1 and t2. Serial samples were tested for HCV RNA by PCR in 18 cases at t0, 1 out of 18 patients had detectable genomic HCV RNA on biopsy-forceps at t0, no suction-biopsy channel was positive at t0. To date samples at t1 and t2 were only tested for 7 patients, they were all negative, either the suction-biopsy channel, either the biopsy-forceps. *Conclusion:* This study emphasizes the difficulty in finding HCV RNA in such samples. It confirms the theoretical possibility of HCV patient-to-patient transmission by endoscopic procedures. Endoscopy, general: Complications Liver and bile ducts, 1: Hepatitis viral, diagnosis }" "Hepatitis C Virus RNA on Digestive Endoscopes"

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## OT84 1591A New Expandable UV-Cured Plastic Endoprosthesis for the Management of Malignant Esophageal Strictures

\*J. Haringsma, J. Ferwerda, W. Dekker, H.L.F. Brom

Depts. of Medicine & Surgery, Kennemer Gasthuis, Haarlem, The Netherlands Expandable stents have provided a major advance in the palliative treatment of dysphagia caused by malignant strictures of the esophagus. Current metal expanding endoprosthesis often require balloon dilatation in assistance to stent placement. After deployment these stents can not be removed, while misplacement and migration occur in up to 20%. In an attempt to produce a more satisfactory modality for palliative stricture and fistula relief, we developed a teflon esophageal endoprosthesis that is inserted over a bow-tie shaped dilatation balloon. Stricture dilatation is combined with stent placement. After correct positioning and deployment, the stent is cured by polymerization with UV light. Potentially, the stent can be disintegrated and removed with a special rescue-catheter. Our initial experience is reported. *Results* Four patients, aged 49–81 years (67 yr), had esophageal carcinoma causing grade 2–4 dysphagia (2.6). Stricture length averaged 5.0 cm. A tubular stent with an internal shaft diameter of 15.5 mm and a 26 mm funnel at both ends was inserted over a guidewire without prior dilatation. Stent placement was successful in all patients and no procedural complications occurred. All patients responded clinically with significant improvement in dysphagia. Complications included pain of limited duration in one, tumor overgrowth in two patients. One early death occurred, unrelated to the procedure. With one patient still in follow-up, average stent survival exceeds 88 days. *Conclusions* This newly developed UV-cured esophageal endoprosthesis is effective in relieving dysphagia in patients with malignant esophageal stenosis. It is safe, easily implanted and has potential advantages over covered metal expanding prosthesis. However, further evaluation is required. Endoscopy, specific: Oesophagus Endoscopy, general: Instrumentation, therapy Oncology, specific: Oesophagus } "A New Expandable UV-Cured Plastic Endoprosthesis for the Management of Malignant Esophageal Strictures"

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**OP1 0001 Early Administration of Natural Somatostatin (S) Increases the Efficacy of Sclerotherapy (ES) in Acute Bleeding Oesophageal Variceal Episodes: The European ABOVE Study**

\*A. Avgerinos, F. Nevens, S. Raptis, J. Fevery, ABOVE Study Group, M. Adler, A. Armonis, D.J. Bac, N. Bourgeois, B. Burtin, T. Darcis, J. Decruyenaere, M. Deman, A. Elewaut, M. Hautekeete, D. Katsaros, L. Lepoutre, S. Manolakopoulos, O. Natens, G. Poulianos, H. Reynaert, Ch. Tzathas, H.R. Van Buuren, P. Van der Spek, A. Zacharopoulos

Athens, Greece

Aalst, Brussels, Gent, Jette, Leuven, Belgium

Rotterdam, The Netherlands

UCB Pharma, Belgium The additional efficacy of S to emergency ES in cirrhotics with an acute upper gastrointestinal bleeding episode was assessed. Immediately after admission, 205 subjects were randomly assigned to receive continuous iv infusion of S (6 mg/24 hr for 120 hr), or placebo (PI) in a double blind way. Additionally, iv boluses S (250 µg) or PI were injected: a) after start of infusion, b) before endoscopy and c) if active bleeding occurred. ES was performed between 1 to 8 h after initiation of treatment. The study drug was continued in 151 pts (74%) in which oesophageal varices were the origin of bleeding (S = 75, PI = 76). Overall failure during the 5 day study period was defined as: death or clinical signs of rebleeding or the requirement of an excess of blood products or rescue therapy. Both groups S/PI were comparable with regards to age (mean – sd = 59.5 yrs – 12.1/58.8 yrs – 3.9), gender (M: 52/52, F: 23/24), Child's-class (A = 10/11; B = 38/39; C = 26/25) and alcoholic origin (40/46). Overall failure was observed in 32 subjects (S) and 51 (PI) with p = 0.003. During the infusion 2 patients (2.7%) died in S and 7 (9.2%) in PI (p = 0.17); units of blood products transfused: 2.6 – 0.35 (S) vs 3.6 – 0.35 (PI) (i.t.t., p = 0.05). In conclusion the results of this study suggest that the early administration of natural S increases the efficacy of ES in the control of acute bleeding from oesophageal varices in cirrhotics. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding Endoscopy, specific: Oesophagus } "Early Administration of Natural Somatostatin (S) Increases the Efficacy of Sclerotherapy (ES) in Acute Bleeding Oesophageal Variceal Episodes: The European ABOVE Study"

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## OP1 0003 The Actin Bundling Protein Fascin, Is Upregulated by Transforming Growth Factor- $\alpha$

\*A.U. Jawhari<sup>1</sup>, P.D. McCrea<sup>3</sup>, M.J.G. Farthing<sup>1</sup>, M. Pignatelli<sup>2</sup>

<sup>1</sup> Digestive Diseases Research Centre, St. Bartholomew's and the Royal London School of Medicine and Dentistry, London, UK

<sup>2</sup> Department of Histopathology, Hammersmith Hospital, London, UK

<sup>3</sup> Department of Biochemistry and Molecular Biology, Anderson Cancer Centre, Houston TX Fascin is a highly conserved, ubiquitously expressed actin-bundling protein, involved in the assembly and reorganisation of actin bundles and networks necessary for locomotion, maintenance of cell polarity, and attachment to intercellular contacts and the substratum. A recent report has suggested interaction of fascin with the cadherin-catenin complex at adherens junctions. *Aims:* 1. To examine the expression of fascin in gastric and colonic carcinoma cell lines and its response to stimulation of the epidermal growth factor receptor (EGFR) by TGF- $\alpha$ . 2. To examine the interaction of fascin with the E-cadherin-catenin complex in these cell lines. *Methods:* Fascin expression was examined in gastric (MKN45 & HSC39) and colonic cell lines (HT29, HCT116, & LS174T) by immunocytochemistry and Western blotting. Intensity of expression was assessed on days 1–4 following seeding and in response to stimulation of the EGFR by TGF- $\alpha$  (10 ng/ml for 24 hrs). Immunoprecipitation of fascin-associated proteins followed by Western blotting was performed. *Results:* Fascin co-localised with E-cadherin at the cell membrane. A 55 kDa band consistent with fascin was demonstrated in all cell lines. Band intensity was inversely proportional to monolayer confluence. Stimulation by TGF- $\alpha$  was associated with increased fascin expression in MKN45 & HT29. Immunoprecipitation experiments confirmed fascin interaction with E-cadherin,  $\beta$  and  $\gamma$ -catenin. *Summary and conclusions:* TGF- $\alpha$  stimulation is associated with upregulation of fascin expression. The interactions between the cadherin-catenin complex, fascin and the EGFR may play a role in modulating cell-cell adhesion and cytoskeletal interaction during cell migration in epithelial repair, and invasion by neoplastic cells. *Hormones and receptors:* Growth factors *Oncology, general:* Proliferation, carcinogenesis *Oncology, specific:* Stomach } "The Actin Bundling Protein Fascin, Is Upregulated by Transforming Growth Factor- $\alpha$ "

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**OP1 0004 Preoperative Radiotherapy in Rectal Carcinoma: Influence of the Interval between Radiotherapy and Surgery: A Multicenter Randomised Trial from Lyon, France**

Department of Surgery, Centre Hospitalier Lyon Sud, Pierre-Benite, France

Preoperative radiotherapy has been shown to decrease local recurrence after surgery in rectal carcinoma. However the best moment for surgery after completion of radiotherapy is not known. Therefore the aim of this prospective multicenter randomised trial was to determine the influence of the interval between radiotherapy and surgery on sphincter conservation, complications of surgery and local recurrences.

*Methods:* Operable patients with rectal carcinoma reachable at digital examination, staged T2–T3, Nx, MO were included. Preoperative radiotherapy delivered 39 Gy in 13 fractions within 17 days. Randomisation was performed before radiotherapy in 2 arms: in the "short" arm, patients were operated on within 2 weeks after completion of radiotherapy, while in the "long" arm, surgery was performed 6 to 8 weeks after radiotherapy.

*Results:* 210 patients were randomised between 1992 and 1995. 177 patients had for the moment completed a 6 month follow-up, 90 in the short arm, 87 in the long arm. There were 113 male and 64 female, mean age 63 yrs (range 35–82). There was no statistical difference between the 2 groups for sex, age, and the mean distance between the lower part of the tumor and the anal verge as determined by rigid endoscopy and endosonography (respectively 5.8 cm and 6.1 cm). 21 patients (12%) could not have curative resection (liver, peritoneum metastasis, parietal invasion). Sphincter preservation was possible in 68% (61/90), short arm and 76% (66/87) (long arm ( $p = 0.25$ )). After radiotherapy, decrease in tumoral size ( $> 50\%$ ) measured by digital examination was observed more in the long arm, 69% vs 55% ( $p < 0.05$ ). Operative specimen showed no or only a few tumoral cells in 11/86 vs 25/83 ( $p = 0.008$ ). Median operative stay, peroperative mortality, anastomotic complications and reinterventions were similar in the 2 groups. With a median follow-up of 20 months, actuarial survival was at 1, 2 and 3 yrs, 89, 83, 78% in the short arm, 91, 77 and 64% in the long arm (NS). Local recurrence was observed in 6 patients in the short arm and 5 in the long arm. All these patients had sphincter saving surgery.

*Conclusion:* In this large series of rectal carcinoma with preoperative radiotherapy, sphincter conservation was possible in 72% of patients. Patients of the long arm has a more important tumor regression than in the short arm. However there was not statistical difference in the percentage of sphincter saving intervention or operative complications. A longer follow-up will confirm the lack of difference in survival and local recurrence.

Oncology, specific: Colon, rectum  
Clinical practice: Management strategy }

"Preoperative Radiotherapy in Rectal Carcinoma: Influence of the Interval between Radiotherapy and Surgery: A Multicenter Randomised Trial from Lyon"

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**OP1 0005 Effects of Smoking on the Clinical Course of Crohn's Disease R. Sostegni,**

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<sup>1</sup> Divisione di Gastroenterologia, Ospedale Mauriziano, Torino, Italia *Purpose* A previous study by our group showed no relationship among 1) years of smoking 2) the cumulative estimate of the total amount of cigarette smoked and the long term medical and surgical course of the disease. This suggested that the effect of smoking is not long-lasting. In order to test the hypothesis of a short-term effect of smoking during long-term follow up a phone interview based on a standardized questionnaire about smoking habits was performed. *Patients and Methods* Of 203 patients (127 M, 76 F) with a follow-up of more than 10 years duration, 73 (36%) stopped smoking after the diagnosis of CD and were excluded from the study. The median follow-up period for the remaining 130 patients is 16 years (10–33). At the time of diagnosis the disease involved: ileum 60 (46%), ileum-colon 29 (22%) and colon 41 (32%). The effect of daily cigarette smoking irrespective of life time exposure was evaluated by dividing patients in 64 smokers (49%) and 66 non-smokers (51%). *Results* The comparison of non-smokers versus smokers shows: mean age 49 and 46 (P = 0.17), mean age at diagnosis 33 and 29 (P = 0.13), months between first symptom of CD and diagnosis 38 and 22 (P = 0.09), pain at diagnosis 45 and 55% (P = 0.09), weight loss at diagnosis 39 and 61% (P = 0.04), mean number of hospital admission 2.9 and 3.6 (P = 0.06), steroid months 18 and 26 (P = 0.08), azathioprine months 7 and 18 (P = 0.12). Disease localization, number of major surgical operations, indications for surgery, number of postoperative recurrences, and mortality are not statistically associated with smoking. There is no difference in the timing of the first, second, third and further operations estimated by life table analysis. *Discussion* This study confirm the absence of both long-standing and cumulative effects of smoking on Crohn's disease. Our data suggest that smoking could have a short-term effect on some symptoms, signs and disease severity as indicated by the statistical association or consistent trend with age at diagnosis, latency between symptoms and diagnosis, hospital admission and therapeutic needs as suggested recently by Cosnes et al. Intestinal disorders: IBD, etiology and genetics } "Effects of Smoking on the Clinical Course of Crohn's Disease"

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## OP1 0006 Hepatitis G Virus Infection in Patients with Hepatocellular Carcinoma

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*Purpose of the study:* Hepatitis G virus (HGV) is a RNA virus and has been implicated as a causative agent in acute and chronic hepatitis. We investigated the prevalence of HGV in patients with hepatocellular carcinoma (HCC). *Methods:* Serum of 76 patients (53 m, 23 f, 61 – 11 yrs) with HCC was studied for the presence of HGV-RNA by reverse-transcription polymerase-chain reaction (RT-PCR). *Results:* 15 (20%) of 76 patients with HCC were infected with HGV. In 6 patients (8%) HGV was the only hepatotropic virus found. In 9 patients (12%) coinfection of HGV with other hepatitis viruses was present. 4 patients (26%) were HBsAg+, 5 others (33%) were HCV-RNA+; in none of our patients triple infection of HBV, HCV and HGV was found. Of 67 patients with HCC 30 patients (39%) had no evidence of infection with hepatotropic viruses, 46 patients (61%) had markers virus infection: of those 12 patients (27%) were HBV infected, 26 patients (59%) were positive for HCV-RNA, and 6 patients (14%) were HGV-RNA+. In 61 control patients with chronic hepatitis B (without HCC) 10 patients (16%) were HGV-RNA+, whereas 4 of 12 HBsAg+ patients with HCC (30%) were infected with HGV. 16 of 68 patients (21%) with chronic hepatitis C (without HCC) and 5 of 26 of HCV-RNA+ patients with HCC (20%) were positive for HGV. The prevalence of HGV in patients with HCC (20%) was significantly higher than that found in healthy controls (3%;  $p = 0.003$ ). *Conclusion:* The prevalence of HGV is significantly increased in patients with HCC as compared to the healthy population. HGV could be a risk factor for HCC. Liver and bile ducts, 1: Hepatitis viral, diagnosisOncology, specific: Liver, biliary } "Hepatitis G Virus Infection in Patients with Hepatocellular Carcinoma"

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**OP2 0007 Circulation of Tumorous Cells and Iatrogenic Spreading of Hepatic Cells in Patients with Liver Cancer (LC)** M. Louha<sup>1</sup>, K. Poussin<sup>1</sup>, N. Ganne<sup>4</sup>, H. Zylberberg<sup>2</sup>, C. Vons<sup>5</sup>, O. Soubrane<sup>3</sup>, S. Pol<sup>2</sup>, B. Nalpas<sup>2</sup>, M. Beaugrand<sup>4</sup>, P. Berthelot<sup>2</sup>, D. Franco<sup>5</sup>, J.C. Trinchet<sup>4</sup>, C. Br'e9chot,

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Prognosis of patients with LC often depends on development of extrahepatic metastasis, particularly after liver transplantation. We have developed a sensitive test, specifically detecting the spontaneous circulation of circulating tumorous cells (CTC) and spreading of liver cells due to chemoembolisation (CE) and alcoholisation (A). *Methods:* Alphafetoprotein (AFP) mRNAs detection in peripheral blood cells by RT-PCR. Test of sensitivity by spiking HepG2 cells (derived from human LC) in blood of healthy volunteers. 76 patients with LC (group A: 39 treated by surgical resection; group B: 37 not treated surgically, including 12 patients tested before, 1 hour after and 24 hours after CE or A), 100 controls (group C: 10 patients with benign liver tumors or liver metastasis from intestinal cancers; group D: 53 patients with chronic hepatitis and/or cirrhosis without HCC, group E: 37 blood donors). *Results:* Sensitivity: one HepG2 cell detected when mixed with 10<sup>7</sup> leukocytes. Controls (group C, D and E): all negative. Group A: 13/39 positive. Group B: 13/37 positive. Patients with metastasis: 4/5 positive. Patients tested before and after CE or A: 6/12 positive after therapy, including 2 positive after CE and 4 after A. Three patients became positive 1 hour and negative 24 hours after therapy. Three other patients became positive 24 hours after therapy. *Conclusions:* 1) We have developed a highly specific and sensitive technique to detect CTC in patients with LC. 2) 30% of patients with LC have detectable CTC 3) Locoregional therapy (CE and A) may spread hepatic cells including tumorous cells in the peripheral blood. Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis Oncology, general: Therapy } "Circulation of Tumorous Cells and Iatrogenic Spreading of Hepatic Cells in Patients with Liver Cancer (LC)"

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OP2 0009 **Pivotal Role of Granulocytes in Immunoregulation in Inflammatory Bowel Disease?** S. Nikolaus, J. Hampe, J. Bauditz, M. Ortner, E. Reichelt, H. Lochs, U. Schindler<sup>1</sup>, S. Schreiber

IVth. Medical Department, Charit'e9, Berlin, Germany

<sup>1</sup> Tularik, San Francisco, USA *Background:* Pro-inflammatory cytokines (IL-1{ b}, TNF-{ a}, IL-8, IL-1ra) are increased in intestinal inflammation in IBD. Monocytes as well as epithelial cells have been discussed as a source. However, predominant cells in inflammatory infiltrates are granulocytes (PMN). The *Aim:* of this study was to evaluate the capacity of PMN to secrete pro-inflammatory cytokines as well as the regulatory capacities of IL-4 and IL-10 in PMN. *Methods:* PMN from 35 patients with ulcerative colitis (UC), 28 patients with Crohn's disease (CD) and 25 normal volunteer controls (NC) were obtained from peripheral blood by dextran sedimentation and density centrifugation. Release of pro-inflammatory cytokines (ELISA) into culture supernatants as well as mRNA (semiquantitative RT-PCR) were assessed. *Results:* Only low levels of pro-inflammatory cytokines were secreted spontaneously. After stimulation with LPS, PMN from patients with active UC or CD secreted significantly more IL-1{ b}, TNF-{ a} and IL-1ra than NC (Figure). Pro-inflammatory cytokine secretion was related to disease activity. IL-4 as well as IL-10 down-regulated pro-inflammatory cytokine secretion as well as mRNA levels in a dose dependent manner without differences between IBD and NC PMN. Elements of IL-4 receptor signal transduction (STAT-6) were induced by stimulation of PMN with IL-4. *Conclusions:* PMN could be an important contributor to enhanced concentrations of pro-inflammatory cytokines in intestinal mucosa or feces of IBD patients. PMN appear to be fully capable to partake in mucosal immunoregulation by anti-inflammatory cytokines. Elements of IL-4 signal transduction (STAT-6) are fully conserved in PMN. Future therapeutic developments need to consider PMN as potent pro-inflammatory cells capable of partaking in mucosal immunoregulation.

Intestinal disorders: IBD, basicIntestinal disorders: IBD, etiology and geneticsIntestinal disorders: IBD, therapy }" "Pivotal Role of Granulocytes in Immunoregulation in Inflammatory Bowel Disease?"

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**OP2 0011 Self-Reported Ulcer Incidence and Changes in Levels of Serum IgG Antibodies to *H. Pylori*; A Prospective Cohort Study Comprising 2,404 Unselected Danes**

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Dept. of Surgery K, Bispebjerg Hospital, the Copenhagen Hospital Corporation, the Glostrup Population Studies, University of Copenhagen, 2400 NV Denmark

**Aim:** To examine the relationship between changes in levels of IgG antibodies to *H. pylori* and the incidence of self-reported peptic ulcers (PUD) in an 11-year period. **Methods:** A random sample of 3,589 Danes aged 30–60 years entered a population-based prospective cohort study in 1983. After 11 years, 2,656 participants attended a follow-up examination. Blood samples were drawn at both attendances (n = 2,404). IgG antibodies against *H. pylori* were measured with an in-house ELISA assay. Antibody levels were categorized as sero-negative, border-line, or sero-positive. People who sero-converted in IgG antibodies to *H. pylori* were regarded as having acquired *H. pylori* infection within the study period. Participants with no history of peptic ulcer disease at study entry reported if they had had an ulcer diagnosed at follow-up. Information on life-style practices, socio-economic factors, and medical history was obtained from a questionnaire. **Results:** Cumulated 11-year incidence of PUD was 28.3 [21.7–34.9] per 1,000 persons at risk. Ulcers were more often reported in those who were seropositive at both attendances (OR 2.18 [1.13–4.21]), in people with an increase in IgG antibodies from border-line to seropositive levels (OR 4.89 [1.13–4.31]), in heavy tobacco smokers (OR 6.24 [2.45–15.91]), and in people categorized as psychical vulnerable at study entry (OR 2.86 [1.45–5.56]). Age, sex, family history of PUD, sero-conversion in IgG antibodies, and alcohol consumption did not act as risk factors to PUD in this study. **Conclusions:** Long-term *H. pylori* infection, tobacco smoking, and psychic vulnerability are independent risk factors to PUD. An increase in IgG antibody levels may be useful as a marker for ulcer formation. Recent infection with *H. pylori* (< 11 yrs.) may not be a risk factor to PUD. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Epidemiology (non cancer) } "Self-Reported Ulcer Incidence and Changes in Levels of Serum IgG Antibodies to *H. Pylori*; A Prospective Cohort Study Comprising 2,404 Unselected Danes"

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**OP2 0012 Diagnosis of Pancreatic Cancer with FDG-PET: Comparison with CT, US and Endoscopic UST. Inokuma, T. Okamoto, T. Ogami, T. Uchida<sup>1</sup>,**

**\*S. Katsushima<sup>2</sup>, T. Higashi, T. Torizuka, T. Honda, N. Tamaki, J. Konishi<sup>3</sup>**

<sup>1</sup> Department of Medicine, Takamatsu Red-Cross Hospital, Kagawa, Japan

<sup>2</sup> Department of Medicine, Osaka Teishin Hospital, Osaka, Japan

<sup>3</sup> Department of Radiology and Nuclear Medicine, Kyoto University Faculty of Medicine, Kyoto, Japan  
*Purpose:* Clinical value of PET for identification of pancreatic cancer was prospectively evaluated in comparison with CT, US and endoscopic US (EUS).  
*Methods:* 74 preoperative patients with suspected pancreatic neoplasm underwent PET, CT and US. EUS was performed in 66 patients. Images were independently interpreted and compared with the histopathologic findings or with clinical follow-up findings for over six months. PET was performed one hour after intravenous injection of 185 MBq of F-18 fluorodeoxyglucose (FDG) under fasting state. Focal FDG uptake in the pancreatic region was considered as sign of malignancy, and was evaluated quantitatively with standardized uptake values (SUVs).  
*Results:* In 54 (96%) of 56 patients, foci of pancreatic carcinomas (10–100 mm in diameter) were identified as an increase in FDG uptake, whereas CT, US, and EUS depicted the foci in 51, 51, and 46 cases, respectively. In 12 (86%) of 14 with chronic pancreatitis, no increased FDG uptake was observed. Specificities of the other modalities were lower. False-positive findings were obtained in two of chronic pancreatitis and in two of vascular-rich benign neoplasms. In the semiquantitative analysis, SUVs accurately differentiated malignant (4.16 – 2.16) from benign (2.05 – 0.93) tumors ( $p < 0.01$ ), and SUV cut-off values of 2.20 best separated the two groups.  
*Conclusion:* FDG-PET, which provides biochemical information, is accurate in identifying pancreatic cancer, and has significantly higher sensitivity and specificity than CT and US. PET CT US EUS  
Sensitivity 54/56 (96%) 51/56 (91%) 51/56 (91%) 46/48 (96%)  
Specificity 14/18 (78%) 10/18 (56%) 9/18 (50%) 12/18 (67%)  
Accuracy 68/74 (92%) 60/74 (81%) 61/74 (82%) 58/66 (88%)  
Oncology, specific: Pancreas  
Radiology and ultrasound: Diagnosis }  
"Diagnosis of Pancreatic Cancer with FDG-PET: Comparison with CT, US and Endoscopic US"

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"P P 1 0013" P 1 0013 **Human Papillomavirus (HPV) Infection and p53 Overexpression as Prognostic Factors in Patients with Esophageal Squamous Cell Carcinoma.** M. Iwasa, S. Ogoshi, A. Takahashi, H. Ono, Y. Ohmori, Y. Iwasa, A. Yamamoto

Department of Surgery II, Kochi Medical School, Okoh, Nankoku, Kochi 783, Japan Infection with high-risk human papillomavirus (HPV) has been detected in high percentages of patients with several types of cancer such as in the uterine cervix, anus, skin and esophagus. On the other hand, p53 protein mutation and overexpression in the multistep process of esophageal carcinogenesis is still under debate. The present study was undertaken in order to investigate the possible involvement of HPV in the esophageal squamous cell carcinoma (ESC) and the relation between p53 overexpression and prognosis of patients in ESC. *Material and Methods.* One hundred twenty three samples, formalin fixed and paraffin embedded, were examined for this study. The detection of HPV was performed with dot blot hybridization (DBH), polymerase chain reaction (PCR) and in situ hybridization (ISH) methods. p53 protein were analyzed immunohistochemically with a monoclonal antibody and the avidin–biotin complex (ABC) procedure. The relationship between HPV infection, p53 overexpression and prognosis of patients with ESC were analyzed by multivariate survival analysis. *Results.* The detection rate of HPV were 21% by DBH and PCR, respectively. In ISH method, HPV types 16, 18 and 33 were detected in 30% (37/123). In addition, 43 of 123 samples (35%), nuclear immunohistochemical reactivity for p53 protein overexpression was detected. The survival rate (Kaplan–Meier methods) in HPV positive group was markedly worse than negative group and in p53 protein overexpression positive group was significantly worse ( $p < 0.05$ ) than negative group. *Conclusion.* These results suggest that the HPV infection and p53 protein overexpression were detected in a high percentage of ESC. The presence of HPV and p53 protein overexpression have strong impact on the prognosis of the patients with ESC. However, additional studies on a large series of patients with ESC will be necessary for verification of these results. Oncology, general: Epidemiology Oncology, specific: Oesophagus } "Human Papillomavirus (HPV) Infection and p53 Overexpression as Prognostic Factors in Patients with Esophageal Squamous Cell Carcinoma."

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"P P 1 0014" P 1 0014 **Esophageal Squamous Cell Papilloma and Human Papillomavirus (HPV) Infection**

\*S. Michopoulos, M. Sotiropoulou<sup>1</sup>, M. Botos, H. Bouzakis, I. Vougiadiotis, E. Papaspyrou<sup>1</sup>, V. Pavlou<sup>1</sup>, P. Tsibouris, S. Markaki<sup>1</sup>, K. Nikolaidis, N. Kralios

Gastroenterology Unit, "Alexandra" University Hospital, Athens, Greece

<sup>1</sup> Pathology Unit, "Alexandra" University Hospital, Athens, Greece Human papillomaviruses (HPV) are involved in the development of cervix, larynx, lung and anus papillomas as well as the progression of the papilloma into cancer. Esophageal squamous cell papilloma (ESCP) is a rare benign condition, considered as precancerous, but its etiology and pathogenesis remain controversial. The prevailing etiological considerations are chronic chemical irritation from gastric juice and HPV infection. In addition HPV and particularly of type 16 or 18, is detected in a percentage of squamous esophageal malignancies. The *aim of our study* was to investigate the possible relationship between HPV and ESCP in an area of low prevalence of squamous esophageal cancer. *Patients and methods:* 14 ESCPs (5–15 mm of diameter) from 12 patients (29–72 years old) were analysed for HPV using in situ hybridization (ISH) from paraffin-embedded tissue (ENZO PathoGene<sup>®</sup>). The HPV types researched according to the DNA probe reagents provided were 6/11, 16/18, 13/33/51. The method was validated as the manufacturer suggests, using 2 control slides inoculated with 6 and 16 HPV types. Gastroesophageal reflux was diagnosed in 5 patients, one patient had gastroduodenal ulcer while the rest of the patients (6) had a fiberoscopy for chronic dyspeptic syndrome. One patient had 2 adjacent but distinct papillomas at mid-esophagus while the other patient had a recurrence at the same place of mid-esophagus, one year after ablation. *Results:* No evidence for HPV DNA was detected in any of the examined specimen. *Conclusions:* 1) We were unable to detect HPV DNA using ISH in all ESCP that we tested 2) Other authors using more sensitive methods, like PCR, rarely report HPV DNA in ESCPs. This supports our findings and suggest that other than HPV infection, pathogenetic mechanisms are more important for ESCP's etiology at least in our area. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Oncology, general: Screening, prevention Endoscopy, specific: Oesophagus } "Esophageal Squamous Cell Papilloma and Human Papillomavirus (HPV) Infection"

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**"P P 1 0015" P 1 0015 Clinicopathological Study of Esophageal Squamous Papilloma- Including Immunohistochemical Staining H. Yamagiwa, N. Onishi, T. Onishi, M. Nishii**

Dept. of Pathol., Mie University Hospital and Onishi Hospital, Mie, Japan Clinicopathological study for 100 cases of esophageal squamous papilloma were performed. Patients were frequently found in 6th and 7th decades. The majority of patients had no remarkable complaint and complication, and esophageal squamous papillomas were accidentally found at the investigation of gastric disease by X-ray and endoscopy. The white colored elevated lesions located frequently in lower 1/3 (60%) and middle 1/3 (30%) of esophagus showing lobulated or villous appearances. Hemispherical and sessile polypoid lesions (94%) were frequently found compared with the pedunculated ones. Single lesion was found in 90% of the cases, and 83% of the lesions were within 5 mm in diameter. Histologically, squamous epithelial thickening and papillomatous growth without atypia were observed. Although several factors like as regurgitation of gastric juice associated with gastric resection, hiatal herniation, gastric ulcer, etc., and HPV (human papilloma virus) infection have been reported in relation to the histogenesis of esophageal squamous papilloma, genuine mechanism has been unknown. According to the immunohistochemical staining, positive rate was 21.2%, 7.6%, 0%, 15.4%, 23.1%, 0% and 7.6% for PCNA (proliferating cell nuclear antigen), p53, c-erbB-2, EGF, EGFR, K-ras and HPV, respectively. These positive rates were extremely low in comparison to those of esophageal carcinoma. It seemed likely that esophageal squamous papilloma is not precancerous. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Oncology, general: Proliferation, carcinogenesis Oncology, specific: Oesophagus } "Clinicopathological Study of Esophageal Squamous Papilloma- Including Immunohistochemical Staining"

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## "P P 1 0016" P 1 0016 A Retrospective Review of a Consecutive Series of 90 Oesophageal Resections

\*P. Kolh, J.L. Gielen, C. Azzam, P. Honore, M. Legrand, N. Jacquet

Digestive Surgery Service, University of Liege, CHU, Liege, Belgium To assess the perioperative mortality and morbidity of oesophageal surgery, we present a retrospective series of 90 patients who underwent oesophageal resection at our institution from 1.1.1989 through 31.12.1995. There were 73 males and 17 females, mean age was 64.2 years (range: 21–78 years). Indications for resection were esophageal cancer in 64 patients, cardiac adenocarcinoma in 20, and benign lesions in six. Twenty-five patients received preoperative radiochemotherapy. In 78 patients surgery was performed in a curative intent and was palliative in twelve. There were thirty-seven total esophagectomies, nineteen thoracic esophagectomies, and thirty-four partial oesophagogastrrectomies. Digestive continuity was restored with a gastric transplant in 62 patients, a colonic graft in 24, and a jejunal loop in four. Hospital mortality was 10%, and 30-day mortality was 7%. Comparing the periods until 1992 and since 1993, hospital and 30-day mortalities decreased respectively from 18.5% to 3.8%, and from 10.5% to 3.8%. Three patients died from myocardial infarction, four from anastomotic fistula, and three from pulmonary complications. Among the 9 patients who died, five had a total oesophagectomy, and in all but one a gastric transplant was used. Nonfatal postoperative complications occurred in 32 patients (nine in the colonic graft group and 23 in the gastric pull-up group), and consisted in pulmonary problems in 26 patients, cerebrovascular accident in one, renal insufficiency in two, recurrent nerve palsy in four, and anastomotic fistula in six. Twelve patients were reoperated for technical reasons: anastomotic fistula (6), anastomotic stenosis (1), hemorrhage (3), and transplant ischemic injury (2). We observed 14 pulmonary complications in the subgroup of patients who received preoperative radiotherapy. We conclude that: 1) with experience, major oesophageal resection can be performed with low mortality, 2) the use of a colonic graft doesn't increase the incidence of perioperative complications, 3) pulmonary complications are responsible for a significant morbidity after oesophageal surgery, particularly in patients with preoperative radiotherapy. } "A Retrospective Review of a Consecutive Series of 90 Oesophageal Resections"

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"P P 1 0017" P 1 0017 **An Original Evaluation of Gastric and Colonic Transplants after Oesophageal Resection**

\*P. Kolh, J. Gielen, C. Azam, P. Honore, M. Legrand, Boverie, N. Jacquet

Digestive Surgery Service, University of Liege, CHU, Liege, Belgium We present a clinical and radiological evaluation of gastric and colonic grafts used to restore digestive continuity after oesophageal resections. Out of 90 patients who underwent an oesophageal resection at our institution, from 1.1.1989 through 31.12.1995, we evaluated the alimentary comfort and the quality of life with a standard questionnaire, and performed a dynamic contrast-swallowed radiography (radiocinema) in 35 patients who were alive more than one year after oesophageal resection. There were 23 males and 12 females; mean age was 64 years. In 30 patients esophageal resection was performed for cancer and for benign lesions in five. 28 patients had a gastric pull-up and in 7 patients an isoperistaltic colon segment was used to restore the digestive continuity. Major long-term complaints were sensation of early fullness during eating in 8 patients, nocturnal cough in seven, postprandial sweating in five, dysphagia in four, and diarrhea in three. Most patients considered the side effects of the operation as mild to moderate and mean rating of alimentary comfort was 8.2/10. Twenty-four patients qualified their quality of life as good, eight as satisfactory, and four as poor. Thirty patients led active lives. With radiocinema the following observations were made: colon transplants were essentially non contractile and emptied by gravity; in gastric grafts, the contrast progressed passively in the non-antral portion but isoperistaltic contractions were observed in the antral segment. The best functional results were seen with partial oesophagectomies and gastric transplants: the proximal oesophageal segment triggered the movement with strong contractions, followed by passive progression in the non-antral segment of the gastric pull-up, and subsequently by antral contractions. These radiological observations correlate well with the clinical evaluation. We conclude that in most patients the quality of life and alimentary comfort are good after esophageal resection and gastric or colonic pull-up. Radiocinema shows a better function of the gastric transplant, as compared to the colonic graft, particularly when the proximal portion of the oesophagus triggers the progression. Motility, specific: Oesophagus Oncology, specific: Oesophagus Radiology and ultrasound: Diagnosis } "An Original Evaluation of Gastric and Colonic Transplants after Oesophageal Resection"

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"P P 1 0018" P 1 0018 **Five-Year Survival Following Resection for Oesophageal Cancer in 733 Patients** J.M. Catheline, B. Meunier, S. Landen, E. Bardaxoglou, B. Chareton, J.P. Champion,

\*B. Launois

Digestive Surgery and Transplantation Unit, University of Rennes, Pontchaillou Hospital, Rue Henri Le Guilloux, 35033 Rennes Cedex, France

The aim of this retrospective study was to determine survival and prognosis factors of a group of 733 patients having undergone surgery for oesophageal cancer between 1981 and 1991. Cancers of the pharyngoesophageal and oesophageal gastric junction were excluded from this study. *Patients and methods:* The group comprised 696 males and 37 females with a mean age of 59 years. 528 resections were performed using various surgical procedures: Sweet (5%), Ivor-Lewis (30%), Akiyama (18%), Thorek (6%), MacKeown (18%), transhiatal oesophagectomy (23%). The tumor was located at the upper, middle and lower third of the oesophagus in 14%, 65%, and 21% of patients respectively. 95% of tumors were squamous cell carcinomas. *Results:* The resectability rate was 72% and 76% of resections were considered as being curative. Thirty-day operative mortality was 9%. Excluding operative mortality, 5-year actuarial survival following curative resections was 25.7% versus 3.4% following palliative resections ( $p < 0.0001$ ). When TNM staging was considered, 5-year actuarial survival was 87% for stage 0 lesions, 51% for stage I lesions, 25% for stage IIA and 13.6% for stage IIB lesions, 6% for stage III lesions and 0% for stage IV lesions ( $p < 0.0001$ ). 5-year survival showed no relationship to patient gender or histology. *Conclusions:* There exists a statistically significant relationship between TNM tumor staging for oesophageal cancer and 5-year survival. Oncology, general: Therapy Oncology, specific: Oesophagus } "Five-Year Survival Following Resection for Oesophageal Cancer in 733 Patients"

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"P P 1 0019" P 1 0019 **Results of the Operative Treatment for Esophageal Squamous-Cell Carcinoma**

\*M. Fraczek, P.M. Paczkowski, M. Krawczyk, W. Otto, A. Karwowski

Medical Academy of Warsaw, Warsaw, Poland From 1988 to 1995 one hundred and fifty eight patients with squamous-cell esophageal carcinoma located in its thoracic part were treated in our Department. According to the preoperative staging (TNM) 84% of patients were classified as stage III/IV. The most common and most important presenting symptom was dysphagia, which occurred in 96% of patients (mean 4.6 months). Patients qualified to the operative resectional procedures included those in good general condition, in whom the weight loss have not exceed 20% of body weight. Resectional operations were carried out in 64 patients (42%). The operation of choice was the resection of thoracic esophagus with tumor as well as the lesser curvature of the stomach. Two-field lymphadenectomy (mediastinal and upper abdominal lymph nodes) was also performed. The continuity of the alimentary tract was achieved by stomach graft placed in the anterior mediastinum, with cervical esophagogastric anastomosis. In only 17% of patients the colon was used for reconstruction. Pulmonary (14 patients – 21.9%) and cardiovascular (6 patients – 9.4%) complications were significant source of morbidity following esophagectomy. Anastomotic leak occurred in 5 patients (7.8%). Early mortality (30-days) was of 19% (12 patients). One-year survival equaled 45% (29 patients). Six patients (9%) survived 3 years and 2 (3%)- 5 years. *Conclusions:* Better results of treatment of esophageal squamous-cell carcinoma depend on early diagnosis and treatment, aggressive surgical procedures and appropriately chosen adjuvant therapy (chemo- and/or radiotherapy). Oncology, specific: Oesophagus }  
"Results of the Operative Treatment for Esophageal Squamous-Cell Carcinoma"

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"P P 1 0020" P 1 0020 **Esophageal Functional Evaluation of Laryngectomees Rehabilitated with Esophageal Voice**

\*S. La Manna, D. Pellicoro, G. Coppola, V. Pellegrini

III Department General Surgery–Surgery Oncology Institute of Otorhinolaryngical Pathology and Clinic and Phoniatics, "Federico II" University, Naples, Italy *Aim:* laryngectomees who had laryngeal Ca and rehabilitated with esophageal voice were studied to evaluate the incidence of alterations regarding the esophageal motility and the presence of gastroesophageal reflux disease (GERD). We studied 75 patients (males, age range: 44–71 years, mean age 54 ys) with larynx Ca and who were to undergo surgical total laryngectomy and subsequent phoniatric rehabilitation with "esophageal voice". GERD symptoms were absent in these patients. All subjects underwent pre and post-operative study protocol (generally after six months) including: anamnesis, video-taped oesophagus-stomach Rx and manometric and 24 hours pHmetric evaluation. No patient showed GERD symptoms or pathologies. The protocol was repeated after the logopedic treatment, generally one year after the surgical intervention. Of the patients investigated: 26 (34.7%) reported GERD symptoms, 12 (16%) dysphagia, 2 (2.6%) presented hiatal, 17 (22.7%) abnormal sliding of abdominal oesophagus, 22 (29.3%) acid pathologic GER at the pHmetry, 37 (49.3%) alterations of esophageal motility. All patients were considered "good speakers" referring to the quality of the esophageal voice. The patients were given Omeprazole 20 mg/die and Cisapride 10 mg 4 times a day for an average period of 8 weeks. GERD symptoms were significantly decreased by this therapy in 24 pts. The result of our study showed a certain incidence of GERD and alterations of esophageal motility following the speech therapy and suggested that a therapy of prokinetics can be useful during logopedic treatment in order to avoid esophageal diseases. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux }

"Esophageal Functional Evaluation of Laryngectomees Rehabilitated with Esophageal Voice"

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## "P P 1 0021" P 1 0021 **Comparison of Double Neoplasms of Oesophagus and Head and Neck: Metachronous Versus Synchronous**

\*J.P. Metges, O. Sparfel, M.A. Giroux, J.P. Malhaire, J.A. J'e9z'e9quel, J.P. Labat, H. Gou'e9rou

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Head and neck neoplasms and oesophageal neoplasms have the same risk factors. They can occur in the same patient. The purpose of this study was to compare our series of metachronous and synchronous neoplasms. *Patients and Methods:* Between 1989 and 1995, 669 oesophageal neoplasms and 569 head (H) and neck (N) cancers have been treated in our institution. Forty-eight patients had a double localization: 25 were synchronous (group I) and 23 metachronous (group II). We have compared clinical features, TNM classification, strategies of treatment, survey. *Results:* The mean age was not significantly different between the two groups: 60 yrs (group I) and 58.21 yrs (group II). In both groups, patients had alcohol and tobacco abuse. In the group I, the first localization found was oesophagus (n = 19) and H and N (n = 6). In the group II, the first localization was H and N (n = 21), oesophagus (n = 2). The oesophageal localization was principally middle third (n = 14) for the group I and upper third (n = 11) for the group II. The H and N localization was principally oropharyngeal (n = 14) in group I and oropharyngeal or hypopharyngeal (n = 14) in group II. The treatment in the group I was radio-chemotherapy (n = 19) with 14 complete responses. Radiotherapy and surgery (n = 11) for head and neck cancers and radio-chemotherapy (n = 15) for oesophageal neoplasms were the principal strategy of treatment in the group II with only 9 complete responses. The major problem was the field of radiotherapy. The survey was 16.85 months in group I and 18 months after the second neoplasm in the group II. *Conclusion:* Oesophagus is the first site found in case of synchronous neoplasm, and head and neck cancers in case of metachronous neoplasm. Main difficulties were the field of radiotherapy in the group I and few possibility of surgery in the group II. Oncology, specific: Oesophagus Oncology, general: Therapy }" "Comparison of Double Neoplasms of Oesophagus and Head and Neck: Metachronous Versus Synchronous"

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"P P 1 0024" P 1 0024 **Perioperative Immunotherapy with Recombinant Granulocyte-Colony Stimulating Factor (rhG-CSF) in Patients Undergoing Surgery for Esophageal Cancer** H. Sch<sup>1</sup>, K. H<sup>2</sup>, V. Diehl<sup>2</sup>, H. Pichlmaier<sup>1</sup>, A. Engert<sup>2</sup>

<sup>1</sup> Department of Surgery, University of Cologne, Germany

<sup>2</sup> I Department of Internal Medicine, University of Cologne, Germany Neutrophilic granulocytes play an important role in host defense mechanisms, including those of microbicide, inflammation and wound healing. We investigated the effects of rh-GCSF (Filgrastim) on the function of neutrophils and the high infection rate in patients undergoing surgery of esophageal cancer. Here we report our results of the first 14 patients. There were 8 males and 6 females. The mean age was 60 years (range 49–75). All patients received 300 µg/d (< 75 kg) or 480 µg/d (> 75 kg) of Filgrastim s.c., starting on day -2 before surgery until day 7 after surgery. Application stopped when leucocytes increased above 50 000/µl. The treatment was well tolerated. One patient was found with low grade wound healing disorder; no other complications or infections were observed. To evaluate the effect of G-CSF on neutrophil function, we measured the percent of neutrophils with phagocytosis and the oxidative burst on day -2, 2 and 10. 10 patients undergoing major surgery served as controls. Phagocytosis increased in the study group (day 2: IgG-beads: +30% – 29%, Albumin-beads: +22% – 47%; day 10: IgG-beads: +9% – 47%, Albumin-beads: +28% – 82%) and decreased in the control group (day 2: IgG-beads: -1 – 35%, Albumin-beads: -1 – 19%; day 10: IgG-beads: -1% – 18, Albumin-beads: -18% – 27%). The microbicidal activity as measured by the oxidative burst was substantially higher in the G-CSF-treated study group (day 2: +219% – 167%, day 10: -37% – 77%) as compared with the control group (day 2: -11% – 55, day 10: -46% – 46%). In conclusion, perioperative immunotherapy using G-CSF to stimulate neutrophil function in patients with esophageal cancer might be effective to prevent infection after surgery. Enrollement is continuing. Immunology and microbiology: Inflammation } " Perioperative Immunotherapy with Recombinant Granulocyte-Colony Stimulating Factor (rhG-CSF) in Patients Undergoing Surgery for Esophageal Cancer"

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## "P P 1 0025" P 1 0025 **Retrospective Analysis of Treatment of 640 Patients with Esophageal Squamous-Cell Cancer**

\*V.A. Chernishov, E.I. Sigal

Clinical Cancer Centre, Kazan, Russia The aim was to study the immediate results of surgical and combined treatment in esophageal cancer. In 1980–1994 640 patients (523 males and 117 females) aged 46–70 years (1/3 being of 60 years and older) were treated in the centre. Superior esophageal cancer was in 33 patients, midesophageal-in 406, inferior-in 201 patients. There were 6 cases of stage I, 226-of stage IIa, 30-of stage IIb, 164-of stage III, 214-of stage IV. We have performed esophagectomy in 393 cases with 48 cases of palliative character. Resectability was 61.4%. 376 patients underwent only surgical treatment, 264-combined treatment with preoperative radiotherapy. Resectability was 56.9% and 67.8%, respectively. Esophagectomy by Torek (without primary esophagoplasty) was performed in 36 patients, with one-stage esophagoplasty through the laparothoracotomic access along with cervicotomy in 231 patients, with one-stage esophagoplasty through the transchylathalic access in 158 patients. Patients underwent esophagoplasty were 301 (using gastric tube), 63 (using solid stomach), 4 (large intestine) and 2 (small intestine). Transplant was performed postromediastinally, presternally and retrosternally in 198, 167 and 2 cases, respectively. One-stage anastomosis was fulfilled in 257 patients, long-term anastomosis in 110 patients. Esophagectomy operative mortality was 14%. Postoperative morbidity was 43%. Among the postoperative complications: pneumonia and pleuritis (17%), mediastinitis (7%), peritonitis (3%). 78 patients had cervical anastomosis failure with most cases of presternal transplant. No postoperative complication dependance upon preoperative radiotherapy was observed. The main mortality reasons were pneumonia (60%) and mediastinitis (25%) irrespective of the type of treatment. So esophageal cancer resectability increases by 10% in patients with combined treatment with no increase of postoperative complications and mortality. Oncology, general: Therapy Oncology, specific: Oesophagus }  
"Retrospective Analysis of Treatment of 640 Patients with Esophageal Squamous-Cell Cancer"

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## "P P 1 0026" P 1 0026 Tissue Polypeptide Specific Antigen in Esophageal Cancer

\*R. Pinto, Ferra M. Am\`elia, P. Fidalgo, A. Oliveira, Leit\`e3o C. Nobre, Mira F. Costa

Servi\`e7o de Gastrenterologia, Instituto Portugu\`eas de Oncologia Francisco Gentil, Lisbon, Portugal Tissue Polypeptide Specific antigen (TPS) is a tumor associated antigen which reflects more accurately cell proliferation than tumor mass. It's clinical use has been studied in several carcinomas, with promising results. *Aim:* This study was undertaken to investigate the importance of TPS in the diagnosis and in the prognosis of the squamous cell carcinoma of the esophagus (SCE). *Methods.* Eighty two patients with SCE were included from 1989 to 1994. Staging was based upon the histopathological analysis of the resected tumors (when resection had been possible), thoracic and abdominal CT scan, echoendoscopy and/or bronchoscopy. Blood samples were collected in the time of diagnosis. TPS was determined by an "in vitro" monoclonal radioimmunoassay; the value of 70 U/L was considered the upper limit of normal. For statistical analysis of data, ANOVA and the proportional hazards survival model were used. *Results.* Seventy three patients (89.0%) were male; mean age was 61.6 – 10.3 years (40–88). In only 24 patients (29.3%) had it been possible to undertake surgical resection. Forty four patients (53.7%) were dead, 28 (34.1%) alive and 10 (12.2%) were lost after a median follow-up of 4.5 months (range: 0–41); 22 (26.8%) were stage II, 36 (43.9%) stage III and 24 (29.3%) stage IV. TPS values were above normal in 34 patients (41.5%). TPS correlated positively with stage ( $p < 0.001$ ) and inversely with survival ( $p < 0.002$ ), the hazard ratio for patients with a TPS value above 70 U/L being 2.7 (95% CI: 1.4–5.1). After controlling for surgical resectability, TPS kept it's independent prognostic significance. *Conclusions.* 1) TPS has little diagnostic accuracy in SCE. 2) TPS values correlated with stage and showed promising prognostic meaning in SCE. This research was funded in part by Beki Diagnostics AB, Bromma, Sweden. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Oesophagus } "Tissue Polypeptide Specific Antigen in Esophageal Cancer"

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"P P 1 0027" P 1 0027 **Multiple Primary Malignancies and Oesophageal Cancer**

\*H. Lombaviana, A. Correia, R. Silva, L. Dias, R. Lombaviana

Dept. of Gastroenterology, Oncology Portuguese Institute, Oporto, Portugal  
The association between multiple primary malignancies, synchronous (s) or metachronous (m) is an interesting subject in Oncology. With the aim of detecting any association between the oesophageal cancer and other malignancies, the authors made a retrospective study in 407 patients, in which oesophageal cancer was diagnosed between July 1974 and December 1995. Among these 407 patients, 20 (4.9%) had at least one other cancer associated. Sixteen patients (80%) presented metachronous malignancies and four (20%) synchronous ones. Fourteen patients (70%) were male, with an average age of 66.1 years old, and six (30%) were female with an average age of 69.6 years old. The oesophageal cancer was associated to another malignancy in 18 cases and with two other cancers in 2 cases. The time interval between the diagnostic of the metachronous primary malignancies ranged from 6 months to 27 years, with an average of 5.6 years. The follow up after the diagnostic of the oesophageal cancer ranged from 1 to 84 months, with an average of 15.7 months. The mortality at the end of the first year was 60% (12 patients) and at the end of the third year was 95% (19 patients). *Conclusions:* 1 – the occurrence of multiple primary malignancies in patients with oesophageal cancer was 4.9%; 2 – high incidence in male; 3 – higher incidence of metachronous malignancies than synchronous ones; 4 – more active association between the oesophageal cancer and others of the head and neck (50%); 5 – reduced time of follow up (15.7 months) of the patients with oesophageal cancer; 6 – very high mortality (95%). Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Oesophagus }  
"Multiple Primary Malignancies and Oesophageal Cancer"

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"P P 1 0032" P 1 0032 **Implantation of Nitinol Self-Expanding Stents for Palliation of Esophageal Malignant Stricture**

\*G. Piccinni, A. Lippolis, M. Lospalluti, A. Scardigno, O. Caputi Iambrenghi Three years' experience in positioning nitinol self-expanding-stent to restore swallowing and improve the quality of life in patients affected by esophageal malignant strictures is reported. In the period 1993–95 eleven patients were treated: five affected by non-resectable lung cancer, four by esophageal cancer and two for cancer of the cardia. All patients had a 3 or 4 grade dysphagia. We always used ULTRAFLEX stents (MICROVASIVE-Boston Scientific Corp. Watertown MA). In the last two patients we positioned a coated self-expanding stent of the same type. The stents were perorally implanted after mild sedation and under combined endoscopic and fluoroscopic guidance; when necessary previous balloon dilation was performed. To evaluate the success of palliation the Grading system of Dysphagia (DG) and Quality of Life Index (QLI) were used. All endoprostheses expanded at a diameter of 14–20 mm. within 24 hrs. and an immediate improvement of dysphagia was achieved (a DG score reduction was observed). One patient died for cardiorespiratory failure 3 days after stenting. The average follow-up of the surviving ten pts. was 97 days (range 30–360): the QLI varied from 5 to 9 with an improvement of nutritional parameters (Lymphocyte count, Albumin, Cholinesterase and Weight). Three pts. presented an episode of stent-obstruction within 3 months; in two cases the obstruction was caused by cancer ingrowth, in the third by food impaction. All were treated endoscopically. The application of Nitinol Self-Expanding Stents, seems to offer safe, fast and effective palliation of malignant dysphagia. Oncology, general: Therapy Oncology, specific: Oesophagus Endoscopy, general: Instrumentation, therapy } "Implantation of Nitinol Self-Expanding Stents for Palliation of Esophageal Malignant Stricture"

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## "P P 1 0035" P 1 0035 Argon Plasma Coagulation in Palliative Treatment of Malignant Dysphagia

\*W. Niezychowski, J. Regula, J. Fijuth, K. Przytulski, E. Butruk

Department of Gastroenterology and Department of Brachytherapy, Institute of Oncology, Warsaw, Poland

**Aim of study** Argon plasma coagulation is a new method of non-contact destruction of tissues by means of argon gas. Argon applicator can be introduced through the biopsy channel of the standard endoscope. The aim of this study was to evaluate the efficacy and safety of this technique in palliative treatment of malignant dysphagia.

**Methods** 23 patients (19 M, 4 F, age 45–85) with oesophageal malignancy (13 adenocarcinoma, 10 squamous-cell carcinomas) not suitable for radical treatment were followed prospectively. Five of them presented with dysphagia causing inability to swallow some solids (grade I), six could swallow semisolids (grade II) and eleven swallowed liquids only (grade III). One patient declared aphagia. Argon plasma coagulation was applied in several sessions every 2–3 days. Seven patients had oesophageal dilation with Savary-Gilliard bougies up to 13 mm prior to coagulation.

**Results** Complete remission of dysphagia as a result of treatment was achieved in 17 patients. Five other patients had improvement in swallowing (one grade at least). These results were achieved after 1 to 6 sessions of argon plasma coagulation. In one patient treatment had to be terminated because tracheo-oesophageal fistula had occurred. The perforation in the tumour region was observed 7 days after treatment in another patient. No other complications were encountered.

**Conclusion** Argon plasma coagulation appeared to be an effective method in palliative treatment of oesophageal malignant stenoses. Although argon beamer causes only 2–3 mm deep tissue damage, the procedure may be complicated by tracheo-oesophageal fistula formation or delayed perforation in the region of the tumour.

Endoscopy, general: Instrumentation, therapy  
Oncology, specific: Oesophagus  
Endoscopy, specific: Oesophagus }

"Argon Plasma Coagulation in Palliative Treatment of Malignant Dysphagia"

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"P P 1 0036" P 1 0036 **Small Cell Carcinoma of the Oesophagus: a Ten-Year Experience 1986–1996**

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Departments of Gastroenterology

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Extrapulmonary small cell carcinoma is becoming more recognised. Small cell carcinoma of the oesophagus (SCCO) is rare and distinct from the squamous cell or adenocarcinoma variety. No more than 200 cases of SCCO have hitherto been reported. We present data on 6 cases of SCCO accounting for 1.84% (6/326) of all primary oesophageal carcinomas seen during a ten year period (1986–1996). Mean age at presentation was 65.3 years (range 49–76) with an equal sex ratio. All patients presented with dysphagia and weight loss while three described odynophagia. Mean time between onset of symptoms and presentation was 15.2 weeks (range 6–24). Putative risk factors include heavy cigarette smoking in 5/6 and previous radiotherapy in 1 patient. The diagnosis of SCCO was made histologically with a primary pulmonary tumor excluded on the basis of a negative CT thorax. 4/6 tumours were located at the lower third of the oesophagus. The tumours took the form of an ulcerated stricture (n = 4) and sessile polyps (n = 2). All but one patient had metastatic disease at presentation. Five were treated with single (VP16) or combination (VAC) chemotherapy. Two underwent palliative endoprosthesis insertion, one receive adjuvant radiotherapy while another had undergone an oesophagectomy at the referring hospital. Overall survival was 7.27 months (range 10 days to 17 months) with only one patient alive at 6 months without metastatic disease.

*Conclusion.* Histology of oesophageal lesions showing small cell carcinoma does not imply pulmonary invasion. SCCO presents late and its natural history and prognosis resemble those of its pulmonary counterpart. Chemotherapy and endoscopic palliation may be beneficial. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux

Oncology, specific: Oesophagus } "Small Cell Carcinoma of the Oesophagus: a Ten-Year Experience 1986–1996"

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"P P 1 0037" P 1 0037 **Conservative Treatment of Oesophageal Perforations after Endoscopic Palliation in Advanced Oesophageal Cancer**

\*T. Bisgaard, M. W\8jdemann, H. Heindorff, L.B. Svendsen

Dept. of Surgical Gastroenterology, Rigshospitalet, Copenhagen, Denmark *Purpose:* The aim of the study was to evaluate the effect of conservative treatment of oesophageal perforations due to endoscopic palliation in patients with unresectable oesophageal or cardiac cancer. *Methods:* From January 1993 to January 1996, 148 consecutive patients with advanced oesophageal or cardiac cancer were subjected to a total of 686 palliation procedures (argon plasma electrocoagulation, Nd:YAG laser photocoagulation, dilatation, intubation and stenting procedures). When palliation-related perforations were diagnosed, patients received conservative treatment: Broad spectrum antibiotics, fasting and nasogastric suction. Pneumothorax or pleural effusions were drained. Stenting or intubation was also regarded as conservative treatment. *Results:* Perforations were seen in 9 patients (6%) corresponding to 1% of palliation procedures. The mean time lap between perforation and treatment was 30 hours (1–56 hours). Conservative treatment succeeded in 6/8 patients (75%) and the perforation-related mortality after conservative treatment was 1/8 (13%). One patient died without further treatment due to age and poor general condition prior to palliation. Two patients did not respond to the conservative treatment (1 patient developed a tracheoesophageal fistula and 1 patient developed pleural empyema, and decortication with drainage was performed). *Conclusions:* Conservative treatment of oesophageal perforations seems sufficient in selected patients with advanced oesophageal or cardiac cancer. Clinical practice: Management strategy Oncology, specific: Oesophagus Endoscopy, general: Complications } "Conservative Treatment of Oesophageal Perforations after Endoscopic Palliation in Advanced Oesophageal Cancer"

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## "P P 1 0040" P 1 0040 **Preoperative Nutritional Status in Esophageal and Gastric Cardia Surgery**

\*Z. Jankovic, Z. Gerzic, P. Pesko, T. Randjelovic, J. Knezevic, M. Popovic

Institute of digestive disease, Clinical center of Serbia, Belgrade, Yugoslavia Using several clinical and antropometric parameters in pts who underwent different oesophageal and gastric cardia surgery: transthoracic oesophagectomy (TT), transhiatal oesophagectomy (TH), coloplasty in benign oesophageal disease (C), total gastrectomy (G), we wanted to assess preoperative nutritional status and its correlation with postoperative pulmonary complications. On table 1 we can see antropometric and nutritional parameters in four groups of pts: Parameter TT (45 pts) TH (41 pts) C (42 pts) G (82 pts) Weight 61.0 – 10.5 59.6 – 12.4 56.1 – 13.6 66.3 – 13.2 Height 168.9 – 8.4 165.8 – 9.1 164.0 – 10.1 170.0 – 8.2 Weight loss 9 – 5.3 11.7 – 11.2 10.8 – 9.1 11.8 – 9.8% w. loss 14.7 19.5 19.4 17.9 MAC 25.5 – 3.6 23.8 – 3 24.5 – 2.9 26.8 – 3.2 TSF 7.1 – 2.7 8.9 – 3.9 8.4 – 4.4 10.8 – 4.8 According to Blookburn classification and MAC and TSF values pts from all groups were severely malnourished. There were no significant difference between groups in any parameter measured (ANOVA,  $p > 0.05$ ), although pts from C group had benign oesophageal narrowing. The incidence of pulmonary complications was 37.7%, 53.6%, 21.4% and 23.1% respectively. Lack of the influence of parameters measuring nutritional state on the incidence of pulmonary complications is the consequence of multifactorial influence on their occurrence. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Nutrition: Techniques of nutrition Oncology, specific: Oesophagus } "Preoperative Nutritional Status in Esophageal and Gastric Cardia Surgery"

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"P P 1 0042" P 1 0042 **Preoperative Chemotherapy and Concurrent Irradiation for Localized Esophageal Carcinoma: Results of a Phase II Study**

\*M. Ychou, P. Senesse, C. Debrigode, P. Rouanet, F. Quenet, S. Salas, B. Saint Aubert, C. Astre, J.B. Dubois

C.R.L.C. Val d'Aurelle- Montpellier- France *Purpose.* A prospective phase II study to determine the outcome of patients (pts) with oesophageal cancer who receive preoperative chemoradiotherapy. *Patients and methods.* Between January 1992 and October 1994, 46 pts, with localized esophageal carcinoma were treated with chemotherapy and concurrent external beam irradiation followed by esophagectomy. Each patient received two courses of chemoradiotherapy on day 1 to 5 and on day 21 to 25. Chemotherapy consisted of leucovorin 200 mg/m<sup>2</sup>/d followed by 5 FU 400 mg/m<sup>2</sup>/d in one hour infusion and Cisplatinum 70 mg/m<sup>2</sup> on day 2. Irradiation was delivered one hour after 5 FU, at 3 Gy per fraction for a total dose of 30 Gy. Twenty three pts had lesions measuring 5 cm or less, 20 had lesions measuring more than 5 cm and data was unknown in 3 cases. Thirty two pts had squamous cell carcinoma and 14 had adenocarcinoma. *Results.* Forty three pts underwent surgical procedure (2 pts died during chemoradiotherapy and 1 became metastatic), 32 had a complete resection and 18% of these pts had no or minimal residual tumor. Post operative mortality rate was 11.6%. The median survival and the 2 years survival were respectively 21 months and 45% for all pts and 44 months and 66% for resected pts. The disease-free survival for the 32 resected pts was 28 months. In the univariate analysis, 3 factors are statistically correlated with a better survival: weight loss less than 10% (p = 0.005), complete tumoral resection (p < 0.001) and complete or major pathologic response (p = 0.001). *Conclusion.* This multimodality treatment for oesophageal carcinoma seems to be efficient in well selected patients but needs further comparative studies. Oncology, specific: Oesophagus Clinical practice: Management strategy Oncology, general: Therapy } "Preoperative Chemotherapy and Concurrent Irradiation for Localized Esophageal Carcinoma: Results of a Phase II Study"

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"P P 1 0043" P 1 0043 **Severe Radiation-Related Pericarditis after Postoperative Concomitant Radio-Chemotherapy for Esophageal Cancer**

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Local failures and metastases are often observed in esophageal cancer and this has induced a great interest for a multimodality approach including radio and chemotherapy. We report a dramatic pericardic complication in order to point out the importance of the dose fractionation and the schedule of the therapeutic sequences. Between March 1983 to December 1993, two phase II studies were performed and forty consecutive patients were included after curative resection. 20 patients (Gr 1) received a split course radiotherapy using a daily dose of 4 Gy on day 1 to day 5 for two cycles. D1 to D1 was 21 days (total dose 40 Gy) and chemotherapy on D1 was cisplatin 100 mg/m<sup>2</sup> IV for 6 cycles. D1 to D1 was 21 days and 2 cycles were concomitant to radiation therapy. 20 patients (Gr 2) received a split course radiotherapy using a daily dose of 2 Gy on day 1 to day 12 of two cycles. D1 to D1 was 28 days (total dose 40 Gy) and chemotherapy cisplatin 75 mg/m<sup>2</sup> on D1 and 5FU 750 mg/m<sup>2</sup> in continuous infusion D1 to D5. Six cycles were performed D1 to D1 = 28 days. The 2 first were concomitant of radiotherapy. Both groups were similar for age, sex distribution, weight loss, serum albumin rate, location of tumor and pathologic findings according to UICC 1987. The median survival was 19 months in group 1 and 18.3 in Gr 2. 6 cases of tamponnade were observed, all in group 1, with a mean time between irradiation and occurrence of ten months (range 6–14). All patients need pericardial evacuated punction in emergency because of hemodynamic failure, and 5 patients underwent a partial pericardectomy. All patients developed pleural effusion. No case of clinical pericarditis was detected in Gr 2 (p < 0.02). We conclude that a split course radiation using a daily dose of 4 Gy is not be used after surgery. If combined therapy is performed it could take place either before surgery with this regimen (Gignoux Ann Chir 1987) or in the postoperative period, but at a lower daily dose.

Oncology, specific: Oesophagus  
Oncology, general: Therapy  
Radiology and ultrasound: Therapy  
}" "Severe Radiation-Related Pericarditis after Postoperative Concomitant Radio-Chemotherapy for Esophageal Cancer"

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**"P P 1 0046" P 1 0046 Clinical, Endoscopic & Pathologic Features of 416 Pts with Esophageal Cancer from Iran H. Froutan Pishbijari, R. Rabiee, G.A. Amirian Mojarad**

Endoscopy Unit, Imam Khomeiny Hospital Tehran, Iran We reviewed the clinical, endoscopic & pathologic findings of 416 Pts with esophageal CA (285 Pts from Tehran & 131 Pts from Sistan Province, south east IRAN). There were 232 (56%) Males & 183 (44%) Female Pts. with a mean age of 57.2 Yrs. (Range 28–81 Yrs), 67% of Pts were in their 5th & 7th decades. Clinically, the most common presenting feature was dysphagia observed in 93% of Pts. with a mean duration of 4 Mths. Anemia (HB < 11 gr/dl) was present only in 20% of Pts. Endoscopically 8.3% of tumors were on upper third, 47.5% on middle third & 44.1% were in lower third of esophagus. Pathologically 84.4% of tumors were adenocarcinoma & 15.6% were S.C.C. 94% of tumors in upper third, 91% in middle third & 75.5% of lower third of esophagus were adenocarcinomas with the remainder being S.C.C. 61% of adenocarcinoma Pts were Males & 39% Females with a mean age of 56 Yrs. 55% of SCC Pts were Males & 45% Females with a mean age of 56.8 Yrs. The adenocarcinoma Pts in Sistan province (Southeast IRAN) Were on average 5 Yrs younger than Pts in Tehran. The SSC Pts. were also 2 Yrs younger than Tehran Pts. } "Clinical, Endoscopic & Pathologic Features of 416 Pts with Esophageal Cancer from Iran"

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"P P 2 0047" P 2 0047 **Histological Features of Chronic Hepatitis C and HCV Genotype: Correlation with Biochemical Data and Knodell Index**

\*A. Coutinho, C. Baptista, R. Albuquerque, A. Figueiredo, C. Machado, B. Rodrigues, M. Ramos, A. Mouro, W. Ferreira, M. Quina

S. Medicina III, S. Anat. Patol\ 'f3gica, H. Pulido Valente Dep. Microbiologia-FCML, Lisboa, Portugal *Purpose:* to study the relation of characteristic histological features of chronic hepatitis C, with HCV genotypes, their eventual correlation with ALT and GGT values, and Knodell Index. *Methods:* the study includes a group of 40 patients (24 M, 16 F; mean age: 44.0 – 15.5 years) with the diagnosis of chronic hepatitis C, confirmed by serological tests (RIBAIII-Chiron), presence of RNA-VHC (PCR-Amplicore) and liver biopsy. Epidemiological inquiry revealed prior history of transfusion (27.5%), IV drug use (30%), and sporadic hepatitis (42.5%). HCV genotype was determined with a line-probe assay (LiPA-Innogenetics), in accordance with Simmonds classification. *Results:* HCV genotype distribution in this patient group was similar to the usually observed in the portuguese population: 1a–22.5%; 1b–45%; 2a–2.5%; 3a–12.5%; mixed infection (all with 1b)–17.5%. Conventional histological diagnosis revealed: Ch. persist. H-15%; Ch. lobular H.-5%; Ch. active H.-57.5%; liver cirrhosis-22.5%. HCV morphological features were observed as follows: lymphoid aggregates (LA)-62.5%; acidophil bodies (AB)-67.5%; perisinusoidal lymphocytes (PL)-20%; bile duct lesions (BDL)-55%; steatosis (STE)-45%. Genotype 1b was more prevalent in the presence of LA and PL and also, more often associated with the absence of BDL and STE (SS- Chi-sq). However, the higher proportion of liver cirrhosis in the genotype 1b patients (27.8%), could have biased the latter data, for loss of typical HCV features due to architectural distortion. A significant correlation between ALT and BDL score was found (linear regression:  $r = 0.397$ ;  $p = 0.001$ ); there was no correlation between any of the 5 specific features and Knodell Index and its subscores (inflammation; fibrosis). *Conclusions:* HCV genotype association with the rate of disease progression, suggested by the higher rate of liver cirrhosis in 1 b patients, may be related to different prevalence of specific morphological lesions, namely lymphoid aggregates. Liver and bile ducts, 1: Hepatitis viral, diagnosis }" "Histological Features of Chronic Hepatitis C and HCV Genotype: Correlation with Biochemical Data and Knodell Index"

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"P P 2 0048" P 2 0048 **Hepatitis C and Rheumatic Diseases**

\*P. Peixe<sup>1</sup>, M. Parente, J. Vaz Pato, H. Madeira, M. Micaelo, H. Santos, M. Marques Silva, A. Vilar, G. Peixe<sup>1</sup>

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<sup>1</sup> Department of Gastroenterology, Hospital Egas Moniz, Lisbon, Portugal  
Hepatitis C infection may induce several immune alterations including rheumatoid factor and type II cryoglobulinemia production. The purpose of our study is to find the prevalence of HCV in a miscellaneous of rheumatic diseases and detect a pattern to suspect the virus presence in this population. *Methods:* We performed a longitudinal study in 279 patients, aged 53.7 – 15.3 years followed at a rheumatology outpatients clinic, regarding ALT, AST, Alkaline Ph, { g}GT, leukocyte count, anti-nuclear antibody (ANA), rheumatoid factor (RF), HCV determination by ELISA (3<sup>rd</sup> gen.) and RNA by PCR. An hepatic biopsy was performed in patients RNA+. We considered 5 major groups of rheumatic diseases: osteoarthritis (n = 43), fibromyalgia (n = 30), Rheumatoid arthritis (n = 61), Sjögren's Syndrome (n = 27), miscellaneous (misc) not belonging to any of the previous groups (n = 118). *Results:* OA (43) Fibrom (30) pSS (27) RA (61) Misc (118) Total (279) HCV (Elisa) 2.3% 3.3% (1) 11.1% (3) 9.8% (6) 16.1% (19) 9.7% (27) RNA (PCR) 2.3% 3.3% 0% 8.2% (5) 8.5% (10) 6.5% (18) RF+ ANA > 1/160 RNA+ in "Misc. Group" (10/118) 80% (8) 40% (4) *Conclusions:* We found a higher prevalence of HCV in a heterogeneous group of 118 patients (16.1%), associated frequently with immunological alterations: Mixed Cryoglobulinemia (3), Cutaneous vasculitis (3), Weber-Christian Disease (1), Peripheral neuropathy (1), Primary Biliar Cirrhosis with Sjögren S. (1), Oligoarthritis (2), MCTD (1), SLE (1), Carpal syndrome (1), Poliarthralgias (1), osteoporosis and tendinitis (3). } "Hepatitis C and Rheumatic Diseases"

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"P P 2 0049" P 2 0049 **Prevalence of a Positive Pathergy Test in Patients with Chronic HCV Infection**. O. Uzunlimoglu, H. Cetinkaya, H. Bozkaya, C. Yurdaydin, H. Erverdi, A. Gurler, S. Cagsin, S. Karayalcin

Ankara University, School of Medicine, Division of Gastroenterology, Ankara, Turkey

**Background:** Chronic HCV infection has been found to be associated with several extrahepatic diseases including mixed cryoglobulinemia, Sjogren syndrome, and Behcet's disease all of which are characterized by vasculitis. Positive pathergy test, a cutaneous hyperreactivity reaction characterized by vasculitis, is detected in 60–92.5% of patients (pts) with Behcet's disease while only 1% of normal population and 1.5% of disease controls including chronic liver disease have positive reaction in Turkey. **Aim:** To evaluate the prevalence of positive skin pathergy test in pts with chronic HCV infection. **Patients and Methods:** Sixty pts, 32 female, 28 male, mean age 50.5 yr, 48 with chronic hepatitis, 11 with cirrhosis and 3 with chronic hepatitis + cirrhosis were studied. HCV infection was diagnosed by using both anti-HCV (ELISA) and HCV RNA (PCR) determinations. None of the pts had co-existing Behcet's disease. Pathergy test was performed by intradermal injection of 0.1 ml sterile saline in five different locations and a positive result was defined as occurrence of erythema, papule and pustule at the injection site 48–72 hrs after the injection. **Results:** Eleven of 60 pts (18%) had a positive skin pathergy test. This ratio was significantly higher compared to those seen in normal (1%) and disease controls including liver diseases (1.5%) in Turkey. Light microscopy showed a vasculitis in 9 of 11 pts (82%). Cryoglobulinemia was found in only 4 of 60 pts (6.6%) and 1 of 11 pts (9%) with a positive pathergy reaction had cryoglobulinemia. **Conclusion:** A positive pathergy test is more frequently seen in patients with chronic HCV infection compared to normal and disease controls and may represent an extrahepatic phenomenon associated with HCV infection. Further studies are ongoing to determine the immunohistological characteristics of the pathergy reaction in this group of patients. Liver and bile ducts, 1: Hepatitis viral, diagnosis }" "Prevalence of a Positive Pathergy Test in Patients with Chronic HCV Infection"

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## "P P 2 0050" P 2 0050 **Infants and Neonates Screening for Hepatitis C Virus Infection**

\*Abou EL Magd Enas, EL Rashidi Zeinab, Saad Eldin Kouka, Khalifa Ahmed, Nabawy Zekry Abdel Rahman

Faculty of Medicine for Girls, Al-Azhar University, Cairo Egypt  
The aim of this study was to screen infants borne to anti-HCV seropositive and seronegative mothers for evidence of HCV markers. Symptoms free 61 mother infants pairs were classified into 4 groups according to infant's age. Blood samples were taken from all mothers and infants. Saliva samples was collected from all infants. Collective and specific (core, NS3, NS4 and NS5) IgG anti HCV antibodies, IgA and IgM anti HCV antibodies by ELISA test, HCV RNA by RT. PCR and HCV antigen in lymphocyte Lysate by Dot ELISA test were done. Eight out of 61 (13.1%) of mothers were seropositive for collective IgG anti HCV antibodies, 5 of them were seropositive for IgG anti-core and NS3, 4 of them were seropositive for IgG anti NS4 and only one was seropositive for IgG anti NS5. 5 mothers were seropositive for IgG anti-core, NS3 and HCV RNA. Only 4 had infants who were seropositive for IgG anti HCV core and NS3 but only 3 were seropositive for IgG anti NS4 and only one was Seropositive for IgG anti HCV (NS5). HCV RNA were detected in 2 out of 4 IgG anti HCV seropositive infants. The same 2 infants were also positive for HCV Ag in Lymphocyte Lysate, but only one was positive for salivary IgA anti-HCV. All seronegative mothers and infants for IgG anti-HCV were also negative for HCV RNA and other markers tested. In conclusion mother to infants transmission of HCV does exist. Clinical practice: Epidemiology (non cancer) Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Infants and Neonates Screening for Hepatitis C Virus Infection"

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"P P 2 0051" P 2 0051 **Hepatitis C Virus Infection among Medical Personnel**

\*El Sherif Ahmas, El Sherif Assem, Saad Eldin Kouka, Aal Maged Abdel, El Shinnawy Gamal

Faculty of Medicine, Al Azhar University, Cairo, Egypt The aim of the present work was to study the prevalence of HCV seromarkers indicative of past or current infection of medical personnel as a high risk group. This study was carried out on 202 volunteer medical and paramedical staff members working in different hospitals and medical institutes. Sera were collected and tested serologically for HCV-antibodies using 3rd generation ELISA Technique and the positive cases were subjected to PCR test, liver function tests, HBsAg and abdominal ultrasonography. Saliva samples were also obtained and examined for anti-HCV. The results revealed that anti-HCV was detected in 13.86% of the medical personnel while only 4.95% of them showed positive PCR reaction indicative of viraemia. A significant increase in the frequency of anti-HCV was noticed with increasing age and duration of employment. A positive correlation was also found between the serum level of anti-HCV (optical Density Level) and the presence of anti-HCV antibodies in saliva. From this study, it is obvious that frequent contact with blood, blood products and body secretions during health care practice carries a definite risk of HCV transmission as high frequency of HCV seropositivity was found among laboratory personnel. Clinical practice: Epidemiology (non cancer) Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Hepatitis C Virus Infection among Medical Personnel"

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## "P P 2 0052" P 2 0052 **HCV Genotypes in French Haemophiliacs: Kinetic and Reappraisal of Mixed Infections**

\*R. Tuveri, C. Rothschild<sup>2</sup>, S. Pol<sup>3</sup>, T. Persico<sup>4</sup>, C. Gazengel<sup>2</sup>, C. Bréchet, V. Thiers<sup>1</sup>

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<sup>5</sup> Dept. Obstetric and Gynecology U of Milan Italy

**Aims:** The aims of this study were to investigate the distribution and kinetic HCV genotypes and prevalence and molecular bases of mixed infections, among haemophiliacs repeatedly exposed to non-virus inactivated clotting factor. **Patients and methods:** We analysed 45 patients with A or B haemophilia or Von Willebrand's disease (37, 7, 1 respectively). All were anti-HCV positive, 21/45 also anti HIV1 positive. For evaluation of HCV genotype dynamics, serum samples from 36 haemophiliacs were genotyped two times with a mean of 98.3 months follow up (min = 56–max = 171). We analysed the HCV genotype in the core and 5' untranslated regions by means of modified core method and InnoLiPA assays, respectively. Serotyping assay based on the detection of type specific NS4 antibodies was performed for 43 patients. **Results** 1) *HCV genotype prevalence:* We revealed genotypes 1 (n = 23: 51%, 1a n = 10: 22%, 1b n = 13: 28%); 2 (n = 10: 22%, 2a n = 3, 2b n = 4 2NC n = 3), and 3a (n = 10: 22%). 2) *"Mixed infections"*: Genotyping in 5'UTR revealed 2/8 mixed infections (1a + 1b and 2nc + 3a). Our core modified method showed 8/45 mixed infections: 6/8 1a + 1b and 2/8 3 + 2. By designing new primers more specific to HCV types 1a and 1b we could confirm such 1a + 1b mixed infection in only 1/6 cases. This result was also confirmed by direct sequencing. 3) *Evolution upon time:* Only 5/33 haemophiliacs showed a change of genotype during follow-up: 2 from 1a to 1b, 1 from 1b to 1a, 1 from 1a to 2a and 1 from 1b to 3a. 4) *Serotyping:* Seventeen of 21 anti HIV-patients showed concordance with 5'UTR genotype; only 6/19 anti HIV+ patients showed detectable serological reactivity. 3 serum samples showed reactivity toward 2 HCV types, whereas genotyping assays only revealed 1 type in these three cases. **Conclusions:** We have 1) observed a similar HCV genotypes distribution between French haemophiliacs and non-haemophilic HCV+ patients; 2) demonstrated the difficulties to assess with the available genotyping and serotyping assays the real prevalence of mixed infections in polytransfused subjects. Immunology and microbiology: Inflammation Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 1: Hepatitis viral, diagnosis } "HCV Genotypes in French Haemophiliacs: Kinetic and Reappraisal of Mixed Infections"

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"P P 2 0053" P 2 0053 **Analysis of the Core Region of HCV Genome Isolated from Patients with Chronic Hepatitis C during Intervals of Normal ALT Concentration**

\*K. Arataki, T. Nakanishi, T. Ohbatake, J. Matsuo, T. Moriya, G. Kajiyama

First Department of Internal Medicine, Hiroshima University School of Medicine, Hiroshima, Japan There are several reports on hepatitis C virus-specific cytotoxic T lymphocytes (CTLs) recognizing an epitope in the core region. In this study, we determined core region nucleotide sequences of specimens from patients with chronic hepatitis C during intervals of normal ALT concentration without treatment. *Materials and Methods:* Six patients analyzed in this study had chronic hepatitis C and their ALT concentrations had remained normal for more than one year without treatment. In one patient, we were able to compare the amino acid sequence during normal ALT concentration with that during elevated ALT. The core region of the HCV genome was amplified by the PCR. PCR products were then cloned. At least 5 independent clones were sequenced. *Results:* In 2 of the 6 patients, some clones that could be sequenced showed deletions. In 3 of the 6 patients, most of the isolated clones that could be sequenced had mutations at specific amino acids. When the ALT concentration was normal, we could sequence 10 independent clones. However, when the ALT concentration in the same patient was elevated, six of ten clones that could be sequenced were equivalent to one clone that was obtained during normal ALT concentration. *Conclusion:* These results suggest that expression of the wild-type HCV core region genome as well as diversity of the HCV core region genome was associated with liver cell damage. Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation } "Analysis of the Core Region of HCV Genome Isolated from Patients with Chronic Hepatitis C during Intervals of Normal ALT Concentration"

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"P P 2 0054" P 2 0054 **Relationship between Hepatitis C Virus (HCV) Genotypes and Sources of Infection in a Sample of Patients from Northern Portugal** T. Vasques<sup>1</sup>,

\*J.A. Sarmiento<sup>2</sup>, F. Carneiro<sup>1</sup>, G. Macedo<sup>2</sup>, A.M. Vale<sup>2</sup>, J.I. Riezu<sup>3</sup>, T. Ribeiro<sup>2</sup>, J. Prieto<sup>3</sup>

<sup>1</sup> Institute of Molecular Pathology and Immunology of University of Porto (IPATIMUP), Medical Faculty, Porto, Portugal

<sup>2</sup> Gastroenterology Unit of H. S. J., Porto, Portugal

<sup>3</sup> Internal Medicine, University of Navarra, Pamplona, Spain  
**Aims:** To study the relationship between HCV genotypes and gender, age, and putative source of HCV infection, in a sample of patients from northern Portugal. **Patients and methods:** The present study included 143 patients anti-HCV-positive (ELISA) (94 men, mean age 43 – 15 years) referred to H.S.J. between 1989/95. Patients were divided according to age (< 40 years and > 40 years) and source of infection (past history of blood transfusions (BT), intravenous drug users (IVDU) and unknown cause of infection (UCI)). HCV-RNA was detected in serum by nested PCR with primers directed to the 5'-UTR. Genotyping was performed by means of a hybridization procedure using specific probes for HCV genotypes 1a, 1b, 2, 2a, 2b, 3a and 4, according to Simmonds *et al.* and the amplified nested PCR product of the HCV Core region. The Chi-square method was used to statistical analysis. **Results:** HCV-RNA was detected in 119/143 patients (83.2%) and genotyping was done in 107 patients from the latter group: 1a (17.8%); 1b (53.3%); 2 (2.8%); 3a (19.6%); 4 (2.8%), 1b + 2b (1.9%); unclassifiable (1.9%). The statistical analysis was performed after excluding double infections and unclassifiable genotypes: Genotypes (%) n 1a 1b 2 3a 4 p value Age < 40\* 41 36.6 19.5 0.0 39.0 4.9 Age > 40 62 6.5 79.0 4.8 8.1 1.6 < 0.0001 Male 71 18.3 50.7 2.8 25.4 2.8 Female 32 18.8 65.6 3.1 9.4 3.1 n.s. BT 16 18.8 50.0 0.0 31.3 0.0 IVDU 22 36.4 4.5 0.0 50.0 9.1 UCI 65 12.3 73.8 4.6 7.7 1.5 < 0.0001 \*IVDU in this group (51.2%) was higher (p = 0.0001) than in > 40 years (1.6%). **Conclusions:** 1. Genotype 1b was the most prevalent in this sample; 2. Genotype distribution by source of infection showed predominance of genotype 3a in IVDU group, in contrast with the predominance of genotype 1b in the other two groups (BT and UCI); 3. Differences in genotyping distribution by age probably reflect the predominance of IVDU in the group of patients younger than 40 years. **Clinical practice: Epidemiology (non cancer) Liver and bile ducts, 1: Hepatitis viral, diagnosis }** "Relationship between Hepatitis C Virus (HCV) Genotypes and Sources of Infection in a Sample of Patients from Northern Portugal"

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## "P P 2 0055" P 2 0055 **Glucose Tolerance, and Insulin and C-Peptide Response to Glucose Load in Chronic HCV Infection**

\*F. G\fcnsar, U.S. Akarca, G. Ers\fcz, O` Topalak, Y. Batur, M. T\fcz\fcn, U. Ege

Medical School, Dept of Gastroenterology, Izmir, T\fcrkiye Diabetes mellitus (DM) has been found often in patients (pts) with chronic HCV infection (HCVi). Although it has not been investigated in detail, it is suggested that this association is a manifestation of autoimmune extrahepatic disorders of HCVi. To clarify the glucose metabolism in HCVi, in this continuing study we studied 39 patients with biopsy proven HCVi (23 noncirrhotics, 16 with compensated cirrhosis), 10 controls, 17 patients with chronic HBV infection with/without (7/10) cirrhosis. OGTT with serum insulin and C-peptide determination with related parameters were studied and compared between the groups. Anti-insulin (AIA) and anti-insulin receptor (AIRA) antibodies were also determined along with the other autoantibodies. The other parameters which can effect the glucose metabolism were also accounted for in the statistical evaluation. *Results:* 1) Of 23 HCVi pts without cirrhosis, 2 were diabetics (9%) and 2 (9%) had glucose intolerance (the rates were not different from in pts with noncirrhotic B hepatitis and controls). Five (31%) cirrhotic pts diabetics and 3 (19%) had glucose intolerance. 2) Glucose values during the OGTT were not different between the groups. 3) Basal insulin and C-peptide levels were found to be higher in noncirrhotic (0.370 – 0.122 nmol/l and 0.867 – 0.103 nmol/l) and cirrhotic patients (0.275 – 0.037 nmol/l and 1.338 – 0.177 nmol/l) with HCVi than in controls (0.144 – 0.069 nmol/l and 0.216 – 0.204 nmol/l) (basal C-peptide values was also higher in cirrhotics (p < 0.05)). 4) C-peptide increment during OGTT was blunted in pts with HCVi either cirrhotics or noncirrhotics while the insulin values were higher in these patients than in controls. 5) Peak insulin response in pts wig HCVi was more strong comparing with the pts with chronic B infection. 6) Of 15 chronic HCV infection pts studied 5 had anti-insulin antibodies (33%); none of the pts in controls and with HBV infection had AIA. AIRA was found to be negative in each pts. The parameters studied were not different between the pts who were AIA positive and negative. *Conclusions:* 1) The prevalence of diabetes mellitus was not higher in pts with chronic HCV infection if they have no cirrhosis. 2) The glucose metabolism in the pts with HCVi is similar with that observed in cirrhosis in general (increased basal insulin and C-peptide values, increased insulin but blunted C-peptide response following glucose challenge and insulin resistance). 2) Although AIA may be positive in some patients, DM if occurs in chronic HCV infection seems to be due to the liver damage, at least partly. Liver and bile ducts, 1: Hepatitis viral, diagnosis }" "Glucose Tolerance, and Insulin and C-Peptide Response to Glucose Load in Chronic HCV Infection"

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"P P 2 0056" P 2 0056 **HCV Genotypes in Relation to Age, Sex and Period of Infection**.  
**Lobello, D. Infantolino<sup>1</sup>, R. Biasin<sup>1</sup>, U. Lorenzoni, A. Floreani, A. Vian, R. Naccarato, M. Chiaramonte**

Dept. of Gastroenterology, Padua University, Italy

<sup>1</sup> Dept. of Patology, General Hospital Castelfranco V., Italy So far, HCV genotypes had been variably correlated to the severity of liver disease, to the prognosis, to the route of infection, to the patient age and the geographical origin. Few studies, however, correlated genotypes to epidemiological clusters or to secular trends of infection. To verify the possible epidemiological clusters and/or secular changes in the genotype spread we studied 120 HCV-RNA positive patients, all caucasians, living in North-East Italy and we correlated HCV genotypes to age, gender, place of birth and area of residence, route of infection and attributable infection period. Epidemiological data were collected before HCV genotype test. HCV-RNA was determined by RT-PCR and genotype was named in accordance with Simmonds' classification. *Results:* Genotype 1b was the most frequent (56%) followed by the 2c (20%), 3a (11%), 1a (8%), 2a (2.5%), 4 (2.5%). 1b 2c 3a 1a 2a 4N 67 24 13 10 3 3M/F 1.0 2.4 3.3 4.0 0.3 2.0 Year of birth before 1945 69% 50% 8% – 67% -after 1945 31% 50% 92% 100% 33% 100% Infection period before 1970 63% 75% – – 100% -1970–1980 27% 13% 31% 50% – -after 1980 10% 12% 69% 50% – 100% *Conclusions:* Genotype 1b was more frequent in more aged patients with suggestions of old infection by parenteral inapparent routes. Genotype 2c was distributed in the old ages and was related mostly to iatrogenic factors. Genotypes 3a and 1a were more frequent in young males and related to drug addiction. These data are consistent with the hypothesis of secular changes in HCV genotype spread. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "HCV Genotypes in Relation to Age, Sex and Period of Infection"

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"P P 2 0057" P 2 0057 **Soluble IL2 Receptor Levels in Peripheral Blood of Patients with Chronic Hepatitis and Asymptomatic Hepatitis Virus Carriers—in Special Comparison with B type and C Type—Hiroaki Ishimaru**

1st Dept of Intern Med, St. Marianna Univ School of Med, Kwasaki, Japan It is known that soluble IL2R (sIL2R) levels in peripheral blood can be used as index of activated T cells. In present study, IL2R levels were measured in peripheral blood of patients with chronic hepatitis positive for HBV or HCV and asymptomatic carriers, using EIA kits for sIL2R measurement. (*Subjects and Methods*) Cases with chronic hepatitis (CH) and asymptomatic carriers (ASCs) were positive for HBV or HCV. Classification (CIH, CAH IIa, CAH IIb) of CH was done due to basis on histological findings, and ASC was diagnosed due to normal level of serum transaminase for two years, non-increased level of  $\gamma$ -globulin and normal finding of liver and spleen by abdominal US. In methods, sIL2R in peripheral blood was measured, using cell-free IL2R measurement kit of EIA (T cell diagnostics company). (*Results*) In HBV carriers, serum sIL2R revealed normal to high levels in order of ASC, CIH and CAH. In HCV carriers, sIL2R revealed the increased levels in each group., which were higher in later in order of ASC, CIH and CAH. The level of sIL2R was higher in C-ASC rather than in B-ASC. In fatty liver with increased level of serum transaminase, it was within normal range. Furthermore there was the significantly positive relationship between the levels of serum sIL2R and transaminase. There was not the significant change of serum transaminase levels at an interval of several months. sIL2R showed the significant high level one week after start of IFN- $\alpha$  therapy, compared with one before it. The change was similar to one of ratios of T cell subsets positive for IL2R on the membrane. The levels of sIL2R and transaminase were lower two months after start of SNMC (glycyrhizin) – intravenous injection, compared with ones before it. Next capacity of IL2 production in peripheral blood mononuclear cells (PBMN) increased in B-CH and B-ASC and in C-CAH IIb. Capacity of IL2R response in PBMN was not significantly different between each group. (*Conclusion*) Circulating sIL2R levels either in HBV or HCV carrier were higher in CH than in ASC, and increased in progression of CH. In comparison with HBV and HCV carriers, it was suggested that the activation of T cells might be accelerated in HCV carrier rather than in HBV carrier. } "Soluble IL2 Receptor Levels in Peripheral Blood of Patients with Chronic Hepatitis and Asymptomatic Hepatitis Virus Carriers /in Special Comparison with B type and C Type/"

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"P P 2 0058" P 2 0058 **Cirrhosis, HCV Infection and Diabetes Mellitus** G. Macedo, A. Correia, N. Fernandes, H. Queiroz, J. Pires, T. Pinto, J.A. Sarmiento, A.M. Vale, T. Ribeiro

Gastro Unit and Faculty of Medicine, Porto, Portugal *Introduction and aim:* It is known for long the association between cirrhosis, glucose intolerance and Diabetes Mellitus (DM), and several contributive factors have been proposed: hyperinsulinemia, insulin resistance, reduced glucose uptake by cirrhotic livers. In cases with pancreatic disease associated (hemochromatosis, alcoholism) or with underlying autoimmune disorders, DM is a common observation. As HCV infection is associated with autoimmune phenomena, and being clinically observed a high prevalence of DM in those patients, we compared the prevalence of DM in cirrhotics from different etiologies. *Material and methods:* In a retrospective study of 95 cirrhotic patients, several parameters were registered: age, sex, etiology, HCV, DM, steroids use, B blockers use. DM diagnosis was based upon the need for oral hypoglycemic agent or insulin, or glucose > 12 mmol/l. *Results:* The distribution of etiology and DM prevalence was: Diagnosis Nr. of cirrhotics Nr. of DM patients Alcohol 38 4 (11%) HCV 28 15 (54%) HBV 13 1 (7%) PBC 5 0 (0) Hemoc. 5 4 80% Crypto. 4 0 (0) PSC 2 0 (0) No patient had been on B blockers before DM diagnosis, and one had been treated with steroids for uveitis. *Conclusion:* DM prevalence is significantly higher in HCV cirrhotic patients than in other common etiologies (HBV, alcohol). This retrospective study supports a genuine link between HCV cirrhosis and DM. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Hepatitis viral, diagnosis Hormones and receptors: Clinical disorders } "Cirrhosis, HCV Infection and Diabetes Mellitus"

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## "P P 2 0059" P 2 0059 **Only Some Autoimmunity Markers Are Associated with Hepatitis C Virus**

\*J. Graus, R. B\`e1rcena, V. Ure\`f1a, A. Moreno

Hospital Ram\`f3n y Cajal de Madrid, Spain *Purpose:* To investigate if the Hepatitis C Virus (HCV) induce autoantibody production in Chronic Hepatitis C patients. *Methods:* We analyzed antinuclear (ANA), antimitochondrial (AMA), antismooth (SMA) and antiliver and kidney microsomes antibodies (LKM) in 153 patients HCV+ (91 males); antimicrosome (AM) and antithyroglobulin antibodies (AT) in 162 patients (92 males), and thyroid stimulating antibody (TSAb), islet cell antibodies (ICA), antipituitary (Ap), antiinsuline (Ai) and antiadrenal antibodies (Ad) in 125 patients (74 males). We determined rheumatoid factor (RF) in 143 patients, 59 of them with liver biopsy. The same antibodies were investigated in 88 people (16 males) not infected by HCV. *Results:* Mean RF in HCV+ patients was 92.8. Mean RF in controls was 21.6 – 0.31, the difference being statistically significant in a Student t test ( $p < 0.001$ ). There was no relation between RF and ALT values. However, RF values correlated with portal necrosis grade ( $r = 0.28$ ). Healthy controls and HCV+ patients showed no significant differences in ANA, AMA, AM, AT, Ad, ICA, Ap, Ai and TSAb titles. HCV+ males showed a significantly higher SMA prevalence if compared to controls ( $p < 0.05$ ). HCV+ females also showed higher LKM prevalence compared to controls ( $p < 0.1$ ). *Conclusions:* 1.- RF titles are higher in CHC patients than in controls, their values being directly related to portal necrosis. 2.- SMA male prevalence and LKM females prevalence are significantly higher in HCV+ patients than in controls. 3.- Other antibodies's prevalence was not significantly higher in HCV+ patients compared to controls. Immunology and microbiology: Host defense mechanisms Liver and bile ducts, 1: Hepatitis viral, diagnosis Immunology and microbiology: Inflammation } "Only Some Autoimmunity Markers Are Associated with Hepatitis C Virus"

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## "P P 2 0060" P 2 0060 **Thyroid Dysfunction in Chronic Active Hepatitis (C)**

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<sup>1</sup> Department of Internal and Tropical Medicine, Mansoura University, Egypt

<sup>2</sup> Department of Clinical Pathology, Mansoura University, Egypt  
Thyroid disorders are now considered as an extrahepatic manifestation of chronic hepatitis C. The aim of this work is to study the changes in thyroid function tests and thyroid autoantibodies in chronic active hepatitis C and also to find if there are correlations between the degree of hepatic damage and these changes. In this study, 20 patients with chronic active hepatitis C (12 males & 8 females) age ranging from 28 to 60 years were included. Statistically significant reduction in Free T<sub>3</sub> level in both compensated and decompensated chronic active hepatitis C groups and in the level of TBG level in decompensated HCV Versus control group (P {\'a3} 0.001) and significant reduction in Free T<sub>4</sub> in decompensated HCV Versus control group (P {\'a3} 0.01). Also statistical difference was observed between chronic hepatitis C patients and control group concerning the antithyroperoxidase titre (51.971 – 64.501 Versus 7.414 – 5.371: P {\'a3} 0.05). And no significant difference was observed concerning the antithyroglobulin titre (55.849 – 26.711 Versus 41.689 – 17.913; P > 0.05). 6 patients revealed border line elevation in anti TPO (30%) and only one female patient showed significantly high anti TPO level > 125 I\`b5/ml (5%). On the other hand only one female (5%) revealed border line increase in anti TG levels. Also, there were statistically significant positive correlation between (the level of albumin and Free T<sub>4</sub>, Free T<sub>3</sub>, and TBG levels), (ALT level and TBG level), and (prothrombin activity and Free T<sub>4</sub>, and Free T<sub>3</sub> levels), and there were statistically significant negative correlation between (Total bilirubin and Free T<sub>4</sub>, and Free T<sub>3</sub> levels) and (Alkaline phosphatase and Free T<sub>3</sub> levels). From this study it can be concluded that, in addition to the characteristic low T<sub>3</sub> syndrome and low T<sub>3</sub>–T<sub>4</sub> syndrome which can occur with any non thyroidal illness. Chronic HCV infection is commonly associated with presence of thyroid autoantibodies indicating that immunologic stimulation and direct effect of HCV on the thyroid gland may play a role in thyroid disturbance in chronically infected HCV patients. Liver and bile ducts, 1: Hepatitis viral, diagnosis }"  
"Thyroid Dysfunction in Chronic Active Hepatitis (C)"

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"P P 2 0061" P 2 0061 **Lack of Autoimmune Disease in Irish Hepatitis C Patients**S.  
**Sachithanandan, J.F. Fielding**

Depts. of Gastroenterology & Hepatology, Beaumont Hospital, Dublin 9, Ireland *Purpose:* To determine the prevalence of autoimmune disease and/or autoantibody positivity in Irish Hepatitis C patients. *Methods:* 90 Irish Hepatitis C patients (55 Anti-D recipients, 25 Intra-Venous Drug Abusers and 10 Transfusion recipients) were surveyed clinically and by autoimmune serology to anti-nuclear (ANA), anti-smooth muscle (SMA), anti-mitochondrial (AMA), liver-kidney microsome (LKM-1), thyroid microsomal, thyroid globulin, gastric parietal antibodies and rheumatoid factor. *Results:* *Anti- D group* (all female); 2 of the Anti-D group and 1 of the transfusion group complained of generalised musculoskeletal symptoms but without clinical signs. In 6/55 (10.9%) thyroid microsomal antibodies were detected (2/6, thyroid globulin antibodies also positive). In 5/55 (9.1%), ANA titres were weakly positive and in 5/55 (9.1%), gastric parietal antibodies were positive. 47/55 were genotype 1 and 8/55 were genotype 3. *IVDA group* (8 females, 17 males); No autoantibodies were detected. Of 7/25 genotypes tested, 3 were genotype 3 and 4 were genotype 1. *Transfusion group* (5 females, 5 males); No autoantibodies were detected. 5 were of genotype 3 and the other 5 were of genotype 1. *Conclusions:* These findings suggest that in Irish Hepatitis C patients, neither genotype nor source (and dose) of inoculum contributes to the development of autoimmune disease. The question of if and how HCV is associated with autoimmune disease remains unknown. If the association exists, it may at least in part be genetic, and HLA typing may provide an answer. Larger numbers are also required before genotypic influence can be excluded. Liver and bile ducts, 1: Chronic non viral hepatitis }" "Lack of Autoimmune Disease in Irish Hepatitis C Patients"

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"P P 2 0062" P 2 0062 **Jaundice at Onset Signifies a Good Prognosis in Anti-D Associated HCV Infection** S. Sachithanandan, J.F. Fielding

Dept. of Gastroenterology & Hepatology, Beaumont Hospital, Dublin 9, Ireland *Introduction:*

Acute hepatitis presenting with jaundice occurs in less than a quarter of patients infected with the hepatitis C virus. These patients may be associated with a more benign clinical course than those who are asymptomatic. *Purpose:* To compare and contrast the PCR and RIBA status, serum ALT levels and histological scores in age, disease duration and viral load matched HCV anti-D recipients with and without a history of jaundice. *Methods:* HCV status was confirmed by detecting HCV-RNA by PCR and antibodies to HCV using ELISA and RIBA-3. Serum ALT levels were measured in all patients and a liver biopsy was performed in 26/34 patients. All patients were genotyped. *Results:* 14/17 jaundiced patients were PCR negative and only 4/17 had RIBA scores greater than nine whereas all non jaundiced patients were PCR positive and all seventeen had RIBA scores > 9. 13/17 jaundiced had normal ALT values; 3/17, mildly elevated (41–100) and 1/17 > 100. 6/17 non-jaundiced had normal ALT levels, 9/17 (41–100) and 2/17 (> 100). 7/9 jaundiced had mild histological scores, 0/9 moderate and 2/9 severe. 5/17 non jaundiced had mild, 9/17 moderate and 3/17 severe. All 34 patients were of genotype 1b. *Conclusions:* Patients with jaundice were associated with lower antibody scores, increased PCR negativity, normal serum ALT levels and low/normal histological scores. Jaundice at onset was an indicator of good prognosis. Liver and bile ducts, 1: Chronic non viral hepatitis } "Jaundice at Onset Signifies a Good Prognosis in Anti-D Associated HCV Infection"

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**"P P 2 0063" P 2 0063 Chronic Cryptogenic Hepatopathy: A Still Puzzling Entity in 1995V. Bourgeois, M.-O. Peny, O. Le Moine, N. Bourgeois, C. Deprez, S. Sa'efkali, L. Debaisieux,**

\*M. Adler

Medico-surgical Department of Gastroenterology, Hospital Erasme-ULB, Brussels, Belgium Even now, chronic elevation of transaminases without evidence of viral, toxic, alcoholic, genetic, autoimmune or vascular liver disease (defined as chronic cryptogenic hepatopathy: CCH) is still a clinically puzzling entity. The charts of 257 immunocompetent patients submitted between 01/93 and 10/95 to liver biopsy (percutaneous: 138, laparoscopic: 2, transvenous: 117) because of chronic elevation of transaminases were reviewed retrospectively. Thirty patients (12%) satisfied the criterion of CCH. Blood HCV RNA measured in 25 of them was always negative. These 30 patients with CCH (group I) were matched according to their sex and age to 30 HCV + VC patients (group II) and clinical, biochemical and histological features were compared between the two groups using univariate analysis (Chi-square or Fisher exact-test). Patients from group I had mean values of 46 y.o. for age, 93 IU (N < 35) for aminotransferases, 25.6 for body mass index (N < 25) and consumed 45 g alcohol per week (N < 140 g for women and < 210 g for men). None of these parameters differed in the two groups even so for blood glucose, ferritin, transferrin saturation index and sex. Cholesterol and triglyceride levels were significantly elevated ( $p < 0.02$ ) in group I. Histological analysis revealed greater inflammatory activity (using Metavir classification), higher number of lymphoid aggregates, greater portal inflammation and greater sinusoidal activation in group II. Final histological diagnosis in group I patients was steatosis/fibrosis in 18, chronic hepatitis in 5, normal liver in 4 and cirrhosis in 1. CCH represents thus 13% of chronic parenchymal liver disease and is characterized by abnormal lipid profile and histologically by steatosis/fibrosis in most cases with minor inflammatory activity. This entity could represent a new metabolic dysregulation or a new non A non B non C viral hepatitis. Liver and bile ducts, 1: Chronic non viral hepatitis } "Chronic Cryptogenic Hepatopathy: A Still Puzzling Entity in 1995"

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"P P 2 0064" P 2 0064 **Prevalence of Anti-HCV Antibodies in Healthy Individuals, Alcoholics and Immigrant Population from Albania in North Western Greece** G.N. Dalekos<sup>1</sup>, E. Zervou<sup>2</sup>, D. Christodoulou<sup>1</sup>, E.V. Tsianos<sup>1</sup>

<sup>1</sup> Division of Internal Medicine, School of Medicine, University of Ioannina, Greece

<sup>2</sup> Blood Bank at the University Hospital of Ioannina, Greece *Purpose:* The aim of the present study was an attempt to the better approach of the real prevalence of anti-HCV antibodies in Epirus region, (north western Greece) where epidemiologic studies can be done with good accuracy. Comparison between the prevalence in Epirus with that of some special groups of individuals belonging to the high risk groups for infectious diseases such as refugees from Albania and alcoholics with or without liver disease (LD), was also done. *Methods:* We investigated 6.742 healthy (5.285 male and 1.457 female, mean age: 38.5 years, range: 0–60 years), 684 refugees from Albania (473 male and 211 female, mean age: 39.2 years, range: 0–70 years) and 151 alcoholics (145 male and 6 female, mean 56.5 years, range: 30–80 years). This latter group consisted from 83 alcoholics with LD and 68 without LD. 5835 subjects from healthy were blood donors who were accounted for only once during the study while more than 50% of them were first time donors. Third generation enzyme immunoassays and immunoblot assays were used (EIA 3.0 and RIBA-III). *Results:* We found that: (a) 0.83% of healthy (56/6742) were reactive with EIA 3.0 but 21.4% (12/56) of them were positive by RIBA-III, (b) 1.75% (12/684) of refugees were positive both with EIA 3.0 and RIBA-III and (c) 1.32% (2/151) of alcoholics (1/83 with LD and 1/68 without LD) were also positive both with EIA 3.0 and RIBA-III. The seropositivity for anti-HCV antibodies was significantly more frequent among refugees than healthy ( $p < 0.05$ ) but not between alcoholics and the other two groups (comparison between male only). In addition, the presence of anti-HCV antibodies in healthy controls was significantly ( $p < 0.01$ ) more frequent in older ages (more than 30 years). The latter finding, however, was not confirmed for the refugees. *Conclusions:* (1) The prevalence of anti-HCV antibodies in our region is approximately similar with that reported in most European countries. (2) The refugees from Albania had significantly higher prevalence of these antibodies than healthy controls. (3) By contrast, the present study did not confirm the presence of high prevalence of anti-HCV antibodies among alcoholics which has been reported by others. *Clinical practice: Epidemiology (non cancer) }* "Prevalence of Anti-HCV Antibodies in Healthy Individuals, Alcoholics and Immigrant Population from Albania in North Western Greece"

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## "P P 2 0065" P 2 0065 The Significance of Hepatitis B Markers in Chronic Hepatitis C Egyptian Patients

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<sup>1</sup> Department of Tropical Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt

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*Purpose:* It is well known that both HCV and HBV share several routes of transmission. It is our aim to assess the prevalence and clinical significance of hepatitis B markers in chronic hepatitis C patients. *Methods:* A total of 372 chronic hepatitis C (CHC) patients with elevated ALT were studied; 306 males and 66 females with a mean age of 42 years. All cases were ELISA-2, repeatedly positive, HCV-RNA-PCR was performed as a prerequisite before antiviral therapy. They were tested for hepatitis B markers (HBsAg, HbeAg/Ab HBcAb IgG, whereas cases positive for HBsAg were screened for HBV-DNA-PCR). Liver biopsy was performed in 242 patients. *Results:* HBV seromolecular data are demonstrated in the following table: No. % anti- HCV-RNA HBsAg { - } HBeAg/ anti-HBc HBV-DNA of pts

Category	No.	%
HCV+ve PCR Ab IgGG1: HCV + HBV	195	53.5
dual infectionG2: HCV + HBsAg	44	12.1
+ve { - }carrierG3: HCV + HBV	207	55.9
infectionG4: Isolated HCV	102	27.4

Histological diagnosis in dual infection versus (vs) isolated HCV infection revealed CPH in 16% vs 19.6%, CAH in 21% vs 58.8%, cirrhosis in 63% vs. 21.5% respectively. *Conclusion:* The results show a high prevalence of markers of past HBV infection among HCV viremic patients. Results also might suggest suppression of HBV replication by coexisting HCV infection. We also concluded that dual HBV & HCV infection hasten the progress & severity of liver disease. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "The Significance of Hepatitis B Markers in Chronic Hepatitis C Egyptian Patients"

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"P P 2 0066" P 2 0066 **Lack of Evidence of IgA Deficiency in Hepatitis C Virus Infection**

\*M.A. Heneghan, L. Geoghegan, J. McWeeney, T.A. O'Gorman, C.F. McCarthy

Department of Medicine, Clinical Science Institute, University College Hospital, Galway, Ireland

A previous study (Ilan et al. Arch. Int. Med. 1993; 3: 1588–1592) has suggested that IgA deficiency predisposes towards chronic Hepatitis C Virus (HCV) infection in some patients. It has also been suggested that IgA deficiency may occur as a secondary event as a result of the viral infection.

**Aims:** To determine the prevalence of both selective IgA deficiency (IgA < 0.05 g/L), and partial deficiency of IgA (IgA < 0.82 g/L) in a group of patients with chronic HCV infection attending our clinics.

**Methods:** Immunoglobulin levels including IgG, IgA and IgM were determined in 67 HCV infected patients using a nephelometric technique. These patients had been infected with HCV contaminated blood, or anti-D immunoglobulin between 1977 and 1990. Mean immunoglobulin concentration (g/L) was compared with 100 controls without HCV infection.

**Results:** 59 women and 8 men were examined with HCV infection, mean age 45.3 years (range 27–72 years). No patient was found to be either selectively or partially deficient in IgA. Mean IgA 2.59 g/L versus 2.81 g/L in the control group (2 tailed p = 0.980). Furthermore, no deficiency of serum IgG or IgM was found in either patients or controls.

**Conclusion:** No evidence of IgA, or other immunoglobulin deficiency states exist among this group of patients with chronic HCV infection. While it is possible that IgA levels may decrease transiently following infection, no evidence exists that this phenomenon persists in the long term (mean duration of infection = 15.01 years). Differences between this study population and the previous report may relate to ethnic factors alone.

Liver and bile ducts, 1: Hepatitis viral, diagnosis }  
"Lack of Evidence of IgA Deficiency in Hepatitis C Virus Infection"

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"P P 2 0067" P 2 0067 **Quality of Life of Italian Patients with Chronic Hepatitis C**

\*F. Arpinelli, G. Visona<sup>1</sup>, G. De Carli, U. di Luzio Papparatti, N. Caporaso<sup>1</sup>, A. Craxi<sup>2</sup>, A. Bellobuono<sup>3</sup>, E. Roda<sup>4</sup>, G. Recchia

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<sup>1</sup> Gastrointestinal Dept. of Naples, Italy

<sup>2</sup> Gastrointestinal Dept. of Palermo, Italy

<sup>3</sup> Gastrointestinal Dept. of Milan, Italy

<sup>4</sup> Gastrointestinal Dept. of Bologna, Italy After the diagnosis, patients (pts) suffering from chronic hepatitis C undergo to several changes of their life style, because of treatments, fear to infect wife/husband, progress of the disease etc. Measurement of health related quality of life (QoL) is an important index to evaluate outcomes induced by therapies and the use of QoL questionnaires is the most suitable way to collect these informations. A multicentre survey to measure the QoL of Italian CHC pts started during the spring of 1996. As in Italy no specific questionnaire for CHC pts is available, the protocol provided for the use of Italian version of the general questionnaire SF36. It was administered to anti-HCV positive males and females with compensated CHC and serum ALT values at least 1.5 times the upper limit of normal, who never underwent a hepatic biopsy, were not previously treated with interferon and/or antiviral drugs and/or corticosteroids, who were free from relevant psychiatric or neurological diseases and were HIV-1 negative. SF36 was administered to over 500 patients by 50 Investigators throughout Italy. Analysis of the first 62 pts (mean age 46 y, 65% males) showed that scores in some domains of SF36 were lower than the norm: role physical { - }2.0%, general health { - }7.0%, social functioning { - }4.4%, role emotional { - }6.4%, mental health { - }3.1%. Other domains scored greater than the norm: physical functioning +3.6%, bodily pain +11.1%, vitality +1.1%. These data suggest that CHC pts perceive their disease as a serious risk for their health, with limitations of social functions in spite of having a good enough physical functioning and lack of symptoms. It is notable that psychological aspects of pts are lower than normal however pts were not treated with any drugs and this does not support hypotheses on psychotropic effects of specific drug for CHC. } "Quality of Life of Italian Patients with Chronic Hepatitis C"

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## "P P 2 0068" P 2 0068 **Hepatic Glutathione Deficiency in Chronic Hepatitis C: Quantitative Evaluation and Correlations with Plasmatic and Lymphocytic Concentrations in HIV-Positive and HIV-Negative Patients**

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Departments of Emergency Medicine, Medical Sciences and Infectious Diseases, University of Torino, Italy

<sup>2</sup> Departments of Emergency Medicine, Medical Sciences and Infectious Diseases, University of Pavia, Italy

<sup>3</sup> Division of Infectious Diseases, General Hospital, Foggia, Italy

**Introduction.** Reduced glutathione (GSH) is decreased in plasma and in peripheral blood mononuclear cells (PBMC) of subjects affected by chronic hepatitis C (CHC) as well as in plasma, lung epithelial-lining fluid and T lymphocytes of Human Immunodeficiency Virus (HIV)- positive subjects. Since the liver is the most important source of plasmatic GSH, we measured the concentrations of GSH in the liver (H-GSH) of HIV-positive and HIV-negative patients with CHC, correlating it with the concentrations of GSH in plasma (P-GSH) and in PBMC (L-GSH), with the replication activity of HCV in PBMC, with the activity of the liver disease and with the state of immunodeficiency in HIV-positive patients.

**Methods.** The study has considered 125 patients with serologically and histologically demonstrated CHC (65 HIV-positive and 60 HIV-negative); 61 healthy individuals served as a control group for P-GSH and L-GSH concentrations. H-GSH concentration was determined by High Performance Liquid Chromatography on liver specimens obtained by ultrasound-guided biopsies according to the method described by Reed et al.. The concentrations of P-GSH and L-GSH were determined according to the method described by Suarez et al. The detection of HCV-RNA strands in PBMC was performed according to the method described by Qian et al.

**Results.** H-GSH, P-GSH and L-GSH were significantly reduced in patients affected by CHC compared with healthy controls ( $p < 0.001$ ); H-GSH was significantly correlated to both P-GSH ( $r = 0.91$ ;  $p < 0.001$ ) and L-GSH ( $r = 0.65$ ;  $p < 0.001$ ). The reduction of H-GSH, P-GSH and L-GSH were significantly correlated to the replication activity of HCV in PBMC [ $r = 0.97$  vs H-GSH ( $p < 0.001$ );  $r = 0.92$  vs P-GSH ( $p < 0.001$ );  $r = 0.97$  vs L-GSH ( $p < 0.001$ )] and to the grade of activity of the liver disease assessed by the values of ALT [ $r = 0.74$  vs H-GSH ( $p < 0.001$ );  $r = 0.83$  vs P-GSH ( $p < 0.001$ );  $r = 0.64$  vs L-GSH ( $p < 0.001$ )] and by the histological score of CHC ( $r = 0.75$  vs H-GSH;  $p < 0.001$ ). H-GSH and, particularly, L-GSH were more significantly reduced in HIV-positive patients compared with HIV-negative ones ( $p < 0.001$ ), without significant correlation with the values of T cells subset CD4+ ( $r = 0.065$ ;  $p = 0.507$  vs H-GSH and  $r = 0.0933$  vs L-GSH;  $p = 0.343$ ). In both groups of CHC patients L-GSH was more significantly reduced in drug addicts compared with non drug addicts patients ( $p < 0.001$ ).

**Conclusions.** In patients with CHC and, particularly, in HIV-positive patients, a systemic depletion of GSH is present. This depletion may be a factor underlying the resistance to interferon therapy and, in HIV-positive patients, to antiretroviral drugs, fostering HCV and/or HIV replication. This may represent the biological basis for GSH replacement therapy with

GSH-prodrugs. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Immunology and microbiology: GI infections in adults }" "Hepatic Glutathione Deficiency in Chronic Hepatitis C: Quantitative Evaluation and Correlations with Plasmatic and Lymphocytic Concentrations in HIV-Positive and HIV-Negative Patients"

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"P P 2 0069" P 2 0069 **HCV Heterogeneity and Response to Alpha IFN Therapy in French Patients with Chronic Hepatitis C. Le Guen<sup>1</sup>, Gio. Squadrito, S. Pol<sup>2</sup>, B. Nalpas<sup>2</sup>, P. Berthelot<sup>2</sup>, C. Brechot**

<sup>1</sup> Inserm U370, CHU Necker, Paris, France

<sup>2</sup> Liver Unit, CHU Necker, Paris, France

<sup>3</sup> Dep. Internal Medicine, Univ. of Messina, Italy *Objectives:* It has been suggested that Hepatitis C virus (HCV) genome heterogeneity might be a predictive virologic parameter for responsiveness to IFN treatment. We have investigated this issue in a serie of French patients treated by IFN for HCV related chronic active hepatitis. *Methods:* Ninety-five patients (19/95 cirrhosis) before IFN treatment were classified into three groups: long term responders (LTR) (n = 20), relapsers (n = 31) and non-responders (n = 44). The HCV genotype was determined by restriction fragment lenght polymorphism analysis (RFLP), 1b (n = 45), 1a (n = 11), 2 (n = 8), 4/5 (n = 2) and 3a (n = 29) and HCV RNA quantitation was analyzed by the Branched DNA assay (Quantiplex<sup>®</sup> 2.0). The quasispecies complexity of HCV HVR 1 was analyzed by PCR-mediated single-strand conformation polymorphism (SSCP) and classified as low (SSCP band {\\a3} 3) or high complexity patterns (SSCP band > 3). Univariate and multivariate analyses were performed (BMDP Statistical Software Inc., Los Angeles, CA, USA). *Results:* In univariate analysis high complexity pattern showed the highest correlation to IFN efficacy followed by age, HCV genotypes and viral load (p < 0.0001). A low complexity pattern was associated with long term response for genotype 3a (10/14). Multivariate analysis showed that the high complexity pattern was the most informative predictive factor of non response or relapse with odds ratio of 19, compared to 11.6 for HCV viremia and 7.48 for HCV genotype. *Conclusions:* The high degree of HCV genome heterogeneity is a negative independent predictive factor of response to IFN in patients infected by HCV types associated to both low (1b) or high (3a) response rates. It should be important to prospectively include the analysis of HCV heterogeneity in the design of therapeutic strategies for HCV infection. Liver and bile ducts, 1: Hepatitis, viral, treatmentLiver and bile ducts, 1: Hepatitis viral, diagnosis }" "HCV Heterogeneity and Response to Alpha IFN Therapy in French Patients with Chronic Hepatitis C"

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"P P 2 0070" P 2 0070 **HCV Core Protein: Subcellular Localization and Intracellular Interaction with Cellular Lipid Metabolism** G. Barba<sup>1</sup>, F. Bono, T. Harada<sup>3</sup>, C. Transy<sup>4</sup>, F. Harper<sup>5</sup>, Y. Matsuura<sup>3</sup>, J. Chapman<sup>6</sup>, T. Miyamura<sup>3</sup>, C. Brechot<sup>1</sup>

<sup>1</sup> Liver cancer and molecular virology, Inserm U370, Paris, France

<sup>2</sup> Policlinico San Matteo, Pavia, Italia

<sup>3</sup> Department of Virology II, National Institute of Health, Tokyo, Japan

<sup>4</sup> Institut Pasteur, Paris, France

<sup>5</sup> Functional Organization of the Nucleus, CNRS UPR9044, Villejuif, France

<sup>6</sup> INSERM U321, Paris, France There are evidences for a role of HCV core in both encapsidation and modulation of gene expression. Its subcellular localization is however controversial. We have analyzed these points by two approaches: 1) *Immunofluorescence and confocal microscopy* were performed in CHO and HepG2 cells stable expressing HCV core. The protein showed a cytoplasmic distribution with a perinuclear (CHO) or peripheric (HepG2) pattern localized in globular structures unrelated to the position of the cell in cell cycle. A nuclear localization was excluded by confocal analysis and by double labelling with a nuclear membrane marker. *Electron microscopy* analysis showed presence of lipidic droplets absent in control cells. Immunostaining with an anti-core antibody revealed a concentration of the signal on the surface of the droplets both in CHO and HepG2 cells. Detailed analysis of the lipidic composition of the droplets showed a prevalent presence of triglycerides and confirm the association to the HCV core. 2) The association of the core to cellular protein was studied by employing *the yeast two hybrid system*. We obtained from a human liver cDNA library 3 independent clones coding for the apolipoprotein AII for 65 currently analysed. Confocal analysis of double immunofluorescence for Apolipoprotein AII and core protein in HepG2 cells showed colocalization of the two proteins. Further studies are in progress in order to confirm the biochemical interaction "in vivo". *Conclusions:* Our results show: 1) Accumulation of lipidic storage vesicles upon HCV core expression. 2) Association of cytoplasmic HCV core to these Triglycerides rich vesicles and colocalisation with AII. These observations stress the potential importance of these interactions in HCV infection pathobiology. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Hepatitis viral, diagnosis } "HCV Core Protein: Subcellular Localization and Intracellular Interaction with Cellular Lipid Metabolism"

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"P P 2 0071" P 2 0071 **Nosocomial Transmission of HCV. Angelis<sup>1</sup>, M. Papadaki<sup>2</sup>, P. Garzonis<sup>1</sup>, K. Liosis<sup>1</sup>, Ch. Papamichail<sup>1</sup>,**

\*A. Simos<sup>1</sup>

<sup>1</sup> Medical Unit of "Sotiria" General Hospital of Chest Diseases of Athens-Greece

<sup>2</sup> Blood Transfusion Centre of "Sotiria" General Hospital of Chest Diseases of Athens-Greece  
*Purpose:* The study's purpose is the determination of HCV dispersion in patients with chronic disease and the investigation of the possible significance of hospitalization as a risk factor for HCV infection. *Patients and Methods:* 657 patients with chronic disease, who were hospitalized in our hospital between Sept. 91 and Dec. 94, were studied. They were classified in two groups. Group A included 248 transfused patients, 157 males and 91 females, with a mean age 65.2 years, a mean number of hospitalizations 15.8, a mean duration of hospitalization 8.8 months and a mean number of transfusions 5.5 units. Group B consisted of 409 non transfused patients, 262 males and 147 females, with a mean age 67.3 years, a mean number of hospitalizations 15.9 and a mean duration of hospitalization 9.2 months. Patients with other risk factors for hepatitis C were excluded from the study. As a control group were used 480 individuals with a history free of chronic disease, hospitalizations or transfusions and with comparable features concerning age and sex. Individuals who were at high risk for hepatitis C were excluded from the control group as well. The determination of anti-HCV was performed by ELISA-2 ABBOTT and furtherly confirmed by RIBA-2 ORTHO. The statistical analysis was made on PC (D Base IV, SPSS). *Results:* Antibodies against HCV, confirmed by RIBA-2, were found in 11.3% in group A, in 9% in group B and in 1.4% in the control group. The statistical analysis showed important difference regarding the presence of anti-HCV between groups A, B and the control group. A positive correlation between serum positivity and number of transfusions in group A and number and duration of hospitalizations in group B was confirmed. *Conclusion:* Our results demonstrate a high dispersion of HCV in patients with chronic disease and multiple hospitalizations, independently of transfusions and indicate that the factor "exposure to hospitalization" represents a significant risk factor for HCV infection. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Nosocomial Transmission of HCV"

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"P P 2 0072" P 2 0072 **The Genotype 1b Replicates More Actively and It Is More Resistant to the IFN in the Patients with Chronic Hepatitis C**

\*A. Castro, M. Hermida, S. L\'opez Calvo, P. Vega, R. Torr\'n, J. Bali\'as, J.D. Pedreira

Internal Medicine Service, Hospital Juan Canalejo, La Coru\'a, Spain *Objective:* To study the influence of viral genotype and viremia on the response to IFN alpha treatment in chronic hepatitis C patients. *Patients and Methods:* 50 hepatitis C patients, diagnosed by liver biopsy and the presence of anti-HCV in serum (ELISA and RIBA-II), were treated with IFN alpha (Welferon, Wellcome) for one year: 3 MU daily for 10 weeks followed by 3 MU thrice to week. Viremia was determined immediately before and after treatment by quantitative PCR (Monitor, Roche). HCV genotype was determined before treatment by INNO-LiPA (Boheringer Ingelheim). To normalize ALT level following treatment was considered as response to IFN. *Results:* Of the 50 patients treated, 34 (68%) showed no response and 16 (32%) responded, 8 of whom (16%) maintained the response after one year of follow-up. HCV RNA level was 100 000 eq/ml for the responders and 600 000 eq/ml for non responders ( $P < 0.0032$ ). All but one of those who didn't respond were RNA HCV positive at the end of treatment but to much reduced level: 150 000 eq/ml ( $P < 0.0058$ ). They were accomplished genotipifications with the basal serum of 37 (74%) of 50 patient. 15 of 16 responders were genotyped (94%) and 22 of 34 non responders (64%). The most frequent genotype was 1b (26/37) (70%). 19 of 22 non responders genotyped were 1b (86.3%), while only 7 of 15 (46.6%) responders genotyped were 1b ( $p = 0.0130$ ). It has been studied the patients that were presenting the genotype 1b as compared to those which were presenting other genotypes in relation to the viremia. The viremia mean of the patients with genotype 1b was 5.7 times;  $10^5$  (standard desviation: 9.7 times;  $10^5$ ) and that of the others genotypes (non-1b) was 9.8  $\times 10^4$  (standard desviation: 1.37 times;  $10^5$ ) ( $p < 0.0019$ ). *Conclusion:* The replication of HCV is greater in the patients infected with the type 1b and the response to IFN treatment in these patients is lower. Furthermore the genotype 1b is the most frequent in the population. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "The Genotype 1b Replicates More Actively and It Is More Resistant to the IFN in the Patients with Chronic Hepatitis C"

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"P P 2 0073" P 2 0073 **Chronic Hepatitis C and Severe Autoimmune Diseases** L. Pascalis,

\*G. Pia, G. Aresu

University Cagliari Italy *Objectives* – To test the effectiveness and tolerance to { b} Interferon combined with low-doses of CsA and steroids for the treatment of patients with chronic hepatitis C virus (HCV) and exacerbation of severe autoimmune diseases. *Methods* – 20 Patients (12 females and 8 males) ages ranging from 25 to 42 years were included in the study. Each patient were affected with chronic hepatitis with actively replicating HCV and/or Rheumatoid Arthritis (new ARA classification criteria) 10 patients, and/or L.E.S. (new ARA classification criteria) 6 patients, vasculitis (histological or arteriographic evidence) 4 patients. Inclusion criteria for patients: a therapy refractory condition after an at least 3-weeks treatment with prednisone at a dose of 1 mg/Kg body weight, which usually corresponded to 40–70 mg. { b} Inteferon (Fron–Serono) was administered at a dose of 5 million U./week on 5 days for 6 months. Cyclosporin A (CsA) was administered initial daily dose of 5 mg per Kg body weight (ideal weight in the case of overweight subjects). Blood levels of the drug were between 100 and 200 mcg/l by the third day of treatment. All the patients also received Fluocortolone at a dose to control disease activity, that is, 80–70 mg/week on 5 days depending on the case, and then tapered in relation to the course down to a maintenance dose of 15–20 mg/week administered on 3 days. *Results* – All Patients presented a significant improvement of the clinical picture. 2 months after onset of treatment the AST had normalized and there was a statistically significant decrease in clinical outcome variables (morning stiffness; Pain, 100 mm VAS; Lee functional index) and biological parameters (C reactive protein, ESR, { a }<sub>1</sub>-glycoprotein acid). The disease activity indexes remained normal for the rest of the follow period (24.12 – 2.33 months, range 21–27). All side effects were mild. No renal toxicity was observed in any patients. Immunology and microbiology: Inflammation Liver and bile ducts, 1: Hepatitis, viral, treatment } "Chronic Hepatitis C and Severe Autoimmune Diseases"

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"P P 2 0074" P 2 0074 **Rheumatic Manifestations of HCV Infection** R.J. Farrell, D. McGonagle, R. Pilkington, E.B. Casey, D. Kelleher

Departments of Hepatology and Rheumatology, St James's Hospital, Dublin 8,

Ireland *Introduction:* Hepatitis C Virus (HCV) infection is associated with several connective tissue diseases. The most well recognized is Cryoglobulinemia, a Sjogren's like syndrome, an asymmetrical inflammatory arthropathy and non-specific arthritis. In 1977–78 Anti-D

Immunoglobulin batches infected with HCV were inadvertently administered as prophylaxis against Rhesus blood group incompatibility. Virtually all patients exposed to HCV whether symptomatic or not have been evaluated thus allowing accurate determination of the true prevalence of rheumatic conditions at a mean time of 18 years since exposure. *Methods:* HCV was diagnosed using RIBA testing and confirmed with PCR. Groups where HCV was acquired by other means (IVDU, blood transfusion, sexually, bone marrow transplant and sporadic) were included for comparison. Patients with suggestive symptoms were carefully re-evaluated with full auto-antibody screen, cryoglobulins and Schirmer test. *Results:* 136 patients who acquired HCV through Anti-D were evaluated. Mean age: 42.5 (range 33–60) yrs. 83 were PCR+ve; 71 type 1b, 2 type 2b, 10 type 3. At mean follow-up of 18 years there was no clinical evidence of cryoglobulinemia. However 1 PCR+ve case with small joint arthralgia had a cryocrit of 2%.

There was 1 case of mild seropositive RA and 1 of palindromic RA. 4 had small hand joint arthralgia while 1 PCR+ve case had Sjogren's syndrome with xerostomia and xerophthalmia, positive ANA, Ro and La antibodies and a positive Schirmer test. Six cases had frozen shoulders, 3 of which were PCR+ve. 90 patients who acquired HCV through means other than Anti-D (All HBV and HIV negative) were evaluated. Mean age: 27.1 (range 17–72) yrs. 64 were PCR+ve; 29 type 1b, 2 type 2, 32 type 3. There was no case of cryoglobulinemia. One PCR+ve lady had long standing RA and thyroiditis and 3 cases of peripheral symmetrical arthralgia. There was no confirmed case of Sjogren's Syndrome, however 2 cases had xerostomia and xerophthalmia but were Ro and La antibody negative. Two cases had frozen shoulders one of which was PCR+ve.

*Conclusions:* Despite the well reported association between HCV infection and cryoglobulinemia the prevalence with chronic HCV infection appears to be low. Sjogren's Syndrome does not appear to be more prevalent than in the general population. 5% of the anti-D group had persistent small joint arthralgia with 2 documented RA cases while 4.5% had frozen shoulders. Liver and bile ducts, 1: Hepatitis viral, diagnosis }" "Rheumatic Manifestations of HCV Infection"

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"P P 2 0075" P 2 0075 **Abdominal Lymphadenopathy and Histological Pictures in Chronic Hepatitis CM. Soresi, G. Bonfissuto, A. Carroccio, V. Agate<sup>1</sup>, C. Magliarisi, F. Bascone, A. Cartabellota, F. Aragona<sup>1</sup>, G. Montalto**

<sup>1</sup> Cattedra di Medicina Interna, Università di Palermo, Italy

Istituto di Anatomia Patologica, Università di Palermo, Italy *Aim:* To evaluate the relationship between ultrasonography (US) findings of upper abdominal lymphadenopathy and histological activity index (HAI) and serum liver function tests (LFTs) in subjects with chronic hepatitis C. *Methods:* 58 subjects (41 M, 17 F) (mean age 46.4 – 12.4 years), with chronic hepatitis C were studied. None were HBsAg +ve, alcoholics or had other known causes of liver disease or neoplasia. US scans were performed using a real time equipment (Toshiba SSA 240 A) with a 3.5-Mhz convex transducer. Liver biopsies were performed with needles 16 G (Surecut, Hospital Service, Rome). HAI was evaluated with Knodell's score (K), which expresses necrosis-inflammation and fibrosis, and Desmet's score which separately determines grading (G) necrosis-inflammation and staging (S) expressing fibrosis. The common LFTs (AST, ALT, ALP, GGT, total bilirubin, prothrombin activity, serum albumin, {g}-globulin) were assayed. Statistical analysis was performed using Student's test, Pearson's and Spearman's coefficient correlation *r*. *Results:* 36 subjects did not present lymph nodes (LN) on US (LN{-}), while 22 did (LN+). Mean values of the K and G scores were significantly higher in the LN+ than the LN{-} subjects: K LN+ (n = 22) 10.0 – 3.0\* 8.4 – 2.47\*\* LN{-} (n = 36) 7.9 – 3.6\* 6.5 – 2.9\*\*\* p < 0.03; \*\* p < 0.02 There was no difference for the serum LFTs. There was a significant correlation between number of LN and K and G scores (p < 0.05 and p < 0.01 respectively) and with serum {g}-globulin (p < 0.04) but not with S or the remaining serum LFTs. *Conclusion:* The presence of LN on US is a parameter of greater inflammation and severe necrosis which can be confirmed histologically; LN are thus indicative of a more severe evolution of liver disease, even in absence of LFTs alterations. Liver and bile ducts, 1: Hepatitis viral, diagnosis Radiology and ultrasound: Diagnosis } "Abdominal Lymphadenopathy and Histological Pictures in Chronic Hepatitis C"

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"P P 2 0076" P 2 0076 **Hepatitis C Infection in Non-Hodgkin Lymphoma**

\*H. Senturk, M. Akdogan, A. Mert, A. Sonsuz, S. Ozdemir, P. Akin

Department of Internal Medicine, Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey Chronic hepatitis C virus (HCV) infection was proposed as a predisposing factor in the development of non-hodgkin lymphoma. Despite its oncogenic mechanism is far from clear, HCV is known to infect both B and T lymphocytes and its long-term presence in immune system may promote the infiltration of bone marrow with expanded clones of Ig-secreting lymphocytes. We examined the serum samples from 30 patients (17 male, 13 female, median age 52, range 16–84 ys) with non-hodgkin lymphoma (NHL) and 18 patients (10 male, 8 female, median age 26, range 17–61 ys) with hodgkin lymphoma (HL) for anti-HCV antibodies by ELISA II (Abott, HCV EIA.) Anti-HCV positive sera was tested for HCV-RNA by nested-PCR as well. The serologic results from sera of 9488 healthy blood donors (age range 18–65 ys) were used as controls. 4/30 (13%) of patients with NHL, and 74/9488 (0.8%) of blood donors were anti-HCV positive ( $p < 0.001$ .) None of the 18 patients with HL was +ve for anti-HCV. There was no correlation between the transfusion history and anti-HCV positivity (2/4 of anti-HCV +ves vs. 13/26 of anti HCV -ves in NHL and 5/18 in HL.) Serum ALT levels of 2/4 of anti-HCV positives were elevated. Liver biopsy showed chronic hepatitis in these patients. Biopsy was not performed for the other two with normal serum ALT. HCV-RNA was present in the sera of all but one of the anti-HCV +ve patients. It was concluded that chronic HCV infection is more common in the patients with NHL in comparison to general population. There is no correlation between the history of transfusion and anti-HCV positivity in lymphoma. Liver and bile ducts, 1: Hepatitis viral, diagnosis Oncology, specific: Lymphoma } "Hepatitis C Infection in Non-Hodgkin Lymphoma"

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**"P P 2 0077" P 2 0077 Intra-Hepatic and Peripheral Blood Lymphocytes (IHL, PBL) in Patients with Chronic Hepatitis C (CHC) Albert Tran<sup>1</sup>, Guang Yang<sup>1</sup>, Michel Ticchioni<sup>2</sup>, Alain Bernard<sup>2</sup>, Patrick Rampal<sup>1</sup>, Sylvia Benzaken<sup>2</sup>**

<sup>1</sup> Liver Unit, Archet Hospital, Nice, France

<sup>2</sup> Department of Immunology, Archet hospital, Nice, France The host immune response have been suggested to play a role in liver injury occurring in patients with chronic hepatitis C. In order to explore the relationship between the relative proportions of intrahepatic and peripheral blood lymphocytes (ILL, PBL), the levels of viremia, and the histological hepatitis activity score, three-colour fluorescence-activated cytometric analysis was performed for 36 patients with chronic hepatitis C before interferon therapy and 6 control subjects without chronic hepatitis. Each liver specimen was divided into two parts: one for histological examination and one for immunological analysis. Tri-color CD45 was used to improve "lymphogating". Fluorescein isothiocyanate- or phycoerythrin-conjugated monoclonal antibodies with specificity for CD3, CD4, CD8, and CD20 (lymphocyte subpopulations), for CD69 (activated lymphocytes), and for CD16/56 (natural killer cells) were used. Levels of viremia were determined by quantitative PCR (Monitor, Roche Diagnostic Systems). The proportion of IHL CD4+ was significantly increased in patients with chronic hepatitis C, resulting in an IHL CD4+/CD8+ ratio significantly higher than in control subjects (0.55 – 0.21 vs 0.23 – 0.12, p = 0.046). The livers of patients with chronic hepatitis C contained a higher percentage of CD8+ T lymphocytes (40.7 – 13.9% vs 26.0 – 6.6%, p = 0.0001) and a smaller percentage of CD4+ T lymphocytes (20.7 – 7.3% vs 48.3 – 6.8%, p = 0.0001) which exhibited marked expression of CD69, compared to peripheral blood. No statistical correlation was found between the intrahepatic CD4+/CD8+ ratio and the level of viremia, Knodell's score, or transaminase activities. Our findings indicate that a cellular immune response does take place in HCV-infected livers, and could contribute to the pathogenesis of HCV-induced liver damage. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Intra-Hepatic and Peripheral Blood Lymphocytes (IHL, PBL) in Patients with Chronic Hepatitis C (CHC)"

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"P P 3 0078" P 3 0078 **High Prevalence of Antibodies to Hepatitis A Virus (HAV) Infection in Healthcare Workers** E. Rajan, S. Ai'Bloushi, M.G. Courtney, B. O'Farrell<sup>1</sup>, A.G. Shattock<sup>1</sup>, J.F. Fielding

Department of Medicine, Beaumont Hospital, Ireland

<sup>1</sup> Virus Reference Laboratory Dublin, Ireland *Objective:* To determine the occupational risk of contracting HAV infection among healthcare workers in a large general adult hospital which should represent the relative risk among healthcare workers in other general hospitals. *Methods:* 625 healthcare workers were recruited of which 264 were student nurses, 98 medical students, 87 staff nurses, 65 administrative staff, 50 physicians, 31 laboratory staff and 30 physiotherapists. Each participant completed a questionnaire by interview and 10 ml of venous blood was withdrawn which was tested for total anti HAV immunoglobulin (primarily IgG) using an ELISA competitive assay. *Results:* 17% of student nurses were HAV antibody positive, 18% of medical students, 48% of staff nurses, 41.5% of administrative staff, 40% of physicians, 41% of laboratory staff and 23% of physiotherapists were also HAV antibody positive. Staff nurses, physicians, laboratory technicians and administrative staff are at significant risk of HAV infection whereas physiotherapists, medical students and student nurses were not. *Conclusion:* These findings suggest that patient exposure does not alone account for the increased susceptibility. This suggests that healthcare workers may be at increased risk of HAV infection and would benefit from a HAV vaccination programme. Clinical practice: Epidemiology (non cancer) } "High Prevalence of Antibodies to Hepatitis A Virus (HAV) Infection in Healthcare Workers"

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## "P P 3 0079" P 3 0079 **Origin and Course of a Local Epidemic of Hepatitis-A in Germany**

\*R. Eissele, U. Kajdan, C. Fischer, R. Arnold

Dept. of Gastroenterology, Philipps University, Marburg, Germany Germany has a low rate of endemic hepatitis-A infection. Therefore, natural immunity is reduced, which predisposes to local epidemics. We report about the origin and the course of a local epidemic with hepatitis-A and discuss possible implications on active vaccination. *Patients:* In 42 patients (19 female and 23 male) with icteric hepatitis-A infection a common origin could be found. The diagnosis of hepatitis-A infection was confirmed by serology. The mean age of patients was 32 (2–62) years. Twenty-six patients were treated in the hospital with a mean duration of 10 (2–42) days, and 16 were out-patients. *Focus of infection:* Primary infection occurred in 3 members of a family running a small restaurant and in one guest. All of them had been infected by contaminated seafood. After 2–6 weeks another 29 patients suffered on acute hepatitis-A. All of them had eaten in the restaurant during the incubation period of the index family. A few weeks later 9 family members of these patients were diseased on hepatitis-A. *Clinical course:* The mean incubation period was 25 (16–37) days. The most common symptoms were: dark urine (69%), nausea (60%), lack of appetite and weight loss (54%), and vomiting (54%). The maximal increase of ALT was below 2000 U/l in 2/3 of patients and above 2000 U/l in 1/3 of patients. Serum bilirubin increased in 13 patients by more than 10 (up to 46) mg %. In 16 patients a transient decrease of the prothrombin-time was measured. In 40 patients no complications were observed, whereas 2 patients had a severe recurrent clinical course. *Conclusions:* In countries with a low rate of endemic hepatitis-A infections limited epidemics can be induced by "food workers". These infections could be prevented by active vaccination of persons working in the food-industry. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment }

"Origin and Course of a Local Epidemic of Hepatitis-A in Germany"

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"P P 3 0080" P 3 0080 **Incidence of HBV Positivity and Behaviour of HBsAg Carrier State in Cancer Patients, during Chemotherapy (CT)** C.G. Alexopoulos<sup>1</sup>,

\*M. Vaslamatzis<sup>1</sup>, G. Hatzidimitriou<sup>2</sup>

<sup>1</sup> Dpt Med. Oncology, Evangelismos Hospital Athens, Greece

<sup>2</sup> Transfusion Unit, Evangelismos Hospital Athens, Greece *Aim:* We prospectively studied: 1) The incidence of HBV markers positivity in cancer pts & 2) the changes in HBV profile of HBsAg carriers during CT. *Patients-Methods:* Serum HBsAg, HBeAg, HBsAb, HBcAb & HBeAb were determined using specific third generation ELISA (Abbott) in 1008 of 1402 (72%) cancer pts admitted in our Dpt between 1986–95 & in all 920 who received CT. Liver biochemistry was also performed. *Results* 1) 443 of 1008 pts (44%) had at least one HBV marker positive: 54 pts (5.3%) were HBsAg carriers while none was HBeAg+ve, 405 (91%) were HBcAb+ve, 321 (72%) were HBsAb+ve & 212 (48%) were HBeAb+ve positive: 50 pts (5.4%) were HBsAg carriers, 374 (41%) were HBcAb+ve, 280 (30%) were HBsAb+ve & 178 (19%) were HBeAb+ve. 2) In the 50 HbsAg carriers, serial HBV profile before, in the middle, after CT & in follow up & liver biochemistry before each CT course, demonstrated: in 43 pts (86%) stable HBs antigenaemia without clinical or biochemical signs of hepatitis. Seven of 50 pts (14%) developed hepatitis with significant increase of hepatocellular enzymes. Hepatitis was very severe in 3 pts (6%) with a bilirubin of 17 mg% & transaminases above 1500 units. In all 7, anti-HBs antibodies appeared in the serum with associated decrease of HBsAg titers. Serum HBsAbs appeared temporarily in 3 & permanently in 4 of 7 pts. *Conclusions:* a. The incidence of HBsAg carrier state in cancer pts is not different than in the general Greek population (5%) b. Reactivation of HBV infection with sometimes severe hepatitis during cancer CT, is not a rare phenomenon (14% in our series) c. Disappearance of HBs antigenaemia as a result of cancer CT is mostly a temporary phenomenon. Oncology, general: Therapy Liver and bile ducts, 1: Hepatitis viral, diagnosis Oncology, specific: Liver, biliary } "Incidence of HBV Positivity and Behaviour of HBsAg Carrier State in Cancer Patients, during Chemotherapy (CT)"

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"P P 3 0081" P 3 0081 **Nosocomial Transmission of HBV. Angelis, M. Kymissis, P. Garzonis, N. Sofoulis, N. Koumentakis,**

\*A. Simos

Medical Unit of "Sotiria" General Hospital of Chest Diseases of Athens-Greece *Purpose:* The study's purpose is the determination of the dispersion of HBV in chronic patients and the investigation of the possible significance of hospitalization as a risk factor for HBV infection. *Patients and methods:* 657 chronic patients, who were hospitalized in our hospital between Sept. 91 and Dec. 94, were classified in two groups. Group A consisted of 248 transfused patients, 157 (63.3%) males and 91 (36.7%) females, with a mean age 65.2 years (23–92), a mean number of hospitalizations 15.8 (2–60), a mean duration of hospitalization 8.8 months (3–30) and a mean number of transfusions 5.5 units (1–25). Group B consisted of 409 non transfused patients, 262 (64%) males and 147 (36%) females, with a mean age 67.3 years (22–92), a mean number of hospitalizations 15.9 (5–70) and a mean duration of hospitalization 9.2 months (3–50). Patients with other risk factors for hepatitis B were excluded from the study. As a control group, fully comparable for age and sex, we used 480 healthy controls without a history of chronic disease, hospitalizations or transfusions. High risk individuals for hepatitis B were excluded from the control group as well. The determination of the dispersion of HBV was made through the search of anti-HBcAg and HBsAg using the ELISA method. The statistical analysis was made on PC (D Base IV, SPSS). *Results:* In group A the prevalence of anti-HBcAg was 60.3% and of HBsAg 8.9%, in group B 54.6% and 7.85%, whereas in the control group 34.5% and 4.5% respectively. The statistical analysis showed important difference regarding the presence of HbsAg and anti-HBcAg between groups A, B and the control group. A positive correlation between serum positivity and number of transfusions in group A and number and duration of hospitalizations in group B was confirmed. *Conclusions:* The results show a high dispersion of HBV in chronic patients and demonstrate that besides transfusion hospitalization consists a significant risk factor for HBV infection as well. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Nosocomial Transmission of HBV"

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## "P P 3 0082" P 3 0082 **Prediction of Severity in Chronic Active Hepatitis B (CAHB) by PCR-RFLP Method**

\*H. Ueda, H. Tanaka, M. Miyano, M. Kinoshita, K. Mimura, S. Yukawa

3rd Dept. Internal Medicine, Wakayama Medical College, Japan We have reported that amino acid substitutions Ile (I) to Leu (L) at codon 87 and Ser to Gly (G)/Asn (N) at codon 97 due to DNA mutation in core region were noted in patients with CAHB, whose serum GPT (sGPT) were below 100 IU/l (published in 4th UEGW). However, it is time consuming to detect mutations by DNA sequencing. We studied whether these mutations could be detected or not by Restriction Fragment Length Polymorphism (RFLP) method. Twenty-six patients with CAHB were studied. CAHB were characterized of two groups according to sGPT value. In group 1 (10 patients) and group 2 (16 patients), sGPT were over 100 IU/l and below 100 IU/l, respectively. HBV DNA were extracted from patient's sera and amplified by PCR with core region specific primer. Digestion study at codon 87 and 97 for PCR products was performed with AluI and DdeI, respectively. To prevent incomplete digestion. PCR products were incubated with restriction enzyme at 37°C over night and analysed for agarose gel-electrophoresis. In group 1, DNA fragments ladder was the same pattern as wild type. The other hand, different ladder pattern (mutant type) were found in group 2. In digestion with AluI, DNA fragment of 88 bp was detected in group 1, but not in group 2. And also, in digestion with DdeI, DNA fragment of 410 bp was detected in group 1, but not in group 2. Further, ladder pattern that mixed both wild and mutant type, mixed type, was frequently found in group 2. Therefore, in group 2, mutant or mixed type were detected by RFLP. In this study, amino acid substitutions Ile to Leu at codon 87 and Ser to Gly/Asn at codon 97 due to DNA mutation in core region were associated with severity in CAHB. And these mutations were simply detected by RFLP. These results showed that PCR-RFLP at codon 87 and 97 is available for prediction of severity in chronic active hepatitis B without DNA sequencing. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment } "Prediction of Severity in Chronic Active Hepatitis B (CAHB) by PCR-RFLP Method"

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## "P P 3 0083" P 3 0083 Is There a Real Nuclear Localization of HBV Core Protein? A Detailed Subcellular Localization Study

\*H. Sirma, O. Rosmorduc, D. Kremsdorf, C. Bréchet

INSERM U370, Paris, France

The subcellular distribution of HBV capsid protein (C) and its implications for the viral life cycle is still a matter of debate. In the present study we examined the localization of C in different cell lines as well as in the livers of humans and replicative transgenic mice (TG) in dependence from cell cycle and viral replication status. *Methods: In vitro:* Huh7, COS and NIH 3T3 cells were stably and/or transiently transfected with constructs containing HBV, dHBV (generated from singly spliced 2.2 kb HBV RNA) or C-ORF alone. Huh7 cells were synchronized using TGF $\beta$ , double thymidine block and nocodazol (N). The intracellular distribution of C was studied by confocal microscopy (CM) and biochemical fractionation of synchronized cells. *In vivo:* Localization of C in the livers of highly replicating HBV TG (kindly provided by F. Chisari) and humans from both high and low HBV replicators was studied by Immunocytochemistry (IC) and CM permitting 3D reconstructions (3D). *Results: In vitro:* There was no evidence for a cell cycle related nuclear translocation of C, contrasting with recently reported data. C was in fact exclusively cytoplasmic characterized by diffuse to granular staining with perinuclear attenuation. Transfection of COS cells stably expressing large T-Antigen (LTA) revealed C is not a nucleoprotein like LTA. Double labelling with antibodies against nuclear pore complex (NPC) and lamin showed further an association of C with nuclear membrane (NM). Biochemical fractionation of synchronized cells confirmed further the in situ localization data. In addition, N-arresting cells in mitosis- led to a diminution of C as revealed by immunoblotting. *In vivo:* TG showed cytoplasmic C staining in centrilobular hepatocytes whereas nuclear C was panlobular revealed by IC as recently reported (Guidotti et al.). The human livers from high replicators showed in virtually all hepatocytes cytoplasmic C in addition to the nuclear staining. In low replicators C was restricted only to the nuclei. A detailed CM analysis of nuclear C distribution in TG and human hepatocytes with a 3D provided evidence for a localization of C only at the NM. *Conclusions:* Our results show 1) that C is restricted exclusively to the cytoplasm. However, we provide evidence for an association of C with the NM and mitotic disassembly of NM destabilize C. 2) In vivo, cytosolic C is an indicator of high viral replication. Altogether our data are consistent with the following scenario: low viral replication is accompanied by low C expression. The reported nuclear localization signal of C leads to its binding to the NM but is not sufficient for a translocation through the NPC. The accumulation and stabilization of C at the NM is disturbed with each mitotic NM disassembly. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Is There a Real Nuclear Localization of HBV Core Protein? A Detailed Subcellular Localization Study"

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"P P 3 0084" P 3 0084 **Randomised Controlled Trial of Interferon { a}2B in Prolonged Hepatitis B\***

\*K.T. Shenov, K.B. Leena

Dept. of Gastroenterology, Medical College, Trivandrum, India *Objective:* With the hypothesis that interferon is effective and well tolerated in prolonged hepatitis B (> 10 weeks), we designed this randomised controlled trial. *Setting:* Tertiary referral centre. *Participants:* Patients with virus B hepatitis of > 10 weeks and positive of anti HBcIgM, HBeAg with elevated alanine aminotransferase (1.5 {b4} N) were recruited. *Intervention:* { a}-interferon (INTRON A) 3 MU thrice weekly (group A) for sixteen weeks or conventional treatment (group B) was given. *Study variables:* Clinical status (weekly), biochemical and haematological parameters (monthly) and HBV markers at 4, 8 and 16 weeks of therapy. Subjects were followed up for 6 months after the trial. Compliance to therapy and side effects were monitored. *Outcome variable:* Clinical improvement, clearance of HBsAg and HBeAg. *Results:* Of 20 patients enrolled, 9 received interferon and 11 conventional treatment. Age ranged from 18 to 42 years and baseline characteristics were similar in both groups. Compliance therapy was 100% and side effects such as malaise and arthralgia were noted two patients. HBsAg became negative in two patients each in group A & B. HBeAg was negative in 3/9 (group A) and 2/11 (group B). One patient in group B progressed to subacute hepatic failure and expired. *Conclusion:* Interferon treatment is beneficial in prolonged B hepatitis and is a promising modality of treatment. Further long term trials are needed in larger samples.\* Study funded by Fulford India Limited (Schering Plough, USA). Liver and bile ducts, 1: Hepatitis, viral, treatment } "Randomised Controlled Trial of Interferon alpha2B in Prolonged Hepatitis B\*"

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"P P 3 0085" P 3 0085 **Pre-Core Stop Codon Mutations among Patients with Chronic HBV Infection in Turkey** A.M. Bozdayi, O. Uzunalimoglu, H. Bozkaya, H. Cetinkaya, H. Aydogan, M. Arslan, H. Ozsan, C. Yurdaydin, S. Karayalcin

Department of Gastroenterology, Ankara University, School of Medicine, Ankara, Turkey *Background:* Pre-core stop codon mutation, G to A substitution at nucleotide 1896 that preclude the production of HBeAg develops around the time of HBe seroconversion. Pre-core stop codon mutation (A1896) is not found in patients (pts) infected with HBV genotypes that have a C at nucleotide 1858 due to base-pairing in the stem-loop structure of the pregenome encapsidation signal. Thus the prevalence of the pre-core stop codon mutant (A1896) among HBeAg{ - }ve pts varies in different geographical areas depending on the predominant HBV genotype. *Aim:* To determine the prevalence of pre-core stop codon mutation (A1896) in Turkish pts with HBeAg+ve and HBeAg{ - }ve chronic hepatitis B. *Patients and Methods:* Sera from 14 HBeAg+ve and 18 HBeAg{ - }ve pts were analyzed by direct sequencing of the pre-core region of PCR amplified DNA. *Results:* All the patients studied had T at nucleotide 1858. Three of 14 HBeAg+ve pts had mixture of wild type and stop codon mutant A1896, the other 11 had wild type sequence only. Fifteen of 18 (83%) HBeAg{ - }ve pts had the stop codon mutation (A1896). Three pts had another commonly described mutation involving the G to A change at nucleotide 1899. Mutations involving the initiation codon was not observed in any pts studied. *Conclusion:* Most HBeAg{ - }ve Turkish pts with chronic hepatitis B have the pre-core stop codon mutation (A1896). The high prevalence of A1896 is related to the fact that the predominant HBV genotype in Turkey has a T at nucleotide 1858 which permits G to A mutation at nucleotide 1896. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Pre-Core Stop Codon Mutations among Patients with Chronic HBV Infection in Turkey"

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## "P P 3 0086" P 3 0086 Hepatitis B X-Protein is Exclusively Located in the Cytoplasm and Colocalizes with Proteasomes

\*H. Sirma, O. Rosmorduc, D. Kremsdorf, C. Bréchet

INSERM U370, Paris, France

In view of the potential implication of HBV X-Protein (X) in hepatocarcinogenesis we have studied its subcellular distribution during the cell cycle for the following reasons: *I.* The subcellular localization of X is still a matter of debate *II.* X may exert, depending on its sublocalization, different effects and interact with proteins which are temporary expressed and compartmentalized in function of the cell cycle. *Methods:* 1) Huh7 cells were stably transfected with HBV and dHBV (generated from singly spliced 2.2 RNA) containing constructs. 2) Expression of X was studied by immunoblotting. 3) Cell synchronization was achieved by TGF $\beta$  (G1), double Thymidine block [dT] (S) and Nocodazol [N] (M). S-Phase was additionally labelled by BrdU pulse. Cellular localization of X was studied by immunofluorescence (IF). 4) To analyse the behaviour of X in living cells we have used the green fluorescent protein (GFP). GFP was used as a C-terminal tag to create X-GFP chimera and was expressed in cells by transient transfection. Subsequently, the distribution of GFP and X-GFP was analysed in living cells by fluorescence microscopy. Using fixed cells, we have further performed double-labelling using 7-Actinomycin D and antibodies against Lamin and Proteasomes. The biological activity of the chimer protein was tested using the stimulation of NF-kB dependent transcription by X. *Results:* 1) The cells could be synchronized to high degree (> 80%). X was distributed irregularly as granules embedded in diffuse cytoplasmic staining with perinuclear dominated corona. 2) GFP alone was diffusely located both in the nucleus and the cytoplasm. In contrast, X-GFP was located only in the cytoplasm as granulo-globular structures and juxtannuclear caps. Using double labelling in fixed cells, CA confirmed the exclusively cytoplasmic location of X as already seen in living cells. IF and CA studies further demonstrated a colocalization of the cytoplasmic proteasomes at sites of X. X-GFP chimera activate NF-kB dependent transactivation consistent with recently reported data. Thus, addition of GFP to X does not alter one of its well characterized biological activity. *Conclusions:* 1) X is located exclusively in the cytoplasm. There is no cell cycle dependent translocation into the nucleus. These data support a model of X acting indirectly on transcriptional process. 2) The colocalization of X with proteasomes suggest that X may interfere with cellular protein degradation leading to modulation of the half-life and activity of transcriptional and other regulatory factors; this would provide an unifying explanation for the markedly pleiotropic effects of X. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Hepatitis B X-Protein is Exclusively Located in the Cytoplasm and Colocalizes with Proteasomes"

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## "P P 3 0087" P 3 0087 **Hepatitis B: Flare of Hepatitis during Alpha Interferon Therapy**

\*J. Areias, I. Pedroto, T. Freitas, A.M. Saraiva

Dept. Gastroenterology, Hospital Geral de Santo António and Instituto de Ciências Biomédicas Abel Salazar, University of Oporto, Oporto, Portugal

Current treatment of HBV-related hepatitis includes alpha interferon (IFN- $\alpha$ ). *Aim* – To assess the incidence and severity of the HBV flare with IFN- $\alpha$ . *Patients and Methods* – We have studied 36 patients with chronic hepatitis B histologically proven, that were enrolled in two randomized controlled trials of IFN- $\alpha$ . Eighteen patients were initially treated with 5 MU of IFN- $\alpha$ . Clinical data were analyzed on 13 (36%) responders (loss of HBe Ag and HBV DNA by dot blot) and 23 (64%) non responders. Flare was defined as an elevation of ALT greater than 3 times of the median pre-treatment value and  $> 200$  U/L during the 24 weeks of therapy. *Results* – Sixteen of 36 (44%) treated patients had a flare during IFN  $\alpha$  therapy. None of 23 untreated control subjects had a flare during a period of observation of 6 months. ALT levels during the flares ranged from 226 to 894 U/L. No patient had decompensated liver disease. Patients with and without a flare were similar concerning age, sex, initial mean ALT level, HBV DNA and liver histology. Patients who had a flare were more likely to loss HBe Ag and HBV DNA (30.5% vs 8.7%). Among the 13 responders, 7 (61.5%) experienced a flare with IFN $\alpha$ , and all had cleared viremia. Flares in responders had higher ALT levels (538 vs 226 U/L,  $p < 0.05$ ) than in non responders. *Conclusions* – During IFN- $\alpha$  therapy for chronic hepatitis B: 1) flares of hepatitis occurred in 44% of patients; 2) there was an association with a higher rate of HBe Ag and HBV DNA loss; 3) Early HBV flare with significant enzyme elevation results in sustained viral clearance. Liver and bile ducts, 1: Hepatitis viral, diagnosis }

"Hepatitis B: Flare of Hepatitis during Alpha Interferon Therapy"

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"P P 3 0088" P 3 0088 **Prevalence of Hepatitis E Virus Antibodies in Tunisia**

\*M.F. Khediri, M.R. Bouali, M. Ben Moussa, H. Ben Abdallah, J. Hamida, A. Amor

Department of Gastroenterology and Department of Microbiology, Military Hospital, Tunis, Tunisia Hepatitis E virus (HEV) infection is common in Asia and Africa, but its prevalence is unknown in our country. Furthermore, although HEV represents the main etiological agent of enterically transmitted non-A, non-B (NANB) hepatitis, the risk factors associated with anti-HEV positivity are not well known yet. *Aim:* This study investigates the prevalence of HEV antibodies in different populations and compares it to hepatitis A and C antibodies prevalence. *Method:* We studied the prevalence of anti HEV IgG in 205 asymptomatic male volunteer blood donors (AVBD), 87 health related staff (HRS), 49 hemodialysis patients and 21 cirrhotic patients. All samples were tested with HEV EIA (Abbott Laboratories). ELISA technique was used to detect anti-HAV IgG and anti-HCV antibodies. *Result:* (see table). n age (years) anti HEV anti HAV anti HCV AVBD 205 24 4.9% 100% 0.49% HRS 87 32 8%\* 98% 1.7%\* Hemodialysed 49 47 14%\* 98% 41%\* Cirrhotic patients 21 60 19%\* 100% 86%\*\* p < 0.05 referring to AVBD *Conclusions:* The prevalence of HEV antibodies varies from 4.9% (AVBD) to 8% (HRS) in healthy people. It is lower than rates encountered in India and other parts of Africa, and higher than European rates. This prevalence is about 14% and 19% respectively in hemodialysis and cirrhotic patients, suggesting that these two conditions may represent risk factors for HEV infections (but this may also be related to the more advanced age in these two groups). *Clinical practice:* Epidemiology (non cancer) Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Prevalence of Hepatitis E Virus Antibodies in Tunisia"

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"P P 3 0089" P 3 0089 **Detection of Hepatitis G/GB-C Viral RNA but not HCV RNA in the Different Semen Fractions of Infected Patients**

\*T. Persico, V. Thiers<sup>1</sup>, R. Tuveri<sup>1</sup>, M. Di Fine<sup>3</sup>, A.E. Semprini<sup>2</sup>, C. Brechot<sup>1</sup>

<sup>1</sup> INSERM-U370 Necker and CBMS Pasteur Institut Paris, France

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<sup>3</sup> C. M. S. Patrignano, Rimini, Italy  
The issue of sexual transmission of HCV is still debated. A new RNA virus, HGV/GB-C, related to HCV, has been recently identified. There is no information on the risk of its sexual transmission. *Objective:* Investigate the presence of HCV and HGV RNA in the different fractions of semen: seminal plasma (SP), spermatozoa (Spz.), round cells (RC, leukocytes and spermatogenesis cells), swim-up (SU) by PCR. *Methods:* 90 anti-HCV (+) Italian previously drug addicted males, were included (27 HIV+). The different fractions of the semen samples were obtained after discontinuous Percoll gradient. HCV RNA was tested in sera and different semen fractions by PCR (5{\'a2} NCR). HGV RNA was tested in sera and in some selected semen samples by PCR (NS<sub>3</sub>/NS<sub>5</sub>). Negative results were only interpreted in semen fractions in the absence of PCR inhibition (previously reported in such samples). *Results: Serum:* HCV RNA was detected in 55/90. 26/90 samples were positive for HGV/GB-C including 15 HCV RNA (+) and 11 HCV RNA ({} -). *Semen fractions:* HCV RNA was detected in none of the 22 SP, 50 RC, 50 Spz and 50 SU tested. HGV/GB-C RNA was detected in the seminal plasma of 6/24 (25%) tested, serum HGV RNA (+) individuals. *Conclusions:* Our results: 1) demonstrate that even in HCV-viremic subjects each semen fraction (SP, RC, Spz) results uninfected from HCV, confirming that sexual transmission of HCV is rare; 2) confirm the high prevalence of HCV/HGV coinfections in IVDU. 3) show, that HGV/GB-C genome can be detected in sperm raising the possibility of distinct modes of transmission from HCV. Liver and bile ducts, 1: Hepatitis viral, diagnosisClinical practice: Epidemiology (non cancer) }"  
"Detection of Hepatitis G/GB-C Viral RNA but not HCV RNA in the Different Semen Fractions of Infected Patients"

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"P P 3 0090" P 3 0090 **Idiopathic Thrombocytopenic Purpura (ITP) and Viral Hepatitides. Is There Any Relationship?** G.N. Dalekos<sup>1</sup>, E. Zervou<sup>2</sup>, S. Tsiara<sup>1</sup>, K. Bourantas<sup>1</sup>, E.V. Tsianos<sup>1</sup>

<sup>1</sup> Division of Internal Medicine, School of Medicine University of Ioannina, Greece

<sup>2</sup> Blood Bank at the University Hospital of Ioannina, Greece *Purpose:* Acute and/or chronic ITP has already been associated with several viral infections. This study was conducted in an attempt to estimate the possible relationship(s) of viral hepatitides (A-E) with well defined ITP cases. *Methods:* We determined the presence of various markers of infection from viral hepatitides (A-E) in serum samples from 23 patients (5 male and 18 female, range 17–74 years) with chronic ITP. Samples were obtained before any treatment, transfusions of blood or blood products and platelet concentrate infusions. Patients with epidemiological, clinical or biochemical data suggestive for infections with viral hepatitides or with a past history of jaundice or first degree relative suffering from liver diseases were excluded from the study. 975 healthy volunteers (682 male and 303 female, range 20–80 years) were also studied. All subjects were investigated for the presence of anti-HAV, HBsAg, HBsAb, HBcAb, HBeAg, anti-HCV, anti-HDV and anti-HEV by commercial enzyme immunoassays. *Results:* None of the markers studied was statistically more frequent in patients compared to those of healthy controls. (Table) Table. Frequency (%) of hepatitides viral markers in patients with ITP and in healthy controls. Patients Healthy controls anti-HAV IgG 65.2 56.3 NS anti-HAV IgM 0 0 HBsAg 0 1.7 NS HBeAg 0 0 HBcAb 30.4 22.5 NS HBsAb 30.4 20.2 NS anti-HDV (IgG) 0 0 Anti-HCV 4.3\* 0.4 NS anti-HEV (IgG) 8.7\*\* 0.1 NS \*The only one patient reactive by third generation enzyme immunoassay was negative by RIBA-III while HCV-RNA was not detected. \*\* Both two patients reactive by enzyme immunoassay were negative by the inhouse immunoblot assay. NS = not significant by  $\chi^2$  or Fisher's exact test. *Conclusions:* Our findings suggest that at least in our region other immunopathogenetic mechanisms may be responsible for the development of ITP. Particularly for HCV, this study can neither confirm the findings observed by others nor indicate a trend for pathogenetic link between HCV and ITP. Clinical practice: Epidemiology (non cancer) } "Idiopathic Thrombocytopenic Purpura (ITP) and Viral Hepatitides. Is There Any Relationship?"

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"P P 3 0091" P 3 0091 **Infections from Viral Hepatitides and HTLV-I/II after Open-Heart Surgery in North Western Greece. A Preliminary Study** G.N. Dalekos<sup>1</sup>, G.K. Liapi<sup>2</sup>, E. Zervou<sup>3</sup>, J. Goudevenos<sup>2</sup>, E.V. Tsianos<sup>1</sup>, D. Sideris<sup>2</sup>

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<sup>2</sup> Department of Internal Medicine (Division of Cardiology), School of Medicine, University of Ioannina, Greece

<sup>3</sup> Blood Bank at the University Hospital of Ioannina, Greece *Purpose:* The aim of the present preliminary study was an attempt to determine the prevalence of several markers of viral hepatitides (B-E) and HTLV-I/II infections in patients (pts) from northwestern Greece who underwent an open-heart surgery. *Methods:* We investigated 104 pts (90 having coronary artery bypass grafting and 14 having replacement of mitral or aortic valve) and 113 healthy controls matched for age and sex. Forty six pts had been operated on before 1991, among them 83 pts had the open-heart surgery done in Greece and the remaining 21 pts abroad. The pts had at least a 6 month period from the time of the operation to the entrance the study. The serological determinations of the various viral markers were done using commercially available enzyme immunoassays as well as confirmatory immunoblot assays (for HCV and HEV). *Results:* We found that none of the pts was positive for the HBsAg or the anti-HTLV-I/II antibodies. By contrast, the markers of a previous infection by HBV were found more frequent in pts (HBcAb: 46.1%, HBsAb: 37.3%, HBeAb: 37.3%) than in healthy controls (30.9%, 24.8% and 7.95% respectively). These differences were statistically significant ( $p < 0.05$ ,  $p < 0.10$  and  $p < 0.0001$  respectively). The presence of the markers of previous HBV infection among pts was not associated with age, sex, place of the operation or the number of transfusions, but with a longer duration from the day of the open-heart surgery (HBcAb: 70.7 – 65.2 in positive vs 49.6 – 38.4 in negative ( $p < 0.05$ ), HBsAb: 75.3 – 68.7 in positive vs 49.9 – 39.1 in negative ( $p < 0.10$ ) and HBeAb: 70.9 – 70.3 in positive vs 52.5 – 38.8 in negative ( $p < 0.0001$ )). Anti-HCV and anti-HEV antibodies were detected in 1.92% and 3.94% of pts respectively but this frequency was not statistically significant when compared to healthy controls (0% for both antibodies). *Conclusions:* We conclude that: (1) this group of pts does not appear to be a high risk group for HTLV-I/II infection as we have already reported it for other groups; (2) although none of the pts was positive for HBsAg, the presence of significantly increased incidence of markers of previous HBV infection compared to healthy could suggest this group as a high risk one for HBV infection and a intensive vaccination schedule against HBV before the operation seems rationale; (3) the presence of anti-HEV antibodies among the pts needs further evaluation, since, the oral fecal route of transmission of HEV may be not the only one. *Clinical practice: Epidemiology (non cancer) }* "Infections from Viral Hepatitides and HTLV-I/II after Open-Heart Surgery in North Western Greece. A Preliminary Study"

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"P P 4 0092" P 4 0092 **Anagraphic, Anthropometric and Metabolic Predictors of Ultrasonographic 'Bright' Liver** A. Lonardo, M. Bellini<sup>1</sup>, P.L. Tartoni<sup>2</sup>, E. Tondelli<sup>3</sup>, A. Grisendi, M. Pulvirenti, G. Della Casa,

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<sup>3</sup> Department of Chair of Medical Statistics, University, Modena, Italy *Background & Aim* Ultrasound (US) finding of a 'bright' liver (BL) is accurately predictive of fatty liver allowing non-invasive surveys of this common condition. Our purpose was to ascertain factors independently associated with a BL US finding in our series. The hypothesis was that a cluster of features characterize the so-called 'Bright Liver Syndrome' (Lonardo A, Endoscopy 1995; 27 A61. Lonardo A, Am J Gastroenterol 1995; 90: 2072–2074). *Series & Method* 97 subjects underwent liver US scanning, anthropometric and laboratory evaluation. Criteria for exclusion were: pregnancy, thyroid disease, exposure to hepatotoxic drugs or chemicals, familial heterozygous hypobetalipoproteinemia (Lonardo A, Gastroenterology 1996; In Press). The following data were registered: age (ys); alcohol consumption (g/day); body mass index (BMI, in Kg/m<sup>2</sup>); serum levels of GOT and GPT (mu/ml), albumin (g/dl), total cholesterol (ch), HDL-ch, triglycerides (tg), apoB, fasting glucose (all in mg/dl). Based on the liver-kidney contrast (Yajima Y. Tohoku J Exp Med 1983; 139; 43–50) cases were classified as controls (n = 50; 40 males) or BLs (n = 47; 35 males). Data were analyzed through SPSS package. *Results* Mean values were as follows (control vs. BL): age 65.6 vs. 56.4; BMI 25.8 vs. 29.2; alcohol 26.1 vs. 35.8; glucose 91.6 vs. 96.8; ch 195 vs. 225; ch-HDL 38.3 vs 43.2; apoB 1.23 vs. 1.44; tg 134.6 vs. 178.1; albumin 3.5 vs. 3.9. Univariate F-ratio analysis selected BMI (0.0001), serum albumin (0.0004), age (0.0005), ch (0.0009), tg (0.005), apoB (0.005) and ch-HDL (0.02) as significantly different in cases with BL vs. controls. Using BL as a dependent variable, logistic regression analysis (LRA) carried out through backward stepwise approach disclosed BMI (0.0072), age (0.0080), apo B (0.0359) and tg (0.0822) to be independent predictors of BL. However, when forward stepwise approach was adopted, BMI (0.0072) ch (0.0143) and age (0.0185) turned out to be significant. LRA allowed correct classification of cases with 74.22% accuracy. *Conclusions* Obesity, younger age, hypercholesterolemia, hypertriglyceridemia and elevated serum apo B levels are independent predictors of BL in our series. These findings support the existence of the "'Bright Liver Syndrome'" and highlight its metabolic significance. *Nutrition: Metabolism Liver and bile ducts, 1: Hepatotoxicity, ethanol Radiology and ultrasound: Diagnosis }* "Anagraphic, Anthropometric and Metabolic Predictors of Ultrasonographic 'Bright' Liver"

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## "P P 4 0093" P 4 0093 **Ultrasonographic Score (USS) of Chronic Hepatitis**

\*G. Palasciano, V.O. Palmieri, F. Ungaro, A. Velardi, P. Portincasa

Chair of Semeiotica Medica, Department of Internal and Occupational Medicine, University of Bari Medical School, Bari, Italy

An ultrasonographic score (USS) has been prospectively correlated to the histological activity index (HAI) in 20 patients with chronic hepatitis (10 HCV, 6 HBV, 1 HBV and HCV, 2 alcohol-correlated). USS was determined within 24<sup>h</sup> from liver biopsy by 3 independent operators without knowledge of the biopsy results, clinical data and previous US. The parameters of USS were classified as hepatic, extrahepatic and vascular: hepatic echogenicity, distal attenuation, liver edge, periportal fibrosis, portal hypertension, echogenicity of hepatic veins wall with doppler waveform, porta hepatis lymphnode, Morrison space thickness and Harbin index (caudate lobe transverse diameter/right lobe transverse diameter). Each parameter was scored as 1, 2 or 3. A recently proposed score (Williams et al., J Hepatol 1995; 22: 513–21) involving 3 parameters (hepatic echogenicity, liver edge and periportal fibrosis) was simultaneously evaluated in each patient. Comparisons were made between the USS and the results of histological examinations using the Spearman Rank correlation coefficient. USS was highly and positively correlated with HAI (n = 20; r = +0.73; p < 0.001) and the results were better than applying the score proposed by Williams (n = 20; r = +0.55; p < 0.05). The accuracy of the USS in the diagnosis of cirrhosis was also evaluated: Cut-off value Sensitivity Specificity Williams score { \b3 } 6 66.7% 99.8% USS { \b3 } 18 83.4% 100% The USS proved to correlate with the histological activity of hepatic disease and allowed the identification of patients with cirrhotic chronic liver disease. The utility of the USS for grading and staging of diffuse hepatic diseases is under evaluation. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis }

"Ultrasonographic Score (USS) of Chronic Hepatitis"

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## "P P 4 0094" P 4 0094 Nitrous Oxide Analgesia for Intercostal Liver Biopsies: Results of a Prospective Randomized Trial

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Pre-mixed 50% nitrous oxide and oxygen mixture (Entonox<sup> </sup>) analgesia has previously been shown to be effective in pediatrics for painful acts. It is widely used during labour, is safe and can easily be administered by the patient. Liver biopsy is essential for the diagnostic and severity assessment of most chronic liver diseases, however it may be painful to the patient. Sedation is not routinely given before biopsy because no protocole has proven to be effective so far.

**Aims:** to study prospectively the effects of Entonox<sup> </sup> on pain relief and comfort in comparison with a placebo in patients undergoing intercostal liver biopsy using a randomized study design.

**Methods:** 48 consecutive patients admitted since march 1996 to our unit for intercostal liver biopsy (chronic hepatitis C: 26, alcoholic liver disease: 12, others: 10) were enrolled after local ethical committee approval and written informed consent. They were randomized to receive during biopsy either (i) a breathing mixture of even parts of oxygen and nitrous oxide (Entonox<sup> </sup>) from a face mask with a demand valve (group E, n = 23), or (ii) a breathing oxygen placebo from the same valve setup (group P, n = 25). Liver biopsy was performed by 2 senior operators according to the Menghini technique after adequate local anesthesia with Xylocaine 1%. Pain after biopsy was assessed at the end of procedure (D0) and the next morning (D1) using visual analogue scales (VAS) scoring from 0 to 100. The following data were also assessed: comfort scored from 0 to 100 (VAS); anxiety scored from 0 to 100 (VAS); amount of analgetic drugs (paracetamol mg) required within the 12 hours following biopsy; acceptance of a new biopsy; incidents and side effects observed.

**Results:** Pain scores at D0 were 10.95 – 2.66 and 29.72 – 4.7 for groups E and P respectively (p < 0.002). Pain scores at D1 were 15.7 – 4.6 and 35 – 5.4 for groups E and P respectively (p < 0.01). Comfort scores were 84.4 – 3.35 and 68.44 – 5.28 for groups E and P respectively (p < 0.02). Anxiety scores were 31.3 – 4.85 and 34.08 – 6.27 for groups E and P respectively (p = 0.7). All patients agreed for new biopsy with the same conditions. No serious adverse effect was observed. Amount of analgetic drugs required was not statistically different between the 2 groups. The average cost of Entonox<sup> </sup> use was 4\$ per biopsy.

**Conclusions:** Administration of Entonox<sup> </sup> during intercostal liver biopsies resulted in a significant decrease in pain at D0 and D1 and in discomfort of patients without influence on anxiety. If such results are confirmed on a larger group of patients, Entonox<sup> </sup> could increase the acceptability of liver biopsy in the follow up of patients with chronic liver diseases.

**Clinical practice:** Management strategy

**Clinical practice:** Quality assurance

Liver and bile ducts, 1: Hepatitis viral, diagnosis }

"Nitrous Oxide Analgesia for Intercostal Liver Biopsies: Results of a Prospective Randomized Trial"

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## "P P 4 0095" P 4 0095 Serum Erythropoietin Level in Cases of Normocytic Normochromic Anaemia in Hepatic Fascioliasis

\*M.N. El-Khashab, A.M. Mahmoud, M.Z. Nasar, I.M. Hegazi, E.G. El-Badrawy

From Tropical Med. and Clinical Pathology Departments, Faculty of Medicine, Zagazig University, Egypt. In Egypt, human fascioliasis is an increasing health problem especially in the Nile Delta. This study was conducted on 35 anaemic\* patients with fascioliasis, 20 anaemic\* patients with schistosomiasis (parasitic control group) and 10 persons (healthy control group). Serum erythropoietin (EPO) and ferritin were measured using a sandwich ELISA technique, as well as other ferrokinetic parameters were done. In patients with fascioliasis, EPO level (19.05 – 13.3 mU/ml) was significantly higher than those of healthy control (7.23 – 1.6 mU/ml) and of schistosomiasis (12.3 – 2.85 mU/ml) groups ( $P < 0.001$ ). Serum ferritin was significantly higher in fascioliasis group (384.8 – 51.1 ng/ml) than in schistosomiasis (174.7 – 83.4 ng/ml) and in healthy control (117.5 – 29.5 ng/ml) groups. ( $P < 0.001$ ). Other ferrokinetic studies showed low serum iron, subnormal transferrin saturation, low total iron binding capacity, in spite of adequate iron stores shown by high serum ferritin, these findings together with normal reticulocytic count were similar to those found in the anaemia of chronic disorders. The presence of anaemia in spite of high EPO level and adequate body iron stores may be explained by unresponsiveness of bone marrow to high EPO level which may be due to blocking the action of EPO by some cytokines as interleukin -1, tumour necrosis factor, and gamma interferon which were proved to be abundant in hepatic fascioliasis, or it may be due to an inhibition of bone marrow by large amount of proline which is usually present in hepatic fascioliasis. After treatment, cases of hepatic fascioliasis showed a good improvement of all parameters which were more or less comparable to those of healthy control. \* Normocytic Normochromic anaemia. Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 1: Chronic non viral hepatitis } "Serum Erythropoietin Level in Cases of Normocytic Normochromic Anaemia in Hepatic Fascioliasis"

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"P P 4 0096" P 4 0096 **Cirrhosis and Cryoglobulinemia: Relation with Severity and Evolutivity of Liver Disease**

\*I. Allemand, M. Perrard, P. Pagliero, P. Bellon, D. Monges, M.A. Chrestian, A. Grolami

Service d'Hépatogastro-entérologie, CHU Timone, 13005 Marseille, France Recent studies have reported a relationship between presence of mixed cryoglobulinemia (CG) and cirrhosis in patients with alcoholic or viral liver disease. The aim of this study was to assess the prevalence and the prognostic significance of CG. *Patients and methods.* 77 cirrhotic patients (53 men, 24 women) were enrolled in this study. All the patients were tested for anti-HCV antibodies by a third generation ELISA test, for HCV-RNA by PCR, and for HBS Antigen. Cryoglobulinemias were characterized by immunoblotting. The causes of cirrhosis were alcohol (31 patients), HCV (30 patients) and miscellaneous (16). In addition, 101 patients with chronic hepatitis caused by HCV but without cirrhosis, were included. *Results.* CG was found in 66% of our patients with cirrhosis (58% in alcoholic cirrhosis, 74% in HCV-cirrhosis: NS), however, the CG level was higher in HCV patients. There was no significant difference in age between patients with CG and without CG (56 – 9 y. vs. 61 – 9 y. in alcoholics, 59 – 12 y. vs. 53 – 14 y. in HCV infected patients). There was no difference in prevalence of CG according to CHILD' score. Among the patients without cirrhosis, CG was found in 54,4%. There was no difference in age between patients with and without CG (42 – 14 y. vs. 41 – 15 y.). *Conclusion.* These results confirm the high prevalence of CG in liver disease, and the role of HCV infection. The fact that CG is unrelated with the CHILD's score nor with and early occurrence of cirrhosis suggests that it is an epiphenomenon without consequence on the evolution of the liver disease. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Cirrhosis and Cryoglobulinemia: Relation with Severity and Evolutivity of Liver Disease"

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## "P P 4 0097" P 4 0097 **Child-Pugh-MEGX Score in Assessment of Prognosis in Cirrhotic Patients**

\*R. Testa, S. Cagliaris, E. Giannini, L. Arzani, S. Alvarez, G.L. Guido, A. Remagnino, G. Celle, D. Risso<sup>1</sup>, P.B. Lantieri<sup>1</sup>, R. Pellicci<sup>2</sup>, L. Mondello<sup>2</sup>, G. Dardano<sup>2</sup>, U. Valente<sup>2</sup>

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Prognostic evaluation of cirrhotic patients is a basic step for liver transplantation. The Child-Pugh's score is the usual tool and monoethylglycine xylylidide (MEGX, lidocaine metabolite) formation was proposed as an additional test. Aim of this study was to verify the prognostic usefulness of the combined score Child-Pugh-MEGX in cirrhotic patients. One hundred forty-three patients (104 males, 39 females, mean age 49 – 9), consecutively admitted to our Units for functional hepatic evaluation, were studied. According to Child-Pugh's score 32 patients were class A, 79 class B and 32 class C. Serum MEGX (ng/ml) at 30 min after i.v. lidocaine (1 mg/Kg) was measured by TDX fluorescent polarization immunoassay. MEGX 30 min were scored as follows: score 1 to > 30 ng/ml; 2 to 30 \f7 10 and 3 to < 10. The modified Child-Pugh-MEGX score was calculated by adding MEGX-score to Child-Pugh original score. In the follow-up period, ranging from 6 to 60 months, twenty patients died and thirty were transplanted. Kaplan-Meier survival curves were calculated for patients: 1) with Child-Pugh scores {\a3} 9 and for those with scores > 9 (whole survival was 93% versus 63%, Cox's test  $p < 0.00001$ ); 2) with MEGX levels {\b3} 10 ng/ml and for those with levels < 10 (94% versus 70% survivors,  $p = 0.001$ ), and 3) for patients with Child-Pugh-MEGX scores {\a3} 12 and for those with scores > 12 (92% versus 58% survivors,  $p < 0.00001$ ). These whole survivals reflect those at 12 months. Excluding Child-Pugh's class A patients, Cox's test significativity was  $p = 0.00008$  for Child-Pugh score,  $p = 0.00049$  for MEGX level and  $p = 0.00001$  for Child-Pugh-MEGX score. These results suggest that MEGX test can improve prognostic evaluation only in Child-Pugh's class B and C patients. Liver and bile ducts, 1: Liver transplantation } "Child-Pugh-MEGX Score in Assessment of Prognosis in Cirrhotic Patients"

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"P P 4 0098" P 4 0098 **The Changes of the Lipid Profile in Hepatitis Patients** Y. Baykal, M.R. Mas,

\*S. Nalbant, H. \d6zotuk, C. G\ 'f6nl\ 'fcsen, F. Kocabalkan

GATA Int. Med. Dept. Ankara/Turkey The liver has an important role in the metabolism of cholesterol, cholesterol esters, phospholipid and triglycerid. The transportation of cholesterol, triglycerid and phospholipid are carried by apolipoproteins. The lipid profile changes in acute and chronic liver disease. Activity of the plasma lesitin cholesterol acil transferase (LCAT) which is produced by the liver and esterifies the plasma cholesterol, decreases. So HDL and VLDL decrease; LDL and triglycerid increase. Some reports declared that annexin-V and apoprotein-H facilitate the bounding of protein-S of HBsAg to hepatosit. We studied lipid fractions in hepatitis-C, chronic active hepatitis (CAH), chronic persistent hepatitis (CPH). Cont (n. 34) HBV (n. 30) HCV (n. 14) CPH (n. 13) CAH (n. 44) Cholest. 208.11 – 31 190.16 – 54 203 – 53.7 192.8 – 39 181.8 – 33.6 Triglycerid 190.02 – 84 155.83 – 83 163.46 – 83.6 126.1 – 50.4 102.55 – 41.1 HDL 37.55 – 6.4 40.66 – 11.1 49.4 – 5.2 38.6 – 4.9 45.17 – 10.1 LDL 138.52 – 27.4 119.33 – 58.6 122.6 – 54.6 133.5 – 39.3 115.42 – 34.4 VLDL 38.4 – 17.4 31.08 – 16 32.6 – 17 25.2 – 15.3 20.4 – 8.1 We found low cholesterol values in subjects, specially in CAH patients. It was nearly the same for triglycerid. HDL-cholesterol was the highest in active HCV infectious patients. LDL-cholesterol was lowest in CAH group. When we compared the CAH with CPH cholesterol, it was obtained that triglycerid and cholesterol values were lower at CAH but it was not statistically significant ( $p > 0.01$ ). HDL was higher and LDL was lower at CAH group. ( $p < 0.05$ ). Cholesterol and triglycerid were lower HBV infection group ( $p > 0.05$ ). HDL was higher at HCV group and LDL was lower at HBV group ( $p > 0.05$ ). As a conclusion, We obtained high lipid levels at all of the subjects according to control group. But you can not explain these changes only with some metabolic changes at the level of hepatosit (disorders of the Lechitin metabolism, decreasing LCAT enzyme activity) and disorders at the level of membrane receptors and changes of the metabolism of the hepatic synthesis. So we need more studies for explaining that pathophysiologic event. Liver and bile ducts, 1: Chronic non viral hepatitis Liver and bile ducts, 1: Hepatitis viral, diagnosis Clinical practice: Management strategy } " "The Changes of the Lipid Profile in Hepatitis Patients"

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## "P P 4 0099" P 4 0099 Increase of Urinary Neopterin Levels in Chronic Liver Disease

\*H. Simsek, A. Kadayifci, Z.Z. Altindag, G. Sahin, M.A. Ozturk, Y. Akcan

Hacettepe University, Ankara, Turkey

Neopterin is a pteridine which is produced under the control of interferon-gamma by human mononuclear phagocytes. Although, physiological role of neopterin is not yet clear, it is generally accepted as one of the indices of cell-mediated immune activation. Increased serum and urinary neopterin levels have been found in conditions causing activity of cellular immunity, including various malignancies, autoimmune disease, certain viral infections and transplant rejection. Therefore, it is a useful tool in the diagnosis and monitoring the therapy of these conditions. This preliminary study was carried out to evaluate the urinary neopterin levels in chronic liver disease (CLD). Fifteen patients with liver cirrhosis, 13 patients with chronic active hepatitis C (CAH-C), and 16 healthy subjects were enrolled to the study. The diagnose was based on clinical findings and liver biopsy in all patients. Early morning urine samples were obtained from all of the subjects and urinary neopterin was measured by high pressure liquid chromatography. The mean levels of urinary neopterin (ng/ml) between three groups were compared by Student's t test (Table 1)

Groups	n	M/F	median age	Neopterin (mean – SEM)
1. Cirrhosis	15	11/4	49	399 – 972.
CAH-C	13	6/7	47	182 – 623.
Control	16	9/7	44	123 – 16

An overall increase of neopterin levels in CLD were observed. This increase was most prominent in liver cirrhosis and statistically significant compared to controls ( $p = 0.007$ ). Therefore, neopterin levels in CAH-C patients did not show marked elevation as found in cirrhosis. Neopterin levels in cirrhotic patients did not affected by etiology of disease, its clinical severity and are not correlated with serum alanine aminotransferase and aspartat aminotransferase levels. *Conclusion:* This study suggest that urinary neopterin value was elevated in CLD, especially in cirrhosis. Cell-mediated immune activation may be responsible for increase in urinary neopterin level in these patients. Immunology and microbiology: Host defense mechanisms

Liver and bile ducts, 1: Cirrhosis: portal hypertension  
Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Increase of Urinary Neopterin Levels in Chronic Liver Disease"

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## "P P 4 0100" P 4 0100 **Increments in Plasma Prothrombin Fragment 1.2 Concentrations in Chronic Liver Disease**

\*H. Simsek, A. Kadayifci, I. Haznedaroglu, S. Kirazli

Hacettepe University Medical School, Ankara, Turkey Prothrombin fragment 1.2 (PF 1.2) is a peptide fragment that is generated during the conversion of prothrombin into thrombin which is a main key event within the coagulation cascade. As a good molecular marker of thrombin formation, quantitative PF 1.2 determination may be used to assess the hypercoagulable/prethrombotic states. Abnormal hemostasis is a common complication of liver diseases, and its underlying pathogenesis is still an enigma. In this study, we have measured the plasma levels of PF 1.2 in patients with chronic liver diseases (CLD) in order to assess in vivo coagulation in these patients. Twenty-six patients with liver cirrhosis, and 14 patients with chronic active viral hepatitis were included. Age and sex matched 15 healthy subjects were also studied as controls. Venous blood samples, which were obtained without venous stasis, were collected in standard citrated tubes and centrifuged. Supernatant plasma was stored at  $-30^{\circ}\text{C}$  until assayed up to 3 months. Plasma PF 1.2 level in all samples was detected by EIA (Enzygnost F1 + 2 micro kit). The reference range and measuring range of kit was 0.44–1.1 nmol/L and 0.04–10 nmol/L, respectively. Data was expressed as mean – SEM and significance of differences between groups was tested by one way analyze of variance and by unpaired student's t test. The mean plasma level of PF 1.2 in patients with liver cirrhosis (4.2 – 0.5) significantly elevated when compared to that of both patients with CAH (2.6 – 10.3) and that of healthy subjects (1.7 – 0.05) ( $p = 0.03$  and  $p = 0.0001$ , respectively). The difference between CAH and controls was also statistically important ( $p = 0.01$ ). *Conclusion:* These results suggest that patients with CLD, especially cirrhosis is often associated with a derangement in hemostatic process. Elevated concentrations of PF 1.2 in these patients might be accepted as a clue of thrombotic risk such as portal and other venous thrombosis. Therefore, long term follow up of CLD patients with elevated plasma PF 1.2 levels is required to assess its clinical importance. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Increments in Plasma Prothrombin Fragment 1.2 Concentrations in Chronic Liver Disease"

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## "P P 4 0101" P 4 0101 The Assessment of Arrhythmogenic Side-Effect of Interferon- $\alpha$ 2A by Heart Rate Variability Tests in Chronic Active Hepatitis

\*A. Kadayifci, K. Aytemir, M. Arslan, S. Aksoyek, M.C. Savas, B. Sivri, B. Kayhan

Hecettepe University Medical School, Ankara, Turkey Cardiac arrhythmia and sudden death have been reported recently in various clinical trials of interferon. In this study, the cardiac arrhythmogenic side-effects of recombinant interferon- $\alpha$  2A (rINF- $\alpha$  2A) were investigated prospectively with heart rate variability (HRV) tests, in a group of patients with chronic active viral hepatitis (CAH). Sixteen patients with CAH type B, 14 patients with CAH type C and one patients with CAH type D were included in the study and 4.5 MIU, 3 MIU and 9 MIU of rINF- $\alpha$  2A was administrated thrice weekly to these patients, respectively. The HRV analysis of all patients were made with a standard record of 7 minutes at the beginning of the study and at the first and sixth month of interferon therapy and also 6 months later ceasing the therapy. Two-time domain variables were calculated as being the mean RR intervals (MRR) and the mean of squared differences between successive intervals (MSD). In addition, power of the low frequency peak (P1) and power of the high frequency peak (P2) are calculated for spectral analysis as the determinants of frequency-domain analyses. The mean values of data obtained from all patients are shown in Table 1. Table 1. The mean values of data obtained from HRV analysis. Parameters MRR (msn) MSD (msn) P1 ( $\text{ms}^2/\text{Hz}$ ) P2 ( $\text{ms}^2/\text{Hz}$ ) Before therapy 71.25 – 55.3 31.8 – 3.7 962 – 460 201 – 180 First month 72.4 – 48.9 30.2 – 4.2 969 – 515 196 – 167 End of therapy 70.7 – 52.4 31.2 – 2.7 966 – 380 198 – 281 After 6 month 70.1 – 47.8 32.3 – 3.9 921 – 338 187 – 1156 No significant difference was observed in all parameters of HRV analysis before, during and after the rINF- $\alpha$  2A therapy. *Conclusion:* These results indicate that rINF- $\alpha$  2A alone does not produce an arrhythmogenic potential. Atrial and ventricular arrhythmia and cardiac sudden death attributed to interferon in previous reports are questionable in CAH patients. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "The Assessment of Arrhythmogenic Side-Effect of Interferon-alpha 2A by Heart Rate Variability Tests in Chronic Active Hepatitis"

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## "P P 4 0102" P 4 0102 Nocturnal Protein Turnover and Liver Glycogen Stores in Patients with Cirrhosis

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In patients with cirrhosis of the liver nocturnal administration of glucose has a sparing effect on the nocturnal protein breakdown. Suggesting an early onset of the use of protein for gluco-neogenesis because of glycogen depletion. To further study this phenomenon the nocturnal protein turnover using  $^{15}\text{N}$ -glycine as a label was studied simultaneously with measurement of the depletion of liver glycogen. For the latter we used a new developed technique of labelling the liver glycogen pool with naturally  $^{13}\text{C}$ -enriched dietary carbohydrate. Oxidation of the labelled glycogen was measured indirectly by  $^{13}\text{CO}_2$ -enrichment in breath. Concurrently insulin, glucagon and the glucose response to glucagon i.v. were studied in 12 cirrhotics (P) and 12 healthy volunteers (V). Though bodyweight did not differ, the body cell mass (BCM) was 25.4 kg (SD4.9) in P versus (vs) 33.0 kg (SD7.0) in V,  $p < 0.01$ . The nocturnal protein break-down was 0.78 gr N/kg BCM/9 hr (SD0.28) in P vs 0.46 gr N/kg BCM/9 hr, (SD0.06) in V,  $p = 0.002$ . The protein balance did not differ between P and V. After 14 hours fasting the contribution of liver glycogen to  $^{13}\text{CO}_2$  production was 44% of initial value in P vs 73% in V,  $p < 0.005$ . The molar insulin-glucagon ratio was 4.48 (SD2.28) in P vs 32.21 (SD22.84) in V,  $p < 0.005$ . The blood glucose rose 0.74 mmol/l (SD.38) in P vs 2.11 in V,  $p = 0.0001$  in response to 1 mg glucagon i.v. after 15 hours of fasting. In patients with cirrhosis the liver glycogen pool is smaller and depleted earlier. The degree of depletion correlates with the molar insulin-glucagon ratio, while in cirrhosis this ratio is significantly lower compared with healthy volunteers. The nocturnal protein breakdown is increased. No correlation between the two phenomena could be demonstrated. Nutrition: Metabolism Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy Hormones and receptors: Clinical disorders } "Nocturnal Protein Turnover and Liver Glycogen Stores in Patients with Cirrhosis"

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"P P 4 0103" P 4 0103 **Randomized Trial Comparing Intravenous Ceftriaxone with Oral Cefixime for Treatment of Spontaneous Bacterial Peritonitis (SBP) in Cirrhotic Patients: Pilot Study**

\*F.A.F. Figueiredo, H.S.M. Coelho, R.G. Alvariz, F.D. Silva, F. Godinho, E. Salgueiro

UFRJ and UERJ, Rio de Janeiro, Brasil *Background/Aims:* SBP is a common and potentially fatal complication of cirrhosis. The use of antibiotics oral will contribute greatly to advance in the treatment of SBP. The aim of this study was to assess the efficacy of cephalosporin orally (cefixime) versus cephalosporin intravenous (ceftriaxone) for the treatment of non-severe SBP in patients with cirrhosis and ascites. *Methods:* We enrolled 37 patients in a prospective randomized trial: 18 in the oral group and 19 in the intravenous group. SBP was defined by an ascitic fluid polymorphonuclear count exceeding 250 cells/mm<sup>3</sup> without evidence of surgically treatable intra-abdominal source of infection. Patients with advanced encephalopathy and arterial hypotension were excluded. The infection was treated with 1 g ceftriaxone every 12 hours or 400 mg cefixime once a day until two days after the ascitic neutrophils count decrease below 250 cells/mm<sup>3</sup>. *Results:* There was no difference between the two groups for age (p = 0.55), underlying liver disease (p = 0.39), recent gastrointestinal bleed (p = 0.58), degree of ascites (p = 0.83), Child-Pugh score (p = 0.33), serum albumin (p = 0.48), prothrombin time (p = 0.19), ascitic fluid total protein (p = 0.53) and ascitic fluid polymorphonuclear count (p = 0.44). The organisms most frequently isolated were gram-negative bacteria. The mean time of treatment was 7.2 – 2.5 days for the intravenous group and 8.3 – 2.5 for the oral group (p = 0.15). The mortality was similar between the two groups (p = 0.59). A total of 89% patients treated with cefixime and 94% of patients treated with ceftriaxone were cured of their infections (p = 0.52). Side-effects could not be attributed to the drugs. *Conclusions:* Our results suggest that cefixime is an efficacious, safe and cost-effective measure to treat non-severe SBP in cirrhosis. Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy Clinical practice: Management strategy }" "Randomized Trial Comparing Intravenous Ceftriaxone with Oral Cefixime for Treatment of Spontaneous Bacterial Peritonitis (SBP) in Cirrhotic Patients: Pilot Study"

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"P P 4 0104" P 4 0104 **Type of Estrogen Receptors (ERs) Determines Response to Antiestrogen Therapy**

\*E. Villa, A. Dugani, L. Camellini, E. Fantoni, P. Buttafoco, A. Grottola, I. Ferretti, F. Manenti

Gastroenterology, University of Modena, Italy Tamoxifen (TAM) for inoperable HCC has given contradictory results, possibly explained by the presence in many HCCs of variant ERs ( $\nu$ ER) modified in the hormone binding domain [1]. These cases might respond to megestrol (MEG), which blocks estrogen action at post-receptor level. We therefore planned a pilot study in which TAM or MEG were used depending on ER transcript type. *Methods:* RNA, extracted from liver tumor of 7 pts with unresectable, multifocal HCC, was reverse transcribed and amplified by RT/PCR with primers localized in exons 4 and 6. Tumor growth was evaluated by magnetic resonance (MR) at baseline and after 3 months without therapy. Pts with *wt*ER were then started on TAM 80 mg/day while pts with  $\nu$ ER were assigned to MEG 160 mg/day. MR was repeated after 9 months of therapy. Success was defined as a growth during treatment not exceeding that in the 3 months without therapy. *Results:* Spontaneous tumor growth was higher in  $\nu$ ER tumors. After 1 year, 4/4 TAM-treated and 2/3 MEG-treated pts showed inhibition of growth. Incremental volume fraction by MR in the 2 periods of observation is indicated in the table:  
 $V_{T3}/V_{T0}$  (no therapy)  $V_{T12}/V_{T3}$  (on therapy) *wt*ER (TAM) 1.6 – 0.4 0.8 – 0.2  $\nu$ ER (MEG) 3.0 – 0.8 2.1 – 0.9 *Conclusions:* 1. growth of tumors characterized by  $\nu$ ERs is extremely aggressive; 2. the choice of antiestrogen in relation with type of ERs determined an overall high response rate, significantly improving the known response rate to tamoxifen.

Reference: Cancer Res 1995, 55: 498–500 (supported by grant 60%) Hormones and receptors: Molecular biology Hormones and receptors: Clinical disorders Oncology, specific: Liver, biliary } "Type of Estrogen Receptors (ERs) Determines Response to Antiestrogen Therapy"

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"P P 4 0105" P 4 0105 **Impaired Hepatocellular Integrity in Pre-Eclampsia as Assessed by Measurement of Plasma Glutathione S-Transferase Alpha1-1**

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Pre-eclampsia is a complication of pregnancy characterized by elevated blood pressure and proteinuria. The term HELLP syndrome describes a group of pre-eclamptic women with Haemolysis, Elevated Liver enzymes, and Low Platelets. Deterioration of hepatic function is a crucial determinant as to whether to terminate pregnancy. Glutathione S-transferase Alpha1-1 (GSTA1-1) constitutes as much as 1% of the cytosolic protein in the liver, has a uniform hepatic distribution, and a plasma half-life of less than 2 hours. Seventy-five women during uncomplicated pregnancy, 26 women with pregnancy induced hypertension, 40 women with pre-eclampsia and 20 women with the HELLP syndrome were included in the study. Plasma GSTA1-1 levels were measured by ELISA. Of the women with non-complicated pregnancy five subjects (7%) had elevated GSTA1-1 levels and two (3%) had elevated alanine aminotransferase (ALAT) levels. Both ALAT and GSTA1-1 were elevated in four (15%) patients with pregnancy induced hypertension. Fifteen patients with pre-eclampsia (75%) had elevated GSTA1-1 levels whereas 10 (50%) had elevated ALAT activities. In the eight patients where both parameters were elevated, the median rise in plasma GSTA1-1 was more pronounced (5.7 times upper normal reference limit; UNRL) than the median rise in ALAT (2.7 times UNRL). All patients with the HELLP syndrome had elevated ALAT and GSTA1-1 levels. However, the median rise in plasma GSTA1-1 (34.4 times UNRL) was significantly ( $P < 0.01$ ) higher than the median rise in ALAT (8.3 times UNRL). *Conclusion:* Plasma GSTA1-1 levels may provide an early and sensitive indicator of hepatocellular damage during pre-eclampsia and the HELLP syndrome. Liver and bile ducts, 1: Liver diseases, children } "Impaired Hepatocellular Integrity in Pre-Eclampsia as Assessed by Measurement of Plasma Glutathione S-Transferase Alpha1-1"

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"P P 4 0106" P 4 0106 **Is Carbohydrate-Deficient Transferrin (CDT) a Valid Marker for Harmful Alcohol Intake among Surgical Patients?**

\*H. T\8nnesen, M. Carstensen, P. Maina

Department of Surgery, Copenhagen County Hospital in Herlev, University of Copenhagen, DK-2730, Denmark Alcohol abusers are at special risk at surgery. Daily consumption of at least 60 g (35 beverages/week) is related to 3–4 fold increased development of complication after colorectal resection. (Lancet 1992; 340: 334–337) *Purpose:* Examination of the validity of CDT as a marker of harmful alcohol intake in surgical patients previous to operations. *Methods:* Consecutive adult patients admitted to the department of surgery were included after informed consent. Until the deadline for abstracts June 1, 1996 213 patients (108 women, 105 men) have been included. Nobody denied to enter the study. Eleven patients were not included due to immediate admission to ICU (4), deafness (1) and by mistake (6). Alcohol interviews were performed and blood samples were obtained. Se-CDT were analysed by a modified radioimmunoassay. Positive CDT was defined as values above 20 U/l for men and above 26 U/l for women. *Results:* The median alcohol intake was 5 beverages per week. (range 0–350). The correlation between alcohol intake and CDT was 0.65,  $p < 0.001$ . The sensitivity and specificity of CDT were high (100% and 95%). The positive predictive value was 62% and the negative predictive value was 100%. *Conclusion:* CDT is a useful marker of harmful alcohol intake among surgical patients. } "Is Carbohydrate-Deficient Transferrin (CDT) a Valid Marker for Harmful Alcohol Intake among Surgical Patients?"

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"P P 4 0107" P 4 0107 **Tissue Inhibitor of Metalloproteinases-1 in Liver in Patients with Chronic Liver Disease**

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Tissue inhibitor of metalloproteinases (TIMP)-1 is an important regulator of matrix metalloproteinase activity. To clarify its changes in diseased liver, we measured TIMP-1 concentrations in liver tissue samples from patients with chronic liver disease using an enzyme immunoassay after the extraction with 2 M guanidine. The subjects were 68 patients, who were classified by the histological findings as 10 almost normal liver/fatty liver, 18 chronic persistent hepatitis (CPH), 24 chronic active hepatitis (CAH) 2A, 10 CAH2B, and 6 liver cirrhosis (LC). As compared with the controls, the liver TIMP-1 level increased 2.2-fold in CAH 2A, 2.9-fold in CAH 2B and 4.1-fold in LC, but not in CPH. Liver TIMP-1 levels were closely correlated with the histological degree of periportal necrosis, of portal inflammation and of liver fibrosis. When the localization of TIMP-1 was examined immunohistochemically, TIMP-1 was stained mainly in hepatocytes, and the intensity was stronger in CAH and LC than in CPH. Gel filtration of the liver extract from a cirrhotic liver showed that the major peak of TIMP-1 was eluted at around 40 kDa, although the TIMP-1 antigenicity was heterogenous. When the relationship between serum and liver levels of TIMP-1 was examined, both levels were closely correlated, indicating that serum TIMP-1 could reflect the change of liver TIMP-1 in patients with chronic liver disease. In conclusion, the liver TIMP-1 concentration increased with the progress of liver disease, where the degradation of extracellular matrix proteins would be decreased, resulting in the development of liver fibrosis. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Tissue Inhibitor of Metalloproteinases-1 in Liver in Patients with Chronic Liver Disease"

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"P P 4 0108" P 4 0108 **Expression of a Non-MDR2-Coded Phosphatidylcholine Membrane Transport Protein from Rat, Mouse and Human Liver in *Xenopus Laevis* Oocytes**.  
Cornacchia, A. L. 'f6chel, J. M. 'f6ssner,

\*F. Berr

Dept. of Medicine II, University of Leipzig, Germany Phosphatidylcholines (PC) are secreted into the bile via hepatocyte canalicular membrane transport protein(s). Evidence for ATP-dependent mdr2-encoded PC transport as well as carrier-mediated PC transport had been demonstrated by expression of specific liver mRNA species/fractions. *Aim:* To test in *Xenopus laevis* oocytes, whether the functional expression of MDR2 is involved in the PC transport induced by functional expression of liver mRNA. Transport was assayed using a water-soluble, radiolabeled PC homolog, <sup>14</sup>C-dibutyroyl-PC (diC<sub>4</sub>PC). *Results:* Functional expression of rat or mouse mdr2 cRNA in *Xenopus laevis* oocytes did not result in detectable uptake of diC<sub>4</sub>PC in presence or absence of ATP. By contrast, expression of rat, mouse and human liver total mRNA resulted in saturable, carrier-mediated and ATP-independent uptake of diC<sub>4</sub>PC with an apparent K<sub>m</sub> of 9.6 mM, 7.7 mM and 11.6 mM, respectively. Antisense inhibition of MDR2 expression increased diC<sub>4</sub>PC uptake encoded by total liver mRNA from mouse and rat by 40%–50%. In addition, a clear difference in mRNA size was shown between MDR2 and the diC<sub>4</sub>PC carrier, after size fractionation of rat liver mRNA. *Conclusion:* The data prove the existence of a specific mRNA for a non-MDR2-coded cell membrane PC carrier in mouse, rat and human liver which exhibits similar transport affinity for diC<sub>4</sub>PC as the PC carrier previously characterized (J Biol Chem 268: 3976; 1993) in rat liver canalicular membranes. Liver and bile ducts, 2: Bile formation, cholestasis } "Expression of a Non-MDR2-Coded Phosphatidylcholine Membrane Transport Protein from Rat, Mouse and Human Liver in *Xenopus Laevis* Oocytes"

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"P P 4 0109" P 4 0109 **Cyclosporine and Hypercholesterolemia. Cyclosporine Down-Regulates Low Density Lipoprotein Receptors in Cultured Liver Cells**

\*C.-H. Florén, O. Al Rayyes, A. Wallmark

Department of Internal Medicine and the Wallenberg Laboratory, Malmö University Hospital, Malmö, Sweden *Purpose:* Cyclosporine is today one of the most widely used immunosuppressive drugs and it is used in most transplantation centres to prevent organ rejection. Patients, who are transplanted, and use this drug are, however, prone to be afflicted by cardiovascular disease, due to the development of atherosclerosis as a result of Cyclosporine-caused elevation of blood low density lipoprotein (LDL) cholesterol levels. The mechanism whereby Cyclosporine causes high LDL cholesterol levels to occur, has not yet been clarified. *Methods:* As the main part of LDL is catabolized in the liver, by its hepatocytes, an in vitro system using cultured hepatocytes was used. HepG2 cells, a hepatoma cell line, which is highly differentiated and with functional LDL receptors, was studied. *Summary:* The results showed that Cyclosporine reduced cellular LDL uptake and degradation by mainly inhibiting the LDL receptor mediated pathway. HMG-CoA reductase inhibitors, which upregulate LDL receptor activity, reversed the Cyclosporine caused downregulation of LDL receptor activity. *Conclusion:* Cyclosporine causes hypercholesterolemia in transplanted patients by inhibiting LDL receptor activity. This effect can be reversed by HMG-CoA reductase inhibitors. This argues for treating patients with Cyclosporine caused hypercholesterolemia with HMG-CoA reductase inhibitors. Liver and bile ducts, 1: Liver transplantation Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Cyclosporine and Hypercholesterolemia. Cyclosporine Down-Regulates Low Density Lipoprotein Receptors in Cultured Liver Cells"

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"P P 4 0110" P 4 0110 **Effects of Oltipraz, { a}-Tocopherol, { b}-Carotene and Phenethylisothiocyanate on Glutathione S-Transferases of the Rat Digestive Tract**

\*E.M.M. Van Lieshout, W.H.M. Peters, J.B.M.J. Jansen

Dept. of Gastroenterology, St. Radboud University Hospital, Nijmegen, the Netherlands Many studies have linked consumption of naturally occurring anticarcinogens, present in vegetables and fruits, to the prevention of gastrointestinal tumours. The mechanism is unclear, but induction of glutathione S-transferases (GSTs) seems crucial. GSTs are a family of isozymes, divided into classes Alpha, Mu, Pi and Theta, which serve a major role in the detoxification of many substances, including carcinogens. In order to understand better their anticarcinogenic potential, four anticarcinogens (oltipraz, { a}-tocopherol, { b}-carotene and phenethylisothiocyanate [PEITC], incorporated in the diet at 0.03, 0.02, 0.02, and 0.045% w/w, respectively) were studied with respect to their effects on oesophageal, gastric, colonic, and hepatic GST activity and GST isoenzyme levels. Male Wistar rats were fed normal or supplemented lab chow for two weeks. Organs were removed and cytosolic fractions were prepared. Herein, GST activity towards 1-chloro-2, 4-dinitrobenzene was measured and GST isozymes were quantified after immunodetection of Western blots. Wilcoxon rank sum test was used to assess statistical significance of differences. GST activity was significantly increased in oesophagus and colon by PEITC and in liver by oltipraz. Oltipraz, { a}-tocopherol, and PEITC induced hepatic GST Alpha. GST Mu was increased by { b}-carotene and PEITC in stomach and liver, by oltipraz in liver and by { a}-tocopherol in stomach. PEITC induced colonic GST Pi. In conclusion, oltipraz, PEITC, and to a lesser extent { a}-tocopherol and { b}-carotene, may exert their chemoprotective effects in liver, colon and oesophagus by enhancing GSTs, resulting in a more efficient detoxification of carcinogens. Oncology, general: Screening, prevention Nutrition: Metabolism }" "Effects of Oltipraz, alpha-Tocopherol,  $\beta$ -Carotene and Phenethylisothiocyanate on Glutathione S-Transferases of the Rat Digestive Tract"

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**"P P 4 0111" P 4 0111 Prospective Evaluation of Circulating Hepatocytes by Alpha-Fetoprotein mRNA in Humans during Liver Surgery A. Lemoine<sup>1</sup>, D. Azoulay<sup>2</sup>, T. Le Bricon<sup>1</sup>, M. Salvucci<sup>1</sup>, P. Pham<sup>1</sup>, H. Bismuth<sup>2</sup>, B. Debuire<sup>1</sup>**

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"Tissue-specific" mRNAs have been used for the detection of circulating micrometastatic tumor foci of hepatocellular carcinoma (HCC). However, the interpretations of the results have been equivocal. The specificity of these tests remains to be clearly established for clinical use, especially to decide chemotherapy. To establish the specificity of detecting liver tumor cells dissemination by alpha-fetoprotein (AFP) mRNA, a prospective study was performed in a random group of 64 consecutive patients (pts) undergoing hepatic resection for various tumors (HCC: n = 20, secondary metastatic liver: n = 27 and non tumoral etiologies: n = 17). AFP mRNA was evaluated in peripheral blood by reverse transcription-polymerase chain reaction (RT-PCR) before surgery and at 2 intraoperative time intervals during surgery. Prior to hepatectomy, AFP mRNA was detected in the blood of 17% of pts which included 5 out of the 20 pts with HCC. Intraoperatively, 53% of the pts (8/20 operated for HCC, 17/27 for secondary metastases and 9/17 for non tumoral etiologies) were found to be AFP mRNA positive, regardless of the disease, the type of surgery or clinical parameters surrounding their disease. Thirty two pts (50% of which were positive intraoperatively) were examined 6 months after surgery and all but one were negative for AFP mRNA. None of the pts treated for HCC in this series had recurrence 6 months after surgery (2 died of liver failure). Although liver surgery seems associated with a transient release of AFP mRNA positive cells in the circulation, this gene transcript is not a specific marker of circulating micrometastases from HCC. It would be imprudent to attempt clinical application of this marker until a more accurate test is devised which can link specific gene markers to circulating tumor foci. }

"Prospective Evaluation of Circulating Hepatocytes by Alpha-Fetoprotein mRNA in Humans during Liver Surgery"

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## "P P 4 0112" P 4 0112 Cholestatic Liver Injury Induces a Rapid Increase in Proliferation and Expression of $\beta$ PDGF Receptor in Hepatic Stellate Cells

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<sup>1</sup> Rhéne-Poulenc Rorer, Alfortville The molecular mechanisms of hepatic stellate cells (HSC) activation have been well described *in vitro* but have not been fully elucidated *in vivo*, particularly in cholestatic liver injury. Increased proliferation is one of the major aspects of HSC activation. PDGF has been identified as the most potent mitogen for HSC *in vitro*. However, the mitogenic effect of PDGF *in vitro*, requires up-regulation of  $\beta$  PDGF receptor in these cells. The aim of our study was to determine the kinetics of HSC proliferation and that of  $\beta$  PDGF receptor expression in HSC, following cholestatic liver injury. **Materials and methods:** Cholestatic liver injury was induced in male Sprague-Dawley rats by double ligation with sectioning of the common bile duct (BDL). Sham-operated rats served as controls. Liver injury induced by biliary obstruction was assessed by liver tissue histology and by the measurement of serum bile acids (Enzabile') and of bilirubinemia. HSC proliferation was assessed by *in vivo* incorporation of bromodeoxyuridine (BrdU), which was administered intraperitoneally (50 mg/kg) one hour before cell isolation. HSC were isolated by *in situ* liver enzymatic dissociation and cell separation on density gradient, 1, 2, 3 and 7 days after bile duct ligation, respectively. Freshly isolated cells were subsequently analyzed by flow cytometry, in order to quantify incorporated BRDU. In separate experiments, HSC plasma membrane expression of PDGF receptors was also analyzed by flow cytometry using an anti-PDGF (R)  $\beta$  polyclonal antibody. **Results:** Cell purity, as determined by fluorescence of retinoid-containing vacuoles under UV excitation, was > 95%. Biochemical determinations, semi-quantitative analysis of ductular reaction, and incorporation of BRDU in HSC are shown in the following table (M – SEM, n = 3).  
D1 D2 D3 D7 BDL SHAM BDL SHAM BDL SHAM BDL SHAM  
Bilirubin ( $\mu$ mol/l) 94 – 21 1 – 0 144 – 31 1 – 0 163 – 25 1 – 0 170 – 15 1 – 0  
Bile acids ( $\mu$ mol/l) 563 – 63 12 – 2 565 – 19 18 – 3 674 – 139 16 – 3 398 – 22 18 – 9  
Ductular reaction + { - } ++ { - } +++ { - } ++++ { - }  
anti-BrdU + cells (%) 5 – 0 4 – 1 19 – 8 4 – 1 19 – 1 5 – 1 25 – 6 10 – 1  
In addition, HSC proliferation was associated with a more than ten-fold increase in  $\beta$  PDGF receptor density on the plasma membrane. In conclusion, complete bile duct obstruction induces ductular reaction and HSC proliferation within 24 h and 48 h following bile duct ligation, respectively. HSC proliferation is associated with an increased expression of  $\beta$  PDGF receptors. These results suggest that cholestatic liver injury induces a rapid increase in HSC proliferation, which could result at least partly from the up-regulation of  $\beta$  PDGF receptors. Liver and bile ducts, 1: Cell biology, collagen, fibrosis }" "Cholestatic Liver Injury Induces a Rapid Increase in Proliferation and Expression of  $\beta$  PDGF Receptor in Hepatic Stellate Cells"

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## "P P 4 0113" P 4 0113 Expression of Gap Junction Protein Connexin 32 in Experimental Rat Liver Cirrhosis

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Gap-junction-protein levels of connexin 32 (Cx 32) were reported to be decreased in neoplastic foci induced by hepatochemicals in rat livers. However, there were no reports whether the expression of Cx 32 was decreased in experimental liver cirrhosis. We examined immunohistochemically the expression of Cx 32 in cirrhotic rat livers induced by diethylnitrosamine (DEN). *Methods*: Male Wistar rats were treated with DEN for 6 weeks. After sacrifice, the livers were resected, and immediately frozen by liquid nitrogen for immunohistochemistry and H&E stain. The immunohistochemical detection of Cx 32 was performed using an avidin-biotin complex peroxidase technique with a mouse monoclonal anti-Cx 32 antibody. The number of Cx 32 positive spots/100  $\mu\text{m}^2$  was counted at random in 15 photographic fields (magnification  $\times 1000$ ). *Results*: Macular Cx 32 spots were observed at intercellular borders of hepatocytes. The number of plaques in control and cirrhotic livers was  $133 \pm 30.7$  spots and  $79.4 \pm 25.8$  spots/100  $\mu\text{m}^2$ , respectively. The number of spots in the cirrhotic livers was significantly decreased compared with that in the control livers ( $p < 0.05$ ). *Conclusion*: The expression of connexin 32 is decreased in cirrhotic rat livers treated with DEN when compared with that in normal livers. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Hepatotoxicity, ethanol Oncology, general: Proliferation, carcinogenesis } "Expression of Gap Junction Protein Connexin 32 in Experimental Rat Liver Cirrhosis"

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"P P 4 0114" P 4 0114 **Trimethylamine-N-Oxide (TMAO) — Important in the Pathogenesis of Hepatic Encephalopathy after TIPSS?**

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<sup>1</sup> NMR Unit, Hammersmith Hospital, Department of Medicine, Royal Infirmary of Edinburgh

<sup>2</sup> ICH, London, Department of Medicine, Royal Infirmary of Edinburgh *Background:* About 20–30% patients become encephalopathic following TIPSS. TMAO is nitrogenous, diet related, produced by gut flora, crosses the blood brain barrier, is present in the portal circulation, is metabolised by the liver and inhibits Ca<sup>2+</sup> ATPase. This study was designed to test the hypothesis whether TMAO or other biogenic amines may contribute to the development of encephalopathy. *Methods:* Plasma was collected prior to TIPSS and at 3 months when the patients attended for routine portography and stored at  $-70^{\circ}\text{C}$ . Two patients were clinically encephalopathic prior to TIPSS. *In vitro* <sup>1</sup>H magnetic resonance spectroscopy was performed on the plasma using a spin echo sequence on an 11.7 Tesla magnet (JEOL). Spectra were analysed on a Sun-Sparc computer. Amino acids were measured in the plasma using HPLC. *Results:* The severity of encephalopathy worsened in the 2 patients who were encephalopathic before TIPSS and 2 others became encephalopathic. The changes in TMAO correlated significantly with the changes in the portal pressure gradient ( $r = 0.58$ ,  $p < 0.02$ ). TMAO levels in controls and patients before and after TIPSS is illustrated in Fig 1. No significant change was noted in capillary ammonia or amino acids.

*Conclusions:* TMAO may be important in the development of encephalopathy and deserves further investigation. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy } "Trimethylamine-N-Oxide (TMAO) / Important in the Pathogenesis of Hepatic Encephalopathy after TIPSS?"

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**"P P 4 0115" P 4 0115 Collagen Type IV and Laminin in Alcoholic and Nonalcoholic Liver Diseases. Relationship with Portal Hypertension**

\*Z. Krastev, L. Mateva, A. Alexiev, B. Alexiev, R. Ivanova

Clinic of Gastroenterology, University Hospital "St. Ivan Rilsky" Sofia, Bulgaria Collagen type IV and laminin are markers of basement membrane formation and sinusoid capillarization. In this study we investigated the localization and expression of collagen type IV and laminin in alcoholic and nonalcoholic liver diseases. The expression of collagen type IV and laminin was studied by immunocytochemistry on liver biopsy specimens from 30 patients with different stage of alcoholic liver disease (15-fatty liver, 5-alcoholic hepatitis, 10-incipient liver cirrhosis), 20 nonalcoholic liver disease (5-viral chronic active hepatitis, 5-viral liver cirrhosis, 12-PBC) and 3 controls. All patients were clinically follow-up for a period over 3 years about severity of liver damage and appearance of portal hypertension. The expression of collagen type IV and laminin was various intensity around blood vessels and bile ducts in the portal tracts, sinusoidal walls, areas with cell infiltration and liver cell necrosis, fibrotic septa and perisinusoidal spaces in all patients. The expression of collagen type IV and laminin in perisinusoidal areas in alcoholic cases was more intensive than other cases. In alcoholic patients there was also relationship between the intensity of staining reactions in perisinusoidal spaces and appearance of portal hypertension ( $r = 0.890$ ,  $p < 0.001$ ) for the follow-up period and the verity of liver damage ( $x = 46.14$ ,  $p < 0.001$ ) for conclusion liver fibrosis and capillarization play a central role in liver function impairment and portal hypertension in chronic liver diseases, especially in alcoholics. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Collagen Type IV and Laminin in Alcoholic and Nonalcoholic Liver Diseases. Relationship with Portal Hypertension"

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"P P 4 0116" P 4 0116 **Longterm Outcome and Predictive Factors of Efficiency, Encephalopathy (EH) and Obstructions after TIPS Placement for Refractory Ascites (RA)** C. Renou, F. Castex, Pascal L. Canva-Delcambre<sup>1</sup>, G. Sergent<sup>2</sup>, C. L'Hermine<sup>2</sup>, R. Sambuc<sup>1</sup>, J.C. Paris

<sup>2</sup> Service d'Hépatogastroentérologie et de Radiologie CHRU Lille, 59037 Lille, France

<sup>1</sup> Département d'Informatique médicale 13000 Marseille The aim of this study was to assess the TIPS efficiency and to evaluate prognostic factors for EH, obstruction, efficiency and mortality after TIPS for RA. *Methods:* Between 04/92 and 11/95, 33 patients with RA followed 18 mo (2 d–38 mo) underwent TIPS placement. A favorable response to TIPS was defined as an improvement of RA, with or without diuretics or occasionally paracentesis (< 1 by 3 mo). 28 parameters of the pre-TIPS screening were examined as potential prognostic factors. *Results:* 12 mo after TIPS placement, RA was resolved or improved in 75% patients. Cumulative rates of obstruction were respectively 19, 50, 66 and 66% at 1, 12, 24 and 30 mo. After reinterventions TIPS free of obstruction were respectively 70, 80, 66 and 80%. 6 parameters were predictive of EH: pre-TIPS EH history (p = 0.05), hypoalbuminemia (p = 0.04), hemoglobinemia (p = 0.0003), Child score (p = 0.03), Prothrombine Time (p = 0.002) and proaccelerin (p = 0.003). 3 were predictive for thrombosis: recent operators experience (p = 0.02), hypoalbuminemia (p = 0.01), lack of anticoagulant therapy (p = 0.02). For TIPS free of obstruction, only 2 parameters were predictive of efficiency: anticoagulant therapy (p = 0.04) and Child score (p = 0.005). None parameters was predictive for stenosis. 5 were predictive of mortality before 15 mo: Child score (p = 0.0004), hemoglobinemia (p = 0.015), Prothrombine Time (p = 0.004), proaccelerin (p = 0.01) and blood alcalin phosphatases (p = 0.02). One-year survival was 70%. After TIPS Child score improved 7.85 – 1.73 vs 9.27 – 0.88 before TIPS (p = 0.0001). *Conclusion:* During long term follow-up, TIPS might be a treatment of RA and complications might decrease under the following conditions: 1) only Child B must be treated, 2) early reintervention in case of obstruction, 3) lactulose and antibiotics treatments should be prescribed before TIPS and anticoagulant therapy after. Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy }" "Longterm Outcome and Predictive Factors of Efficiency, Encephalopathy (EH) and Obstructions after TIPS Placement for Refractory Ascites (RA)"

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## "P P 4 0117" P 4 0117 Utility of Thoracentesis in Cirrhotic Patients

\*X. Xiol, M. Delgado, R. Cortés, J. Guardiola, E. Sesé, M. Da Costa, L. Guerrero, J. Castellote

Gastroenterology Service, Hospital de Bellvitge L'Hospitalet, Barcelona, Spain About 10% of cirrhotic patients with ascites have an associated pleural effusion, but the utility and safety of thoracentesis is not well established. *Aim:* To prospectively study complications of thoracentesis in cirrhotic patients with pleural effusion. *Material and methods:* From October 1994 to December 1995 a diagnostic thoracentesis (DT) was performed on all cirrhotic patients with pleural effusion at admission or when a spontaneous bacterial empyema was suspected. A therapeutic thoracentesis (TT) was performed in patients with dyspnea secondary to the effusion. To detect complications, a chest radiograph and exhaustive follow up were done after the procedure. *Results:* 106 thoracentesis have been performed in 33 cirrhotic patients, 77 DT and 29 TT. Of the 77 DT, no pleural fluid was obtained in 4 (5.2%), pleural fluid analysis was compatible with hydrothorax in 57 (74%) and pleural fluid analysis provided a definitive diagnosis in 16 (20.8%): tuberculosis in 2 cases, malignancy in 2 and spontaneous bacterial empyema in 12. In 23 (79.3%) of the 29 TT pleural fluid could be evacuated (mean volume 1990 – 685 ml). Major complications were pneumothorax in 6 (5.66%), 4 of them required chest tube insertion, and uncomplicated wall haematoma in 4. Pneumothorax appeared in 2 (2.6%) of the 77 DT and in 4 (13.8%) of the 29 TT ( $p < 0.05$ , Fisher exact test). *Conclusions:* 1. – In 20% of the thoracentesis performed in cirrhotic patients, pleural fluid analysis provides a definitive diagnosis other than hepatic hydrothorax. 2. – Diagnostic thoracentesis in cirrhotic patients is a useful and safe procedure. 3. – Therapeutic thoracentesis is an effective procedure having greater morbidity than diagnostic one. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy } "Utility of Thoracentesis in Cirrhotic Patients"

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"P P 4 0118" P 4 0118 ***Helicobacter Pylori* Infection and the Risk of Peptic Ulcer among Cirrhotic Patients**

\*C.H. Wang, L.R. Mo, R.C. Lin, J.Y. Kuo, K.K. Chang

Department of Internal Medicine Tainan Municipal Hospital, Tainan, Taiwan, R.O.C. *Helicobacter pylori* and peptic ulcer are known to be associated and there is a high prevalence of peptic ulcer in cirrhotic patients. However, whether *H. pylori* is a risk factor for peptic ulcer in cirrhosis remain controversial. The aim of the present study was to determine whether there is a significant correlation between *Helicobacter pylori* infection and peptic ulcer in liver cirrhosis. In a prospective study, 49 cirrhotic patients were endoscoped regardless of symptoms. Another group of 75 controls without liver disease were also examined routinely. Both groups of patients were subdivided into ulcer and non-ulcer patients. The presence of *H. pylori* was assessed by culture, histologic findings, and rapid urease test of antral biopsy specimens. The prevalence of *H. pylori* in cirrhosis was significantly lower than in control group (49% vs. 68%,  $p < 0.05$ ). The presence of *H. pylori* was more frequent in ulcer than non-ulcer patients in controls (91.3% vs. 57.6%,  $p < 0.005$ ), whereas this difference was not significant in cirrhosis (56.7% vs. 36.8%,  $p > 0.05$ ). As for peptic ulcer between two groups, *H. pylori* was identified in 56.7% of cirrhotic patients compared with 91.3% of controls ( $p < 0.01$ ). The positive rate of *H. pylori* in cirrhosis group is directly related to the presence of serum hepatitis B surface antigen. There is no strong evidence to substantiate an etiologic role of *H. pylori* in the development of peptic ulcer among cirrhotic patients. *H. pylori* may frequently infect hepatitis B virus-related cirrhotics. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, specific: Stomach, duodenum Liver and bile ducts, 1: Cirrhosis: portal hypertension } "*Helicobacter Pylori* Infection and the Risk of Peptic Ulcer among Cirrhotic Patients"

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"P P 4 0119" P 4 0119 **The Effect of Ceftazidime on the Prevention of Peritonitis after Recurrent Ascites Paracentesis** C. Petrogiannopoulos, A. Zacharof, A. Tzoumani, J. Panagopoulos, N. Papageorgiou, J. Poulidakos

2nd Department of Medicine, Hellenic Red Cross Hospital, Athens, Greece A common complication of recurrent paracentesis of ascites in cirrhotics is the appearance of bacterial peritonitis. *Aim of the study:* was to evaluate the efficacy of Ceftazidime (Solvetan) on prevention of bacterial peritonitis due to recurrent ascites paracentesis in cirrhotic patients with tense ascites. *Material and methods:* This study included 26 patients with non compensated cirrhosis and tense ascites. During their hospitalization (1–2 months) all the patients got recurrent paracentesis every once or twice weekly. After each procedure 15/26 patients (Group A) were received Ceftazidime (Solvetan) 1 gr IV while the rest of them (Group B) received nothing. Clinical and laboratory investigation was done every day. *Results:* Only one patient (6%) from group A appeared clinical symptoms of bacterial peritonitis (fever, local pain and increased blood and ascitic fluid white cells), while in group B 4/11 (36.6%) patients got typical clinical picture of bacterial peritonitis with positive ascitic fluid cultures in 2 of them. *Conclusions:* Ceftazidime (Solvetan), a third generation cephalosporin, is quite effective on the prevention of bacterial peritonitis due to recurrent evacuant paracentesis in cirrhotics with tense ascites. Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy Immunology and microbiology: Inflammation } " "The Effect of Ceftazidime on the Prevention of Peritonitis after Recurrent Ascites Paracentesis"

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"P P 4 0120" P 4 0120 **Pattern of Dapsone Induced Liver Injury and Outcome** Joeffe<sup>1</sup>,

\*K.T. Shenoy

<sup>1</sup> Dept. of Dermatology, Medical College, Trivandrum, India

Dept. of Gastroenterology, Medical College, Trivandrum, India *Objective:* Paucibacillary Hansen's disease (PHD) is emerging as a major public health problem in developing countries. We studied the pattern of liver injury and their outcome in paucibacillary Hansen's disease administered Dapsone. *Setting:* Tertiary referral centre. *Participants:* 362 cases of PHD administered Dapsone (100 mg), Clofazimine (50 mg) daily and Rifampicin (600 mg) monthly. *Study variables:* Onset of jaundice, its temporal relationship with drug therapy, alcoholism, biochemical parameters (S. bilirubin, transaminases, alkaline phosphatase and S. albumin), tests for haemolysis, HBsAg and haematology. *Results:* Of 362 subjects (190 males and 172 females), 15 developed jaundice (M:F = 2:1). Jaundice occurred 3 to 6 weeks after drug therapy; fever and erythematous rash with exfoliation 100%; body pain and malaise 50%; altered behaviour 20%; congestion of eyes 20%. Clinical signs were tender liver (100%), asterixis (14%), leg edema (14%) and lymphadenopathy (20%). Five males were alcoholics. Serum bilirubin and transaminases were elevated in all those with jaundice and HBsAg was negative. One patient progressed to hepatocellular failure and expired. None had evidence of haemolysis. *Conclusion:* Multidrug therapy for PHD resulted in hepatocellular injury in 4.1% and has significant morbidity and mortality. Liver and bile ducts, 1: Hepatotoxicity, ethanol } "  
"Pattern of Dapsone Induced Liver Injury and Outcome"

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## "P P 4 0121" P 4 0121 **Helicobacter Pylori: Is It a Risk Factor for Hepatic Encephalopathy in Cirrhotic Patients?**

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Department of Internal Medicine (Gastroenterology & Hepatology Unit), Faculty of Medicine, Assiut University, Assiut, Egypt

<sup>1</sup> Department of Biochemistry, Faculty of Medicine, Assiut University, Assiut, Egypt *Objective:* To determine whether *Helicobacter pylori* (Hp) infection is a risk factor for hepatic encephalopathy in patients (pts) with liver cirrhosis. *Methods:* 108 cirrhotic pts undergoing upper GI endoscopy for detection of oesophageal varices were included in this study: 34 pts Child-Pugh grade A, 60 pts grade B and 14 pts grade C. The aetiology of liver cirrhosis was either posthepatic or mixed; Bilharzial fibrosis and posthepatic cirrhosis. Diagnosis of Hp infection was done by histopathology using antral and fundal biopsies, hp fast test and serologically by estimating Hp IgG antibody titers by ELISA (more than 20 u/ml). Estimation of serum NH<sub>3</sub> using an enzymatic assay for all pts was done and the results were compared with that of 24 normal subjects as a control group. *Results:* Serum NH<sub>3</sub> is significantly higher in cirrhotics than in normal controls (P < 0.001) 86 cirrhotic pts with Hp +ve were similar 22 Hp. { - }ve with regard to age, sex, aetiology of cirrhosis and Child score. Hp. +ve had significantly high NH<sub>3</sub> in comparison with Hp { - }ve pts (P < 0.01). Also significant high NH<sub>3</sub> in pts grade C compared with grade A (P < 0.01) and grade B (P < 0.01). Detection of Hp IgG antibodies by ELISA is a sensitive test as it was positive (more > 20 u/ml) in all pts with positive hp fast test and positive histopathology for Hp. There was a significant positive correlation between serum NH<sub>3</sub> levels and Hp IgG antibody titers in cirrhotic pts (r = 0.9, P < 0.001). *Conclusion:* Hp infection as ammonia producer can be considered as a risk factor for hepatic encephalopathy in cirrhotic patients and may warrants eradication. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy }" "Helicobacter Pylori: Is It a Risk Factor for Hepatic Encephalopathy in Cirrhotic Patients?"

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"P P 4 0122" P 4 0122 **The Reduction of Cerebral Blood Flow in Cirrhotic Patients Precedes the Appearance of Overt Encephalopathy** M.R. Biagini, B. Mallardi, A. Galli, E. Surrenti, O. Morelli, M.T. Passaleva, M. Romano, S. Faenzi, C. Surrenti

Gastroenterology Unit, Department of Clinical Physiopathology, University of Florence, Italy Several studies have shown cerebral morphologic abnormalities by CT and MNR and reduction of cerebral blood flow by single photon emission tomography (SPECT) in cirrhotic patients. However, it is unknown if these abnormalities precede or accompany the appearance of overt encephalopathy. *Aim of the study:* to analyze whether alterations in cerebral blood flow evaluated by SPECT in cirrhotic patients is associated with or precedes the onset of hepatic encephalopathy. *Patients and Methods:* SPECT was performed in 20 cirrhotic male patients (50–70 years), without history of alcoholic abuse, diabetes, cardiovascular and neuropsychiatric diseases. The presence of encephalopathy was assessed by clinical examination, EEG, ammonia blood levels, event related potentials (ERPs) and psychological tests. Latent encephalopathy was defined as absence of clinical signs, in the presence of normal EEG, normal blood ammonia levels, abnormal ERPs and psychological tests. *Results:* 6\20 patients showed clinically assessed encephalopathy and reduction of thalamic blood flow by SPECT; 14\20 showed neither signs nor symptoms of encephalopathy but 7\14 showed ERPs, psychological tests and SPECT abnormalities. Two of these seven patients showed a specific SPECT alterations while five showed the same alterations of overt encephalopathy patients. *Conclusions:* Our data suggest that SPECT might be useful to detect subclinical encephalopathy in cirrhotic patients. } "The Reduction of Cerebral Blood Flow in Cirrhotic Patients Precedes the Appearance of Overt Encephalopathy"

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"P P 4 0123" P 4 0123 **Effect of Somatostatin on Renal Functions in Cirrhotic Patients with Ascites**

\*Y. Uzun, A. D'f6kmeçi, H. \d6zkan, H. Bozkaya, \d6. Uzunalimoglu

Department of Gastroenterology, Ankara university, School of Medicine, Ankara, Turkey *Purpose:* Somatostatin therapy is known to be effective in ceasing of bleeding oesophageal varices. Effects of somatostatin in renal functions in patients (pts) with cirrhosis is controversial. Purpose of the study is to evaluate the effect of somatostatin on renal functions in cirrhotic pts with ascites. *Patients and methods:* Twenty cirrhotic pts with ascites were studied. None of the pts had bleeding oesophageal varices and received no diuretic therapy at least 1 week before the study, During the control period Dextrose 5% solution (2 ml/min) for 2 hr was infused. 24 hr after control period somatostatin infusion (250 \b5l/hr in Dextrose 5%) was given for 2 hr. Urine was collected during the infusion and 2 hr postinfusion period in both control and somatostatin experiment. Basal and postinfusion blood samples were collected and mean arterial blood pressure (MABP) was monitored. *Results:* There was no change in MABP. Changes in urine volume (V), urine osmolarity (U<sub>osm</sub>), creatinine clearance (C<sub>cr</sub>), free water clearance (C<sub>H2O</sub>, urinary Na (U<sub>Na</sub>), fractional Na excretion (FE<sub>Na</sub>) under somatostatin infusion were given below table. V U<sub>osm</sub> C<sub>cr</sub> C<sub>H2O</sub> U<sub>Na</sub> FE<sub>Na</sub> (ml/min) (mOsm/kg) (ml/min) (ml/min) (\b5m/min) (X10) Control P. 0.7 – 08 406 – 27 92 – 14 100 – 18 12 – 3 0.7 – 0.6 Test P. 1.2 – 0.1 318 – 29 153 – 18 126 – 18 21 – 6 0.06 – 0.03 p value < 0.05 < 0.05 < 0.0001 NS NS NS NS: non-significant *Conclusion:* Somatostatin therapy has no deteriorating effect on renal functions in cirrhotic patients with ascites. It increases creatinine clearance and urine volume and may be beneficial in this group of patients. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy } "Effect of Somatostatin on Renal Functions in Cirrhotic Patients with Ascites"

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"P P 4 0124" P 4 0124 **Relationship Between KLA Genotype and Phenotypic Expression in Irish Families with Genetic Haemochromatosis**

\*E. Ryan, M. Kelly, S. Pathmakanthan, P. MacMathuna, J.C. O'Keane<sup>1</sup>, K. Ennis, J. Crowe

Mater Misericordiae Hospital

<sup>1</sup> Liver Unit and Dept. of Pathology, Dublin, Ireland *Introduction.* The association between genetic Haemochromatosis (GH) and HLA locus has allowed early identification of affected siblings. The proportion of subjects vulnerable to iron overload that are homozygous (HH) or heterozygous (Hn) is unclear. Studies correlating clinical features with HLA type in families from Ireland — a putative source of this Celtic trait have not been described. *Methods.* This study correlated clinical, biochemical and pathologic features of GH with HLA typing (lymphocytotoxicity assay) in 67 first degree relatives of 12 probands. *Results.* Initial analyses identified 12 HH, 40 Hn and 15 nn (normal) individuals. Eleven of 40 individuals initially thought to be Hn had stainable iron on liver biopsy confirming GH and therefore HH status. Further HLA analysis revealed 7 homozygous x heterozygous matings and identification of all disease haplotypes within each pedigree allowed final classification of 30 HH, 25 Hn and 12 nn individuals. *Conclusions.* (1) Initial HLA haplotyping misclassified 18 GH homozygotes mainly due to unsuspected homozygous x heterozygous matings (7 in 12 families). (2) Correlation of HLA haplotype with iron saturation and biopsy findings identifies homozygotes and HH x Hn matings. (3) High frequency of HH x Hn matings in this Irish population supports a Celtic origin of the GH gene. Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Relationship Between KLA Genotype and Phenotypic Expression in Irish Families with Genetic Haemochromatosis"

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## "P P 4 0125" P 4 0125 **Activation of Human Neutrophil Phospholipase D (PLD) is Impaired in Alcoholic Liver Diseases (ALD)**

\*L. Lora, S. Pigozzo, A. D'Odorico, D. Martines, R. Naccarato

Department of Gastroenterology, University of Padua, Padua It is well known that alcoholics have higher morbidity and mortality in bacterial infections. Defect in the superoxide anion production of polymorphonuclear granulocytes (PMN) has been suggested as pathogenic mechanism. PLD contributes to the production of phosphatidic acid (PA) that plays a second messenger role in the activation of NADPH-oxidase (responsible for the respiratory burst) in human PMN. One widely used method for the detection of PLD is based on the formation of phosphatidylethanol (PEth), an uncommon phospholipid that is generated selectively through PLD by transphosphatidylation when ethanol is present. To evaluate whether PLD activity is altered in patients with ALD, we compared PEth synthesis in response to chemotactic peptide (fMLP) or PKC stimulator (PMA) by PMN from patients with alcoholic steatosis (AS, n = 8), alcoholic cirrhosis (AC, n = 18), acute alcoholic hepatitis (AAH, n = 6) and from control subjects (n = 17). *Methods:* peripheral blood PMN isolated by dextran sedimentation and Ficoll-Hypaque separation were labeled with  $^3\text{H}$ -lysophosphatidylcholine ( $10 \text{ }^3\text{Ci}$ ), stimulated with fMLP or PMA in the presence of ethanol (0.5%) and cytochalasin B ( $10 \text{ }^3\text{mol/l}$ ). PEth was separated by TLC using chloroform:methanol:acetic acid (65:17:2 v/v) as solvent system. Plates were scraped and the radioactivity incorporated in the various phospholipids was analyzed through liquid scintillation counting. The amount of radioactively labeled PEth was expressed as percent of phospholipid labeling. Results (mean – ES): Stimulus Controls AS AC AAH fMLP\* 1.81 – 0.27 1.21 – 0.13 1.29 – 0.11 1.01 – 0.22 PMA 1.09 – 0.16 0.96 – 0.17 0.96 – 0.13 1.28 – 0.22\* ALD vs Controls p < 0.03 Kruskal-Wallis analysis of variance *Conclusions:* fMLP-induced activation of PLD is impaired in ALD whereas PLD activity in response to PMA is normal. This defect may be of significance for the enhanced susceptibility to infectious agents in ALD. Immunology and microbiology: Host defense mechanisms Liver and bile ducts, 1: Hepatotoxicity, ethanol Liver and bile ducts, 1: Chronic non viral hepatitis } "Activation of Human Neutrophil Phospholipase D (PLD) is Impaired in Alcoholic Liver Diseases (ALD)"

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"P P 4 0126" P 4 0126 **Cytokin (IL-1 beta, IL-2, IL-4, IL-6) Concentration in Patients with Chronic Hepatitis during the Treatment with Interferon-Alpha** M. Pawlowska<sup>1</sup>, M. Czerwionka-Szaflarska<sup>1</sup>, W. Halota<sup>2</sup>

<sup>1</sup> Department of Gastroenterology and Pediatric Clinic, University School of Medical Sciences in Bydgoszcz, Poland

<sup>2</sup> Department of Infectious Diseases, University School of Medical Sciences in Bydgoszcz, Poland  
In the present studies we investigated the effect of interferon-alpha (INF-alpha) treatment on the concentration of IL-1 beta, IL-2, IL-4 and IL-6 in the serum patients with chronic hepatitis. Serum levels of IL-1 beta, IL-2, IL-4 and IL-6 were measured by a specific immunoassay (ELISA method) in 46 patients (24 children and 22 adults) with chronic hepatitis in the 6-th week of INF-therapy and after the end of the treatment. Patients have been treated with INF-alpha for six months. Statistical analysis was performed with use of the matched pairs test. In the 6-th week (compared to the time before the treatment) IL-1 beta, IL-2, IL-4 and IL-6 concentrations did not show significant changes in examined children. In adults an increase of the IL-6 level was observed (p, 0.02). After the end of the INF-alpha treatment an increase of the IL-6 level both-in children and in adults was shown (p, 0.05). *Conclusion* The assessment of the IL-6 concentration in serum in patients with chronic hepatitis who received INF-alpha may have any prognostic importance mainly in the adults. } "Cytokin (IL-1 beta, IL-2, IL-4, IL-6) Concentration in Patients with Chronic Hepatitis during the Treatment with Interferon-Alpha"

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## "P P 4 0127" P 4 0127 **Interest of a Higher Dose of Interferon Alpha in Non Responder Patients with Chronic Hepatitis C: A Prospective Randomized Study**

\*A. Rolachon, G. K\ 'e9zachian, X. Causse, M. Baud, J. Fournet, J.P. Zarski

Services d'H\ 'e9patologie de Grenoble et d'Orl\ 'e9ans, et Laboratoire de Virologie M\ 'e9dicale Mol\ 'e9culaire, C.H.U. de Grenoble, BP 217, 38043 Grenoble Cedex 9 The aim of our study was to evaluate the interest of a higher dose of interferon (IFN) in non-responder patients to a first treatment by IFN 3 MIU TIW 6 months. Open prospective randomized and bicentric study concerned 23 patients (17 males, 6 females) with histologically proved chronic hepatitis C. Mean age was 38.7 – 9.1 years. Non-response was defined by ALT  $\{ \backslash 'b3 \} 2$  ULN during first treatment duration. Patients were randomized in simple blind in 2 groups: group 1 (n = 14): IFN  $\{ a \} 2b$  10 MIU TIW 2 months then 6 MIU TIW 4 months; group 2 (n = 9): IFN  $\{ a \} 2b$  6 MIU TIW 6 months. The 2 groups were similar for age, sex, mode of contamination, duration of disease, genotype, quantitative viremia (MONITOR'), Knodell score and Metavir index. ALT activity (ULN) and viremia (AMPLICOR', MONITOR') were evaluated for each patients at M3 D1, M7 D1, M13 D1, and Knodell score and Metavir index at M13 D1. No difference was observed between the two groups at M3 D1, M7 D1, M13 D1 concerning ALT normalisation [respectively 29%, 30% and 0% in group 1 and 33%, 37% and 25% in group 2 (NS)], and HCV RNA negativation [respectively 69%, 50% and 10% in group 1 and 75%, 56% and 14% in group 2 (NS)]. A significant decrease of Knodell score (9.2 – 2.5 vs 5.4 – 3) ( $p < 0.05$ ) and Metavir index was observed in group 2, particularly for activity index (1.8 – 0.7 vs 0.9 – 0.7) ( $p < 0.05$ ). On the other hand, HCV RNA negativation was statistically more frequent at M7 D1 in non 1b (82%) than in 1b genotype patients (14%) ( $p < 0.01$ ). The Knodell score (8.7 – 6.4 vs 6.4 – 3.5) and the Metavir index was significantly decreased (1.7 – 1.8 vs 1.1 – 0.8) in non 1b genotype patients. In conclusion, our results suggest that it is possible to obtain an immediate biochemical and virological response in non-responder patients to first treatment by using higher dose of IFN, particularly in non 1b genotype patients. Indeed, a significant histological improvement is observed in non 1b genotype patients. Further studies should compare this schedule with a longer duration to IFN-Ribavirine association in this group of patients. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Interest of a Higher Dose of Interferon Alpha in Non Responder Patients with Chronic Hepatitis C: A Prospective Randomized Study"

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"P P 4 0128" P 4 0128 **Influence of Flumazenil on Hepatic Coma: Clinical and Neurophysiological Study**

\*G. Golubovic, L. Burg, A. Vlahovic, N. Djukic

Clinical-Hospital Center Zemun, Belgrade, Yugoslavia *Purpose.* It has been shown that flumazenil, a benzodiazepine receptor antagonist, has beneficial effect on cerebral function in patients with hepatic coma caused by liver cirrhosis. The aim of this study was to examine the influence of flumazenil on clinical and neurophysiological changes in 10 patients with hepatic coma as a consequence of underlying alcoholic liver cirrhosis. *Methods.* Clinical and neurophysiological (electroencephalogram-EEG, and visual evoked responses by "flash" stimulation) parameters were analyzed after administration of flumazenil. *Results.* The initial dose of flumazenil was 0.2 mg, while the full dose varied from 0.8–6.0 mg. Positive effect of flumazenil was expressed by patients' awakening and manifested in the first 6 hours by motoric excitability, aggressiveness and mental confusion, followed by drowsiness, but without pyramid deficit. After flumazenil administration, acceleration of average electrical activity from 2.9–4.6 cycles per second was noted on EEG, and shortening of latency period (P-100) on visual evoked responses from 69 to 61 msec (average values). In summary, flumazenil administration showed positive effect on awakening, EEG and visual evoked responses in 8/10 patients (80%). Survival rate was 60% (6/10 patients) at 6 months and 40% (4/10 patients) at one year. *Conclusion.* Our results suggested that endogenous bezodiazepines have significant role in pathogenesis of hepatic coma. The administration of flumazenil should be recommended in patients with hepatic coma. Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy } "Influence of Flumazenil on Hepatic Coma: Clinical and Neurophysiological Study".

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"P P 5 0129" P 5 0129 **Epidemiology of Hepatocellular Carcinoma in the Department of Calvados (France). Risk Factors and Prognostic Factors in a Non-Selected Population**

\*C. Even, G. Launoy<sup>1</sup>, M.A. Piquet, O. Duval, T. Collet, M. Gignoux<sup>1</sup>, J.C. Verwaerde, T. Dao

<sup>1</sup> Departments of Hepato-gastro-enterology, Registry of digestive tumours of Calvados, C.H.U., CAEN, France  
The aim of this study was to determine the epidemiological characteristics of hepatocellular carcinoma (HCC), and to study risk factors and prognostic factors in a non-selected population.  
*Methods:* Between 1984 and 1990, every case of HCC was registered by the registry of digestive tumors of Calvados. Standardized incidence rates were calculated for male and female. Prognostic factors were determined with the Cox's multivariate method.  
*Results:* 213 HCC have been registered. Diagnosis of HCC was based on: histology (50p.100), imaging + AFP  $\{ \backslash b3 \}$  250 ng/ml (34p.100), imaging alone (16p.100). Standardized incidence rates were 7.5/100.000 in men and 0.4/100.00 in women. Sex-ratio was 17.1. Mean age was 66.4 – 1.2 years. HCC was uncommon before age of 50 (3p.100). HBsAg was present in 10/119 cases (8p.100), anti-HCV antibodies (EIA 1) were present in 6/22 cases (27p.100). Presence or absence of an underlying liver disease was established in 191 cases: normal liver (histologically proven) in 10p.100, cirrhosis in 86p.100, non cirrhotic liver disease (histologically proven) in 4p.100. The cause of cirrhosis was known in 150 cases: alcoholic 73p.100, cryptogenetic 9p.100, viral 7p.100, alcoholic + viral 5p.100, hemochromatosis 5p.100. The global survival (n = 203) at 1 year, 3 years and 5 years was respectively 21p.100, 8p.100 and 3p.100. The multivariate study pointed out 4 prognostic factors: number of tumors  $\{ \backslash a3 \}$  2, lack of ascitis, AFP  $\{ \backslash a3 \}$  10 ng/ml, HCC revealing a liver disease well-compensated until diagnosis time.  
*Conclusion:* In a french non-selected population, at least 10p.100 of HCC occurs on normal liver. Occurrence of HCC seems to be linked to cirrhosis, male sex and age > 50, which could constitute main selection criterias for HCC screening. Unknown cirrhosis is associated with a better prognostic, suggesting the interest of early cirrhosis diagnosis. Oncology, specific: Liver, biliary }" "Epidemiology of Hepatocellular Carcinoma in the Department of Calvados (France). Risk Factors and Prognostic Factors in a Non-Selected Population"

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"P P 5 0130" P 5 0130 **HB X RNA and Antigen Detection and Sequence Analysis of the X Gene in the Tumorous and Non Tumorous Tissue of HB<sub>s</sub>AG Negative Patients with HCC. Poussin<sup>1</sup>, H. Dienes<sup>2</sup>, M. Minami<sup>1</sup>, C. Br<sup>\</sup>e9chot,**

\*P. Paterlini<sup>1</sup>

<sup>1</sup> INSERM U-370, CHU Necker, Paris, France

<sup>2</sup> Department of Pathology, Mainz, Germany

<sup>3</sup> Liver Unit, Hospital Necker, Paris, France Deleted HBV genomes persist in hepatocellular carcinomas (HCC) developed in HBsAg negative patients and the X region is often selectively transcribed [1]. In order to understand the role of HBV in these tumors we have: 1) looked for the X protein in the tumorous (T) and non tumorous tissues (NT) and 2) analysed by sequencing the X and the preC/C regions in HBsAg negative patients with HCC. *Methods:* HBV-DNA PCR with 8 sets of primers covering the HBV genome; HBV-RNA analysis with primers on the S, X and C gene; X antigen detection by immunohistochemistry; sequence analysis of the X and, as a ""control"", preC/C region by a combination of direct and after cloning sequencing. *Results:* The structure and RNA expression of the HBV genome were analysed in the T and NT of 9 HBsAg negative patients. HBV-DNA PCR revealed frequent genomic deletions. S and C RNAs were never expressed in the T and NT: conversely, X specific transcripts were found in the T and NT tissues of 7/9 patients. Seven patients were tested for the HBxAg in the T and NT: 5 scored positive and 2 negative, the results being in agreement with RNA results. In 2 of these patients the sequence analysis of the X region showed a high T/NT aminoacid divergence rate (23.3% and 11.6%): mutations were found in cell protein binding and transactivating domains and in the common AA with kunitz domain of serine protease inhibitors, suggesting a modification of the X function. By contrast, a very low rate of T/NT nucleotide divergence was found in PreC/C sequences (0.28% and 0.34%). *Conclusions:* Our study demonstrates the expression of both the X RNA and protein in the T and NT liver tissues of HBsAg negative patients and identifies mutations which might modify the X function. These results are consistent with a role for the X protein in the HBV related liver oncogenesis in HBsAg negative patients.

Reference: Hepatology, 21: 313, 1995. Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis } "HB X RNA and Antigen Detection and Sequence Analysis of the X Gene in the Tumorous and Non Tumorous Tissue of HBSAG Negative Patients with HCC"

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## "P P 5 0131" P 5 0131 Mass Screening for Detecting Hepatocellular Carcinoma

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<sup>1</sup> Health Care Center, Yamanashi Prefectural Welfare Federation of Agricultural Co-operatives

<sup>2</sup> First Department of Medicine, Yamanashi Medical University, Yamanashi, Japan A total of 278,448 inhabitants of Yamanashi prefecture, Japan, were screened for hepatocellular carcinoma (HCC) by using ultrasonography (US) from April 1986 through March 1994. Among 80 HCC patients detected by US, 25 patients were screened annually (group A), the other 55 patients were found at the first screening or at screening after two or more years interval (group B). The detection rate of HCC was calculated as 28.7 per 100,000. The male/female ratio was 5.7 : 1. All patients were asymptomatic at the time of detection. In respects to most important risk factors for HCC, 12 patients were positive for HBsAg from 79 examined, and 40 patients were positive for anti-HCV from 53 examined. Five patients were negative for both HBsAg and anti-HCV, but they showed the same abnormalities in liver function tests. As compared with group B, group A had a tendency to detect in more smaller size and at more earlier stage. Small HCC ( $\leq 2$  cm) in group A and B were 9 patients (36%), 15 patients (33%) each. Solitary HCC in group A and B were 19 patients (76%), 32 patients (58%) each. For the survival rate of HCC, group A (1/3/5 year : 92/74/31 %) was significantly higher than group B (73/35/0 %). In conclusion, repeated mass survey by US within one year interval was effective for detecting the HCC at early stage and for expecting good prognosis. Oncology, general: Screening, prevention Oncology, specific: Liver, biliary } "Mass Screening for Detecting Hepatocellular Carcinoma"

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**"P P 5 0132" P 5 0132 Albumin mRNA in Peripheral Blood a Poor Prognostic Marker for Recurrence of Hepatocellular Carcinoma after Orthotopic Liver Transplantation**

\*M. Peck-Radosavljevic, M. Bergmann, P. Ferenci, M. Riegler-Keil, C. Seelos, E. Lipinski, F. L'engle, R. Steininger, A. Gangl, F. M'chlbacher, J. Pidlich

Dept. of Gastroenterology, Dept. of Transplant Surgery, University of Vienna, A-1090 Vienna, Austria Survival after orthotopic liver transplantation for hepatocellular carcinoma is limited by a high rate of tumor recurrence. A PCR-assay based on the detection of albumin mRNA expression in peripheral blood for detection of hematogenous micrometastasis of hepatocellular carcinoma has been described, which may help to select candidates for orthotopic liver transplantation. The prognostic value of a highly sensitive nested RT-PCR assay was evaluated in comparison to the TNM-classification of the UICC in a population of liver transplant candidates. 80 patients with liver disease and 42 control patients were evaluated. Six of 21 patients with hepatocellular carcinoma and 11 of 59 patients with diseases of the liver were positive on albumin RT-PCR, making this assay a good indicator of ongoing liver damage without absolute specificity for hepatocellular carcinoma. Twelve patients with hepatoma were followed after liver transplantation and 7 of those patients had a tumor recurrence within 12 months. Six of these patients with recurrence had UICC stage IV A tumors preoperatively, while only one of them were positive on albumin RT-PCR before transplantation. Only one patient with a stage I to III tumor had a recurrence within 12 months. Albumin mRNA RT-PCR seems to be an unreliable marker for assessing hematogenous spread of hepatocellular carcinoma before orthotopic liver transplantation. UICC stage IV A was a much better predictor of tumor recurrence compared to albumin mRNA RT-PCR. The practical value of albumin mRNA RT-PCR for patients undergoing liver transplantation seems to be very limited. Oncology, specific: Liver, biliary Liver and bile ducts, 1: Liver transplantation } "Albumin mRNA in Peripheral Blood a Poor Prognostic Marker for Recurrence of Hepatocellular Carcinoma after Orthotopic Liver Transplantation"

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## "P P 5 0133" P 5 0133 **Diagnostic Value of Color Doppler Ultrasonography in Hepatocellular Carcinoma**

\*Vedat G\u00f6ral, Levent Mumbul\u00e7, Arslan Bilici, Aydin Kemaneci

Dicle University School of Medicine, Division of Gastroenterology, Diyarbakir,

Turkey Hepatocellular carcinoma accounts for 80 to 90 percent of liver carcinomas. There is a

wide variation in the incidence of hepatocellular carcinoma in different parts of the world, and a

numbers of etiologic factors may be important. *Aim:* A differential diagnosis of liver tumors was

attempted on the basis of the pattern of blood within and around tumors on color Doppler flow

images. *Methods:* The study comprised 47 patients with liver mass lesions: 22 patients had

hepatocellular carcinoma, 15 had hemangiomas, 4 had metastatic liver cancer, 3 had liver

abscess, 3 had liver cyts. Color Doppler flow imaging and Doppler flow velocity were

established and compared according to the Tanaka classification. *Results:* Color Doppler flow

imaging was observed in masses of all of 22 patients with hepatocellular carcinoma, of 3 patients

with liver metastasis, of 3 patients with hemangiomas. Doppler signals were not observed in 1

patient with liver metastasis, in 3 patients with liver abscess, in 3 patients with liver cyts. The

mean of maximum blood flow velocity was 80.7 cm/sn in hepatocellular carcinoma, 49.3 cm/sn

in metastatic liver cancers, 10.3 cm/sn in hemangiomas. A basket pattern (a fine blood-flow

network surrounding the tumor nodule) was observed in 17 (77%) of the 22 hepatocellular

carcinomas. An image of vessels within the tumor (blood flow that runs into and branches within

the tumor) was observed in 5 (23%) of the 22 hepatocellular carcinomas. These two findings

were observed only in hepatocellular carcinomas. In three of 15 hemangiomas, a spot pattern

(color-stained dots or patches in the central region of the tumor) was seen. *Conclusion:*

According to the this results, hepatocellular carcinomas have some characteristic appearances on

Doppler flow images. Therefore, color Doppler ultrasonography can aid in the diagnosis of liver

mass lesions. Radiology and ultrasound: Diagnosis Oncology, specific: Liver, biliary Oncology,

general: Screening, prevention } "Diagnostic Value of Color Doppler Ultrasonography in

Hepatocellular Carcinoma"

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## "P P 5 0134" P 5 0134 **Cholangiocellular Carcinoma: Pathological, Ultrasonographic and Angioechographic Correlation**

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Clinic of Gastroenterology, Medical Faculty, Skopje, Macedonia

<sup>1</sup> Institute of Gastroenterology, Tokyo Women's Medical College, Tokyo, Japan  
Correlation were sought among histopathologic, ultrasonographic (US) and angioechographic findings in 27 resected cholangiocellular carcinoma (CCC) cases. According to macroscopic appearance CCC was classified into three types: nodular, periductal and intraductal. This classification was accepted because clinico-pathological features, as well as prognosis, differed among tumor types. A tumor mass was clearly visible in nodular type tumors. 17 were large tumors and 3 were small less than 3 cm. The large tumors were ill-defined (70%), showed hypoechoic rim (65%), had an echo pattern which tended to be more echogenic and were associated with bile duct dilatation (59%). Vascular structures within the tumor were of importance as US characteristics of CCC: Portal tract passing through the tumor (23%), disappearing portal tract (29%) and the "vessel like structures" sign (53%). Tumor mass could not be identified or was poorly visualised in periductal and intraductal type CCC. A disappearing portal tract sign was noted in four while bile duct dilatation was seen in all five periductal type cases. The two cases had intraductal type CCC. Tumor mass filling the bile duct was seen in one case. In addition angioechography was performed in 9 of these CCC cases. After CO<sub>2</sub> gas injection three angioechographic patterns were discernible, peripheral enhancement in three cases, whole tumor enhancement in four cases and partial tumor enhancement in two cases. There was a tendency for the angioechographic pattern to change from whole to peripheral enhancement as the tumor increased in size. The comparisons contribute to understand the significance of the different US and angioechographic appearances of CCC. Oncology, specific: Liver, biliary Radiology and ultrasound: Diagnosis }  
"Cholangiocellular Carcinoma: Pathological, Ultrasonographic and Angioechographic Correlation"

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## "P P 5 0135" P 5 0135 Cytology Study of Localisation of Hepatitis B Surface Antigen in Hepatocellular Carcinoma Using Orcein Staining

\*K.T. Shenoy, J.V. Panicker Jalesh, Joy Augustine

Department of Gastroenterology and Pathology, Medical College, Trivandrum, India *Objective:* To test the hypothesis that orcein staining of cytological specimen from hepatocellular carcinoma (HCC) can detect hepatitis B surface antigen (HBsAg) and to determine the observer variability and agreement. *Methods:* 20 cases of suspected HCC were evaluated clinically and cytological examination of fine needle aspiration cytology material for malignancy by papanicolaou and orcein staining for HBsAg was carried. Modification of orcein staining was done to suit cytology. Using cytomorphological features, HCC was diagnosed. HBsAg was detected in serum using ELISA. Observer variability and agreement were assessed on orcein positivity by two independent cytopathologists. Data were analysed using Kappa statistics for observer agreement. *Results:* Of 20 suspected HCC, 13 had definite HCC. 8 HCC had HBsAg positivity and 8 had orcein positivity as judged by observer 2 and 7 by observer 1. A Kappa value of 0.837 was statistically significant. *Conclusion:* A high degree of observer agreement between cytopathologists in the interpretation of orcein positivity was noted and there was excellent correlation with HBsAg status. This technique is cheap, safe and quick and need further evaluation as a test for laboratory diagnosis of HBV related HCC. Oncology, specific: Liver, biliary } "Cytology Study of Localisation of Hepatitis B Surface Antigen in Hepatocellular Carcinoma Using Orcein Staining"

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"P P 5 0136" P 5 0136 **HCC Prevalence in Liver Cirrhosis: A Prospective Study on 121 Cases**. S. Pistoso, G.P. Aimo, W. Piubello

Med. Dept. Salo' General Hospital, Salo' Italy Prevalence of Hepatocellular carcinoma (HCC) in patients suffering from cirrhosis is high and its prognosis generally poor. The early detection of HCC could improve treatment chances and survival. We monitored 121 consecutive patients (73 men, 48 females ages, average age 58, ranging from 28–73) with semiannual controls of alfafetoprotein and ultrasonography. Cirrhosis was viral in 48 patients, ethanol related in 63 and due to other causes in 10. At the moment of enrollment 64 of the patients were classified in class A of Child, 39 in B and 18 in C. The average length of our observation was 48 months (range 11–102). There were 20 HCC diagnosed, 15 of them male. In relation to aetiology, 12 HCC developed in patients with viral cirrhosis (25%) and 8 in alcoholic disease (12.6%). In 11 HCC underlying cirrhosis was classified in Child grade A, in 8 B, and in one case C. In 10 cases tumor size was smaller than 5 cm in diameter. The levels of Alfafetoprotein were high in 12 patients with HCC (60%) and in 7 (8%) with cirrhosis. Cumulative incidence of HCC became greater with the length of follow up: 2.5% at the first year, 22.4 at the sixth, with annual incidence of about 4%. In conclusion our results suggest that the semiannual screening of cirrhotic patients permits the diagnosis of HCC in its early stages in 50% of the cases. Alfafetoprotein measurement alone is an unsatisfactory index of HCC development for its low sensibility. In patients with Child grade C cirrhosis background liver disease itself determine the prognosis, so that screening for HCC development seems to be unnecessary. Oncology, specific: Liver, biliary Oncology, general: Screening, prevention } "HCC Prevalence in Liver Cirrhosis: A Prospective Study on 121 Cases"

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## "P P 5 0137" P 5 0137 Serum Carbohydrate-Deficient Transferrin in Patients with Nonalcoholic Liver Disease and with Hepatocellular Carcinoma

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Serum carbohydrate-deficient transferrin (CDT) test is a reliable and specific marker for detecting alcohol consumption. However, recent studies have shown false-positive of CDT test results in nonalcoholic liver disease. We examined the clinical significance of serum CDT in nonalcoholic liver disease and especially in hepatocellular carcinoma (HCC), using alcoholic liver disease as a positive control. The subjects included 23 teetotalers, 56 patients with alcoholic liver disease (39 liver fibrosis and 17 LC), 84 patients with chronic viral liver disease (24 CPH, 33 CAH, 27 LC) and 67 patients with HCC. Serum CDT was measured with an Axis % CDT RIA kit (Axis Biochemicals AS, Oslo, Norway) and expressed as percentages of the total transferrin (% CDT). The serum % CDT was 1.2 – 0.8% in the teetotalers. The mean serum % CDT value was increased 1.8-fold in alcoholic liver fibrosis and 3.8-fold in alcoholic LC compared with the teetotalers. The serum % CDT values in viral chronic hepatitis were similar to those in teetotalers, and were increased 2.0-fold in nonalcoholic LC. False-positive results were found in 10 (37%) of the 27 patients with nonalcoholic LC, but not in viral chronic hepatitis. The mean serum % CDT value was increased 2.5-fold in HCC, and false-positive results were found in 31 (46%) of the 67 patients. CDT was also recognized by isoelectric focusing followed by immunofixation in the false-positive serum from patients with HCC. The serum % CDT value in HCC was related to the size of tumor and the grade of histological differentiation. These results suggest that the ability of serum CDT measurement to detect chronic alcoholism may be reduced in patients with nonalcoholic liver cirrhosis and with hepatocellular carcinoma. Liver and bile ducts, 1: Hepatotoxicity, ethanol } "Serum Carbohydrate-Deficient Transferrin in Patients with Nonalcoholic Liver Disease and with Hepatocellular Carcinoma"

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"P P 5 0138" P 5 0138 **Precancerous Potentiality of Macroregenerative Nodules in Liver Cirrhosis**

\*M. Bonelli, S. Signorelli, B. Paris, F. Negrini, E. Marzo, M. Girola

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Italy *Background/Aims.* A close follow-up with ultrasonographic (US) examination and alpha-fetoprotein (AFP) measurement is the current policy for early diagnosis of hepatocellular carcinoma (HCC) in patients with cirrhosis. Large hepatocellular nodules, histologically defined as benign macroregenerative nodules (MRNs), are sometimes picked-up by ultrasound. The significance of these lesions, which have a differing sonographic texture, is still debated. In the present study the pre-malignant potential of these nodules is evaluated, by following them up with regularly scheduled US examinations and US-guided fine needle biopsy (FNB). *Methods.* 14 focal lesions (with an average size of 24 mm in diameter) in 11 cirrhotic patients (10 males and 2 females, age 52–75 years), with histological diagnosis of MRNs, made by US-guided fine needle biopsy, were followed from 1989 to 1996. Mean follow-up was 41 months (range 12 to 77). During the observation period a regular US and clinical evaluation at an interval of 4 months was carried out. When some changes occurred in nodules size, US pattern or AFP levels, a rebiopsy was performed. US and clinical features, including Child's classification, alcohol intake, AFP and HBV/HCV positivity were investigated (chi-square test was used for statistical analysis of data). *Results.* 12 out of 14 nodules (78.5%) increased in size during the follow-up period, and became histologically malignant (HCC) after  $28.7 + 10$  months (mean + SD). There was no statistical correlation between neoplastic transformation and US pattern or clinical data at the time of entry into the study. *Conclusions.* The pre-malignant nature of MRNs in cirrhotic liver is very likely and the treatment of these lesions should be encouraged. Oncology, specific: Liver, biliary }" "Precancerous Potentiality of Macroregenerative Nodules in Liver Cirrhosis"

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"P P 5 0139" P 5 0139 **Retroviral Thymidine Kinase Gene Transfer and Ganciclovir Therapy (GCV) Generate Anti-Tumoral Immunity and Bystander Effect Against Non Transduced Liver Tumors Cells in Rat**

\*Rad A.R. Kianmanesh, Y. Panis, M. Fabre, D. Houssin, D. Klatzmann

Surgical Research Lab. (Hospital Cochin), Pathology (Hospital Kremlin-Bic\eatre) and CNRS (Hospital de la Piti\e9-Salp\eatrière), Paris, France Significant regression of liver metastases in rats was observed after in situ retroviral transfer of thymidine kinase gene from Herpes Simplex Type 1 (HSV1-TK), followed by GCV. However, few tumor cells were effectively transduced. This could be explained by bystander effect (intercellular crossing of toxic form of GCV) and/or anti-tumoral immunity. The aim of this work was to study these two mechanisms in rat liver metastases and hepatoma. *Material and Methods:* (a) *bystander effect* was studied in 16 rats after intrahepatic injection of colon cancer cells mixture with variable rates of transduced TK+ (0, 25%, 50% and 100% TK+) and TK{ -} cells. After 5 days, rats were treated with GCV for 5 days. Rats were sacrificed at Day 12; (b) *anti-tumoral immunity* was studied in 12 rats after intrahepatic injection in 2 different locations of hepatomas cells: in each rat, left lobe received TK{ -} cells and right lobe TK+ cells. At Day 14, 6 rats were treated with GCV for 5 days. The 6 others rats received no treatment. Two weeks later, all the rats were sacrificed. *Results:* (a) significant tumor regression was obtained from tumors with 25% TK+ cells: mean tumor volumes were: 30 – 16 mm<sup>3</sup> (0% TK+) vs 10 – 5 (25% TK+; p < 0.04) vs 4 – 4 (50% TK+) vs 0.2 – 0.2 (100% TK+); (b) in control rats with double liver tumors, mean tumor volume for TK+ was 4895 – 4360 and TK{ -} 6494 – 7329 mm<sup>3</sup> (N.S.). After GCV, mean tumor volume for TK+ was 11 – 13 (p < 0.006 vs control TK+) and TK{ -} 30 – 41 mm<sup>3</sup> (p < 0.004 vs control TK{ -}). *Conclusions:* (a) bystander effect was responsible of a significant anti-tumoral effect even if only 25% of tumor cells were effectively transduced; (b) the unexpected significant regression of TK{ -} liver tumors suggested a possible role of host immunity. This study demonstrated that 2 different mechanisms could amplify the therapeutic effect observed after HSV1-TK retroviral gene transfer and GCV: the bystander effect and the generation of anti-tumoral immunity against TK{ -} cells after destruction of TK+ cells. Oncology, specific: Liver, biliary Oncology, general: Molecular biology, genetics }" "Retroviral Thymidine Kinase Gene Transfer and Ganciclovir Therapy (GCV) Generate Anti-Tumoral Immunity and Bystander Effect Against Non Transduced Liver Tumors Cells in Rat"

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"P P 5 0140" P 5 0140 **Assay of Trace Elements and Superoxide Dismutase Activity on Bioptic Specimens from Chronic and Neoplastic Liver Diseases** A. Grattagliano,

\*G.L. Rapaccini, P. Marino, O. Senofonte<sup>1</sup>, N. Violante<sup>1</sup>, M.E. De Leo<sup>2</sup>, L. Riccardi, T. Galeotti<sup>2</sup>, S. Caroli<sup>1</sup>, G. Gasbarrini

<sup>2</sup> Dept. of Internal Medicine and Institute of General Pathology, Italy

<sup>1</sup> Catholic University, Istituto Superiore di Sanit'e0, Rome, Italy Oxygen radicals play an important role in multistep carcinogenesis and antioxidant substances can inhibit the carcinogenesis. Hepatocellular carcinoma (HCC) is a neoplasm mostly arising on cirrhotic liver. The aim of our study was to evaluate on liver specimens obtained by echo-guide percutaneous biopsy from patients with neoplastic and/or chronic liver diseases: A) the activity of the two types of antioxidant enzyme Superoxide Dismutase (Mn-SOD and CuZn-SOD); B) the level of some elements (Mn, Cu, Zn, Fe) involved in free radicals metabolism. We evaluated: the SOD activity on specimens from 8 normal livers, 17 chronic hepatitis (CH), 11 cirrhosis, 4 dysplastic nodules (DN) and 11 HCC; the element levels on specimens from 4 normal livers, 14 CH, 16 cirrhosis, 1 DN and 4 HCC. Total-SOD \b5g/mg prot Mn-SOD \b5g/mg prot CuZn-SOD \b5g/mg prot Normal liver 12.4 – 1.0 6.4 – 0.8 6.0 – 0.4 CH 7.9 – 0.6<sup>bullet</sup> 4.5 – 0.5<sup>Ø</sup> 3.4 – 0.4<sup>bullet</sup> Cirrhosis 7.0 – 0.8<sup>bullet</sup> 3.6 – 0.4<sup>Ø</sup> 3.4 – 0.5<sup>bullet</sup> DN 5.2 – 0.8<sup>bullet</sup> 3.1 – 0.6<sup>Ø</sup> 2.1 – 0.2<sup>bullet</sup> HCC 4.9 – 0.9<sup>bullet</sup> 3.6 – 0.6<sup>Ø</sup> 1.3 – 0.5<sup>bullet</sup><sup>bullet</sup> p < 0.001 vs. normal liver, Øp < 0.05 vs. normal liver Mn \b5g/g dw Cu \b5g/g dw Zn \b5g/g dw Fe \b5g/g dw Normal liver 4.08 – 0.08 3.90 – 1.04 65.2 – 10.2 156 – 85 CH 5.43 – 0.52 6.30 – 1.12 165.7 – 59.3 388 – 65 Cirrhosis 6.89 – 1.56 9.96 – 1.14 222.3 – 60.4 715 – 202 DN 5.28 15 68.2 200 HCC 4.62 – 0.91 3.17 – 1.83 81.8 – 28.6 1024 – 246 In present study a reduction of SOD activity has been found progressing from chronic liver diseases to HCC; this reduction could to be involved in the pathogenetic mechanism underlying the natural history of HCC. In our study the level of Mn, Cu and Zn (cofactors of the two types of SOD) aren't lower in liver diseases, thus they aren't involved in down regulation of SOD. On the contrary, the iron, element involved in free radicals production, is higher in all liver diseases. Oncology, specific: Liver, biliary } " Assay of Trace Elements and Superoxide Dismutase Activity on Bioptic Specimens from Chronic and Neoplastic Liver Diseases "

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"P P 5 0141" P 5 0141 **Hepatocellular Carcinoma (HCC) in HCV-Related Cirrhosis Treated and Not Treated with Interferon**

\*A. Vian, U. Lorenzoni, S. Lobello, A.R. Floreani, F. Farinati, R. Naccarato, M. Chiaramonte

Dpt of Gastroenterology, University of Padova Hepatocellular carcinoma (HCC) is a complication of long-standing cirrhosis, especially with viral aetiology. In an Italian population the HCC incidence/100 pts/year in Child A HCV-related cirrhosis is 3.62 (Ital J Gastroenterol, 1994; 26; 164) Recent reports suggested that IFN treatment can reduce the risk of HCC development in HCV related cirrhosis (Lancet, 1995: 346; 1051, J Hepatol, 1996: 24; 141). With the Aim to verify whether in our population IFN treatment can reduce the incidence of HCC in Child A cirrhotic patients, we studied two group of patients, prospectively followed up, and treated or not with IFN. *Methods:* IFN treated group: 44 patients (26 M, 12 F; mean age 56 Range 28–64) enrolled in Alpha-IFN trials between 1991–1994 and followed-up for at least 12 months (mean 37.6 Range 12–56) after the end of full treatment. Control group: 157 non treated patients (81 M, 76 F; mean age 54.2 Range 30–72) enrolled in a prospective follow-up study between 1981–1994. All patients had well compensated cirrhosis (Child A), biopsy proven at the enrolment, and no statistically significant differences in demography were detectable. In the treated group 8 pts (18.2%) were responders, 27 (61.3%) non-responders and 9 (20.5%) responders with relapse. The results were statistically analysed by the Mantel Haenszel life table analysis. *Results:* 5 (11.4%) patients in the treated group developed HCC. The respective incidences in responders, non responders and relapsers were 2/5 (female), 3/5 (all males) and 0/5. In non treated patients 32/157 (20%) developed HCC. After adjustment for the follow-up period, the Mantel Haenszel life table analysis showed that the probability of remaining HCC free was not statistically different between the two groups ( $p = 0.30$ ). *In Conclusion* our results, based on a prospective follow-up study of cirrhotics, treated or not with IFN, failed to confirm the above early evidence that IFN treatment reduce the HCC incidence in well compensated cirrhosis. Oncology, specific: Liver, biliary Oncology, general: Epidemiology Oncology, general: Therapy } "Hepatocellular Carcinoma (HCC) in HCV-Related Cirrhosis Treated and Not Treated with Interferon"

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## "P 5 0142" P 5 0142 Trial of a New Therapy Combining DDS with Hyperthermia for Liver Cancer

\*M. Imamura, T. Seki, K. Kunieda, T. Tamai, T. Nakagawa, A. Nishimura, K. Inoue, Y. Obiya<sup>1</sup>, K. Harada<sup>1</sup>

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<sup>1</sup> PL Botanical Inst., PL Gakuen Women's Jr. College, Tondabayashi, Osaka 584, Japan We have been developing a new form of therapy to achieve more effective local control of liver cancer. First, we designed a new anticancer drug delivery system (DDS) targeting liver cancer. Then, we developed a drug complex bound to hydroxyapatite (HAP) including doxorubicin hydrochloride (DOX) and buthionine sulfoximine (BSO). This drug complex was named the HAP system. DOX is an anthracycline anticancer drug, and BSO is a selective inhibitor of GSH (intracellular glutathione;  $\gamma$ -glutamyl-cysteinyl-glycine) biosynthesis. GSH is a scavenger of free radicals in tumor cells. We found in an *in vitro* experiment that DOX and BSO were eluted from the HAP system over the first 3 hrs of incubation, and that from 4 hrs onwards the remaining DOX was released continuously, showing a slow-release property. This property is likely to be favorable because it allows continuous attack on tumor cell DNA after the initial depletion of GSH by BSO. Also, we performed an *in vivo* experiment using sarcoma 180 tumors transplanted into the thigh of the right hind leg of mice. After measuring the tumor volume every day we evaluated the inhibitory effect of the HAP system on tumor growth. The inhibitory effect of the system was remarkable, the tumor volume ratio (DOX-HAP complex-treated group/DOX & BSO-HAP complex-treated group) on the 31st day being 1.93. We then examined experimentally the inhibitory effect on tumor growth of the HAP system + hyperthermia (42°C for 40 min) on the 7th day after HAP system transplantation. On the 28th day after transplantation of this system, the tumor volume in the DOX & BSO-HAP group was  $6.36 \times 10^4 \text{ mm}^3$  whereas that of the DOX & BSO-HAP + hyperthermia group was  $2.29 \times 10^4 \text{ mm}^3$ . The latter group showed significant suppression of tumor volume to 64%, as compared with the former group (t-test,  $t < 0.05$ ). Therefore, it was assumed that the HAP system + hyperthermia treatment was more effective for cancer therapy than the other treatments. We have also been studying the inhibitory effect on tumor growth of the HAP system + hyperthermia using VX<sub>2</sub>-transformed livers (hepatic tumor) in Japanese white rabbits, and obtained results similar to those for sarcoma 180. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Oncology, general: Therapy Oncology, specific: Liver, biliary } "Trial of a New Therapy Combining DDS with Hyperthermia for Liver Cancer"

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**"P P 5 0143" P 5 0143 Arterial Infusion Chemotherapy Using in vitro Chemosensitivity Test for Unresectable Hepatocellular Carcinoma (HCC) M. Yoshikawa<sup>1</sup>, T. Denda<sup>2</sup>, M. Ebara<sup>1</sup>, H. Fukuda<sup>1</sup>, N. Sugiura<sup>1</sup>, M. Kimura<sup>3</sup>, H. Tokita<sup>2</sup>, H. Saisho<sup>1</sup>**

<sup>1</sup> Chiba University, Chiba, Japan

<sup>2</sup> Chiba Cancer Center Research Institute, Chiba, Japan

<sup>3</sup> Chiba Kaihin Municipal Hospital, Chiba, Japan We studied the clinical usefulness of hepatic arterial infusion chemotherapy based on an chemosensitivity test. Seventy eight patients with unresectable HCCs were treated by hepatic arterial chemoinfusion using a percutaneously implanted reservoir. Before chemoinfusion, we selected an anticancer drug by in vitro chemosensitivity test using a biopsy specimen, in which karyologic changes of cancer cells were observed microscopically as an indicator of drug sensitivity. Forty four patients were treated by chemosensitivity-positive drugs (group A). The remaining 34 patients (group B), failing to have chemosensitivity-positive drugs, were treated by randomly selected 1 of 4 drugs (pirarubicin, epirubicin, carboplatin, mitoxantrone). The overall response rate by WHO criteria was 46% in group A and 12% in group B. The 1-year and 2-year survival rates of group A were 69% and 42%, while, those of group B were 58% and 0%, respectively. The arterial infusion chemotherapy based on the chemosensitivity test improved therapeutic results in the patients with unresectable HCCs. Oncology, general: Therapy Oncology, specific: Liver, biliary } "Arterial Infusion Chemotherapy Using in vitro Chemosensitivity Test for Unresectable Hepatocellular Carcinoma (HCC)"

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"P P 5 0144" P 5 0144 **High Preoperative Serum Alanine Transaminase Level Increases the Risk of Liver Resection for Hepatocellular Carcinoma (HCC) in Childs' Grade A Cirrhotic Patients**

\*O. Farges, P. Jagot, R. Noun, J. Belghiti

Department of Digestive Surgery, Hospital Beaujon, University Paris VII, Clichy, France Liver resection in patients with liver cirrhosis (even in the absence of overt liver insufficiency) is associated with a greater risk than in patients without underlying liver disease. Because the incidence of HCV-cirrhosis related HCC is anticipated to increase rapidly in the near future we have assessed, by multivariate analysis, parameters associated with in-hospital mortality and morbidity in a consecutive series (1984–1994) of 108 Childs' grade A cirrhotic patients undergoing liver resection of an HCC (1 or less liver segment, 2 segments or 3 or more segments in 42, 23 and 43 patients respectively). Parameters entered for analysis included age, aetiology of cirrhosis, preoperative serum bilirubin, AST, ALT, GGT, albumin, creatinine levels as well as prothrombin time, presence or absence of pathological features of superimposed active hepatitis, extent of resection, type and duration of vascular clamping and amount of intraoperative blood loss. Overall incidence of in-hospital death and major postoperative complications were 8.3% and 48.1% respectively. By univariate analysis, preoperative serum ALT levels ( $p = 0.001$ ) and intraoperative transfusions ( $p = 0.01$ ) were the only parameters significantly associated with in-hospital death. However, only serum ALT concentrations was an independent risk factor. In-hospital mortality in patients whose preoperative serum ALT was below 2 N ( $n = 77$ ), comprised between 2 and 4 N ( $n = 23$ ) and greater than 4 N ( $n = 8$ ) was 3.9%, 13.0% and 37.5% respectively. Increased ALT levels ( $> 2 N$ ) was also associated with an increased incidence of postoperative ascites (58 vs. 32%,  $p = 0.01$ ), kidney failure (16 vs. 0%,  $p = 0.0003$ ) and UGI bleeding (6.4 vs 0%,  $p = 0.02$ ). *Conclusion:* Preoperative serum ALT level is an independent and reliable predictor of in-hospital mortality and morbidity following liver resection in Child A cirrhotic patients. Our results suggest that cirrhotic patients with ALT  $> 2 N$  should undergo only a limited resection. If a larger resection is necessary other therapeutic option should be considered. Oncology, specific: Liver, biliary } "High Preoperative Serum Alanine Transaminase Level Increases the Risk of Liver Resection for Hepatocellular Carcinoma (HCC) in Childs' Grade A Cirrhotic Patients"

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## "P P 5 0145" P 5 0145 **Low Morbidity after Liver Resection with Ultrasonic Dissector in Cirrhotic and Non-Cirrhotic Patients**

\*R. Dionigi, L. Dominioni, A. Benevento, A. Ferrari

Department of Surgery, University of Pavia in Varese, Varese, Italy Aim of this study is to evaluate the postoperative (30 days) morbidity and mortality in a consecutive series of 144 liver resections carried out with the ultrasonic dissector (CUSA). From 1987 to 1996 144 patients (M/F: 90/54, mean age 64 years) underwent liver resection for hepatocarcinoma (n = 51), liver metastases (n = 62), bile ducts carcinoma (n = 5), hemangioma (n = 11), and other benign tumors (n = 15). Fortysix patients were cirrhotic and 98 patients had a normal residual liver. Hepatic resections included: 43 major resections (left, right or extended right hepatectomy), 21 segmentectomies and 80 atypical or subsegmental resections. Surgical technique included the use of CUSA, which allowed the meticulous identification and ligation of major as well as minor hepatic vessels and ducts crossing the resection plane, thus preventing local surgical complications. The morbidity and mortality observed are detailed in the table: Complications All patients Cirrhotic Non cirrhotic (n = 144) (n = 46) (n = 98) Liver failure 6 (2\*) 2 (1\*) 4 (1\*) Liver bleeding 1 1 – Gastrointestinal bleeding 2 (1\*) – 2 (1\*) Biliary leakage 2 – 2 Septic shock 2 (1\*) 1 (1\*) 1 Heart, lung, renal failure; MOF 11 (3\*) 5 (1\*) 6 (2\*) Total complications 24 8 15 Total pts with complications 16 (11%) 7 (15%) 9 (9%) Mortality 7 (5%) 3 (7%) 4 (4%)\*fatal outcome In conclusion, our results indicate that liver resection can be done in cirrhotic and non-cirrhotic patients with low morbidity (11%) and low mortality (5%), by using the ultrasonic dissector, which allows a better hemostasis and control of biliary leakage of the liver transection surface, as compared to the finger dissection technique. Oncology, specific: Liver, biliary Oncology, general: Therapy Clinical practice: Management strategy } "Low Morbidity after Liver Resection with Ultrasonic Dissector in Cirrhotic and Non-Cirrhotic Patients"

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"P P 6 0146" P 6 0146 **Quantification of Intra-Hepatic HCV-RNA According to Histology and to Genotypes after Liver Transplantation** V. Di Martino, C. F'eyray, F. Saurini, D. Samuel, M. Gigou, M. Reynés<sup>1</sup>, H. Bismuth

<sup>1</sup> Hepato-Biliary Surgery and Liver Transplant Unit, Pathology, CHU Kremlin-Bic\eatre, France

Paul Brousse Hospital, Villejuif, CHU Kremlin-Bic\eatre, France A relation between genotypes 1b and severity of recurrent liver disease due to HCV has been described after liver transplantation. However, the mechanism of such severity remains unknown. *The aim* of this study was to analyse in liver transplanted patients remaining serum HCV RNA positive, the relations between the level of intrahepatic replication of HCV, the severity of liver disease and the genotypes. *Samples and methods:* 98 post-transplant biopsies from 33 liver transplanted patients (21 were genotype 1b) were available. Intrahepatic HCV RNA was quantitated by competitive PCR on serial dilutions of HCV cDNA. For all biopsies, a similar competitive method was used for the quantification of 28S ribosomal RNA permitting to normalize the quantitation of HCV between the biopsies. *Results:* Levels of intra-hepatic replication was higher in case of lobular hepatitis than in case of chronic active hepatitis, rejection, cholestasis and subnormal histology (10 competitor Unit (CU) vs 2; 1; 1.8 and 2.2  $p < 0.01$ ). Level of replication decreased with time after LT and was not related to genotype 1b. *Conclusions:* Our results show that intra-hepatic replication of HCV 1) exist in liver graft with normal histology; 2) was only increased in case of acute lobular hepatitis; 3) decreased with time after transplant. 4) was not related to genotype 1b. These findings suggest a direct cytopathic effect of HCV at the time of acute hepatitis and that pathogenicity of HCV type 1b is an intrinsic property not related to an increased level of replication. } "Quantification of Intra-Hepatic HCV-RNA According to Histology and to Genotypes after Liver Transplantation"

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"P P 6 0147" P 6 0147 **Value of Transjugular Intrahepatic Portosystemic Shunt in Cirrhotic Patients Awaiting Liver Transplantation** D. Azoulay, J. Raccuia, D. Castaing, H. Bismuth

Hepato-Biliary Surgery and Liver Transplant Center, Paul Brousse Hospital, Villejuif, France From November 1991 to January 1995, 34 transjugular intrahepatic portosystemic shunt (TIPS) were attempted in 34 cirrhotic patients (mean 46.4 ± 2.4; 22–66) candidates for liver transplantation (LT). Patients were classified Child class A in 5 cases, B in 11 cases, C in 18 cases. Indication for TIPS was sclerotherapy failure in 23 cases and intractable ascites in 11 cases. Two patients were excluded because of technical failures which were treated by OLT in one case and open calibrated porta-caval shunt in one case. The follow-up with LT as end point was 1 to 34 months (7.6 ± 1.6 M). *Results:* Early thrombosis (< 3 months) occurred in 8 cases: 6 were desobstructed via the internal jugular vein and 2 were desobstructed surgically together with calibrated porta-caval shunt. Late thrombosis occurred in 1 case with portal vein thrombosis and was treated by mesenterico-caval shunt followed by LT 6 months later. Recurrence of hemorrhage occurred in 2/22 patients who underwent TIPS for sclerotherapy failure (one rupture of varices, one duodenal ulcer). Ascites disappeared in 7/10 patients who underwent TIPS for intractable ascites and was controlled together with diuretics in 2 patients. Ascites remained unchanged in 1 patient. 21 patients were transplanted following TIPS with a mean delay 6.4 ± 1.6 (range: 1–26) months. During the same period, 7 patients with cirrhosis and surgical open porta-caval shunt were transplanted. Comparison of patients with TIPS to patients with surgical open shunt showed a shorter duration of operation for patients with TIPS (332 ± 351 vs 467 ± 480 min,  $P > 0.05$ ), less blood transfusion (3.5 ± 2.1 vs 7.3 ± 2.6 L,  $P < 0.05$ ). Graft and patient survival at 3 months were comparable. We conclude that TIPS controls the complications of portal hypertension in patients awaiting transplantation. TIPS diminishes blood requirement during liver transplantation procedure. } "Value of Transjugular Intrahepatic Portosystemic Shunt in Cirrhotic Patients Awaiting Liver Transplantation"

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"P P 6 0148" P 6 0148 **Prospective Evaluation of Serum GST{ a} in Liver Transplantation**

\*D. Azoulay<sup>1</sup>, A. Lemoine<sup>2</sup>, M. Salvucci<sup>2</sup>, R. Adam<sup>1</sup>, H. Bismuth<sup>1</sup>, B. Debuire<sup>2</sup>

<sup>2</sup> Biochemistry Dept, Paul Brousse Hospital, Villejuif, France

<sup>1</sup> Hepato-Biliary Center, Paul Brousse Hospital, Villejuif, France  
The cytosolic enzyme, Glutathion S transferase { a} (GST) has been proposed as a marker of acute graft rejection following liver transplantation (LT). GST may offer significant clinical advantages over conventional liver function tests (LFT; wide hepatic distribution and shorter in vivo plasma half life). The value of this test over LFT remained to be assessed and was the impetus for the present study. A prospective daily evaluation of plasmatic GST using a new enzyme immunometric assay (Hepkit, Biotrin, Ireland) was performed in 45 recipients (men: 46%, 46 – 13 y), in the first 20 days following LT. The results were compared to conventional LFT and significant clinical events. Twenty patients experienced biopsy proven acute graft rejection episodes (only 15 were treated); 15/20 had an increased GST vs 11/20 for transaminases. The sensitivity of GST assay for the occurrence of treated acute graft rejection was 100% and the specificity 73% vs 73% and 88% for ALT, respectively). The positive predictive value was 75% and the negative one was 100%. GST increased earlier than the conventional LFT before acute graft rejection and decreased also more rapidly when treatment was efficient. GST remained elevated in case of steroid-resistant graft rejection. In the first 3 days of the post operative period, GST was significantly correlated with the prothrombin time at D3 and D5 ( $p < 0.007$ ) and with the occurrence of acute graft rejection. The slower was the decrease, the higher was the occurrence of acute graft rejection. According to the early increase before acute graft rejection and the rapid decrease following efficient treatment of graft rejection, GST assay seems to be a useful marker of acute graft rejection to use in combination with conventional LFT. Moreover the initial GST release following LT was correlated with early graft function. }" "Prospective Evaluation of Serum GSTAlpha in Liver Transplantation"

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"P P 6 0149" P 6 0149 **Liver Transplantation for Hepatocellular Carcinoma on Cirrhosis: Prognostic Impact of an Adapted Patient Selection** H. Bismuth, R. Adam

Hepato-Biliary Surgery and Liver Transplant Research Center, Paul Brousse Hospital, Villejuif, France

Hepatocellular carcinoma (HCC) is an established but still debated indication of liver transplantation (LT). The high risk of recurrence and five year- survival rates significantly lower (0–50% in different series) than those of benign diseases have questioned the place of LT for HCC in the current period of organ shortage. We report in this study the consequences of a new selection of patients adapted from prognostic indicators established in the first phase of a same series. From November 1985 to March 1994, 109 patients with cirrhosis were transplanted for HCC. Of these 109 patients, only 95 patients with HCC diagnosed before LT were included in the study. The presence of extrahepatic deposits on pretransplant staging or pre-operative exploration was considered as a contraindication to LT. In the first period of our experience (November 85–December 91), the selection criteria only included the absence of any extrahepatic tumour (60 patients). After assessment of prognostic factors in this first period (mainly tumor size > 30 mm, number of nodules > 3 and presence of a portal thrombosis), we proceeded to a more restrictive selection of those patients at very high risk of recurrence. Results in terms of patient selection and 3 year-survival were as follows:

	1st period (85–91)	2nd period (92–94)	p
n	60	35	
No nodules > 3	24 (40%)	6 (17%)	0.03
Size > 30 mm	29 (48%)	12 (34%)	0.01
Portal thrombosis	6 (10%)	1 (3%)	NS
No and Size < 30 mm < 3 nod	21 (35%)	22 (63%)	0.04
> 30 mm > 3 nod.	14 (23%)	5 (14%)	
Recurrence	20 (33%)	4 (11%)	0.013
yr-Surv. (Overall – Disease free)	55% – 49%	76.5% – 70%	NS – 0.07

**Conclusion:** An adapted selection of patients with HCC for LT allows a significant decrease of the recurrence rate and a trend to improved survival. This warrants the indication of LT for HCC even in the current period of organ shortage. }

"Liver Transplantation for Hepatocellular Carcinoma on Cirrhosis: Prognostic Impact of an Adapted Patient Selection"

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**"P P 6 0150" P 6 0150 Impact of Cytomegalovirus (CMV) on Morbidity and Mortality after Liver Transplantation (LT) F. Saliba, O. Farges, D. Samuel, P. Ichai, M.F. David, D. Mathieu, E. Dussaix, H. Bismuth**

Hepato-Biliary and Liver Transplantation Center, Paul Brousse Hospital, Villejuif, France CMV is the predominant cause of viral infection after LT. The aim of this study was to analyse the impact of the CMV on the results of LT. From January 1987 to December 1992, 789 LT were performed in 688 patients. 76 CMV seronegative recipients (R{-}) received livers from CMV seronegative donors with CMV free blood transfusions (D{-}) (group I: 34 M, 42 F; mean age 44.3 – 16 years) and the 612 other patients were either seropositive (R+) or acquired the virus from the graft or from transfusions (D+) (group II: 365 M, 247 F; mean age 46.3 – 13 years). LT was performed in emergency for fulminant liver failure in 18.4% of the R{-}D{-} group and in 19.2% of the other group. ABO incompatible graft were used in 5.2% and 4.6% of group I and group II patients respectively. Among group II patients, 37.5% developed a CMV infection, 21% a CMV disease and two died of CMV disease. None of the R{-}D{-} patients developed a CMV infection. There was no statistical difference in the cumulative actuarial incidence of acute rejection between group I (36%) and group II (35%). The cumulative actuarial incidence of chronic rejection was comparable in the two groups (7%). There was a statistical difference in actuarial patient survival rate (group I: 81% vs group II: 70% at five years,  $p < 0.01$ ). No statistical difference was seen in actuarial graft survival rate (group I: 70% vs group II: 64%). *In conclusion:* Despite improvements in early diagnosis, prevention and treatment of CMV disease, morbidity is lower and survival better in R{-}D{-} patients than in R+ or R{-}D+ patients. Despite scarcity of organ donors, it is of the utmost importance to match CMV seronegative recipients with CMV seronegative donors. } "Impact of Cytomegalovirus (CMV) on Morbidity and Mortality after Liver Transplantation (LT)"

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## "P P 6 0151" P 6 0151 RNA-HCV Higher Levels in Orthotopic Liver Transplantation Treated with Steroid because of Acute Rejection

\*R. B\elrcena, S. Campo, M. Garc\eda, E. Vicente, A. Candela, A. Moreno

Ram\fn y Cajal Hospital, Alcala de Henares University Madrid, Spain *Aim:* To study the influence of steroid treatment on hepatitis C virus (HCV) RNA titres in orthotopic liver transplantation patients (OLT) because HCV chronic hepatitis. *Materials and Methods:* 26 OLT patients with HCV infection were studied. All of them comprise: a) HCV-RNA positive by PCR before OLT and in the 5-day determination after OLT; b) At least 3 months post-OLT survival; c) no receiving antiviral or autoimmune treatment after OLT. All of them were treated with immunosuppressive therapy (cyclosporin, steroids, azathioprine). Rejection episodes were treated with 3 methylprednisolone pulses (1 gr/d). OKT<sub>3</sub> was used in those who no response was observed. In the 6–7 months follow-up steroid doses were tapered. At 12th month all patients received 8–4 mg/d of steroid treatment and at 15th month has been suppressed in all patients. Acute rejection episode was observed in 14 patients. OKT<sub>3</sub> was administered to one patient. In 16 patients serum samples had been stored on 5th day post-OLT, 9 of them before the acute rejection episode. Another serum sample of these patients were stored between 15–30 days post-OLT. In all patients serum samples were stored 2 months after-OLT, in 23 at 6 months after-OLT, and in 8 patients after steroid therapy suppression. RNA-HCV titre was assessed by amplification. Mean age: 51 – 10 yrs (16 males). Follow-up: 456 – 235 d. (r: 95–924) *Results:* No differences were observed in relation to age, sex, mean ciclosporin levels, time of azathioprine treatment and infections in patients who developed or not an acute rejection episode. RNA-HCV levels at 5 days post-OLT were 912 – 1220  $\times 10^3$  Eq/ml. Patients treated with 3 pulses of steroids had higher titres of RNA-HCV at second samples (15–30 d) (4153 – 7692  $\times 10^3$  Eq/ml) than at 5 day (657 – 393  $\times 10^3$ ) ( $p > 0.05$ ). Titres at 2 months (9435 – 10868  $\times 10^3$  Eq/ml) and 6 month (8348 – 8217  $\times 10^3$ ) were higher than titres at 5 day post-OLT ( $p < 0.05$ ) and higher than RNA-HCV levels in patients without acute rejection episodes. After steroid withdrawal RNA-HCV titre fallen to 1298 – 1029  $\times 10^3$ ; no statistically difference was observed. *Conclusions:* OLT-HCV positive patients treated with steroid pulses present higher levels of HCV viremia at 2 and 6 months after-OLT than immediately post-OLT levels and than patients no treated with steroid pulses. Steroid suppression was followed by a decrease HCV viremia, although no difference was observed with 6 months values. Liver and bile ducts, 1: Hepatitis, viral, treatment Liver and bile ducts, 1: Liver transplantation } "RNA-HCV Higher Levels in Orthotopic Liver Transplantation Treated with Steroid because of Acute Rejection"

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"P P 6 0152" P 6 0152 **Transjugular Intrahepatic Portosystemic Shunt (TIPS) is of Benefit to Orthotopic Liver Transplantation (OLT)** H. Sunyach<sup>1</sup>, J.-M. Perarnau<sup>1</sup>, S. Bramli<sup>1</sup>, J.-J. Raabe<sup>1</sup>, P. Wolf<sup>2</sup>, K. Boudjema<sup>2</sup>

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<sup>2</sup> Fondation Transplantation C.H.U. 67000 Strasbourg, France Although patients waiting for a liver transplantation are considered as the better indication for TIPS, interest of this procedure has not been clearly demonstrated and results show some discrepancies. *Aim:* To determine the benefit of TIPS in OLT, we have compared in a retrospective case-control study, patients who, during the same period, underwent OLT after TIPS (T+) and control OLT patients without TIPS (T-). *Method:* 15 Patients and 15 controls were matched for age (<math>\leq 5</math> yrs), gender, Child-Pugh stage and cirrhosis etiology. *Results:* No difference between the two groups was observed in Apache Scores, previous ascites, previous encephalopathy episodes and previous abdominal surgery; delay between registration on the waiting list and OLT was identical in the 2 groups. Differences were significant concerning the presence of peritoneal adhesions (0 (T+)/5 (T-));  $p < 0.02$ ) and portal thrombosis (0 (T+)/5 (T-));  $p < 0.02$ ). A trend toward a decrease in procedural time (5.6 h. - 1.2 (T+)/7.2 h. - 3.3 (T-)); ns) and a decrease of amounts of transfusion (5.3 blood unit - 3.5 (T+)/9 - 10 (T-)); ns) was noticed. There was a significant decrease in the intensive care unit stay: (3.9 d. - 1.2 (T+)/6.5 d. - 4.5 (T-));  $p < 0.05$ ). *Conclusion:* Because of the reduction of portal hypertension, TIPS allowed to simplify the OLT procedure and to reduce the length of post OLT intensive care unit stay. A prospective randomized study is necessary to confirm these data for patients waiting for OLT with and even without complications. Liver and bile ducts, 1: Liver transplantation Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Transjugular Intrahepatic Portosystemic Shunt (TIPS) is of Benefit to Orthotopic Liver Transplantation (OLT)"

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## "P P 6 0153" P 6 0153 **Bile Duct Reconstruction affects the Results of Orthotopic Liver Transplantation**

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Aim of the study was to assess the effect of bile duct reconstruction (splint technique according to *Zimmermann*) on the postoperative course, the liver function parameters and on the histomorphological changes in the liverparenchima after orthotopic liver transplantation (ORLT). Three groups, each consisting of 10 syngenic rats, were compared: I. sham operation, II. bile duct reconstruction, III. ORLT. After the operation the clinical course and the serological parameters were monitored. 4 weeks postoperatively the histomorphological changes according to a semiquantitative score (scale: 0–103 points) and the proliferation rate (using the proliferation marker BrdU) were evaluated. Survival rate was 100% in I and II, 90% in III; early postoperative elevation of transaminases was normalized after 4 weeks in all groups. Morphological changes as bile duct alterations, Kupffer cell proliferation, increase in fibrous tissue and hepatocellular necrosis and regeneration were minimal in I (2.5 points), accentuated in II (36.5 points) and prominent in III (45 points). Hepatocellular proliferation was low after sham operation, significantly increased after bile duct reconstruction, and again doubled after ORLT. The lasting effect of bile duct reconstruction on the morphological results necessitates the inclusion of a mere bile duct reconstruction as a control group in ORLT-experiments. Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 2: Bile formation, cholestasis } "Bile Duct Reconstruction affects the Results of Orthotopic Liver Transplantation"

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## "P P 6 0154" P 6 0154 HCV Recurrence after Liver Transplantation

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Recurrence of HCV infection is extremely frequent after liver transplantation (OLT) for HCV-induced cirrhosis. The incidence and severity of graft disease occurring after HCV infection recurrence is still controversial. Aim of our study was to evaluate the features of HCV recurrence after OLT. From November 1990 until November 1995, 41 patients (33%) were transplanted for HCV-related cirrhosis out of a total of 123 patients transplanted at our institution. Patients who died in the perioperative period were excluded from analysis. A total of 35 patients were included in the study: 28 males and 7 females, with a mean age of 49 years (range 25–61 yrs); 17 pts (49%) had HCV alone, 7 (20%) concomitant alcohol abuse, 5 (14%) HCC, 4 (11%) coexistent HBV infection, 1 Wilson's disease and 1 PSC. Mean age at OLT for patients with HCV alone was 52.5 – 6.9 years, compared with 42.6 – 12.6 years in patients with multiple etiology ( $p < 0.02$ ). All patients were anti HCV(+)<sup>ve</sup> prior to OLT, whether 29 (83%) were HCV-RNA by PCR(+). A total of 28 recipients (96%) remained HCV-RNA by PCR positive during the post-transplant follow-up. None of the 6 antiHCV(+)/HCV-RNA({ - }) recipients became HCV-RNA(+) after OLT. Post-OLT liver histology 6 months 12 months 24 months N m M C N m M C N m M C {\\ab}AST/ALT 7 1 – 4 1 – 4 – 1 {\\ad}AST/ALT 6 3 – 2 6 1 2 2 1 Total 13 13 4 – 5 6 7 1 1 6 2 2  $p < 0.01$  N = normal, m = mild, M = moderate, C = cirrhosis Two patients died as a result of HCV recurrence: 1 died of sub-acute HCV recurrence and the other with cirrhosis respectively at 4 and 27 months after OLT. *Conclusion:* 1) HCV-RNA positivity prior to OLTx is the best predictor of HCV recurrence; 2) Recurrent histologic HCV disease is very common after OLT, and as a result end-stage liver disease can occur even within 2 years from OLT; 3) Serum transaminases are not a reliable follow-up marker of recurrent disease. Liver and bile ducts, 1: Liver transplantation Liver and bile ducts, 1: Hepatitis viral, diagnosis } "HCV Recurrence after Liver Transplantation"

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"P P 6 0155" P 6 0155 **Predictors of Survival in Acute Hepatic Failure** M.K. Mohana Das,

\*K.T. Shenoy

Dept of Gastroenterology, Medical College, Trivandrum, India *Objective:* To determine the prognostic factors and survival in hyperacute, acute and subacute liver failure. *Setting:* Tertiary referral centre. *Study Design:* Prospective prognostication and survival. *Participants:* 60 subjects with hepatic failure (8 hyperacute, 29 acute & 23 subacute) selected as per Roger Williams criteria, 1993. *Study Variables:* 32 clinical and laboratory variables which included liver span, h/o seizures, asterixis, biochemical and haematological parameters. *Outcome variables:* Prognostic factors and survival or death in the hepatic failure subgroups. *Data Analysis:* Descriptive, independent \quotet\quote test, proportions by chi square, survival rate by Kaplan Meier (KM) product limit method and univariate & multivariate analysis using Cox Proportional Hazard Model. *Results:* 17 subjects expired (hyperacute 2, acute 6, subacute 9). Age, onset of encephalopathy, liver span, blood glucose, transaminases and platelet count did not differ between survivors and non-survivors. Serum bilirubin (mg/dl) was 20.96 – 7.43 among survivors & 24.95 – 5.76 in non survivors (P = 0.048). KM survival probability for hyperacute, acute and subacute were 0.75 (95% CI 0.31–0.93), 0.79 (95% CI 0.59–0.90) and 0.61 (95% CI 0.38–0.77). Hazard ratio was 3.77 for those with encephalopathy gr 3 & 4 and prothrombin time > 25 sec (P = 0.001). *Conclusion:* Acute and subacute hepatic failure have poor prognosis and grade of encephalopathy with abnormal prothrombin time and low platelet count are poor prognostic factors. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Predictors of Survival in Acute Hepatic Failure"

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## "P P 6 0156" P 6 0156 Cholestatic Liver Disease in Protoporphyrin: Treatment with Cholic Acids and Liver Transplantation

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In erythropoietic protoporphyria with ferrochelatase deficiency an unpredictable hepatobiliary course of the metabolic disease develops in a quarter of patients: erythrohepatic protoporphyria. The effect of ursodeoxycholic acid (UDCA) was studied in 7 patients (age 33–71 years; 2 females, 5 males) with protoporphyrin (PP)-induced liver cirrhosis and cholestasis. PP accumulating in liver tissue is hepatotoxic in high concentrations. Five patients underwent liver transplantation.

*Patients and methods.* The patients with protoporphyria-associated liver disease exhibited an excessive PPemia ( $> 30 \mu\text{mol/l}$ , normal  $< 1$ ), elevation of fecal PP and a pathologic coproporphyrinuria up to  $700 \text{ nmol/24 h}$  (normal  $< 120$ ) with dominance of isomer I. They were treated with UDCA (10 mg/kg) for 1–19 months. Porphyrins were analyzed by HPTLC and HPLC.

*Results.* A decrease was observed concerning 1. hyperbilirubinemia ( $200\text{--}400 \mu\text{mol/l}$ ) of 65% up to normal levels, 2. PPemia of 40–70%, and 3. coproporphyrinuria of 70% ( $p < 0.001$ ). In spite of improved biliary PP elimination a clinical remission occurred only in one case; 5 patients were liver-transplanted after UDCA therapy; the other died of liver failure. All patients were treated with UDCA after liver transplantation. In two patients UDCA treatment was continued up to 5 years. Porphyrin parameters remain moderately elevated. The clinical status improved in 4 patients.

*Conclusion.* The dissociation observed between metabolic and clinical course results from irreversible liver disease caused by PP accumulation in liver cells. A long-lasting remission of hepatobiliary involvement by UDCA therapy can be achieved only in the early phase of complicated protoporphyria. A pathologic coproporphyrinuria with isomer I increase and red cell PP ( $> 20 \mu\text{mol/l}$ ) are first signs for hepatic component in protoporphyria. This is the indication for starting UDCA treatment. The PP-reducing effect of UDCA may be due to mobilisation of accumulated PP crystals in liver cells and improved bile flow in cholestasis. A marked decrease of fecal PP excretion reflects PP induced progressive toxic liver injury leading to reduced clearance of PP from the liver. In these patients with protoporphyria-associated irreversible cholestatic cirrhosis liver transplantation is the therapy of choice.

(Supported by the Hans-Fischer-Gesellschaft, Munich)

Liver and bile ducts, 1: Liver transplantation  
Liver and bile ducts, 2: Bile formation, cholestasis }

"Cholestatic Liver Disease in Protoporphyrin: Treatment with Cholic Acids and Liver Transplantation"

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## "P P 6 0157" P 6 0157 **Liver Transplantation (OLT) for Hepatocellular Carcinoma (HCC): Role of Selection and Chemotherapy**

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The role of OLT for patients with HCC is still controversial because of high disease recurrence. The aim of our study was to evaluate if careful pre-OLT selection and multimodal chemotherapy could improve the results after OLT. Twelve out of 108 patients transplanted at our unit were affected by HCC. Our policy is to transplant only the patients in which a diagnosis of HCC is obtained while already on the waiting list. In 5 out of 12 the diagnosis of HCC was incidental. One case, a 24 year old patient, with a 15 cm unresectable HCC in HBV-related chronic hepatitis, was an exception to the rule. Pathologic TNM staging was T1 in 9 patients, T3 in 2 (both incidental HCC) and T4 in the last. Seven patients received pre-OLT lipiodol-mediated arterial chemoembolization with adriamycin plus at least three courses of systemic chemotherapy (5-fluorouracil, folinic acid, carboplatin). After OLT the patients received systemic chemotherapy weekly for a total of 24 cycles. The same treatment was administered in 3 patients with incidental HCC. Two patients with incidental HCC refused chemotherapy. In one patient a severe HCV-related hepatitis contraindicated the chemotherapeutic regimen. Therefore, a total of 9 patients underwent post-OLT chemotherapy. Mean follow up is presently 24 months (range 4–46 months). One patient died for HBV-related cirrhosis at 44 months after OLT, free of HCC recurrence. Overall and disease-free survivals are 100% and 92% at 36 months, respectively. The only recurrence was observed 3 months after OLT in one incidental HCC who did not receive adjuvant chemotherapy. *Conclusion:* 1) patients with small HCC are good candidates for OLT if proper selection is adopted; 2) once a patient with HCC is selected for OLT, or once HCC is an incidental finding at OLT, also multimodal chemotherapy can improve the results in terms of overall and disease-free survival

Liver and bile ducts, 1: Liver transplantation  
Oncology, specific: Liver, biliary } "Liver Transplantation (OLT) for Hepatocellular Carcinoma (HCC): Role of Selection and Chemotherapy"

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## "P P 6 0158" P 6 0158 Liver Transplantation in Patients with Cirrhosis and Hepatocellular Carcinomas

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It has been recently shown that liver transplantation (LT) is an effective treatment for small unresectable hepatocellular carcinoma (HCC) in patients with cirrhosis (NEJM 1996; 334: 693–9). In this study, we report our experience on LT for HCC. Between January 1987 and December 1995, 244 LT were undertaken for patients among which 152 had cirrhosis (except for secondary biliary cirrhosis). Among these 152 patients, 48 (31.6%) had an HCC. Retrospectively, the indication for LT was HCC (group A, n = 21), cirrhosis and HCC (group B, n = 13), and cirrhosis (group C, n = 14). In group C, HCC was incidentally discovered by pathological examination in resected livers not originally thought to contain tumors. As of May 1996, 29 patients (60.4%), with a mean age of 54.8 – 1.8 years (range, 28 to 68) were alive without apparent recurrence, with an overall survival of 33 – 3.9 months (range, 6 to 83). 14 patients (29.2%), with a mean age of 57.4 – 1.4 years had died after LT complications without apparent tumoral recurrence within 1.6 – 0.5 months (range, 0 to 7), whereas 5 patients (10.4%), with a mean age of 62.2 – 1.7 years (range, 56 to 66) had died of tumoral recurrence within 15.6 – 4.2 months. Group C had the highest survival rate (79%) compared to groups A and B (52% and 54%, respectively). Patients alive from Group C had tumors, at the time of LT, whose diameter never exceeded 1.7 cm. From 9 patients, of the three groups, with tumors > 5 cm, 6 died and 3 of them of tumoral recurrence. All the patients who died of tumoral recurrence belonged to group A; the diameter of the tumor exceeded 7 cm (3 out of 5), there were tumoral nodes in the hilum (1/5), or adherence of the tumor to the diaphragm (1/5) (lung metastasis after LT). Of seven patients, out of 11, who had more than 3 tumor masses < 5 cm, except for 1 tumor, are alive. Hepatic resection (three cases) nor chemoembolization (12 cases) before LT seem to be linked to mortality since all patients undergoing hepatic resection and 8 out 12 patients undergoing chemoembolization were alive. Among the 104 patients transplanted for cirrhosis without cancer, 76 were alive (73%) and 28 (27%) died. These patients had a mean of 50.8 – 1.1 (range, 27 to 69) and 51.4 – 3.6 (range 9 to 70) years, respectively, at the time of LT and had a survival time of 50.2 – 3.2 months (range 7 to 102) and 11 – 3.6 months (range 0 to 86). In conclusion, it seems reasonable to propose LT to cirrhotic patients with a single or multiple HCC < 5 cm without loco-regional spread. However, in this study, patients with cirrhosis and HCC presented a high rate of mortality, possibly linked to the age of patients at the time of LT. Liver and bile ducts, 1: Liver transplantation } "Liver Transplantation in Patients with Cirrhosis and Hepatocellular Carcinomas"

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"P P 6 0159" P 6 0159 **Diagnostic Accuracy of Sonography (US), Computed Tomography (CT) and Angiography in the Diagnosis of Hepatocellular Carcinoma (HCC): Comparison with Histopathological Findings in 169 Transplanted Patients**. Veltri, M. Grosso, D. Regge, M.C. Martina, U. Soldano, J. Galli

Istituto di Radiologia, Universit'e0 di Torino, Italy *Purpose* To assess the diagnostic accuracy of US, CT, and angiography in the diagnosis of HCC based on histopathological examination of explanted livers. *Materials and Methods* The presence or absence of HCC based on US, CT, and angiography performed in 192 patients before liver transplantation was retrospectively reviewed. The radiological findings were compared to the histopathological studies. *Results* Histopathological examination detected 81 nodules of HCC in 58/192 patients, whose diameter ranged from 0.7 to 9.0 cm (mean 2.65 cm). US, performed in 188/192 patients, diagnosed 59/79 nodules with a sensitivity of 82.1% (46/56 true positive patients), specificity of 90.9% and diagnostic accuracy of 88.3%. In 152/192 patients, CT detected 35/54 nodules (29/40 true positive patients; sensitivity 72.5%), with a specificity of 95.5% and diagnostic accuracy of 89.5%. The sensitivity of integrated diagnostic imaging studies was 89.6% with a specificity of 84.3% and diagnostic accuracy of 86%. *Conclusions* Our study, which supports the findings reported in the literature on explanted livers, underlines the low sensitivity of CT in detecting HCC. The integration of US, CT, and angiography, indispensable in the presurgical assessment when newer imaging methods (helical CT, angio-MR) are not available, is more sensitive for the diagnosis and staging of HCC but has a slightly reduced specificity and diagnostic accuracy. Liver and bile ducts, 1: Chronic non viral hepatitis Oncology, specific: Liver, biliary Radiology and ultrasound: Diagnosis } "Diagnostic Accuracy of Sonography (US), Computed Tomography (CT) and Angiography in the Diagnosis of Hepatocellular Carcinoma (HCC): Comparison with Histopathological Findings in 169 Transplanted Pati"

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"P P 6 0160" P 6 0160 **Radiological Treatment of Hepatocellular Carcinoma (HCC): Review of Results in 58 Transplanted Patients** A. Veltri, M. Grosso, D. Regge, M.C. Martina, J. Galli, U. Soldano

Istituto di Radiologia, Universit\`e di Torino, Italy *Purpose* To evaluate the results of radiological treatment performed in patients with HCC before liver transplantation *Materials and Methods* Fifty-eight transplanted patients with a total of 81 nodules of HCC, whose diameter ranged from 0.7 to 9.0 cm (mean 2.6 cm) were studied. 43 lesions in 34 patients were previously treated with transcatheter arterial chemoembolization (TACE) (24), percutaneous ethanol injection (PEI) (10), or combined TACE + PEI (9). On histopathological examination of the explanted livers, tumor necrosis was judged to be complete, partial, or absent. The percentage of recurrence after transplantation was also calculated. *Results* After TACE, necrosis was complete in 6/24 lesions (25%), partial in 6/24 lesions (25%) and absent in 12/24 (50%). After PEI, necrosis was complete in 8/10 (80%) and partial 2/10 (20%). After combined therapy, complete necrosis was obtained in 9/9 (100%). 4/34 patients (11.8%) had complications (2 vascular and 2 parenchymal) without significant consequences for transplantation. 4/34 (11.8%) treated patients had post-transplantation recurrence; these patients had previously undergone only TACE and explanted livers showed no tumor necrosis. *Conclusions* TACE alone is ineffective in treating HCC. The high efficacy of combined radiological therapy and the low incidence of recurrence in treated patients suggests using this approach even before liver transplantation. Oncology, specific: Liver, biliary Liver and bile ducts, 1: Liver transplantation Radiology and ultrasound: Therapy } "Radiological Treatment of Hepatocellular Carcinoma (HCC): Review of Results in 58 Transplanted Patients"

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"P P 8 0173" P 8 0173 **Ultrastructural Characteristic of Papilla Vateri's Carcinoma**  
**B. Damyanov, B. Vladimirov, S. Babourov**

Medical University, Sofia, Bulgaria

The microscopic picture of carcinoma of papilla Vateri makes its endoscopic diagnostics comparatively easy. However, sometimes even ERCP and histomorphological differential diagnostics with chronic odtis is too hampered. *Aim* of this investigation was to define more accurately the ultrastructural characteristic of carcinoma through subcellular organelles features and hence the possibilities for electronmicroscopic examination in the differential tumor diagnostics of the papilla. *Material and methods.* Tumor material was received by clip biopsy during endoscopic duodenopapilloscopy and ERCP of 14 patients, with following electronmicroscopic exploration. *Results and discussion.* The tumor's cells general appearance was uncertain, but here and there with elements of altered cover epithelium of tubular organs. In the irregular in shape and magnitude intercellular spaces of the tumor clusters there were sometimes microvilles, even binding structures of the type tight junction. General characteristic of the nuclei of the tumor cells was the different pattern of the wavy course of the nuclear membrane, often with formations of deep canyon-like engravements, improving characteristic monstrous appearance of the nucleus. All such nuclei were with enlarged quantity and atypical perichromatic granules and with 2–3 or more hypertrophic nucleoluses. For patients with chronic odtis, preceding or accompanying the malignus growth all elements of expressed fibrosis have been observed. *Conclusion.* The monstrous hyperactive nuclei are the main features of the malignus carcinoma of papilla Vateri. The lack of such nuclei, especially at present fibrosis proves sooner a chronic odtis. Oncology, specific: Liver, biliary }  
"Ultrastructural Characteristic of Papilla Vateri's Carcinoma"

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## "P P 8 0175" P 8 0175 Analysis of p53 Abnormalities in a Serie of 34 Tumors of the Ampullary of Vater

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INSERM U410, Facult'e9 Xavier Bichat, Paris, France

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**Background and Aims:** As described in colon, epithelial tumors of the ampulla of Vater (AV) develop through a filiation from adenoma to adenocarcinoma with increasing grade of dysplasia. The diagnosis between adenocarcinoma and epithelial dysplasia of the AV may be difficult on endoscopic biopsies. p53 protein immunostaining has been proposed as a new marker of malignancy. Because controversies exist on the relationship between p53 protein immunostaining and the stage of resected ampullary tumors, we have investigated the presence of p53 abnormalities in 34 tumors of the AV.

**Methods:** We studied 29 invasive adenocarcinomas and 5 adenomas with foci of mild (n = 3) or severe (n = 2) dysplasia of the AV. Immunohistochemistry was performed on formalin fixed tissue with DO7 antibody. In 19 cases, DNA was extracted from frozen specimens or paraffin sections and analysed for mutations of the p53 gene (exon 5–8) by PCR/denaturant gradient gel electrophoresis (DGGE) and sequencing technique.

**Results:** One of the 5 adenomas (20%) and 16 of the 29 adenocarcinomas (55%) were positive on immunohistochemistry for p53. This positivity was present through all stages of ampullary adenocarcinomas. No significant difference in p53 protein expression was observed between adenomas and adenocarcinomas. A mutation of the p53 gene was detected on DGGE and confirmed by sequencing in 6 cases with a good correlation with immunohistochemistry in all 19 cases but 2.

**Conclusion:** p53 gene mutation appears as a common event in ampullary tumors. It can be detected in most cases by immunohistochemistry. However our serie suggest that its detection does not help to appreciate the stage of the tumors.

Oncology, specific: Liver, biliary  
Oncology, general: Molecular biology, genetics }

"Analysis of p53 Abnormalities in a Serie of 34 Tumors of the Ampullary of Vater"

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## "P P 8 0178" P 8 0178 Surgical Treatment of Klatskin's Tumor: Our Experience

\*I. Zoricic, B. Bakula, Z. Pasini, Z. Perko

University Department of Surgery, Sveti Duh General Hospital, Zagreb, Croatia Between January 1991 and February 1996 we operated ten patients with primary cancer originating in the hepatic duct confluence (Klatskin tumor). We got six males and four females. Average age was 59.6 years. The tumors were Type I, Type II, Type IIIa and IIIb in two, one, six and two patients respectively. Three tumors were unresectable: two Type IIIa and one Type IIIb. In these cases transtumor stents have been placed. Stent in right, left and the both ("Y" prosthesis) hepatic ducts were placed in one case each. In this group the average postoperative survival was 11 months. At three patients with the tumor Type I and II, tumor excisions in hepatic parenchyma and reconstructions with hepatico-jejuno-anastomosis Roux-en-Y were done. In the last four patients with the tumor Type IIIa, liver resections were done. Right hepatectomy and left hepatectomies were done in three and one case, respectively. From this group of patients, one patient had liver cirrhosis and died twenty days after operation, because of liver insufficiency. Other patients did not have complications in the postoperative course. In this group, one patient died 2.5 years after the operation, and other patients are still alive. The longest postoperative survival has a patient who 3.5 years after operation has not signs of the tumor recidive. Other patients are alive and without any recidive disease among 0.5 and 2 years. Our experience supports an aggressive surgical approach in patients with Klatskin tumor, and enables longer survival rate, than when only transtumor stent is placed. Oncology, specific: Liver, biliary Clinical practice: Management strategy } "Surgical Treatment of Klatskin's Tumor: Our Experience"

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"P P 8 0179" P 8 0179 **Hepatic Intraarterial Chemotherapy in the Treatment of Pig Experimental Biliary Cancer: A Comparative Study**

\*V. Dufek, J. Petr, P. Klener

1st Medical Department, Charles University, Prague, Czech Republic (CR) Human cholangiocarcinoma (CHC) is one of the most dismal biliary tree cancers to cure. In Central and Eastern Europe, resectability of CHC does not exceed 6%, in general. If untreated, the median survival is 99 days. *Aims:* This study was performed to assess the feasibility of hepatic intraarterial (HIA) chemotherapy by FUDR to experimental pig CHC in comparison with those by FUDR conjugate (FUDR-Cathepsin B-like). *Methods:* In 23 male pigs (strain BU) – weight 23 kg, a CHC was induced by intraportal application of a combination of aflatoxin B<sub>1</sub> and 4-methylcholantren. After the end of cancerogenesis (affected about 30% of the liver by US and CT) a HIA chemotherapy was started in 16 animals. Seven pigs were left without any treatment (control group). *Results:* In the *nil treated group*, the median survival was 67.5 days. Neither tumour mass regression in US or CT nor tumor necroses were observed during the autopsy. In the *FUDR group*, the median survival was 116.6 days; in US and CT, the reduction of tumour tissue was predicted in 3 and 5 pigs, respectively. In autopsy, partial necroses of CHC were observed in such an animals. In the *FUDR-Cathepsin B-like group*, the results of HIA chemotherapy were quite expressive. The median survival reached 205.7 days. Autopsy, the same as US and CT revealed a significant reduction of the tumour tissue. For surprise, no differences in the size of tumour necroses were found, between the FUDR and FUDR-Cathepsin B-like groups. *Conclusions:* FUDR-Cathepsin B-like conjugate seems to be much more potent drugs in the pig CHC palliation as FUDR alone. The same is possible to expect in human primary cholangiocarcinoma. Supported by grant 2227 of IGA MH CR Oncology, specific: Liver, biliary Oncology, general: Therapy } "Hepatic Intraarterial Chemotherapy in the Treatment of Pig Experimental Biliary Cancer: A Comparative Study"

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"P P 8 0180" P 8 0180 **Neuroendocrine Carcinomas of the Gallbladder: Report of Three Cases** N. Giannakou<sup>1</sup>,

\*Ch. Dervenis<sup>2</sup>, P. Parissi<sup>1</sup>, J. Voulgaris<sup>2</sup>

<sup>1</sup> Dept. of Pathology, Konstantopoulion General Hospital, N. Ionias Agia Olga, Athens, Greece

<sup>2</sup> Dept. of Surgery, Konstantopoulion General Hospital, N. Ionias Agia Olga, Athens, Greece  
Neuroendocrine carcinomas of the gallbladder are extremely rare. Three cases with tumors of that kind are presented. The tumors were found in patients operated for cholelithiasis and revealed histological immunohistochemical features of adenocarcinoma and endocrine cell carcinoma, of small or intermediate cell type. One out of the three cases was a composite lesion, consisted of adeno- and endocrine cell carcinoma with apparent transitions between the two types. Two of the patients died shortly after the operation from liver metastases and the third is alive for five months. We describe the pathology of these tumors as well as a review of the literature. Neuroendocrine carcinomas should be recognised and distinguished as they carried worse prognosis compared with true adenocarcinomas. Oncology, specific: Liver, biliary }  
"Neuroendocrine Carcinomas of the Gallbladder: Report of Three Cases"

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"P P 9 0182" P 9 0182 **Does Computed Tomography Have an Impact on the Management of Acute Diverticulitis?** N. Siauve<sup>1</sup>, A. Berger<sup>2</sup>, C.A. Cu'e9nod<sup>1</sup>, P. Wind<sup>2</sup>, N. Bely<sup>1</sup>, M.P. Revel<sup>1</sup>, P.H. Cugnenc<sup>2</sup>, G. Frija<sup>1</sup>

<sup>1</sup> Department of Radiology, Hopital Laennec, Paris

<sup>2</sup> Department of Radiology, Hopital Laennec, Paris *Purpose:* To analyze whether computed tomography (CT) could influence the therapeutic management of acute diverticulitis. *Material and Methods:* Thirty-seven of patients hospitalized with the clinical diagnosis of acute diverticulitis were retrospectively reviewed. Each of these patients underwent a CT scanner with water-soluble enema within the first hours after admission. CT scanners were analyzed for complications like abscess, fistula or peritoneal gas effusion. The initial therapeutic option based only on clinical data (medical treatment or immediate surgery) was compared to the final decision which took into account the CT findings. *Results:* Eleven patients demonstrated one of the following complications on CT: abscess (n = 6), fistula (n = 3), and peritoneal gas effusion (n = 2). The 2 cases with peritoneal gas effusion were not suspected clinically or on plain films, and led to immediate surgery after CT. CT did not influence the initial decision of medical treatment in 4 of the 6 cases with abscess: in 2 cases the percutaneous drainage was not technically possible, and in 2 cases the collection was very small. Only one abscess was drained percutaneously, while the last one required surgery because it was associated with peritoneal gas effusion. In the 3 cases with fistula, there was no change in the initial decision and the patients received medical treatment. *Conclusion:* In this series of acute diverticulitis the therapeutic strategy based solely on clinical data was modified only in 3 cases (8%) by the CT findings. Radiology and ultrasound: Diagnosis Radiology and ultrasound: Therapy } "Does Computed Tomography Have an Impact on the Management of Acute Diverticulitis?"

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"P P 9 0184" P 9 0184 **Severe Colonic Ischemia in Chronic Hemodialysis Patients: CT Scan Allows an Early Diagnosis** A. Berger<sup>1</sup>, N. Siauve<sup>2</sup>, M. Nseif<sup>1</sup>, C.A. Cuenod<sup>2</sup>, M. Zanoun<sup>2</sup>, M.P. Revel<sup>2</sup>, G. Frija<sup>2</sup>, P.H. Cugnenc<sup>1</sup>

<sup>1</sup> Department of Surgery, Hospital Laennec, Paris

<sup>2</sup> Department of Radiology, Hospital Laennec, Paris Colonic ischemia may be related to chronic hemodialysis, causing a high mortality and morbidity. This ischemia is distinctive due to its non occlusive character and to the frequency of right colon involvement. Clinical diagnosis may be difficult since patients symptoms are usually non specific. We report retrospectively the value of CT scan for the diagnosis of severe colonic ischemia in hemodialysis patients. *Patients and methods:* Severe colonic ischemia was suspected in four chronic hemodialysis patients on clinical findings (mean age 59 years); symptoms were abdominal pain of variable intensity starting just after an hemodialysis session. CT scan with water soluble enema was performed within 12 hours after the onset of the symptoms. *Results:* In all cases, CT scan showed a ring thickening of the bowel wall located in the right colon (mean 17.5 mm; 10–20), measuring 55 mm in length (30–90). In 3 cases a parietal pneumatosis was observed. These features were exactly correlated with operative and histological findings. Parietal pneumatosis was predictive of colonic gangrene. *Conclusion:* CT scan allowed an early diagnosis of severe colonic ischemia in chronic hemodialysis patients. Parietal pneumatosis is the main finding reflecting colonic necrosis and indicates immediate surgery. Radiology and ultrasound: Diagnosis Radiology and ultrasound: Therapy } "Severe Colonic Ischemia in Chronic Hemodialysis Patients: CT Scan Allows an Early Diagnosis"

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"P P 9 0185" P 9 0185 **The Ischemic Bowel and Its Myoelectric Activity an Experimental and Clinical Studies**

\*R. Sendur, P. Thor, W. Dutkiewicz, W.W. Pawlik

Univ. Med. Sch. Inst. Physiol. CMUJ Krakow, Poland Evaluation of the intestinal electrical control activity (ECA) has been proposed as a method for determining of the bowel viability. However its diagnostic value has not been definitively established. The purpose of the present investigations was to evaluate intestinal myoelectric activity in the normal and ischemic bowel in experimental animals and humans. Experiments were performed on 15 cats anesthetized with pentobarbital. After laparotomy total intestinal blood flow (BF) was measured in superior mesenteric artery (SMA) with ultrasonic blood flowmeter and microcirculatory blood flow with laser Doppler flowmetry (LD). Myoelectric bowel activity was recorded simultaneously with BF and LD using three monopolar silver electrodes implanted on the serosal surface of the jejunum and Dynograph Recorder R-611. Bowel ischemia was induced by perfusion of SMA with saline or by temporal occlusion of both SMA and/or superior mesenteric vein (SMV). In clinical studies ECA was analysed in 10 patients during abdominal surgery due to bowel ischemia, using EMG technique. In patients comparison was made between ECA in ischemic and normal bowel. Intestinal ischemia in experimental conditions induced reduction in amplitude and frequency of ECA by 50%, whereas in patients about 60% reduction in amplitude and frequency of ECA was observed. Most sensitive parameter appears to be phase lag of ECA which even in small degree of ischemic changes to the bowel was doubled. Most dramatic changes with reduction of amplitude and frequency were observed during simultaneous SMA and SMV occlusion. Our results indicate that amplitude, frequency and the coupling of ECA are sensitive myoelectric parameters which could be used in clinical assesment of bowel viability. Motility, specific: Small bowel Intestinal disorders: Splanchnic circulation, ischemia } "The Ischemic Bowel and Its Myoelectric Activity an Experimental and Clinical Studies"

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"P P 9 0186" P 9 0186 **Nitrate Reducing Bacteria in the Excluded Colon: A New Clue to Diversion Colitis?** C. Neut,

\*F. Guillemot, E. Lederman, J.F. Colombel

Laboratoire de Bactériologie, Faculté de Pharmacie, Clinique des Maladies de l'Appareil Digestif, CH et U Lille, F 59037 Lille

**Background/aim:** Arguments have accumulated favouring a pathogenic role of nitric oxide (NO) in intestinal inflammation. NO is metabolized in the colon in nitrite and nitrate which subsequent reduction implicates the colonic flora. There is no data about nitrate-reducing bacteria in the colon of patients with chronic inflammation. In this work, we evaluated the nitrate-reducing flora in patients with diversion colitis which is a model of inflammation with no exogenous nitrite or nitrate supply. **Patients and methods:** Thirty patients (17 M, 13 F, mean age 45 yrs) having an excluded colon for various reasons (inflammatory bowel disease, n = 15; colon cancer, n = 5; diverticulitis and abscess, n = 7; miscellaneous, n = 3) were studied. Presence of diversion colitis was assessed using endoscopic and histologic criteria. Fecal material was collected by rectal swabs. Bacteriological analysis was performed in anaerobic conditions. Results were compared to those of 30 healthy controls (11 M, 19 F, mean age 28 yrs). **Results:** The percentage of nitrate-reducers among the total count of subcultured bacteria was 46 – 41% (mean – SD) in patients with diversion colitis as compared to 19 – 24% in healthy controls (p < 0.05). In patients with diversion colitis, 75/254 (29.5%) different isolated bacterial strains were nitrate-reducers as compared to 61/294 (21%) (p < 0.05) in controls. Among the 75 nitrate-reducing strains isolated from patients with diversion colitis, 55 (73%) were aerobes as *Pseudomonas*, *Proteus*, *Providencia* and *Morganella*. In healthy controls, nitrate-reducing anaerobes were nearly as frequent as aerobes. **Conclusion:** The bacterial flora of patients with diversion colitis is characterized by a quantitative and qualitative enrichment in nitrate-reducing bacteria. NO synthase might produce a bacterial substrate increasing the growth of bacteria with a high pathogenic potential creating conditions for chronic inflammation in patients with an excluded colon.

Intestinal disorders: Anorectal disorders Immunology and microbiology: Inflammation }

"Nitrate Reducing Bacteria in the Excluded Colon: A New Clue to Diversion Colitis?"

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"P P 9 0187" P 9 0187 **Sodium Cromoglycate in the Treatment of Eosinophilic Colitis** F. Hamsioglu, N. Bagatur, A. Dobrucali, A. Çelik, C. Davutoglu, K. Bal, M. Tuncer, I. Yurdakul, H. Uzunismail, E. Oktay

Gastroenterology Section, Internal Medicine, Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey Eosinophilic colitis is (EC) an uncommon inflammatory process marked by colonic eosinophilic infiltration. Despite of the discrepancy in the treatment, Sodium cromoglycate (SCG) seems to be effective. We report 3 cases of eosinophilic colitis with good response to SCG treatment. *Patient 1:* N.Y 30 year old woman, with recurrent abdominal pain, bloody diarrhoea, tenesm, artralgia and weight loss for 3 years treated with Salazopyrine (SZP) because of the diagnosis of Ulcerative Colitis. Eosinophilia was observed. By rectosigmoidoscopy, colitis with hyperemia, edema and friability was observed. Colonic biopsy showed severe colitis, remarkable infiltration of lamina propria with eosinophils: regular crypt structure with depletion of goblet cells. The disease was limited only to colon. The prick test was normal. After the diagnosis EC which developed during the SZP therapy, she was treated with SCG 300 mg twice daily. After 2 weeks of therapy, her symptoms and endoscopy findings improved. *Patients 2:* K.Ç 33 year old woman with recurrent abdominal pain, diarrhoea, artralgia and weight loss for 14 months. By her admittance only IgE and IgG were elevated. The colonoscopy showed edema, hyperemia, friability and ulcers in the entire colon including terminal ileum. Crohn disease was the first diagnosis. But the biopsy showed chronic colitis with significant infiltration of the mucosa with eosinophils, intraepithelial eosinophils and regular crypt structure, Like patient 1 the colitis was limited to the colon. By the time of the diagnosis she had also cholecystitis. The clinical condition of the patient including cholecystitis improved after 2 weeks therapy with SCG 400 mg twice daily. *Patient 3:* N.B 39 year old woman with bloody diarrhoea, nausea for 2 months. She had allergy to various food, animal products and pollens. The prick test was positive. Eosinophilia was determined. We observed colitis with erosions at rectosigmoidoscopy. The biopsy result was the same as the one of patient 1. Like the previous patients the disease was limited only to the colon and the patient responded well to SCG 300 mg daily after 2 weeks. The results provide evidence of SCG efficacy in the treatment of EC, suggests its application as a first choice of drug. Intestinal disorders, absorption: Malabsorption syndromes Immunology and microbiology: Inflammation } "Sodium Cromoglycate in the Treatment of Eosinophilic Colitis"

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"P P 9 0188" P 9 0188 **Treatment of Radiation Proctitis with Sucralfate Suspension Enema** Masahiro Tada

Department of Gastroenterology, Kyoto Cancer Association, Kyoto, Japan We conducted a pilot study to evaluate the utility of sucralfate suspension enema for the treatment of radiation proctitis. *Subjects and method:* Seven cases with radiation proctitis after irradiation for uterus cancer were included. Per anal administration of 10% suspension of sucralfate was performed twice a day for at least three months. Effectiveness of treatment was determined endoscopically. *Results:* After treatment with sucralfate enema for three months, improvement of endoscopic finding was observed in six (85.7%) out of seven cases. In five cases, further treatment was continued for six months and more improvement of the mucosa was observed in four cases. No adverse effects were encountered. *Conclusion:* Sucralfate suspension enema was useful for the treatment of radiation proctitis. Intestinal disorders: Anorectal disorders Endoscopy, specific: Colon, rectum } "Treatment of Radiation Proctitis with Sucralfate Suspension Enema"

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## "P P 9 0190" P 9 0190 **Intestinal Neurofibromas with von Recklinghausen's Disease: Report of a New Case**

\*P. Kasapidis, V. Milonakis, V. Delis, V. Balatsos, A. Konstantinidis, N. Skandalis

Department of Gastroenterology of the Athens General Hospital, Greece Multiple neurofibromas (MN), which may occur either on familial basis with autosomal dominant inheritance or sporadically, were first described by von Recklinghausen (vR) in 1882. MN is a mesodermal and ectodermal dysplasia with a broad spectrum of clinical and radiological findings. The gastrointestinal tract and in particular the small intestine is involved in 10%–20% of the cases with MN (vR disease). Intestinal neurofibromas (IN), with or without vR disease, are rare. Only 6% of benign tumors in the small intestine are of neurogenic origin. The index case is a 42 year old female, without familial disease, who was admitted to our Department with a lifelong history of melena. Three such episodes had occurred eight, ten and twelve years prior to admission, which were attributed to a duodenal ulcer. On physical examination there was a soft skin nodule on the left heel, measuring 3 cm, and multiple café-au-lait spots predominantly on the trunk. No abdominal masses were palpable. Gastroscopy and colonoscopy were normal. Enteroclysis revealed one unstable smooth filling defect in the central jejunum, while intestinal angiography of superior and inferior mesenteric artery showed an abnormal ringlike enhancement formed by congested veins in the distal part of the fourth branch of jejunal artery. The biopsy of the skin nodule on the heel revealed a neurofibroma and the diagnosis of vR disease was established. At laparotomy two extraluminal neurofibromas, 6 cm and 1 cm respectively, were found and the segment (8 cm) of the proximal jejunum, containing the lesions, was resected. Immunohistochemically some malignant cells showed a positive reaction to S-100 protein. Intestinal neurofibromas with neurofibromatosis are rare. Radiographic examination or enteroscopy reveals multiple smooth tumors predominantly in the distal part of the ileum. As the neurofibromas are hypervascular, angiography is useful in defining the number and extent of the lesions. Surgical resection is indicated because of the danger of: a) malignant degeneration of intestinal neurofibromas (15% of > 40 years patients), b) bleeding and c) other serious complications such as, intestinal or biliary obstruction, ischemic bowel perforation, intussusception and megacolon. Clinical practice: Management strategy Oncology, specific: Small bowel Oncology, general: Therapy }" "Intestinal Neurofibromas with von Recklinghausen's Disease: Report of a New Case"

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## "P P 9 0191" P 9 0191 **Dermatitis Herpetiformis Duhring in Long-Term Clinical Follow-Up**

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Dermatitis herpetiformis Duhring (DH) is nowadays considered one of the ways of clinical manifestation of gluten enteropathy. The frequency of this disease has been increasing considerably, affecting even younger persons and if its gastrointestinal symptoms remain hidden it may be source of serious complications. Group of 92 patients (52 men, 40 women) has been followed up for a long time, at the average follow-up time 7.4 years (2–24 yr). Even if 83% of patients have never had any digestive troubles and physical examinations have been normal in almost all of them, 16% had anaemia, 52% light signs of malabsorption and in 73% of them various degrees of jejunal mucosa damage was proved at the time of the first enterobiopsy. In patients on gluten-free diet with repeated biopsy (n = 44) the intestinal as well as skin changes have improved in 94% of persons. Malignant tumors occurred in 4 patients (2 died). Evaluation of the changes in jejunal mucosa is impossible by current laboratory findings or functional tests, but only using enterobiopsy. In patients with proved changes permanent gluten-free diet is necessary, with a view to the usual absence of difficulties, however, the motivation to observing it is markedly lower than in the coeliacs. The course of DH, complications and the risk of malignancy are the same as in coeliac disease and prove the necessity of steady follow-up by the gastroenterologist. Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption syndromes } "Dermatitis Herpetiformis Duhring in Long-Term Clinical Follow-Up"

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## "P P 9 0192" P 9 0192 Collagenous Colitis Versus Inflammation of Collagenous Type as Nosologic Entity Versus Reaction Form

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<sup>1</sup> Dept. Pathology, Budapest, Hungary In years 1993–1996 we examined 1340 patients with colonoscopy. Among them we found 36 cases with mostly mild mucosal hyperaemia in macroscopic picture and with broad subepithelial collagenous band in histology, mainly in the sigma, in 6 cases in other part of colon. All of them presented only with moderate symptoms not with watery diarrhoea which is characteristic of collagenous colitis. 22 had abdominal pain, 16: diarrhoea, 6: diarrhoea/constipation, 3: constipation, 10: meteorism, 2: without any abdominal complaint. In history 13 had had chronic gastritis, 2 ulcerative colitis, 1 m. Crohn, 2 aspecific colitis. 3 had simultaneously colon erosions, 2 ulcers, 6 diverticulosis, 4 lactose intolerance, 2 starch intolerance, in 2 patients the collagen layer appeared in the subepithelial part of a polyp. 14 were treated with Salazopyrin. We had opportunity to follow up 10 cases, in all the collagen disappeared within 3–6 months. In 4 cases we observed a transitional phase with fragmented collagen layer. *Conclusion:* on the basis of the data of the literature and our findings, we raise a hypothesis: it must be distinguished between 1. a collagenous colitis as a pathologic and clinical entity and 2. a collagenous inflammation reaction type which is manifested in certain person's colon to various stimuli (per analogiam: lupus erythematosus vs. lupoid reaction). Intestinal disorders, absorption: Pathophysiology of diarrhea Endoscopy, specific: Colon, rectum Immunology and microbiology: Inflammation } "Collagenous Colitis Versus Inflammation of Collagenous Type as Nosologic Entity Versus Reaction Form"

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"P P 10 0193" P 10 0193 **Malabsorption of Lactose (25 G), Fructose (25 G) and Sorbitol (5 G) in Patients with Irritable Bowel Syndrome (IBS): Effect of Ethnic Origin, Sex and Age**.  
Mishkin, L. Sablauskas, M. Yalovsky,

\*S. Mishkin

Faculties of Medicine and Management, McGill University and Division of Gastroenterology, Royal Victoria Hospital, Montreal, Quebec, Canada The aim of this study was to determine whether the prevalence of fructose (F) and sorbitol (S) malabsorption was dependent on ethnic origin as is the case for lactose (L). The effect of sex and age were also analysed. *Methods:* 520 ambulatory patients with IBS all underwent H<sub>2</sub> breath testing after challenges of L, F and S. Using criteria of  $\geq 20$  ppm H<sub>2</sub> rise for L and  $\geq 10$  ppm for F and S, 56.3%, 52.7% and 57.5% were malabsorbers of L, F and S resp. *Results:* Tests for equality of prevalence for L malabsorption across 6 ethnic groups was significant at  $p < 0.005$  with Northern Europeans ( $n = 58$ ) and French Canadians ( $n = 92$ ) clustered as one group with a prevalence  $< 35\%$  compared to another group consisting of Arabs ( $n = 35$ ), Greeks ( $n = 60$ ), Italians ( $n = 53$ ) and Jews ( $n = 167$ ) with an average prevalence exceeding 60%. Equivalent testing among F and S malabsorbers was not significant. Prevalence of malabsorption for all ethnic groups ranged between 41.5–55.4% and 47.2–63.0% for F and S resp. L malabsorption was greater among males: 63.0% male vs 52.6% female  $-p < 0.029$ . Females predominated among F and S malabsorbers; 55.8% and 60.8% female vs 45.7% and 50.0% males resp.  $-p < 0.033$ . The effect of age could be analyzed among Jewish patients ( $n = 167$ ). 78.6% malabsorbed L, F and S in the age group 25–34 years. A progressive decline in L malabsorption was noted between 25–55 followed by a significant rise in later years. For F and S, prevalence progressively fell to 51.9% and 48.2% resp by 75–84 years. *Conclusions:* In contrast to L, ethnic origin does not influence F and S absorption in IBS patients. Malabsorption of L was more common among males, the reverse with F and S. While L malabsorption increased after 55 years, that for F and S fell progressively in the ethnic group analyzed. Intestinal disorders, absorption: Malabsorption syndromes } "Malabsorption of Lactose (25 G), Fructose (25 G) and Sorbitol (5 G) in Patients with Irritable Bowel Syndrome (IBS): Effect of Ethnic Origin, Sex and Age"

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"P P 10 0194" P 10 0194 **Quality of Life (QOL) of Irritable Bowel Syndrome Patients in the Community**

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Pentland Medical Centre, Currie, Midlothian, UK

Eastern General Hospital, Edinburgh, UK Although irritable bowel syndrome (IBS) is common, little is known about the quality of life (QOL) in IBS patients in the community. 181 patients, aged 19–74 yrs, with a diagnosis of IBS were randomly selected from the lists of 3 general practices in Lothian. Patients were contacted by letter or telephone and invited to complete a postal questionnaire. Part 1 was the Mayo Bowel Questionnaire and part 2 was the Medical Outcome Survey SF36. A single reminder was sent to non-respondents. Responses were coded for analysis and results compared to known values for the general population, taken from a sample of 6212 residents of Lothian and a sample group of patients with angina pectoris. 110 questionnaires were returned: a response rate of 61% of whom 53% were female. Symptoms fulfilling the Rome criteria for IBS were reported by 79 patients. These patients were classified by the severity, Group 1 with mild or moderate pain and symptoms (39 patients (23 F 16 M) mean age 41 yrs) and Group 2 with severe pain and symptoms (40 patients (30 F 10 M) mean age 43 yrs). The remaining 31 patients (10 F 21 M), mean age 49 yrs, no longer had active IBS and appeared to be largely symptom free. MOS questionnaires showed the symptom free IBS patients had a QOL similar to that of the general population. For the mild/moderate group, QOL was minimally affected whereas in the severe group, QOL was markedly affected. The severity of abdominal pain in patients with IBS living in the community is significantly associated with lower scores in all domains of the MOS. Even relatively well IBS patients have impaired QOL. Patients with severe abdominal pain have a reduction in QOL comparable to that observed in patients with angina pectoris. Clinical practice: Quality assurance Motility, general: Functional GI disorders } "Quality of Life (QOL) of Irritable Bowel Syndrome Patients in the Community"

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## "P P 10 0195" P 10 0195 Is There a Gender Difference in the Natural History of Irritable Bowel Syndrome (IBS)?

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Eastern General Hospital, Edinburgh, UK IBS is a common functional gastrointestinal disorder in both primary and secondary care, with a reported prevalence of 14–20%, incidence of 9% and a female predominance of 2:1. Little is known about the gender difference in relation to the progression and severity of the condition in the community. 181 patients, aged 19–74 yrs, with a diagnosis of IBS in the last five years were randomly selected from the lists of 3 general practices in the Edinburgh area. Patients were contacted by telephone or letter and invited to complete the Mayo Bowel Questionnaire. A single reminder was sent to patients not responding. Questionnaires were coded for analysis. Of the 181 questionnaires sent out, 110 were returned (a response of 61%) of whom 53% were female and 47% male. Symptoms fulfilling the Rome criteria for IBS were reported by 79 patients (72% of responders, 53 F 26 M). The remaining 31 patients (mean age 49 yrs) appeared to be substantially symptom free. Of this group 10 were female, 21 male. The 79 patients with active IBS were classified according to the severity of their condition. Group 1 with mild/moderate pain and symptoms comprised 39 patients (23 F 16 M) mean age 41 yrs: Group 2 with severe pain and symptoms comprised 40 patients (30 F 10 M), mean age 43 yrs. There was a statistically significant association between female gender and symptom severity:  $X^2 = 13.3$ ,  $P < 0.01$ . These data show that among patients in the community diagnosed as IBS, symptom resolution is more common in men than women. To our knowledge, this gender difference in the natural history of the disorder has not previously been reported and emphasises the importance of community-based population studies. Clinical practice: Epidemiology (non cancer) Motility, general: Functional GI disorders } "Is There a Gender Difference in the Natural History of Irritable Bowel Syndrome (IBS)?"

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## "P P 10 0196" P 10 0196 Colonic and Extra-Colonic Symptoms of 1032 Patients with Irritable Bowel Syndrome

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<sup>2</sup> Laboratoires Vedim (UCB-Pharma), 92003 Nanterre, France Aim of this survey was to describe demographic and clinical features of patients complaining of irritable bowel syndrome (IBS) and consulting a non-hospital gastroenterologist. *Materials and methods.* Patients included had abdominal pain related to defaecation associated with altered bowel habit and/or bloating. From september 1994 to february 1995, 271 French gastroenterologists filled-in 1032 questionnaires during a consultation. *Results.* Average age of patients was 49 – 16 years, with a high percentage of women (sex ratio: 2, 3). Average duration of IBS was 11 – 11 years; for only 1% of patients, symptoms appeared less than one year before the study, but for 65% of patients, symptoms were present since more than 5 years. At the time of the study, 96% of patients had abdominal pain and 93% a bloating, both symptoms for which intensity was mostly scored 3 to 5 on a 6 point-scale, and 64% of patients had constipation. The frequency of onset of symptoms was at least once per week for 81% of patients; for 30% of them, symptoms occurred daily. Most of patients (93%) had at least an other digestive symptom such as excess of gas, borborygmus, flatulence, eructation or nausea. 65% of patients complained of one or several non-specific symptoms such as fatigue, insomnia or headache. 67% of patients described symptoms reflecting psychological disorders, mostly anxiety and depression. Number of consultations for IBS during the last 12 months was 3 – 3, but 19% of patients had more than 5 consultations. 7% of patients were out of work and 9% were hospitalized during the last year because of IBS. Rest and holidays alleviated symptoms for half of patients; stressful events, food, job and family worsened symptoms of a majority of patients. 83% of patients went under at least one diagnostic procedure, a colonoscopy most frequently. 90% of patients had already at least one digestive drug prescription and 34% a sedative or anti-depressant drug. *Conclusion.* IBS, expresses by many and frequent symptoms which occur during many years. IBS is associated with anxiety and depressive symptoms. Thus IBS is surely to impair quality of life. This research was funded by Laboratories Vedim (UCB-Pharma). Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Motility, general: Functional GI disorders } " Colonic and Extra-Colonic Symptoms of 1032 Patients with Irritable Bowel Syndrome "

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## "P P 10 0197" P 10 0197 Descriptive Study of Quality of Life in 1032 Patients with Irritable Bowel Syndrome

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<sup>2</sup> Laboratoires Vedim (UCB-Pharma), 92003 Nanterre, France Irritable bowel syndrome (IBS), through its frequent, intense and chronic symptoms, affects the daily life of patients. This is not explored correctly by current clinical criteria such as abdominal pain. The aim of this survey was to evaluate health related quality of life in patients with IBS consulting a non-hospital gastroenterologist. *Methods.* Patients had to present abdominal pain related to defaecation and altered bowel habit and/or bloating. Self-questionnaire was filled-in in waiting-room. It consisted in 34 items reflecting different domains. Answer for each item was a 4-point Likert scale. This questionnaire has been developed specifically for this study, and it has not been validated for evaluative purpose in therapeutic trials. *Results.* Among 1032 patients included by 271 gastroenterologists, 1021 (99%) completed the questionnaire. 68% of patients are afraid about not knowing when the next bout of IBS will arise. 69 to 85% patients declare having difficulties in the different aspects of their daily life (daily activities, job, leisures, social, family, affective) because of IBS. There is a significant correlation ( $p < 0.001$ ) between the severity of pain and bloating (but not for bowel habit) and the impact on the daily life, diet and health perception. 57% of patients consider their health to be good and 51% to be identical to other people. 81% of them are unsatisfied, anxious or afraid by their health. 66% of patients think that their health did worsen during the last years and 21% that it will worsen during the next years. They are only 23% to be convinced that IBS will improve in the next years. 83% of patients declare having sleeping disorders because of their health, 55% feel fatigue and 7% declare to be exhausted. 86% of patients judge their mind as medium to very bad and 65% of them take hypnotic or anxiolytic drugs. 75% of patients follow a diet, which is judged cumbersome or unbearable by 65% of them and not efficient by 49%. *Conclusion.* Quality of life is daily altered in patients with IBS, in terms of discomfort, poor health perception, unsatisfiedness and fear. For an optimal therapeutic management of patients with IBS, quality of life should be evaluated as well as symptoms. This research was funded by Laboratories Vedim (UCB-Pharma). Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Motility, general: Functional GI disorders } "Descriptive Study of Quality of Life in 1032 Patients with Irritable Bowel Syndrome"

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## "P P 10 0198" P 10 0198 Health Status Survey Questionnaire (SF-36) in Dyspepsia and Irritable Bowel Syndrome

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In a validation study of a specific quality of life questionnaire in functional digestive disorders (FDD) (results presented elsewhere), patients from France, Great Britain and Germany were asked also to fill-in the general health status questionnaire SF-36. *Materials and methods.* From June to November 1995, 187 practitioners recruited 401 patients: 191 with dyspepsia, 210 with irritable bowel syndrome (IBS). Patients were asked to fill-in alone the questionnaire SF-36. SF-36 has been given also to 97 control patients: among them, 12% had hypertension, 19% arthrosis, 12% rheumatism, 9% insomnia. The SF-36 questionnaire consists of 36 items in 8 domains: physical functioning (PF), physical problems (RP), bodily pain (BP), general perception of health (GH), vitality (VT), social functioning (SF), emotional problems (RE), mental health (MH). Period recall is the last 4 weeks. For each domain, items answers are summed and transformed on to a scale from 0 (worse health) to 100 (best). *Results.* The acceptability of SF-36 is good, a missing data being found in 11.5% of questionnaires (IBS and French patients are less compliant). Median scores of each domain are significantly different between control group and patients, but not between dyspeptic and IBS:

*Conclusion.* Quality of life is impaired in patients with FDD, in comparison of a control group of patients having other chronic diseases. SF-36 is a useful general tool to compare health status between patients with different clinical conditions. This research was funded by Laboratoires Jouveinal. Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Motility, general: Functional GI disorders } "Health Status Survey Questionnaire (SF-36) in Dyspepsia and Irritable Bowel Syndrome"

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## "P P 10 0199" P 10 0199 European Psychometric Validation of a Specific Quality of Life Questionnaire in Functional Digestive Disorders

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<sup>3</sup> Institut de Recherche Jouveinal, 94260 Fresnes Through several studies, we developed a french specific quality of life questionnaire in functional digestive disorders, translated in english and german, consisting in a self-administered questionnaire of 68 items with answers on a five-point Likert scale, reflecting 12 domains. Aim of this study was to assess the final psychometric properties (acceptability, validity, reliability) of the questionnaire. *Materials and methods.* From june to november 1995, 187 general practitioners and specialists recruited 401 patients in France, Great Britain and Germany: 191 dyspeptic (D), 210 with irritable bowel syndrome (IBS). Patients were asked to fill-in alone the specific questionnaire and the general health survey questionnaire SF-36. *Results.* Average age of patients was 50 – 15 years, with 52% (D) and 70% (IBS) of women. For 80% (D) and 86% (IBS) of patients, symptoms were present since more than 1 year. Disease was severe as 53% (D) and 46% (IBS) of patients complained of more than 10 symptoms. Handicap scored by doctor was at moderate to huge for 59% (D) and 69% (IBS) of patients. Acceptability of our questionnaire is good and similar to the SF-36 as 1 missing data occurred in 10.9% of questionnaires. Construct validity was assessed by a factor analysis. It resulted through several multitrait scaling analysis in a reduction of the questionnaire to 43 items in 8 domains having a good convergent and divergent validity. Reliability is shown by the overall { a } Cronbach coefficient at 0.94. Clinical validity is good as ""food"", ""discomfort"" and ""stress"" domains discriminate dyspepsia from IBS patients. IBS patients and women report a lesser quality of life. There is a correlation between quality of life and the handicap scored by doctor, the number of symptoms and the duration of disease. Finally, correlation with SF-36 is high especially with the ""daily activities"" and ""coping"" domains of the specific questionnaire. *Conclusion.* The good psychometric properties of this specific quality of life questionnaire in functional digestive disorders, translated in french, english and german, allow to use it in comparative therapeutic trials. This research was funded by Laboratoires Jouveinal. Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Motility, general: Functional GI disorders } "European Psychometric Validation of a Specific Quality of Life Questionnaire in Functional Digestive Disorders"

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"P P 10 0200" P 10 0200 **Kruis Scoring System and Manning's Criteria in Diagnosis of Irritable Bowel Syndrome: Is It Better to Use Combined?**

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Gazi University, Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey Irritable bowel syndrome (IBS) is characterized by abdominal pain and alteration of bowel habits. Manning et al. have reported that certain symptoms distinguished IBS from organic gastrointestinal disease (OGD); these were pain relieved by defecation, looser or more frequent stools at the onset of pain, abdominal distention, mucus, and a feeling of incomplete evacuation. Another simple scoring system for discriminating IBS from OGD that incorporated historical data, physical examination findings, and basic investigations was first devised by Kruis et al. In differential diagnosis of IBS from OGD, to evaluate the reliability of Manning's criteria and Kruis scoring system when used apart or combined; we studied 347 outpatients who completed a bowel disease questionnaire which objectively measured Manning's criteria and scoring system of Kruis. The group included 165 patients with IBS and 182 patients with OGD. The Manning's criteria discriminated IBS from OGD with a sensitivity of 90% and a specificity of 87% if three or more items were regarded as positive. Also the Kruis scoring system discriminated IBS from OGD with a sensitivity of 81% and a specificity of 91%. When used together, these systems discriminated IBS from OGD with a sensitivity of 80% and a specificity of 97%. Manning's criteria and Kruis scoring system had a strong correlation when compared in IBS, but not in OGD. Clinical practice: Epidemiology (non cancer) } "Kruis Scoring System and Manning's Criteria in Diagnosis of Irritable Bowel Syndrome: Is It Better to Use Combined?"

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"P P 10 0201" P 10 0201 **Impaired Quality of Life in Irritable Bowel Syndrome as Compared to Inflammatory Bowel Disease**

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<sup>3</sup> Dept. Psychology, UCD, Dublin, Ireland *Introduction* Chronic bowel diseases such as IBD and IBS can have a profound effect on patients' Quality of Life (QoL). Poor QoL may be more pronounced in IBS than IBD. Disease and non-disease related factors can impact significantly on QoL and symptomology alone rarely gives the full clinical picture. *Methods* Adult patients with a clinically confirmed diagnosis of IBS and IBD were assessed using validated interview based and self administered questionnaires as follows: QoL using the Schedule for the Evaluation of Individual Quality of Life (SEIQoL); Somatic symptoms (Tally's-modified); Psychological – Hospital anxiety and depression scale (HAD); Disease Knowledge and support (visual analogue). *Results* 110 patients, IBS (n = 40), Ulcerative Colitis (UC) (n = 40), Crohn's Disease (CD) (n = 30) were studied. QoL (SEIQoL) was significantly (P < 0.01) poorer in IBS 51.56 as compared to CD (64.21) and UC (67.03). Anxiety, depression and somatic symptom scores were significantly (P < 0.01) greater in IBS. Disease knowledge and support were significantly (P < 0.01) poorer in the IBS group. Preliminary data suggests impaired IBS QoL is not directly associated with symptom severity. *Conclusion* QoL is significantly impaired in IBS as compared to IBD and does not appear to be directly associated with symptom severity alone. Other aspects such as psychological non-colonic symptoms and poor disease knowledge and support are likely to be important. Clinical practice: Quality assurance Intestinal disorders: IBD diagnosis, monitoring Motility, general: Functional GI disorders } "Impaired Quality of Life in Irritable Bowel Syndrome as Compared to Inflammatory Bowel Disease"

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"P P 10 0202" P 10 0202 **Symptoms and Colonic Transit Time in the Irritable Bowel Syndrome Treated with Psyllium and Cisapride or Placebo** R. Meier<sup>1</sup>,

\*Ch. Beglinger<sup>2</sup>, R. Brignoli<sup>3</sup>, IBS-CIS study group

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<sup>2</sup> University Hospital Basle, Switzerland

<sup>3</sup> Janssen Research Foundation, Baar, Switzerland Since cisapride (CIS) has been reported to be efficacious in the treatment of constipation and of IBS, it was considered of interest to investigate whether the addition of CIS to Psyllium in pts. not responding to the bulk forming agent could improve the clinical and objective result. *Material and Methods:* IBS was defined as lower abdominal pain eventually relieved by defecation and 1 additional target symptom (see table). Adult pts. with an IBS since at least 6 months and who did respond to with Psyllium during at least 1 month, with a negative Barium-X-Ray or colonoscopy, were randomized to additionally receive either cisapride 5–10 mg tid or placebo tid. The treatment was continued for 12 weeks followed by 4 weeks of drug-free observation. The target symptoms were rated every 4 weeks (from absent = 0, to severe {inhibiting daily activities} = 3). Before and at the end of the treatment period Colonic Transit Time (CTT) was measured. Significance was accepted if two tailed  $p < 0.05$ . *Results:* 101 pts. were randomized but only 51 had 2 CTT determinations (26 CIS and 25 placebo) and are reported here. In both groups all target symptoms improved significantly during the study, however lower abdominal pain improved significantly more in the CIS treated pts. The CTT values were correlated to the constipation scores before and after treatment, but not with the treatment given nor with the other symptoms rated. *Delta CTT and daily scores of Target Symptoms (Mean – S.D.)*

Parameter	Placebo	Cisapride	Intergroup
Abdominal pain	0.85 – 0.43	0.57 – 0.32	$p < 0.01$
Flatulence/meteorism	0.77 – 0.37	0.76 – 0.52	n.s.
Constipation	0.81 – 0.48	0.74 – 0.50	n.s.
Urge to defecate	0.34 – 0.42	0.35 – 0.41	n.s.
Incompl. evacuation	0.32 – 0.32	0.41 – 0.56	n.s.
CTT (END-Start) hours	10.9 – 28.7	9.2 – 24.4	n.s.

*Conclusions:* The adjunction of CIS to Psyllium translated in a significantly larger pain relief. This effect can not be explained by an effect on colonic motility. }" "Symptoms and Colonic Transit Time in the Irritable Bowel Syndrome Treated with Psyllium and Cisapride or Placebo"

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"P P 10 0203" P 10 0203 **Experimental Gut Pain in Man**

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Visceral pain is a substantial clinical problem. Experimental pain stimuli may elucidate physiological aspects of the pain, but only few human models are available. In the current study the findings using electrical stimuli of the gut mucosa were evaluated in patients with ileo/sigmoidostomy. Nine patients participated. Four had an ileostomy and five had sigmoidostomy. In all subjects the stomy was normally functioning. A flexible catheter containing six stimulation electrodes separated by 4 mm was introduced into the stomy. The gut mucosa was stimulated by single, five repeated and continuous electrical stimuli. The sensation threshold, pain detection threshold (PDT) and pain tolerance threshold (PTT) was determined. Also the location and size of the referred pain area was characterized. Finally, brain potentials to single stimuli were measured. PDT and PTT to single stimuli were difficult to determine whereas these thresholds were easily found when repeated stimuli were used. The pain thresholds to single stimuli were twice as high as thresholds to repeated stimuli indicating the importance of central temporal summation in visceral pain. During continuous stimulation the pain intensity as well as the referred pain area gradually increased. Also the amplitude of the brain potentials increased for increasing pain intensity. In conclusion the model demonstrated the importance of repetitive stimuli for eliciting visceral pain. The brain potentials may be useful in the study of basic pain physiology. Visceral stimuli seems adequate to evoke referred pain with profiles similar to those found in patients with different gastrointestinal diseases. Motility, general: Receptors and signals } "Experimental Gut Pain in Man"

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## "P P 10 0204" P 10 0204 Irritable Bowel Syndrome (IBS) Observatory: Clinical and Therapeutic Aspects in 1571 Patients Treated by Town GPs

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<sup>1</sup> CHU du Haut L'e9v\ 'eaque, Bordeaux, France *Purpose:* the prevalence of irritable bowel syndrome (IBS) among the general public is high. Similarly, it presents in a wide range of ways and is treated by various means. The objective of the present work was to describe the characteristics and symptoms of patients consulting a GP for symptoms suggesting IBS, and to measure developments in the medium term. *Methods:* a representative sample of GPs from the whole of France was randomly selected, and their patients consulting for IBS symptoms were included. The clinical and therapeutic data were collected at this consultation and a second time three months later. Prescription of treatment or further examinations was left to the GPs' discretion, and recorded. *Results:* between February 1995 and January 1996, 463 GPs recruited 1571 patients aged 15 to 88 (mean – SD: 53 – 14), with women predominating (64%). 49% of the patients were in employment. 36% had had their appendix removed, and 12% their gall bladder. The IBS had existed for a mean of 8.9 years, chronically in 40% of cases and intermittently in 54%. During the initial consultation, 94% of patients reported pain, for 30.2% on a daily basis. Stool frequency was > 3 per day in 10% of patients, and < 1 per three days in 10.6%. Stool consistency was considered normal in 18%, soft or liquid in 42%, and hard in 14%. 30% of patients alternated between diarrhoea and constipation, and 86% exhibited meteorism. At three months, the pain had disappeared in 13% of patients, and occurred on a daily basis in only 8.8%. The intensity of pain had significantly decreased. Stool frequency anomalies previously noted now occurred in 3.6% and 3.4% of patients. Stool consistency was considered normal in 48% soft or liquid in 46%, and hard in 8.4%. 12% of patients alternated between diarrhoea and constipation, and 58.9% exhibited meteorism. During the three months preceding the study, 93% of patients were already on a treatment and 62% on a diet for their IBS. At the end of the first consultation, 95% of the patients were prescribed a medical treatment and 84% a diet. The mean number of medicines prescribed was 2.38 before the consultation and 2.16 after; the reduction largely concerned prescriptions involving four or more medicines. The most commonly prescribed therapies were intestinal dressings (diosmectite), antispasmodics of the musculotropic (mebeverine) and non-anticholinergic (phloroglucinol) types, and modifiers of digestive motricity (trimebutine). *Conclusion:* the IBS observatory enabled a profile of patients consulting for IBS out-patient treatment to be established. Symptoms at three months were significantly improved. The therapy given, the patterns of disease development or even the conditions of observation could be responsible for this improvement. Intestinal disorders: Constipation Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance }" "Irritable Bowel Syndrome (IBS) Observatory: Clinical and Therapeutic Aspects in 1571 Patients Treated by Town GPs"

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## "P P 10 0205" P 10 0205 Economic Aspects of Irritable Bowel Syndrome in 1571 Patients Treated by Town GPs

\*J.M. Raymond<sup>1</sup>, P. Michel<sup>1</sup>, D. Jessueld<sup>2</sup>, O. Plique<sup>2</sup>, J. Westerloppe<sup>2</sup>, M. Amouretti<sup>1</sup>

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<sup>1</sup> CHU du Haut Lévêque, Bordeaux, France Purpose: irritable bowel syndrome (IBS) is a common, benign pathology. The economic impact of its treatment is not exactly known. The objective of the present work was to assess consultation for treatment of patients presenting with IBS under usual non-hospital practice. *Methods:* a representative sample of GPs from the whole of France was randomly selected, and their patients consulting for IBS symptoms were included. The entire medical consumption over the three months preceding the consultation was recorded as was any prescription of examinations or treatment during this and/or another consultation three months later. *Results:* 1571 patients were recruited over 12 months by 463 GPs. During the three months preceding the consultation, 1364 patients stated having consulted a GP and 335 a gastro-enterologist for IBS at least once out of respective totals of 3348 and 403 consultations (mean of 2.1 and 0.26 per patient per three months). 49 patients were hospitalised, four of which twice and one three times (mean stay in hospital 3.1 days). 94 patients were put on sick leave at least once over the same period for a mean of 8.7 days. 534 patients stated having had a least one extra examination. The examinations included 326 colonoscopies, 90 abdominal echographies, 46 barium enemas, 6 rectoscopies, 5 abdominal scanners, 38 coprocultures and 6 thyroid check-ups. 1461 patients were on medical treatment (involving less than 4 medicines in 86.2% of cases) and 976 were on a diet. At the end of the first consultation, a medical treatment was prescribed to 1494 patients, with less than 4 medicines in 92.3% of cases, and combined with a diet in 1329 patients. Further examinations were prescribed for 93 patients. During the three months of the study, 1081 patients saw a GP and 98 a gastro-enterologist for a total of 2130 and 126 consultations. 18 patients were hospitalized for a mean of 3.3 days, and 39 were put on sick leave for 7.2 days. *Conclusion:* IBS treatment may be improved through an analysis of its various components, taking their corresponding cost: efficiency ratios into account. Clinical practice: Quality assurance Intestinal disorders: Constipation } "Economic Aspects of Irritable Bowel Syndrome in 1571 Patients Treated by Town GPs"

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## "P P 10 0206" P 10 0206 Analysis of the Effect of Irritable Bowel Syndrome (IBS) on the Well-Being of 1571 Patients Treated by Town GPs

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<sup>1</sup> CHU du Haut L<sup>\</sup>e9v<sup>\</sup>eaque, Bordeaux, France *Purpose:* irritable bowel syndrome (IBS) is one of the most common pathological conditions encountered in day-to-day practice. The effect of colonopathy on patients' everyday life has rarely been examined. The objective of the present work was to estimate the physical well-being of patients consulting a GP for symptoms suggesting IBS and to measure its progress three months later. *Methods:* a representative sample of GPs from the whole of France was randomly selected, and their patients consulting for IBS were included. A questionnaire asking for answers formulated on a four-point scale (enormously, fairly, a little, not at all) and analogue visual scales (AVSs) were filled in by the doctor and patient during the first consultation and at a second one three months later. Prescription of treatment or further examinations was left to the GPs' discretion, and recorded. *Results:* Between February 1995 and January 1996, 463 GPs recruited 1571 patients aged 15 to 88 (mean – SD: 53 – 14), with women predominating (64%). The IBS was chronic in 40% of cases and intermittent in 54%, and caused discomfort in various aspects of the patients' lives; according to aspect, the IBS bothered the patients ""enormously"" in 7.4 to 19.5% of cases. It bothered 69.3% of patients ""fairly"" or ""enormously"" for social life, 63.1% for leisure, 62.6% for family life, 57.4% for domestic life, 43.9% for work, and 30.2% for sex. During the initial consultation, stress was accused of triggering abdominal pain by 80.5% of patients and transit disorders by 69.3%. At the end of the study, no matter what the aspect, less than 2% of patients were ""enormously"" bothered by IBS and over 72% ""a little"" or ""not at all"". Assessment of discomfort by AVS demonstrated that the results changed on average between the two consultations from 4.7 to 2.6 for pain, 5 to 2.7 for swelling, 3.3 to 1.7 for diarrhoea, 3.2 to 2 for constipation, and from 5.2 to 3 for an AVS assessing overall discomfort. Age, sex and patterns of disease development were not significantly associated with differences in disease stage at three months. *Conclusion:* measuring the effect of IBS by AVS and discreet-answer questions were in agreement. IBS deteriorated various aspects of physical well-being in day-to-life and, to improve care, must be taken into consideration. The improvements observed during the study could be due to the treatments given, but also to the patterns of disease development or even the conditions of observation. Intestinal disorders: Constipation Clinical practice: Epidemiology (non cancer) } "Analysis of the Effect of Irritable Bowel Syndrome (IBS) on the Well-Being of 1571 Patients Treated by Town GPs"

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"P P 10 0207" P 10 0207 **Enterocyte Covering Agent Versus Intestinal Motility Inhibitor in the Irritable Bowel Authors A.L. Oproiu,**

\*M. Diculescu, A. Iov, S. Calin, A. Dumitrescu, G. Calin, M. Manuc, D. Pitigoi

""Carol Davila"" University of Medicine, Bucharest Romania *Purpose.* Irritable bowel syndrome (IBS) is a rather frequent disease in adults, with a complex pathogenic mechanism. Our aim was to assess whether enterocytes are more involved than smooth muscle cells in IBS with accelerated bowel transit. *Methods:* Our study was a prospective monocentric study. We had 2 groups of patients: group D had 30 patients with IBS who were treated with diosmectite 9 g/day. Group L had 32 patients and was treated with loperamide 4 mg/day. Both groups were treated for 30 days and had a definite IBS diagnosis based on clinical data and laboratory exclusion of organic, infective or systemic diseases who could mimic IBS. All the 62 patients were evaluated at the beginning, and at days 10, 20, 30. Statistic analysis evaluate the median, maximal, and minimal values for quantitative variables, and Wilcoxon's test for qualitative variables. *Results.* The number of stools had reduced from 3.4 – 1.0 to 1.0 – 0.7 in the D group comparative with a reduction from 3.6 – 1.0 to 1.8 – 0.3 in the L group. The frequency of abdominal pain was reduced from 6.5 – 2.4 to 1.6 – 2.1 and from 5.8 – 1.8 to 2.9 – 2.2 respectively. Flatulence was absent in 16.7% before treatment and 83.3% after 30 days in group D compared with 21.9% and stil 37.5% in group L. Global efficacy at 10 days was 46.7% very good and 26.7% good in the D group compared with 31.25% and 18.75% in group L. *Conclusion* Global efficacy at 30 days was 96.7% with diosmectite and 62.5% with loperamide which may mean that usually in IBS smooth muscle hypermotility may be in some conditions more dependent upon the enterocyte and intraluminal status than upon the nervous system. Intestinal disorders, absorption: Pathophysiology of diarrhea Motility, specific: Small bowel Motility, specific: Colon, anorectum }" "Enterocyte Covering Agent Versus Intestinal Motility Inhibitor in the Irritable Bowel Authors"

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## "P PP0 0220"PP0 0220 Comparison of Pantoprazole and Omeprazole in Acute Reflux Esophagitis

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<sup>2</sup> University Hospital A-Graz

<sup>3</sup> Medical Center CH-Locarno Pantoprazole, a new proton pump inhibitor, was compared with omeprazole in the treatment of reflux esophagitis in a large multicenter trial. *Methods:* Outpatients with acute reflux esophagitis (Savary-Miller grade 2 or 3) and at least one leading symptom (heartburn, regurgitation or pain on swallowing) were recruited into a double-blind randomized multicenter trial in Germany, Austria and Switzerland. They received either pantoprazole 40 mg or omeprazole 20 mg s.i.d. before breakfast. Endoscopies: at 0, 4 and, if not healed after 8 weeks. Clinical assessments: at 0, 2, 4, 6 and 8 weeks. Laboratory parameters including thyroid hormones were measured at 0, 4 and 8 weeks. Antacids were not allowed. Compliance had to be above 70% for per protocol evaluation. *Results:* Pantoprazole Omeprazole 40 mg 20 mg Patients (int. to treat) 263 258 Median age (range) 54 (21–95) 54 (18–84) Male/female 171/92 173/85 Grade II/grade III 205/58 200/58 Healing 4 w (per protocol) 77% (181/236) 75% (175/233) Healing 8 w (per protocol) 91% (215/236) 92% (214/233) Protocol violators 27 25 Dropouts 5 7 Adverse events (AEs) were comparable in both groups with respect to type (most common: diarrhea, headache), frequency (pantoprazole: 16 patients, omeprazole: 19 with possible or definite relation to medication) and intensity. No clinically relevant changes in laboratory parameters including T3, T4 and TSH were observed on either treatment. *Conclusion:* Pantoprazole and omeprazole are similarly effective and safe in the treatment of acute reflux esophagitis. Oesophageal gastric duodenal disorders: EG Reflux }" "Comparison of Pantoprazole and Omeprazole in Acute Reflux Esophagitis"

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## "P PP0 0221"PP0 0221 A Double-Blind, Randomized, Placebo-Controlled Study of Cisapride in Pediatric Gastroesophageal Reflux

\*R.B. Scott, C. Ferreira, L. Smith, A.B. Jones, H. Machida, M.J. Louhoues, C.C. Roy

Divisions of Pediatric Gastroenterology and Nutrition, Universities of Calgary and Montreal, Canada Gastroesophageal reflux is a common condition affecting infants and may lead to serious complications such as aspiration, apnea, esophagitis, stricture and failure to thrive. The present study was designed to assess the efficacy and safety of oral Cisapride suspension in the treatment of pediatric gastroesophageal reflux disease. A randomized, prospective, double-blind, placebo-controlled clinical trial was conducted at three study sites. After a one-week run-in period, 45 evaluable infants (aged 6 weeks–2 years) were randomized to receive a 6 week double-blind treatment with Cisapride (0.2 mg/kg q6h) or a placebo suspension. Efficacy was assessed with 24 h esophageal pH monitoring, esophageal manometry, esophageal biopsy before and after the treatment period. A diary was kept by parents of regurgitation frequency and severity, and global evaluation by parents and physician were performed at every visit. Safety was assessed by means of adverse event monitoring and standard laboratory measurements. Compared with placebo, Cisapride significantly ( $p < 0.05$ ) reduced the mean duration of upright and supine reflux episodes by the end of the trial. Compared to baseline, Cisapride significantly reduced the duration of the longest reflux episode, and placebo increased the number of reflux episodes  $> 5$  minutes. Cisapride was not significantly different from placebo for the following measurements: % total time pH  $< 4$ , number of reflux episodes, lower esophageal sphincter pressure, swallow pressure, regurgitation frequency or global evaluation scores. The incidence of adverse events was comparable in both groups. No serious adverse events were reported during the study. Cisapride is a safe, well-tolerated prokinetic agent which improves some parameters of 24 h pH measurements in children with GERD under the age of 2 years. It may be effective in reducing secondary complications of GER in pediatric patients. Oesophageal gastric duodenal disorders: EG Reflux Clinical practice: Management strategy } "A Double-Blind, Randomized, Placebo-Controlled Study of Cisapride in Pediatric Gastroesophageal Reflux"

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## "P PP0 0222"PP0 0222 **Reflux Esophagitis: A Complication of Helicobacter Pylori (HP) Eradication Therapy?**

\*N. Sacc'e0, A. De Medici, S. Rodin\f2, M. De Siena, A. Giglio

Servizio di Endoscopia Digestiva, Ospedale Ciaccio, Catanzaro, Italia Recently some authors reported in a preliminary study an high incidence of reflux esophagitis in patients after HP eradication therapy. Aim of our study was to evaluate this phenomenon in our endoscopical population. *Methods:* 276 patients affected by peptic ulcer and HP infection were treated with different therapeutic regimens (various antisecretory drugs: Omeprazole or Ranitidine and various antibiotics: Clarytromicine (C) + Tinidazole, C + Metronidazole (M), Amoxicillin (A) + Bismuth, A + M. The patients were investigated clinically and endoscopically at 1–6 months after therapy and when dyspeptic symptoms occurred. HP status was assessed by urease test and histology in antrum and body of the stomach and in third inferior of esophagus as well. *Results:* 169 (61.2%) were eradicated at 6 months after therapy: 24 of them developed an endoscopically proven reflux esophagitis which was mild (grade I) in all patients. *Conclusions:* our study confirmed the evidence of reflux esophagitis development in patients treated for Hp infection. Such evidence can be explained by different theory: changed eating and drinking habits that can reduce lower esophageal sphincter pressure or the interruption of a chronic therapy with antisecretory drugs for peptic disease. Any evidence of HP has been found in esophagus as and in stomach as well. We believe that this phenomenon isn't casual finding in patients without previous evidence of reflux esophagitis and that further studies are needed to clarify this phenomenon. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: EG Reflux Endoscopy, general: Instrumentation, therapy } "Reflux Esophagitis: A Complication of Helicobacter Pylori (HP) Eradication Therapy?"

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**"P PP0 0223"PP0 0223 Treatment of Candida Esophagitis in the Acquired Immunodeficiency Syndrome: Evaluation of Long-Term Therapeutic Efficacy of Fluconazole and Itraconazole**

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*Introduction.* Little information is actually available regarding the long-term response of Candida esophagitis to antifungal therapy. Aim of the study has been to assess the long-term therapeutic efficacy of fluconazole and itraconazole in the treatment of Candida esophagitis in a selected population of HIV-positive patients. *Methods.* The study has considered 2213 HIV-positive patients at first episode of esophageal candidiasis diagnosed by endoscopy; 1105 received fluconazole (100 mg b.i.d.), 1108 received itraconazole (100 mg b.i.d.) for 2 week. The patients who presented, after 2 weeks of treatment a partial endoscopic response (Kodsi's grade I), even if asymptomatic, continued the pharmacological treatment up to week 5. At week 5 they underwent endoscopic examination and only the patients with endoscopic cure were considered for long-term follow-up. The other patients were withdrawn from the study. Beginning from week 5, clinical examination was performed every week up to month 3, every two weeks up to month 6 and then every month up to the end of follow-up (month 12); endoscopic examination was performed at months 3, 6 and 12. Endoscopic examination could be performed also if relapses of esophageal symptoms were observed during the follow-up period, in order to assess if Candida infection was responsible or not for symptomatic relapse. *Results.* At week 2, endoscopic cure occurred in 81.2% of patients treated with fluconazole and in 65.6% of patients treated with itraconazole (relative risk: 1.23; 95% C.I.: 1.08–1.33;  $p < 0.001$ ). Clinical cure was observed in 81.5% of patients treated with fluconazole and in 75.2% of patients treated with itraconazole (relative risk: 1.08; 95% C.I.: 0.95–1.18;  $p < 0.001$ ). A total of 2158 patients were clinically and endoscopically evaluable at week 5 and were considered for long-term follow-up. At the end of follow-up, endoscopic and clinical cure were observed in 96.2% of patients treated with fluconazole and in 96% of patients treated with itraconazole (relative risk: 1.00; 95% C.I.: 0.87–1.08;  $p = 0.816$ ). By intention-to-treat analysis endoscopic and clinical cure were observed in 93.6% of patients treated with fluconazole and in 93.3% of patients treated with itraconazole (relative risk: 1.00; 95% C.I.: 0.87–1.08;  $p = 0.857$ ). Symptomatic relapses of endoscopically-demonstrated esophageal candidiasis were observed in 6% of fluconazole-treated patients and in 6.5% of itraconazole-treated patients presenting endoscopic and clinical cure at week 5 (relative risk: 0.92; 95% C.I.: 0.79–0.99;  $p = 0.650$ ). *Conclusions.* Both fluconazole and itraconazole are provided with a good long-term therapeutic efficacy in the treatment of Candida esophagitis in HIV-positive patients. Fluconazole is associated with a higher rate of endoscopic and clinical cure than itraconazole in short-term treatment. Immunology and microbiology: GI infections in

adultsEndoscopy, specific: Oesophagus }" "Treatment of Candida Esophagitis in the Acquired Immunodeficiency Syndrome: Evaluation of Long-Term Therapeutic Efficacy of Fluconazole and Itraconazole"

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## "P PP0 0227"PP0 0227 **TP53 Gene and MTS1 Gene Alterations in Oesophageal Squamous Carcinomas**

\*M.A. Giroux, M.P. Audr\`e9zet, J.P. Metges, J.B. Nousbaum, B. Mercier, C. F\`e9rec, H. Gou\`e9rou, M. Robaszkiewicz

CHU de la Cavale Blanche, 29609 Brest cedex, FranceThe TP53 gene is the most commonly mutated gene in human cancers. Another tumor suppressor gene called MTS1 encoding for p16 protein is frequently mutated in melanoma cell lines. Recent data have reported homozygous and heterozygous deletions involving 9p21. The aims of this study were: 1) to establish the prevalence of TP53 gene mutations, 2) to analyze the rate of deletions of 9p21 and 3) to detect MTS1 mutations in a large series of oesophageal squamous cell carcinomas (SCC).*Material and Methods:* One-hundred tumors were studied. TP53 mutations were identified using a GC clamp Denaturing Gradient Gel Electrophoresis (DGGE) and DNA sequencing. Deletion mapping of 9p21 was performed using microsatellites. MTS1 mutations were identified using DGGE and DNA sequencing.*Results:* TP53 gene mutations were detected in 78 patients (78%). The mutations identified were transitions (48.5%), transversions (34.8%) and frameshift mutations (16.7%). Five patients had a germline mutation of the TP53 gene. Loss of heterozygosity of 9p21 was investigated in 82 samples. Allelic loss involving at least one of the 2 microsatellites was detected in 11 of 75 informative cases (14.7%). We found 6 somatic mutations in exon 2; 3 consisted in deletions of 5, 10, and 33 base pairs and an identical missense mutation (A140T) was detected in the 3 other cases. Two patients had a genomic point mutation identical to that found in somatic DNA, and a loss of the other allele in the tumour.*Conclusion:* this study shows that TP53 gene alterations occur frequently in oesophageal SCC. On the other hand, somatic mutations of MTS1 gene are rare during oesophageal tumorigenesis. Oncology, specific: OesophagusOncology, general: Molecular biology, genetics }" "TP53 Gene and MTS1 Gene Alterations in Oesophageal Squamous Carcinomas"

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## "P PP0 0228"PP0 0228 Sensory Nervous Fibers and CGRP in Gastric Adaptation to Stress

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Gastric mucosa is capable to adapt to ulcerogenic action of stress but the mechanism of this phenomenon is unclear. Stimulation of capsaicin-sensitive sensory nerves and calcitonin gene-related peptide (CGRP) exhibit protective effects against mucosal damage in various models of gastric lesions, and for this reason, we investigated the influence of sensory nerves and sensory neuropeptide such as CGRP on gastric adaptation to stress. Acute gastric lesions were produced by water immersion and restrain stress (WRS) in rats. WRS was applied either once or repeatedly every other day for up to 8 days in animals with intact or capsaicin deactivated sensory nerves. It was found that WRS applied once produced multiple gastric erosions (19.0 ± 0.9 per rat) accompanied by an increase in basal gastric acid secretion (+ 30%), a decrease in gastric blood flow (determined by laser Doppler technique) by about 50% and a reduction of DNA synthesis by 57% as compared to intact rats without WRS. Repeated WRS insults resulted in a significant reduction of number of gastric lesions. This adaptation to stress ulcerogenesis was accompanied by a gradual decrease in gastric acid secretion, an increase in gastric blood flow and a return of mucosal DNA synthesis to the control value. Capsaicin-induced deactivation of sensory nerves eliminated gastric adaptation to WRS as manifested by a failure to decline of gastric lesions after repeated WRS and sustained decrease in GBF. Pretreatment with CGRP in capsaicin denervated rats prevented the formation of acute gastric mucosa lesions by WRS. One exposure to WRS in CGRP-pretreated rats resulted in a decrease of gastric lesions number to the value similar to that observed after gastric adaptation to stress but repeated WRS insults did not result in any additional significant reduction of gastric lesions. We conclude that the stomach is able to adapt to repeated stress insults due to enhancement of GBF and mucosal cell proliferation, and this adaptation depends upon the activity of sensory nerves and probably the release of CGRP.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Sensory Nervous Fibers and CGRP in Gastric Adaptation to Stress"

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## "P PP0 0229"PP0 0229 **Clinical Guidelines for Dyspepsia in Primary Care**

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St James's University Hospital, Leeds, England

**Background** Clinical guidelines have been suggested as a means of improving the quality and uniformity of patient care, though are easier to produce than to implement successfully. We have developed local consensus-based management guidelines for dyspepsia in co-operation with local general practitioners (GPs), and report a prospective audit of their implementation in a primary care setting.

**Methods** A heterogeneous group of 9 GPs from 3 practices were recruited to pilot the guidelines. Consecutive consultations for dyspepsia were recorded on a *dyspepsia management record* (DMR), kept in each patient's casenotes. The DMR was designed to summarise clinical information, facilitate guideline compliance, and simplify audit.

**Results** 217 DMR's were completed, relating to 396 consultations for dyspepsia. Prescribing patterns (%), and guideline compliance, are summarised for selected dyspepsia sub-groups (274 consultations): [N = consultations. Nil = no prescription; Ant = antacid; Mot = motility agent; H2R = H2-antagonist; PPI = proton pump inhibitor; HpE = *H. pylori* eradication; % PP = % prescriptions per protocol; parentheses "(n)" = prescriptions outside protocol; "empirical" = uninvestigated patients]

Sub-group	N	Nil	Ant	Mot	H2R	PPI	HpE	% PP		
New patient	29	7	48	3	38	(24)	3	(3)	0	73
Past dyspepsia, "empirical"	47	4	30	4	38	23	(11)	0	89	
Past reflux, "empirical"	37	3	46	0	19	32	0	100		
Non-ulcer dyspepsia	42	2	5	14	43	29	(24)	5	(5)	71
Reflux (-ve investigations)	32	3	16	0	38	44	0	100		
Reflux oesophagitis	37	0	5	0	22	(3)	68	5	(5)	92
Duodenal ulcer disease	50	4	2	0	62	(36)	8	(4)	24	60

**Conclusions** Although dyspepsia guidelines were well received by GPs, with overall compliance relatively good, some therapeutic agents were still used "inappropriately", and *H. pylori* eradication therapy was under-prescribed in DU disease. Even when guidelines are introduced under "ideal" conditions, with ongoing audit, prescribing practice may prove difficult to modify. Continuing medical education, targeted at specific aspects of disease management, is vital, particularly if guidelines are to be viable on a larger scale.

**Clinical practice:** Management strategy  
**Clinical practice:** Quality assurance  
**Oesophageal gastric duodenal disorders:** GD disorders, acid peptic } "Clinical Guidelines for Dyspepsia in Primary Care"

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"P PP0 0230"PP0 0230 **Ultrastructural Evidence of H. Pylori Penetration into the Gastric Cells**J.N. Giannios,

\*J.A. Karagiannis

Gastroenterology Unit, St. Savvas Anticancer Hospital, Athens, GreeceH. Pylori is considered as exerting its damaging effects to the gastric mucosa by adhering to the gastric mucosa cells without invading them. Aim of the study was to examine intrastructurally the sequence of H. Pylori interaction with the gastric mucosa. Twenty-eight patients with active chronic gastritis and peptic ulcer disease were diagnosed to have been infected with H. pylori, by <sup>13</sup>C-urea breath test, histology, culture and rapid urease test (CLO-test). Biopsy specimens from these patients were randomly selected and were fixed in 2.5% glutaraldehyde sodium cacodylate and then post-fixed in osmium tetroxide. After dehydration and gold coating, samples were examined under a Scanning Electron Microscope (SEM). A second set of biopsies were embedded in epoxy resin and cut to ultrathin sections which were stained with uranyl acetate and lead citrate for enhancing electron scattering for Transmission Electron Microscopy (TEM) analysis. Both SEM and TEM showed that, initially, bacteria adhere to the glycocalyx layer of microvilli, destroying them. Then the bacteria attach directly via filamentous material to the gastric cell surface, where the phospholipase A<sub>2</sub> activity of H. pylori degradate the external phospholipid membrane of gastric cells especially around the areas of tight junctions. Subsequently, the bacteria penetrated into the cytoplasmic region of the gastric cells where bacterial VacA toxin induces formation of large cytoplasmic vacuoles leading to cellular disintegration. Some bacteria were still adhered to cytoplasmic parts and granules which were floating free in the gastric milieu. Furthermore, generation of complement products and cytokines released after urease induction activated the chemotaxis of polymorphonuclear leucocytes which migrated through the epithelium into the gastric lumen, phagocytosing H. pylori and inducing inflammation to the gastric tissue. H. pylori strains having the GagA gene detected by Western Blotting showed greater polymorphonuclear leucocyte infiltration of the gastric tissue and hence induced more severe inflammation. The above observations reveal the ultrastructural mechanism under which H. pylori causes gastritis and peptic ulcer disease by actually invading the gastric cells. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Ultrastructural Evidence of H. Pylori Penetration into the Gastric Cells"

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**"P PP0 0232"PP0 0232 Seroepidemiology of *H. Pylori* Infection and Hepatitis A in a Rural Area. Evidence Against a Common Mode of Transmission**

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Dipartimento di Medicina Sperimentale, Universita' di R. Calabria, Catanzaro, Italy

<sup>1</sup> Cattedra di Microbiologia, Universita' di R. Calabria, Catanzaro, Italy *Background:* Recent studies showed that the age-specific prevalence of *H. pylori* infection parallels Hepatitis A (HAV) suggesting similar modes of transmission. *Aim:* To investigate risk factors for *H. pylori* and HAV and the possibility that the two infections could be associated. *Methods:* Between January and September 1995, a random sample of 705 resident subjects who attended the outpatient medical center of the rural county of Ciro' (11.000 inhabitants, Southern Italy) for blood testing were recruited. All subjects completed a questionnaire for general demographic details, height, weight, current and childhood socio-economic circumstances, history of cardiovascular diseases, diabetes, dyspepsia, smoking and alcohol. Serum sample was drawn from each subject and stored at  $-20^{\circ}\text{C}$ . Blood pressure was measured. All sera were assayed for *H. pylori* specific IgG by an in-house ELISA using a crude *H. pylori* sonicate as antigen (sensitivity and specificity 97% and 91%). In 466 subjects, antibodies to HAV were detected by means of a commercial ELISA kit (Behring, USA). In subsets of subjects, serum fasting cholesterol, triglycerides and glucose were also measured. Data were analysed by multiple logistic regression analysis, Spearman's test,  $\chi^2$  statistic and expressed also as odds ratio (OR) and 95% confidence intervals (CI). *Results:* Of the 705 (273 M, 468 F; age range 1–87, median 50) subjects, 446 (63%) were positive for *H. pylori*. Among the 466 (163 M, 303 F; age range 1–87, median 49) subjects screened for HAV, 291 (62%) were positive for *H. pylori* and 407 (87%) for HAV. Cross-tabulation of this data showed that 275 (59%) were positive and 43 (9%) negative for both *H. pylori* and HAV, 16 (3%) were positive only for *H. pylori* and 132 (28%) were positive only for HAV (OR = 5.6, CI: 3–10). There was an age-specific increase in the prevalence of the two infections and a fair correlation ( $r = 0.287$ ) whereas the association was more weak ( $\chi^2 = 0.21$ ) or not significant ( $\chi^2 = 0.064$ ) when assessed in the first two decades. In multivariate analysis, current and childhood socio-economic features were differently associated with *H. pylori* [dyspepsia (OR = 1.6, CI: 1.1–2.3), occupation (OR = 0.7, CI: 0.6–0.9)] and HAV [n. of siblings (OR = 1.3, CI: 1.05–1.7), refrigerator (OR = 5.6, CI: 1.3–24)]. *Conclusion:* The correlation between *H. pylori* and HAV reflects the age-specific high seroprevalence of both infections more than a true association. The fecal-oral spread of *H. pylori* is unlikely. *Clinical practice:* Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Seroepidemiology of *H. Pylori* Infection and Hepatitis A in a Rural Area. Evidence Against a Common Mode of Transmission"

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## "P PP0 0233"PP0 0233 Regression of Lymphoid Follicles in Gastric Mucosa of Helicobacter Pylori Infected Patients 12 Months after Eradication

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<sup>4</sup> Division of Gastroenterology of Padova, Italy *Introduction.* Only few studies, on small samples, demonstrated that eradication of Helicobacter pylori (Hp) infection causes a decrease of number of lymphoid follicles (LF) and a regression of low grade B cell gastric MALToma. *Aim.* To verify whether the cure of Hp infection could determine the regression of LF in the gastric mucosa. *Methods.* 100 patients (59 M, 41 F, mean age 59) with Hp infection and treated with either double, triple or quadruple therapy for 7–14 days entered the study. Hp colonization was confirmed by histology of 4 biopsies (Hematossilin-eosin and Giemsa modified stain), CLO test and culture. Pathologists were blinded as regards either therapy carried out or clinical results. An endoscopy was performed at baseline, three and twelve months after the end of eradication therapy. Patients with active lesion undergone a further endoscopy after 1 month. *Statistic.* Mc Nemar test of symmetry. *Results.* 55 patients were proven to have LF at baseline endoscopy (Group A) while 45 did not (Group B). After three months 46/55 subjects of the Group A were proven to be Hp negative and the follicles were still present in 20 (36%); 22 out of the Group B patients were reevaluated 1 month after the immission and 11 (50%) were found to have LF, while after 3 months the presence was in 18/45 (40%): eradication was obtained in 36/45 (80%). 44 patients were evaluated after 12 months: LF were detected in 8/24 patients of Group A (3 Hp+ve, 5 Hp{-}ve) and were absent in 16 (1 Hp+ve, 15 Hp{-}ve) while in Group B LF were present only in 1/20 patients; all the patients of this group were Hp{-}ve. The differences between baseline and long-term check-up were proven statistically significant ( $p = 0.0022$  after 3 months and  $p = 0.0003$  after 12). *Conclusion.* The cure of Hp infection significantly reduces the presence of LF in the gastric mucosa. } "Regression of Lymphoid Follicles in Gastric Mucosa of Helicobacter Pylori Infected Patients 12 Months after Eradication"

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## "P PP0 0234"PP0 0234 **Helicobacter Pylori Infection and Antral Intestinal Metaplasia: One Year Follow-up after Eradication**

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<sup>1</sup> Servizio di Endoscopia Digestiva Ospedale degli Infermi di Rivoli, Torino (I)  
*Purpose of the study:* To evaluate Helicobacter Pylori (HP) significance in development of intestinal metaplasia (IM) and how HP eradication modifies IM evolution.  
*Methods:* In 99 consecutive IM histological diagnosis in specimens obtained during upper endoscopic investigation we performed four biopsies, two from angular mucosa and two from fundic mucosa and detected HP presence histologically by Giemsa stain. All patients were endoscopically reinvestigated one year later. The group of patients presenting IM and HP positivity underwent eradication therapy immediately after diagnosis. Statistical analysis was performed by chi-square method.  
*Results:* 82 (82.8%) out of 99 patients resulted HP positive and 17 (17.2%) were HP negative. All IM and HP positive patients underwent eradication by triple therapy (omeprazole 20 mg daily for one month, amoxicillin 1 g twice a day for one week, claritromycin 250 mg twice a day for one week). 69 patients out of 82 resulted eradicated by immunological method two months after therapy. After 12 months 98 patients out of 99 underwent endoscopic control; one patient IM positive and HP negative dropped out of the study. 14 (87.5%) out of 16 patients (87.5%) IM positive and HP negative at time 0 showed IM in histological specimen and one of them was HP positive to Giemsa stain. At the same time only 53 (64.5%) patients out of 82 treated demonstrated intestinal metaplasia on histological specimen; 40 patients out of 53 were HP negative and 13 resulted HP positive. Among 29 patients IM positive at time 0 and IM negative twelve months later 27 were HP negative and 2 HP positive to Giemsa stain. Comparing the IM and HP positive patients before and after eradication, data analysis by chi-square method shows statistical significance ( $P < 0.005$ ).  
*Conclusions:* 82.8% patients affected from IM is HP positive. HP eradication allows regression of histological intestinal metaplasia in 30% cases one year after eradication. According to Correa's gastric carcinogenesis model, eradicating HP positive patients with proven IM. could be suggestable. Oesophageal gastric duodenal disorders: Helicobacter Pylori  
Clinical practice: Epidemiology (non cancer) Clinical practice: Management strategy }  
"Helicobacter Pylori Infection and Antral Intestinal Metaplasia: One Year Follow-up after Eradication"

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"P PP0 0235"PP0 0235 <sup>13</sup>C-Urea Breath Test — A Reliable Diagnostic Technique for Assessment of Eradication P.G. Johnson<sup>1</sup>, A.E. Duggan<sup>2</sup>, C. Olson<sup>3</sup>

<sup>1</sup> BSIA Ltd., Brentford, Middx, U.K.

<sup>2</sup> Glaxo Wellcome Research and Development, U.K.

<sup>3</sup> Abbott Laboratories, Illinois, USA *Introduction:* The sensitivity of any diagnostic test for *H. pylori* is most rigorously tested post-treatment. Here post-treatment results are presented from 7 multinational studies conducted to standards of Good Clinical and Laboratory Practice. *Methods:* 1029 patients, who had active DU and a positive CLOtest<sup>TM</sup> pre-treatment, were evaluated post-treatment in a total of 1815 visits. *H. pylori* was assessed by <sup>13</sup>C-Urea Breath Test (UBT) and at least one other test, [CLOtest, histology (Hx), or culture (Cx)], before and 1, 3, 6, or 12 months post-treatment, dependent on study. UBT, Hx and Cx were processed by central laboratories. Antral and corpus biopsies were taken. The effect of a cut-off of 5 compared to 3.5 excess <sup>13</sup>CO<sub>2</sub> per mil for the UBT is examined. *H. pylori* status was assigned from the combined results of at least two tests. Single positive tests or otherwise anomalous results were reviewed using data from previous and subsequent visits. *Results:* Test Sensitivity Specificity UBT (3.5) 98.7% 98.3% UBT (5.0) 96.9% 99.1% Histology (Giemsa) 98.8% 99.1% Culture 75.0% 98.8% CLOtest 95.6% 98.9% *Conclusion:* The UBT is a convenient, non-invasive test which yields similar sensitivity for assessment of eradication as histology or CLOtest alone (using multiple biopsies and sites). A cut-off of 3.5 is recommended for increased sensitivity but the test is robust even at 5.0 excess <sup>13</sup>CO<sub>2</sub> per mil. Oesophageal gastric duodenal disorders: Helicobacter Pylori } " <sup>13</sup>C-Urea Breath Test / A Reliable Diagnostic Technique for Assessment of Eradication "

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**"P PP0 0236"PP0 0236 Cost-Impact of Clarithromycin Plus Omeprazole Compared to Traditional Therapies for Treatment of *H. Pylori* Associated Duodenal UlcersA. Sonnenberg**

VA Medical Center, Albuquerque, NM USA and The Gastrointestinal Utilization Trial Study Group

**Introduction:** The NIH Consensus Development Conference recommended a comprehensive economic analysis of the impact of treating or not treating *H. pylori* (HP) associated ulcers. Patients were enrolled in a multicenter (n = 132), controlled clinical trial to determine cost savings of eradicating HP with clarithromycin plus omeprazole (C + O) versus conventional anti-ulcer therapy (omeprazole (O) or ranitidine (R) alone). **Methods:** Adult patients with HP and active duodenal ulcer were randomized to double-blinded treatment (Rx): 1) C 500 mg TID + O 40 mg QD for 14 days followed by O 20 mg QD for 14 days; 2) O 20 mg QD for 28 days; or 3) R 150 mg BID for 28 days. Visits were performed at pre-Rx (EGD + biopsy), post-Rx (safety), and 4–6 weeks post-Rx (eradication). After the third protocol directed visit, investigators followed patients for one year by monthly telephone calls to assess ulcer symptoms and collect economic data. Additional management was to be "standard of care" for that investigational site. **Results:** Of the 819 patients enrolled, 750 patients were eligible (confirmed ulcer and HP infection) for economic analysis. The demographics of the three groups were similar. Analysis of health resource utilization is given in the table below: Resource utilization C + O O R(beyond protocol) (n = 253) (n = 255) (n = 242)EGDs 31 76 69Ulcer related clinic visits 84 136 161Ulcer days lost from work 116 122 787All hospitalizations 26 47 42Ulcer related hospitalizations 0 5 6All hospital days 158 318 205Ulcer hospital days 0 24 37**Conclusion:** Ours is the first prospective study to show that using antibiotics to eradicate *H. pylori* in patients with duodenal ulcer results in decreased utilization of health care resources, overall and ulcer related, when compared to conventional anti-ulcer therapy with omeprazole or ranitidine. Oesophageal gastric duodenal disorders: Helicobacter PyloriClinical practice: Management strategy } "Cost-Impact of Clarithromycin Plus Omeprazole Compared to Traditional Therapies for Treatment of H. Pylori Associated Duodenal Ulcers"

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"P PP0 0237"PP0 0237 **A Management Plan for Upper Gastrointestinal (GI) Disease in Primary Care**. J. Brun, S.A. Brunton, F. Carelli, H. Haslbauer, P. Heyse, H. Maurer, P. O'Connor, W. Peterz, K. R\fcy,

\*M.J. Whitaker

International Gastro Primary Care Group  
The International Gastro Primary Care Group (IGPCG) was formed in May 1994 and includes primary care physicians from seven European countries, the USA and Australia. Based on their collective clinical and research experience, they devised a practical guide for the management of upper gastrointestinal (GI) disease. In the absence of alarm symptoms or use of Non Steroidal Anti-inflammatory Drugs (NSAIDs) the IGPCG management plan allocates patients based on predominant symptoms into three subcategories: motility disorder likely (bloating, abdominal discomfort, early satiety, fullness and nausea), ulcer disease likely (localised epigastric pain), gastro-oesophageal reflux disease (GORD) likely (heartburn, regurgitation). For each sub category particular management is recommended. The motility group is treated with a prokinetic. In the ulcer group the *Helicobacter pylori* (Hp) status is checked: Patients positive for Hp are referred for endoscopy and receive eradication treatment if an ulcer is confirmed. For GORD patients a step-up approach is recommended, starting with a prokinetic or and H2 antagonist. Treatment failures receive proton pump inhibitors (PPIs) or combination therapy or are referred. A pilot project in the form of a survey was set up to test the practical application of the IGPCG upper GI management plan in primary care. The age range was < 20 to over 80 [mean 45 years] and the male/female ratio was close to 50:50. Of the 58 patients included, 25 (44%) were allocated to the motility group, 22 (40%) to the ulcer group and 12 (21%) to the GORD group. Only three patients (5%) could not be placed into a specific group. Overall a satisfactory response was obtained in 34/58 (59%) patients, [21/25 (84%) in the motility group, 9/22 (41%) in the ulcer group and in 5/12 (42%) in the GORD group]. The IGPCG protocol postulates the use of predominant symptom in primary care management. This is contrary to symptom clustering which has been shown to be impractical in the management of upper GI disease. However, prospective validation of this plan is required to evaluate its cost-effectiveness. Clinical practice: Management strategy } "A Management Plan for Upper Gastrointestinal (GI) Disease in Primary Care"

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"P PP0 0239"PP0 0239 **Has Spiral Computed Tomography Improved the Staging of Patients with Gastric Carcinoma?**

\*J. Davies, A.G. Chalmers, J. May, G.V. Miller, H.M. Sue-Ling, D. Johnston

Centre for Digestive Diseases, Leeds General Infirmary, England Much controversy exists as to the value of computed tomography (CT) in the pre-operative staging of gastric cancer, due to its limited ability to correctly identify lymph node (LN) metastases, adjacent organ invasion and peritoneal metastases. The third generation of spiral CT scanners has a number of potential advantages including; minimal respiratory misregistration, image reconstruction smaller than scan collimation and optimization of intravenous contrast enhancement. The aim of this study was to assess the sensitivity and specificity of spiral CT, compared with both a formal operative staging and the final pathological (TNM 1987) staging. 105 consecutive patients who underwent both spiral CT and operative assessment were reviewed, median age 71 years (range 33–91 years). A single radiologist reviewed all scans which were assessed for LN metastases, adjacent organ invasion and hepatic and peritoneal disease. A similar assessment was made at the time of surgery. Both were then compared with the final histological staging. *Results:* Spiral CT staging

Operative staging	Sensitivity	Specificity	Sensitivity	Specificity
N1 nodes	24%	100%	94%	63%
N2 nodes	43%	100%	84%	74%
Mesocolon	76%	95%	94%	95%
Pancreatic	50%	99%	100%	98%
Hepatic	57%	100%	100%	99%
Peritoneal	70%	93%	100%	100%

There has been some improvement in spiral CT ability to detect both adjacent organ invasion (mesocolon) and peritoneal disease. Moderate sensitivity with high specificity in detecting spread means that a positive spiral CT result can be relied upon. Spiral CT has the potential to identify those patients who would be suitable for neo-adjuvant chemotherapy before surgery. Oncology, specific: Stomach Radiology and ultrasound: Diagnosis } "Has Spiral Computed Tomography Improved the Staging of Patients with Gastric Carcinoma?"

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**"P PP0 0240"PP0 0240 Incidence of Inflammatory Bowel Disease Across Europe: Is There a Difference between North and South?**

\*S. Shivananda, EC-IBD study group

University Hospital Maastricht, The Netherlands *Background:* It has been suggested that the incidence of inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is higher in the North than in the South of Europe. The aim of this European Collaborative study was to investigate the hypothesis of the North-South gradient. *Methods:* Over 2 years (1 Oct. 1991 to 30 Sept. 1993) all new patients with IBD were identified in 20 European centres according to a standard protocol for case ascertainment and definition. *Findings:* 2201 patients aged 15 years or more were identified, of whom 1379 were diagnosed as UC (including proctitis), 706 as CD and 116 as indeterminate. The overall incidence per 100,000 at ages 15–64 years (standardised for age and sex) of UC was 10.4 (95% confidence interval (CI): 7.6–13.1) and of CD was 5.6 (95% CI: 2.8–8.3). Rates of UC in northern centres were 40% higher than those in the South (rate ratio (RR) = 1.4, 95% CI: 1.2–1.5) and for CD they were 80% higher (RR = 1.8, 95% CI: 1.5–2.1). For UC, the highest incidence was in Iceland (24.5) and for CD, in Maastricht (The Netherlands) (9.2) and Amiens (NW France) (9.2). The lowest incidence of UC was in Almada (S. Portugal) (1.6) and of CD in Ioannina (NW Greece) (0.9). An unexpected finding was that in UC the incidence in women but not in men declined with age. The higher incidence rates in northern centres was not explained by differences in tobacco consumption or education. *Conclusions:* The magnitude of the North-South difference for both conditions was less than expected which may reflect recent increases in the incidence of IBD in southern Europe. Nevertheless there are substantial differences in incidence of UC and CD across Europe which are not readily explained by differences in case ascertainment. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics } "Incidence of Inflammatory Bowel Disease Across Europe: Is There a Difference between North and South?"

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"P PP0 0241"PP0 0241 **Inhibition of Cytokine Formation by the Novel Thiol Modulating Agent OR-1384**

\*P. Aho, E. Serkkola, K. Haasio, I.-B. Lind

Orion Pharma Research, Espoo, Finland Elevated levels of proinflammatory cytokines, (IL-1, IL-8 and TNF- $\alpha$ ), have been associated with the pathogenesis of inflammatory bowel disease (IBD). The key regulatory proteins in the signalling cascade leading to the induction of cytokine genes are thiol sensitive. OR-1384 (3-[[4-(methylsulfonyl)phenyl]methylene]-2,4-pentanedione) is a novel thiol modulating agent, which forms reversible adducts with thiol groups. The aim of this study was to evaluate the effect of OR-1384 on the formation of the major proinflammatory cytokines. We also tested the efficacy of OR-1384 in experimental colitis induced by a hapten, TNBS. *Methods:* Isolated human monocytes were used for the *in vitro* cytokine studies. The monocytes were stimulated with lipopoly-saccharide (50 ng/ml) and incubated with different concentrations of OR-1384. IL-1 $\beta$ , TNF- $\alpha$  and IL-8 were measured from the incubation medium by specific ELISAs. Colitis was induced in mice and in rats by a single intracolonic administration (i. col.) of 5 and 15 mg of TNBS, respectively. In rats, 3–30 mg/kg of OR-1384 was administered i. col. once daily for 5 days and in mice 30 mg/kg was given i. col. 24 and 1 h before TNBS. The rats were killed 96 h and the mice 4, 8, 16, 24, 48 or 72 h after the induction of colitis. Colonic inflammation was assessed by macroscopic and histological scorings and by measurement of tissue myeloperoxidase (MPO) activity. In mice, IL-1 $\alpha$ , IL-1 $\beta$  and TNF- $\alpha$  were measured in mucosal homogenates of the colon. *Results:* OR-1384 inhibited the formation of IL-1 $\beta$ , TNF- $\alpha$  and IL-8 in human monocytes the IC<sub>50</sub> values being below 10  $\mu$ M. In rats, OR-1384 protected against TNBS-induced injuries and decreased the MPO activity significantly and dose-dependently, maximally by more than 70%. In mice, the colonic injuries were visible already 4 h after TNBS, but they were most severe at 48 h. Colonic cytokine levels, IL-1 $\alpha$ , IL-1 $\beta$ , and TNF- $\alpha$  were increased several fold reaching the maximum at 16 h. OR-1384 inhibited the formation of these cytokines and protected against the lesions and inflammation. *Conclusion:* OR-1384 was shown to effectively protect against hapten-induced colonic injuries and inflammation. The marked suppression of the key inflammatory mediators IL-1, IL-8 and TNF- $\alpha$  suggests the anti-inflammatory activity of OR-1384 to be cytokine mediated. The locally acting OR-1384 offers a new alternative for the treatment of IBD. Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } " "Inhibition of Cytokine Formation by the Novel Thiol Modulating Agent OR-1384"

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"P PP0 0242"PP0 0242 **Interleukin-8 in Inflammatory Bowel Disease**

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First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan

**Background and purpose:** Increasing evidence points to various pathogenic roles for cytokines in inflammatory bowel disease (IBD). Interleukin-8 (IL-8) is a major cytokine for recruitment and activation of neutrophils. Neutrophils play a central role in the active stages of IBD. This study aimed to characterize secretion of IL-8 by mucosa in vitro and to visualize its distribution and its positive cell types in the affected intestine of patients with IBD.

**Materials and methods:** Biopsies or resected segment were obtained from 12 patients with active Crohn's disease (CD) and 18 with active ulcerative colitis (UC). In 11 patients, macroscopically normal portion was obtained from large bowel resected because of colorectal carcinoma. IL-8 content of organ culture supernatants was determined by enzymed linked immunosorbent assay, and IL-8 gene expression was analyzed by in situ hybridization with IL-8 DNA probes.

**Results:** The secretion of IL-8 (ng/mg biopsy protein) in 24 hours from inflamed mucosa of patients with CD (median 135.4, range 52.4–352.4) or UC (median 179.5, range 57.4–385.8) was significantly higher than that from normal mucosa (median 51.9, range 35.3–107.9:  $p = 0.0006$  vs. CD,  $p = 0.0001$  vs. UC), and correlated with the number of neutrophils infiltrating in the affected intestinal mucosa of IBD ( $r = 0.760$ ). In situ hybridization with IL-8 DNA probes revealed strong signals in the involved mucosa. The number of cells expressing IL-8 mRNA correlated with histological grades of disease activity. Most of IL-8 mRNA producing cells were focally distributed in erosive or ulcerative intestine of patients with CD, whereas they were diffusely distributed over the entire inflamed mucosa in patients with UC. IL-8 mRNA was mainly expressed by macrophages, neutrophils, and epithelial cells in the involved intestine of IBD.

**Conclusion:** The results of this study suggest that IL-8 play an important role in the pathogenesis of IBD. The distinct distribution of IL-8 gene in CD and UC may indicate that there exists a difference of inflammatory responses between these two forms of IBD.

Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Interleukin-8 in Inflammatory Bowel Disease"

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**"P PP0 0243"PP0 0243 Intestinal Cytotoxic CD4+ TH1-Like Cells in Crohn's DiseaseA. Bachetoni, P. Mariani, M. D'Alessandro, D. Lomanto, P. Mazzocchi, G. Dalsasso, L. Strolighi, V. Speranza**

2 Cl. Chirurgica, Univ. La Sapienza, Roma, Italy Cytotoxic function of isolated lamina propria T lymphocytes (LP-CTL) in inflammatory conditions is not well established. Our previous results show that LP-CTL, mediated by TCR-CD3, is slightly increased in Crohn's disease (CD). Aim of our study is to evaluate which kind TH subset is involved in inflammatory conditions. We have examined the toxic function and cytokine profile (IFN- $\gamma$ , IL4 and IL5) of CD4+ enriched or CD4 $\{-$  depleted LPL, from terminal ileum of CD pts (n = 10) and controls (n = 10). LPL are isolated using DTT-EDTA-Collagenase digestion followed by discontinuous Percoll density gradients and CD4+ cells were purified by Dynabeads. The cytotoxic activity of freshly isolated LPL is assessed against the NK-resistant B7 P815 cell line; anti-CD3 (5 mcg/ml, TR66), anti-CD2 (T11<sub>2,3</sub>) or PHAp (1 mcg/ml) were added to effector and target cells, ratio of 50:1, and incubated for 6 hrs at 37°C. The results are:

\*Contr vs Crohn p = 0.03; CD4+ vs CD4 $\{-$  p = 0.02 The present data unexpectedly indicate that CD4+ have cytotoxic activity and TH1 profile ( $\gamma$ -IFN concentration 6 ng/ml). The CD4+ function is significantly arisen from tissues of all Crohn's pts by TCR/CD3 engagement. Furthermore showing that both CD4+ and CD4 $\{-$  mediated lysis are independent from costimulatory signal. Therefore, the present findings could be of interest because they point out the relevance of activated CD4+ subset with an inflammatory function in the pathogenesis of CD. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Immunology and microbiology: Host defense mechanisms } "Intestinal Cytotoxic CD4+ TH1-Like Cells in Crohn's Disease"

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## "P PP0 0244"PP0 0244 **High Validity of Transabdominal Bowel Sonography for Detection of Complications in Crohn's Disease**

\*C. Gasche, G. Moser, T. Krutt, G. Oberhuber, P. Moeschl

Depts. of Gastroenterology, Pathology and Surgery, Univ. of Vienna, Austria

*Aim:* Transmural bowel inflammation with alteration of the echoarchitecture of the bowel wall and luminal narrowing in Crohn's disease (CD) can be located and visualized by transabdominal bowel sonography (TABS). The significance of these findings has been demonstrated in previous studies regarding the diagnosis of CD (Eur J Gastroent Hepatol 1992, 4: 173–182). Since TABS is a noninvasive, radiation-free method that is well tolerated by the patients, repeated investigations can be easily performed during the follow-up. This study was initiated to investigate the validity of TABS in detection of disease specific complications in CD. *Methods:* Between 1994 and 1996 repeated TABS were performed by two investigators (GC, MG) using 3.5 and 7.5 MHz transducers (Ultramark 9, ATL Inc.) in the follow-up of 213 CD patients. In this study all patients who underwent bowel resection were evaluated (n = 25). The presence and location of intraabdominal fistulas, abscesses or bowel obstruction was assessed by TABS and compared with results obtained by surgery and by histopathology. *Results:* Peri-intestinal hypoechoic lesions were considered to be fistulas and with a diameter > 2 cm to be abscesses. Bowel obstruction was defined by luminal narrowing and evidence of prestenotic dilatation. TABS turned out to have a high validity in detection of such complications: In 14/17 patients, fistulisation was correctly detected by TABS (sensitivity 82%). 7/8 patients were identified to have no fistulas (specificity 88%). Intraabdominal abscesses were detected in 6/6 patients (sensitivity 100%) and excluded in 17/19 patients (89% specificity). Intestinal obstruction was detected in 19/19 and excluded in 6/6 patients (sensitivity and specificity 100%). *Conclusion:* TABS is a valid method to detect specific intraabdominal complications in patients with CD. We therefore recommend TABS for monitoring patients with CD.

Intestinal disorders: IBD diagnosis, monitoring

Radiology and ultrasound: Diagnosis }

"High Validity of Transabdominal Bowel Sonography for Detection of Complications in Crohn's Disease"

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## "P PP0 0245"PP0 0245 Maintenance Therapy May be Discontinued in Ulcerative Colitis Patients in Remission for Over 2 Years with Salicylates

\*S. Ardizzone, V. Imbesi, R. Cerutti<sup>1</sup>, S. Desideri, G. Bianchi Porro

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<sup>1</sup> Bracco S.p.A, Milan, Italy *Aims* To compare the efficacy of a delayed-release 5-ASA (ASACOL) against placebo in patients with ulcerative colitis (UC) in remission and to verify if duration of disease remission affects the relapse rate. *Patients and methods* 112 patients (66 M, mean age 35), with intermittent chronic UC in clinical and endoscopic remission with salicylates for at least one year, were treated in a double-blind, double-dummy, randomized fashion, with 5-ASA (1.2 g/daily) versus placebo (PI), for a follow-up period of one year. Assuming that a minor duration of remission may be associated to higher relapsing risk, the patients were stratified according to the length of their disease remission, in groups (A) (5-ASA 26, PI 35, in remission from 12 to 24 months) and (B) (5-ASA 28, PI 23, in remission over 2 years, median 4 years). Clinical, endoscopic and histologic findings were assessed every 6 months. "End point" of the study was considered the finding of clinical and endoscopic relapse. A Kaplan-Meier life table analysis was used to calculate the relapse rate. Cox model was used to identify predictive factors of relapse. *Results* Fifty-four patients were treated with 5-ASA and 58 with PI. The relapse rate was similar in both groups after 6 months (5-ASA 8/54 (15%), PI 14/58 (24%),  $p = 0.15$ , IC95  $0.23 + 0.05$ ), while a statistically significant difference was found after 12 months of therapy (5-ASA 11/54 (20%), PI 23/58 (40%),  $p = 0.016$  IC95  $-0.35 - 0.02$ ). 5-ASA was significantly more effective than PI in preventing relapse at 12 months in group A (5-ASA 6/26 (23%), PI 17/35 (49%),  $p = 0.037$ , IC95  $\{-\}0.48 - 0.02$ ). In contrast, no statistically significant difference was observed between the two treatments, either at 6 months (5-ASA 3/28 (11%), PI 5/23 (22%),  $p = 0.24$ , IC95  $0.31 - 0.09$ ) or 12 months (5/28 (18%), PI 6/23 (26%),  $p = 0.37$ , IC95  $0.31 - 0.14$ ) of follow up, in group B. Patients in group B are older and have had the disease longer than those in group A. The probability of relapse was independently affected by the 5-ASA treatment and remission duration of disease. In contrast, the relapse rate was not affected by age, sex, age at onset of symptoms, duration of disease, extent of disease, familial aggregation. *Conclusions* This study shows that 5-ASA prophylaxis is really necessary for preventing UC relapses in patients in remission for less than 2 years, and may be discontinued in those with a remission duration longer than 2 years. } "Maintenance Therapy May be Discontinued in Ulcerative Colitis Patients in Remission for Over 2 Years with Salicylates"

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**"P PP0 0246"PP0 0246 Efficacy of 5-ASA Suppositories (Pentasa<sup>®</sup>) 1 g Three Times a Week to Prevent Relapse of Ulcerative Proctitis. A Double Blind, Randomised, Placebo Controlled, Multicentre Trial**

\*P. Marteau, J. Crand, M. Foucault, J.C. Rambaud

Gastroenterology Unit, Saint-Lazare Hospital, Paris

Ferring SA, Gentilly, France The efficacy of daily administration of oral or rectal formulations of 5-aminosalicylic acid (5-ASA) in the prevention of recurrence in patients with ulcerative colitis is well established. *Our aim* was to compare the efficacy of 5-ASA suppositories (Pentasa<sup>®</sup> 1 g, 3 times per week) versus placebo (PI) to maintain remission in patients with cryptogenetic proctitis. *Subjects and methods:* 95 patients (44 M, 51 F, mean age 41 yr.) with cryptogenetic proctitis were randomised immediately after remission (clinical remission + endoscopy score 0 or 1) to receive for 1 year or till relapse 3 suppositories per week of either 1 g 5-ASA or PI. Follow up was performed at 1, 3, 6, 9 and 12 months or in case of relapse. The major end point was the finding of relapse. Data were analysed in intention to treat using ANOVA, Chi<sup>2</sup> tests and Kaplan-Meier life table analysis. In case of relapse, the patients received blindly 1 sup/d till remission. *Results:* comparable demographic and proctitis severity variables existed between the 2 groups. The figure depicts survival curves for time to relapse (log rank:  $p = 0.06$ ). A significant reduction of the recurrence risk was observed for the following time intervals: 0–90 d (19% relapse in the 5-ASA group vs 38%,  $p = 0.035$ ), 0–180 d (29% vs 54%,  $p = 0.017$ ), 0–270 d (38% vs 60%,  $p = 0.031$ ). The risk of recurrence was not influenced by the endoscopy score at entry. Treatment of relapse was significantly better in the group treated with pentasa<sup>®</sup> 1 g/d: 61% of the pts had benefit vs. 8% with PI ( $p = 0.001$ ).

Adverse events were reported in 12% and 10% of the 5-ASA and placebo group respectively.

*Conclusion:* 5-ASA suppositories 1 g 3 times per week are effective for preventing relapses of cryptogenetic proctitis, and well tolerated. Pentasa<sup>®</sup> 1 g/d is effective in the majority of subjects who relapse with the 3 per week schedule. Intestinal disorders: IBD, therapy Clinical practice: Management strategy } "Efficacy of 5-ASA Suppositories (Pentasa<sup>®</sup>) 1 g Three Times a Week to Prevent Relapse of Ulcerative Proctitis. A Double Blind, Randomised, Placebo Controlled, Multicentre Trial"

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"P PP0 0247"PP0 0247 **Gut Permeability Test in Subjects with and without Exercise-Induced Gastrointestinal Symptoms**

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<sup>3</sup> Dept. of Surgery, University of Maastricht, the Netherlands

*Introduction:* Up to 30% of endurance athletes suffer from gastrointestinal symptoms during physical exercise. Splanchnic blood flow drastically decreases during exercise, and may lead to gut hypoxia or ischemia. The aim of this study was to investigate whether the permeability of the gut changes as a result of strenuous exercise. *Methods:* After an overnight fast, 5 well-trained subjects with exercise-induced intestinal symptoms, and 5 well-trained controls ingested a test solution on 3 different occasions; at rest, during a 90 min. running period on a treadmill at 70% of their previously determined Vmax, and 24 h post-exercise, respectively. The test solution consisted of 10 gram lactulose (L) and 1 gram rhamnose (R) in 65 ml water. Before the solution was ingested, the subjects emptied their bladder. Urine was collected for 5 h, and during this period the subjects were not allowed to eat or drink. The L and R excretion was determined by a validated, sensitive, newly developed fluorescent detection HPLC system. Glucose excretion was determined as well. Data are presented as mean – SEM. Statistical analysis was performed by using a two-way ANOVA (time and group). *Results:* During exercise, both the L and the R recoveries were increased, compared to pre- and post-exercise (L: pre = 0.15 – 0.05%, exc. = 0.21 – 0.04% and post = 0.14 – 0.04%, R: pre = 8.9 – 1.2%, exc. = 12.2 – 1.0%, post = 8.4 – 1.0%). R recovery shows a significant difference (p = 0.033) between the three periods. Comparing these periods, no significant difference was found in the L/R ratio. The increase of the R recovery was higher (p = 0.04) in subjects with exercise-induced symptoms. This increase was related to urinary glucose excretion (p = 0.008). *Conclusion:* Alterations in gut permeability seem not to occur during strenuous exercise on a treadmill in our experiment. Rise in rhamnose recovery coincides with an increased glucose excretion. Whether this observation is related to fluid balance differences in these subjects remains to be established. Supported by grants of Sandoz Nutrition and the Dutch Olympic Committee

Intestinal disorders, absorption: Epithelial transport  
Intestinal disorders, absorption: Pathophysiology of diarrhea  
Motility, general: Functional GI disorders }

"Gut Permeability Test in Subjects with and without Exercise-Induced Gastrointestinal Symptoms"

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## "P PP0 0248"PP0 0248 **The Influence of Small Bowel Bacterial Overgrowth in Patients after Total Gastrectomy**

\*R. Brägelmann<sup>1</sup>, U. Armbrecht<sup>2</sup>, D. Rosemeyer<sup>3</sup>, B. Schneider<sup>4</sup>, W. Zilly<sup>5</sup>, R.W. Stockbrügger<sup>1</sup>

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<sup>4</sup> Medizinische Hochschule Hannover

<sup>5</sup> Bad Brückenau *Purpose:* To elucidate whether small bowel bacterial overgrowth (SBBO) after total gastrectomy influences abdominal symptoms, nutrient assimilation, and/or medico-social functioning. *Methods:* 127 consecutive patients (f = 47, m = 80; mean age 56.9 (95% confidence interval (CI) 55.1 to 58.7) years) after potentially curative total gastrectomy for gastric malignancy 573 days earlier (mean; CI 364 to 782) were evaluated for abdominal symptoms (reflux, dysphagia, dyspepsia, early satiety, vomiting, dumping, meteorism), objective signs of malassimilation (haematological and biochemical values, body mass index, weight loss since operation, calorie intake per kg body weight, bowel habits, faecal mass, faecal fat excretion, fat assimilation), Karnofsk index, and the degree of medico-social functioning (Edinburgh Rehabilitation Status Scale, (ERSS), range 0 to 28, best to worst). Patients without SBBO as assessed with a radiographically controlled H<sub>2</sub>-breath test (n = 80) were compared with patients with SBBO (n = 47). *Results:* Mean time since operation was significantly shorter in patients with SBBO (370 days, CI 96 to 645) than in patients without SBBO (687 days, CI 397 to 976) (p < 0.01). Controlling for the difference in the time span since operation, there were no significant differences between the subgroups regarding basic parameters, the haematological and biochemical evaluation, the frequency of abdominal symptoms, the bowel habits, the different factors of nutrient assimilation, and the Karnofski index. However, the mean ERSS on admission was significantly lower in patients without SBBO (3.7 (2.2–5.2)) compared in patients with SBBO (5.1 (3.0–7.0)) (p < 0.05). *Conclusions:* In 127 patients after total gastrectomy, the frequency of SBBO decreased with time past operation. Although patients without SBBO did not differ from patients with SBBO concerning abdominal symptoms, biochemistry, or nutrient assimilation, medico-social functioning is significantly impaired in the latter. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Malabsorption syndromes Oncology, general: Therapy }" "The Influence of Small Bowel Bacterial Overgrowth in Patients after Total Gastrectomy"

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"P PP0 0249"PP0 0249 **B-Cell Primary Gastrointestinal Lymphomas (PGIL) (188 Cases)**

\*P. S\`e1nchez-Fayos, J.M. Castrillo, J. S\`e1nchez Fayos, C. Montalban, A. Gonz\`e1llez Guirado, C. Rivas, J.C. Porres

Dept. of Gastroenterology, Fundaci\`o3n Jim\`e9nez D\`edaz, Universidad Aut\`f3noma of Madrid, Spain  
*Aims.*- To analyse B-PGIL (PGL 143 cases, PIL 45 cases) with the purpose of: 1) differentiate behaviours between themselves and between "low grade" (LG) and "high grade" (HG) forms and 2) identify prognostic factors.  
*Methods.*- 1) Records review; 2) histopathological reclassification after immunophenotyping (Isaacson); 3) staging (Ann Arbor/Musshoff); and 4) conventional statistical analysis ( $X^2$ , log-rank test, etc.).  
*Results.*- The significantly more common features in LG PGL (84 cases) were male sex, infiltrative endoscopic/pathologic aspect and localised stages (IE-IIIE1) and in HG PGL (51 cases) they were weight loss, vegetative endoscopic/pathologic aspect, serosa invasion and an advanced stage (IIE2-IV). The following were favourable prognostic factors: LG character, localised stages, normal LDH, complete surgical resection (cSR) and achieving a complete remission (CR). The significantly more common features in LG PIL (20 cases) were a long pre-diagnostic history, diarrhoea/steatorrhea, finger clubbing, malabsorption, hypoproteinaemia/oedema, multisegment involvement and a nodular radiologic pattern and in HG PIL (25 cases) they were a palpable mass, surgical emergencies, ileo-coecal involvement and a high PC10-positive cell rate. Favourable risk factors were: female sex, normal LDH, unicentric tumour, lowPC10-positive cell rate, use of polychemotherapy (+/{ -} cSR) and achieving a CR.  
*Conclusions.*- B-PGL and B-PIL show different clinico-pathological features between themselves and when compared with their nodal counterparts. The different behaviour of the LG and HG seems to translate unequal biological entities, nonetheless united by the mixed histology forms (LG/HG) which are more proximal to HG in PGL and to LG in PIL. Finally, in the group with PIL a small patient subgroup was discovered suffering a form of lymphoma which resembled the so-called "immunoproliferative small bowel disease".  
Oncology, specific: StomachOncology, specific: Small bowelOncology, specific: Lymphoma } "B-Cell Primary Gastrointestinal Lymphomas (PGIL) (188 Cases)"

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## "P PP0 0250"PP0 0250 **Bone Mineral Density in Adult Coeliac Disease**

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The association between overt coeliac disease (CD) and clinical bone disease has long been recognized. However, evidence is mounting that bone demineralization may occur even in relatively young patients with latent gluten sensitivity. We examined bone mineral density (BMD) and biochemical markers of bone metabolism in a group of otherwise healthy, treated, adult CD patients, and compared these results with those obtained in untreated CD patients. *Subjects and methods:* 36 CD patients (31 F, 5 M) diagnosed in adult life and already established on a gluten free diet participated in the study. The average age of the men was 28.2 yr (range 20–40 yr) and that of the women was 37.9 yr (range 20–74 yr). Thirty-six coeliac patients (30 F, 6 M) who had been recently diagnosed, or who were not receiving a gluten free diet formed the group of newly diagnosed/untreated patients. The average age of the men was 36.5 yr (range 23–65 yr) and that of the women 36.8 yr (range 20–68 yr). BMD of total skeleton was measured by dual energy x-ray absorptiometry (DEXA), and serum and urinary parameters of mineral metabolism (serum and urinary calcium and phosphate, 25-OH vitamin D<sub>3</sub>, alkaline phosphatase, PTH, osteocalcin, and urinary deoxypyridinoline) were determined by standard methods. BMD was expressed both in terms of absolute values (g/cm<sup>2</sup>) and as the Z-score, calculated from age- and sex-matched control subjects. *Results:* 20 out of 36 (55%) asymptomatic CD patients on a gluten free diet had reduced values of BMD, defined as a Z score < { - } 1 SD; of note, severe osteopenia, defined as a BMD > 2 SD below mean normal values for sex and age, was found in 4 young patients (3 F, 1 M) aged 20–26 yr. Overall, reduced BMD was found in 29 out of 36 (80.5%) newly diagnosed/untreated patients; however, while 23 out of 25 (92%) symptomatic patients presented osteopenia, reduced BMD was found only in 6 of 11 (54%) symptomatic patients. No difference in BMD was found between treated and asymptomatic untreated CD patients. Serum and urinary markers of bone metabolism did not show conclusive abnormalities. *Conclusions:* our findings provides evidence that osteopenia is common in adult CD, even in treated asymptomatic patients, and emphasize the importance of early diagnosis and treatment. Intestinal disorders, absorption: Gluten enteropathy }" "Bone Mineral Density in Adult Coeliac Disease"

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**"P PP0 0251"PP0 0251 Evaluation of the Effects of 2 'Spasmolytic' Agents on Gut Motility Using Prolonged Ambulant Small Bowel Manometry (PSBM)X.Y. Qin, D.F. Evans,**

\*D.L. Wingate, S. Allouche<sup>1</sup>

GI Science Research Unit, St. Bart's and the Royal London Medical School, London, UK

<sup>1</sup> Laboratoire Jouveinal, Paris, France Small bowel motility can be evaluated by PSBM during waking and sleeping, during fasting and after food, at rest and under mental or physical stress, and in response to medication; its precision is increased by computer analysis. In the past, PSBM has shown that oral medications do not always have the effects predicted from *in vitro* studies or "bolus" i.v. administration. We have previously shown that the "prokinetic" cisapride does not alter the amplitude and incidence of contractions, and the main action of trimebutine, a gut-selective enkephalinergic agonist, is the preservation of normal motility during exposure to stress. We used PSBM to study the effect of 2 "spasmolytic" medications – alverine citrate 60 mgm and phloroglucinol 80 mgm – on small bowel motility in healthy volunteers. PSBM was carried out twice for 24 hrs in 6 subjects, once with twice daily dosing with one drug, and again with twice daily dosing with the other. After intubation on Day 1 of each study, recording started at mid-day. Subjects were freely ambulant and went home after an evening meal. On Day 2 they were exposed to 2 2-hr periods of mental stressors separated by a 1-hr rest period before extubation. Efficacy of stressors was monitored by serial measurements of heart rate and blood pressure. After computer analysis, motility variables were compared for the 2 drugs against established control values. Stress significantly increased heart rate ( $p < 0.001$ ). Neither agent had any effect on the incidence or amplitude of contractions. No effects of phloroglucinol on any aspect of motor activity were detected. Alverine blocked the effect of stress on migrating motor complexes (MMC) ( $p < 0.05$ ) and on blood pressure ( $p < 0.001$ ); it also blocked ( $p = 0.02$ ) the normal diurnal lengthening of the MMC cycle. These findings are not consistent with an effect of either agent on gut smooth muscle; the effects of alverine are best explained by blockade of the central modulation of gut motility during CNS arousal in waking and under stress. Motility, specific: Small bowel Motility, general: Functional GI disorders Motility, general: Innervation } "Evaluation of the Effects of 2 'Spasmolytic' Agents on Gut Motility Using Prolonged Ambulant Small Bowel Manometry (PSBM)"

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## "P PP0 0252"PP0 0252 **Discrimination of Irritable Bowel Syndrome by Nonlinear Analysis of 24 H Jejunal Motility**

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**Background:** Conventional analysis of ambulatory long-term manometry of the small intestine has revealed an abnormal result in only 43% of patients with the irritable bowel syndrome (Gastroenterology 1995; 108: A605), mainly during phase 2. The aim was to use methods from nonlinear dynamics to discriminate motility in IBS from healthy subjects.

**Methods:** Ambulatory 24 h jejunal motility was obtained with digital data logger and catheter-mounted pressure transducers under standardized caloric intake in 30 diarrhea-predominant IBS patients and 30 controls. The variability and dynamics of the amplitudes of successive phasic contractions during phase 2 was described as a symbolic dynamical system, which means that the dynamics of a system is represented by a sequence of symbols. The sequence was quantified with the entropy, a specific complexity measure, which characterizes the degree of randomness inherent in the time series. For a completely regular process the entropy is 0, for a purely random process the entropy takes the maximum value of 1.

**Results:** Phase 2 motility was characterized by two parameters, the mean value of amplitudes and the entropy. In 19 IBS patients (63%), but only 1 control subject (3%), mean amplitudes exceeding 22 mm Hg and entropies greater than 0.976 were found. Lower contraction amplitudes and entropies > 0.976 were present in 17 controls (57%) and 6 IBS patients (20%). Entropies below 0.976, independent of mean contraction amplitudes, were identified in 12 controls (40%) and 5 patients (17%). A diagnostic accuracy of 80% was obtained.

**Conclusion:** In diarrhea-predominant IBS, phase 2 contractions exhibit a more random dynamics than in healthy subjects. Symbolic dynamics seems to be a promising new method for the analysis of long-term motility data of the small intestine.

Motility, general: Functional GI disorders  
Motility, specific: Small bowel } "Discrimination of Irritable Bowel Syndrome by Nonlinear Analysis of 24 H Jejunal Motility"

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## "P PP0 0253"PP0 0253 Diagnosing Whipple's Disease in Feces

\*M. Gross, Ch. Jung, W.G. Zoller

Medizinische Poliklinik, University of Munich, Germany Whipple's disease is caused by the bacteria *Tropheryma whippelii* that still cannot be cultured. The diagnosis is based on the examination of a duodenal biopsy. Part of the bacterial 16S rRNA gene sequence is known. We investigated the possibility to diagnose Whipple's disease non-invasively by analysing bacterial DNA isolated from feces. DNA was extracted from stool of an untreated patient with Whipple's disease and from 18 healthy control subjects. Since the known sequence of *T. whippelii* shows a high homology to other bacteria, we increased both sensitivity and specificity by performing three subsequent PCRs with nested primers: P52: 5{\a2}-AGA GAT ACG CCC CCC GCA A (position 965 of the TWRG16S sequence in the EMBL GenBank), P53: 5{\a2}-ATT CGC TCC ACC TTG CGA (position 1214), P54: 5{\a2}-CCG CAA CGA GCG CAA CCC TC (1046), P55: 5{\a2}-ACG CGT GAA GCC CAA GAC CG (1163), P56: 5{\a2}-CGT CCT GTG TTG CCA GCG CG (1065), P57: 5{\a2}-CCC AAG ACC GAA GGG GCA TG (1153). The annealing temperatures were 55\b0C (P52-P53), 52\b0C (P54-P55) and 58\b0C (P56-P57). After the third PCR, the product was analysed by gel electrophoresis. A single strong band was visible using DNA extracted from the patient's stool and in 10/18 samples from control subjects. Sequencing the PCR product of the patient resulted in the known *T. whippelii* sequence. In control samples superposing sequences were seen representing DNA from various bacteria. This result shows that Whipple's disease can be diagnosed by detection of DNA of *T. whippelii* in the stool. As long as only part of a highly conserved gene of this bacteria is known, the PCR product has to be sequenced to confirm the diagnosis. However, as soon as more specific sequences of the bacteria are known, the diagnosis can be based on PCR with DNA from stool and subsequent specific tests such as restriction analysis or dot blot tests to exclude amplification of DNA of other bacteria. Intestinal disorders, absorption: Malabsorption syndromes Immunology and microbiology: GI infections in adults }" "Diagnosing Whipple's Disease in Feces"

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**"P PP0 0254"PP0 0254 Multicenter Double Blind Randomized Placebo Controlled Study to Assess the Effect of Sucralfate in Prevention of Acute Enteric Toxicity Secondary to Pelvic Irradiation**A. Valls, I. Pestchen, C. Prats, J. Pera, G. Arag'f3n, M. Vidarte

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Hospital Virgen del Rocío, Sevilla1. *Purpose of the study:* To demonstrate the efficacy of Sucralfate in the prevention of the acute enteric toxicity induced by pelvic irradiation with linear accelerator in patients with primary diagnosis of gynaecologic (cervix and endometrium), prostate or urinary bladder neoplasia, compared with placebo.2. *Methods:* 120 patients (without metastasized neoplasia) between 18 and 80 years old, with a Karnofsky index  $\{ \backslash ' b 3 \}$  80% and usual defecation range (3–10 defecations/week) undergoing whole pelvic irradiation, were included. The whole duration of the study was 7 weeks, following weekly controls. The first week all the patients received placebo. In the second week the patients were randomized into two groups: Sucralfate (61 patients, 2 gr/tid p.o. before meals) and placebo (59 patients). The pelvic radiotherapy started in the beginning of the third week after the patient inclusion and lasted until the end of the study. All patients received 45–50 Gy total dose (1.8–2 Gy/day, 5 days/week) with the ""box technique"". The principal variable was percentage of diarrhoeal stools per week. The statistical analysis of the clinical records was carried out by means of a two way analysis of variance with a repeated measurements design over the principal variable between the groups Sucralfate and placebo.3. *Results:* Intention to treat analysis of the main variable studied showed a statistical significance in favour of Sucralfate vs placebo ( $p = 0.03$ ) concerning the evolution of this study variable from the baseline (first week) to the finalization of the pelvic radiotherapy treatment (seventh week). Per protocol analysis also showed a statistical significance in favor of Sucralfate vs placebo group ( $p < 0.03$ ) in this study variable.4. *Conclusion:* Sucralfate is effective in the prevention of acute enteric toxicity induced by pelvic irradiation with linear accelerator compared to placebo. Intestinal disorders, absorption: Pathophysiology of diarrheaOncology, general: Screening, preventionOncology, general: Therapy }" "Multicenter Double Blind Randomized Placebo Controlled Study to Assess the Effect of Sucralfate in Prevention of Acute Enteric Toxicity Secondary to Pelvic Irradiation"

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## "P PP0 0256"PP0 0256 **Microsatellite Instability in Sporadic Colorectal Carcinomas**

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**Background:** Microsatellite instability (MIN) has been observed in the large majority of tumors from patients with Hereditary Non Polyposis Colorectal Cancer (HNPCC) as well as in 10 to 15% of sporadic colorectal carcinoma (CRC). **Aims:** To evaluate the prevalence of MIN tumors in a series of sporadic CRC as well as to analyse their clinical and pathologic characteristics. **Patients and Methods:** Sixty three patients with sporadic CRC were included in the present study. Mean age was 64 (36–83) years, 36 were male and 27 were female. MIN was detected by evaluating the length of CA repeats sequences at 7 loci: D1S216, D2S118, D3S1611, D5S404, D8S260, D17S783, D22S282. DNA was amplified in a radioactive PCR, the products were run in a 6% polyacrylamide denaturing gel and autoradiography was performed. MIN was defined as the presence of an extra band in one or in the two alleles in DNA from tumor as compared to DNA from normal colonic mucosa. **Results:** MIN in one or more loci was found in 15 (24%) patients, while 7 (11%) patients displayed MIN in at least 2 markers. We found that among patients with MIN+ tumors, familial history was more prevalent (33% vs 11%) although not significantly and these tumors were more frequently located on the right side of the colon ( $P = 0.01$ ). From a pathological point of view, MIN+ tumors were more frequently mucinous (29% vs 17%) and a higher percentage of them presented at an earlier stage (TNM staging stage II: 57% vs 30%). When considering solely patients with right sided neoplasms, the differences were even more striking. Patients with MIN+ tumors were younger (59 – 11.4 vs 70 – 8.5); familial history was found in 50% of the cases as compared to 0% in patients with MIN- tumors. Also, right sided MIN- tumors relapsed in 50% cases but no relapses were detected in those MIN+. **Conclusions:** MIN seems to identify a subset of patients in whom familial history is more prevalent, tumors are more frequently located on the right colon and despite a more aggressive morphology, they seem to have a better prognosis. Mutation analysis of the mismatch repair genes are needed to elucidate whether these patients are part of the HNPCC syndrome. **Oncology, general:** Proliferation, carcinogenesis **Oncology, specific:** Colon, rectum }"  
"Microsatellite Instability in Sporadic Colorectal Carcinomas"

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"P PP0 0259"PP0 0259 **Non Specific Anal and Complex Fistulae: Results of MRI in the Diagnosis and Follow-Up**J.P. Grandjean,

\*L. Henry, O. Daville, O. Tissot, B. Milox, H. Damon, P.J. Valette

Clinique Sainte Marie Th\`e9rése, 1 rue Laborde 69500, Bron, France *Purpose:* to assess the interest of MRI in the surgical management of problematical anal fistulae in ano and in the follow-up of the cases treated by long term seton drainage with two or three stage fistulotomy. *Method:* (1) 24 patients, crohn disease excluded, with recurrent high trans-sphincteric or supra-sphincteric fistula (n = 13) and/or important anal or rectal sclerosis (n = 11) and/or active suppuration (n = 5) were prospectively assessed with MRI before treatment [*pre-op MRI*]. Surgery consisted in excision (n = 24) eventually completed by fistulotomy and long term seton drainage (n = 14). (2) In the later cases a second MRI [*post-op MRI*] was systematically performed in order to assess the result of the drainage (n = 14). (3) Long term (> 6 months) overall results were obtained in 20 patients (18 month mean follow-up). *Results:* (1) [*pre-op MRI*]: the systematic comparison with surgical findings showed an overall accuracy of 84% for the visualization of internal opening, primary and secondary tracts, and 100% for the detection of horse-shoe fistula tracts (7/7) (2) [*post-op MRI*]: in 5 cases, MRI modified the planed treatment indicating the necessity of a prolonged seton drainage or a new surgical excision by demonstrating the evidence of persistant infection. (3) Long term clinical follow-up showed no evidence of recurrence for 19/20 patients (96%) *Conclusion:* MRI accurately demonstrates the extension of high complex fistulae in ano and is helpfull to assess the healing in cases treated with seton drainage and two or three stage fistulotomy. Therefore it appears to be usefull in the conservative surgical management of fistulae in ano. Intestinal disorders: Anorectal disorders Radiology and ultrasound: Diagnosis }" "Non Specific Anal and Complex Fistulae: Results of MRI in the Diagnosis and Follow-Up"

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**"P PP0 0260"PP0 0260 Immunohistochemical Study About the Neuronal Intestinal Dysplasia Type B in Whole Mounts of the Human ColonH.-J. Krammer,**

\*F. Krieger, W. Meier-Ruge<sup>1</sup>, M.V. Singer

Dept. of Med. IV, Univ. Hosp. of Heidelberg at Mannheim, Germany

<sup>1</sup> Dept. of Pathology, Univ. of Basel, Switzerland Neuronal intestinal dysplasia (NID) is well known, but its definition is a topic of debate. The histopathological diagnosis of NID is based on traditional enzyme-histochemical methods such as the acetylcholinesterase and lactate-dehydrogenase reaction on native sections. In this study, we have investigated the enteric nervous system in whole-mount preparations of resected intestinal segments affected by NID of the plexus submucosus (type B). The plexuses of the tunica mucosa and tunica submucosa were visualized by immunohistochemical methods using a polyclonal antibody to protein gene product 9.5 (PGP 9.5). PGP 9.5 is a novel general cytoplasmatic marker specific for the nervous system. The morphology of the plexuses is revealed in full, making possible changes easily discernible. Known pathological findings of the NID can be identified and judged more precisely with this method. Numerous enlarged nerve trunks run within the tunica submucosa and tunica mucosa. Hyperplastic ganglia with an unusually high nerve cell number in the tunica submucosa can be demonstrated as well as heterotopic nerve cells in the tunica mucosa. In the present study is shown that PGP 9.5 immunostaining overcomes many problems observed with other neuronal and glial markers. It has been possible to demonstrate the histopathological features of NID with PGP 9.5 in whole mount preparations. Sponsored by DFG Kr 1257/2-1 Motility, general: Innervation Motility, specific: Colon, anorectum } "Immunohistochemical Study About the Neuronal Intestinal Dysplasia Type B in Whole Mounts of the Human Colon"

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## "P PP0 0262"PP0 0262 A Comparison of Lansoprazole and Placebo in the Prevention and Treatment of Ulcers Induced by Oesophageal Varices Sclerotherapy (O.V.S.)

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**Introduction:** O.V.S. may result in ulcers which may cause severe bleeding or delay further sclerosant injection. A study was conducted to determine if lansoprazole could prevent ulcers or accelerate their healing.

**Methods:** 98 cirrhotic patients with active (n = 74) or recent (n = 24) variceal haemorrhage and starting an O.V.S. protocol (sessions performed on days 1, 7, 14, 28, 49 and 70 with 10–70 cc of 1% polidocanol) were randomly allocated to lansoprazole 30 mg o.a.d. (gp 1, n = 50) or placebo (gp 2, n = 48) in a double-blind 70-day study. At each session, ulcers severity was assessed by a 1–5 index taking into account height and oesophageal circumference. It was planned to compare the % of patients with at least one ulcer of index  $\geq 2$ , D14 being the main endpoint. The biological safety was assessed at each session.

**Results:** The two groups were comparable for age, sex, Child's score, % of active bleeding at inclusion and total dose of injected sclerosant at each visit. 39 patients (19 in gp 1 and 20 in gp 2) were withdrawn before D70 mainly due to complications of the underlying disease. % of patients with at least one ulcer of index  $\geq 2$  on D14 were 31.7% (13/41) in gp 1 and 23.1% (9/39) in gp 2 (p = 0.38). At D7 this criteria was: gp 1 = 0% (0/45) vs gp 2 = 14.6% (6/41); p = 0.008. At D28, D49 and D70 no significant difference was found between groups. 12 and 14 severe adverse events were declared in groups 1 and 2 respectively. One of them was related to treatment in each group (2 cases of ulcer bleeding). For each liver and kidney function test, % of patients with a clinically relevant change was similar in the two groups. 6/33 (gp 1) and 3/30 (gp 2) patients had a gastrin level  $> 2$  N at the end of the treatment.

**Conclusion:** Anti-secretory treatment is not likely to prevent or accelerate healing of O.V.S.-induced ulcers after the 2nd sclerosis session. In cirrhotics, clinical and biological safety of lansoprazole was excellent. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy Endoscopy, general: Complications } "A Comparison of

Lansoprazole and Placebo in the Prevention and Treatment of Ulcers Induced by œSophageal Varices Sclerotherapy (O.V.S.)"

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"P PP0 0264"PP0 0264 **Percutaneous Microwave Coagulation Therapy for Liver Cancer**

\*T. Seki, T. Nakagawa, M. Wakabayashi, M. Imamura, T. Tamai, A. Nishimura, K. Inoue

The Third Dept. of Internal Medicine Kansai Medical University, Osaka 570, Japan *Aim:* Percutaneous ethanol injection therapy (PEIT) is widely performed as a percutaneous local treatment for liver cancer. It has been reported by many that the effects of PEIT were satisfactory. However, PEIT is occasionally ineffective for intracapsular or extracapsular invasion of cancer cells. In some cases, injected ethanol flows into the vessels around the tumors, instead of causing tumor necrosis. There is therefore a need for a more effective technique to destroying liver cancer. We designed ultrasonically guided percutaneous microwave coagulation therapy (PMCT) as a new method of percutaneous local treatment for liver cancer. In this presentation, we introduce the technique of PMCT and report the effect of PMCT comparing with that of PEIT for liver cancer. *Subjects and Method:* Percutaneous local treatments were performed for the 94 patients having a single liver cancer (tumor size  $\leq 3$  cm) between Ja. 1990 and Ap. 1996. There were 46 patients treated by PMCT alone (Group M) and 48 who were treated by PEIT alone (Group E). The microwave electrode (2.0 mm in thickness, 25 cm in length) was inserted through a guide needle (13G) to be placed in the tumor area which was then irradiated with microwave. PEIT was performed conventionally with a 21G-fine needle. The therapeutic results of these two groups were evaluated on the basis of survival rate, disease free survival rate, pattern of recurrences, and kind of re-treatment for recurrent cases. *Results:* For Group M and E, the 5 yr-survival rates (4 yr-disease free survival rate) were 62% (39%) and 30% (17%), respectively. The recurrent rate of Group M and Group E at treated subsegment area within one year after treatment was 4% (2 cases) and 13% (6 cases), respectively. In recurrent cases of Group M and E, TAE was performed for 3 cases and for 8 cases, respectively. *Conclusion:* Compared with PEIT, PMCT is an effective for liver cancer in producing local necrosis. *Oncology, general: Therapy* *Oncology, specific: Liver, biliary* *Radiology and ultrasound: Therapy* } "Percutaneous Microwave Coagulation Therapy for Liver Cancer"

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**"P PP0 0265"PP0 0265 Long Term Ganciclovir Therapy for Hepatitis B Virus Infection after Liver TransplantationB. Roche,**

\*D. Samuel, C. F\`e9ray, M. Gigou, M.F. David, M. Reynes, H. Bismuth

Hepato-Biliary and Liver Transplantation Center, Paul Brousse Hospital, Villejuif, FranceHBV infection of liver graft is characterized by a severe outcome leading to graft failure and is associated with high level of HBV replication. It has been suggested that GANCICLOVIR (Roche-Syntex, USA) is active against HBV. We have studied the efficacy of long term IV GANCICLOVIR therapy for HBV infection on liver graft. 17 patients (pts): 12 with HBV reinfection and 5 with de novo HBV infection were studied. HBV DNA was positive in all pts, HBeAg in 8. Pts received IV GANCICLOVIR 10 mg/kg/day for 14 days, 5 mg/kg/day for 30 days then 5 mg/kg 3 to 5 times a week for a mean of 8.6 months (0.5–34). HBsAg and HBV DNA (Digene Hybrid Capture System; Murex, France), were tested for every month. At time of onset of treatment, mean HBV DNA titer was 756 pg/ml (12–2000), liver graft histology showed no specific changes (n = 1), acute hepatitis (n = 5), chronic active hepatitis (n = 8), cirrhosis (n = 3). GANCICLOVIR was well tolerated. During therapy, HBV DNA negativation (complete response (CR)) was observed in 11 pts, decrease of more than 50% of initial HBV DNA values (partial response) in 3 and absence of response in 3. Among the 11 complete responders, 4 pts relapsed under (n = 3) or after (n = 1) therapy. This last pt presented a CR after a second course of GANCICLOVIR. HBsAg clearance occurred in 3 pts. A dramatic clinical improvement was observed in 4 pts. Last histology showed cirrhosis in 6 pts, CAH in 3 and submassive hepatitis in 2 who were retransplanted. One pt died from variceal rupture. Among the 3 partial responders, none died or was retransplanted, last histology showed cirrhosis in 2 and CAH in 1. Among the 3 non responders, 1 was retransplanted for HBV related graft failure and 2 developed chronic active hepatitis.*Conclusion:* GANCICLOVIR is effective to inhibit HBV replication after LT and is well tolerated. Despite HBV DNA negativation and clinical improvement, an histological deterioration may be observed. }" "Long Term Ganciclovir Therapy for Hepatitis B Virus Infection after Liver Transplantation"

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**"P PP0 0266"PP0 0266 Prevention of Hepatitis B Reinfection after Liver Transplantation by Post Transplant Long-Term Administration of Ganciclovir IV and Anti-HBs Immunoprophylaxis in Patients at High Risk of Viral RecurrenceB. Roche,**

\*D. Samuel, C. F'eyray, M. Gigou, J.L. Arulnaden, M.F. David, A. Bismuth, M. Reynes, H. Bismuth

Hepato-Biliary and Liver Transplantation Center, Paul Brousse Hospital, Villejuif, FranceThe risk of HBV recurrence after liver transplantation (LT) is high in patients (pts) with HBV replication despite use of long-term anti-HBs immunoprophylaxis even associated with preLT Interferon (IFN). The aim of this study was, in HBV DNA positive pts, to associate pretransplant antiviral therapy with post-LT long-term administration of anti-HBs immunoglobulins and GANCICLOVIR IV (Roche-Syntex, USA). 9 pts (8 M, 1 F, mean age 45.8 yrs), HBs Ag and HBV DNA positive were included. The initial diagnosis was: HBV recurrence on first graft (4), acquired HBV infection post-transplant (1), HBV cirrhosis (3), and subacute HBV hepatitis (1). Each patient received antiviral therapy prior to LT: ARA AMP then GANCICLOVIR (4), GANCICLOVIR (2), IFN (2), ARA AMP then IFN (1). After LT, all pts received long-term anti-HBs immuno-prophylaxis to achieve anti-HBs Ab titer above 500 IU/l and IV GANCICLOVIR 10 mg/kg/d for 2 weeks then 5 mg/kg 3 times/week for a mean of 11.9 months (3–24). HBsAg was tested every month, HBV DNA (Digene Hybrid Capture System, Murex, France) was detected every 3 months. Pre-LT negativation of HBV DNA occurred in 7/9 pts, a mean of 2.7 months before LT. After LT, recurrent HBV infection was diagnosed in 1 pt at 3 months which leads to cirrhosis on the graft. 8 pts remained HBs Ag and HBV DNA negative – a mean of 20.5 months (11–36) after LT. Graft histology was available in 7 pts at 1 year and was normal. Tissue antigen detection of HBsAg and HBcAg was negative. One pt died at 2 years of carcinoma unrelated to HBV infection.*Conclusion:* This open study demonstrates the efficacy of a combination of post-transplant long-term anti-HBs immunoprophylaxis and IV GANCICLOVIR in pts at high risk of HBV recurrence. }" "Prevention of Hepatitis B Reinfection after Liver Transplantation by Post Transplant Long-Term Administration of Ganciclovir IV and Anti-HBs Immunoprophylaxis in Patients at High Risk of Viral Recurre"

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## "P PP0 0267"PP0 0267 Hepatitis G Virus Infection in France: Preliminary Epidemiologic Data and Analysis of Viral Tropism

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INSERM U271, Lyon, France

*Goal:* The two main goals of the present study are: 1) to evaluate the prevalence of the newly discovered hepatitis GB virus type C (GBV-C) in different groups of French patients 2) to analyze, in the patient group displaying the highest prevalence, the cellular tropism of GBV-C viruses.

*Methods:* Prevalence of infection was assessed by means of RT-PCR-amplification of viral sequences from the NS3 region (nested amplification) using degenerated primers (adapted from Simons et al., Nature Medicine 1995) as well as using non-degenerated primers from the 5' non-coding region (single PCR followed by Southern Blot detection). The following samples, obtained from 10 positive patients are being analyzed for the presence of both the positive and negative strand viral RNA: 1) sera, 2) liver biopsies, 3) PBMC (peripheral blood mononuclear cells) 4) T and B cells and 5) monocyte/macrophages. PBMC cellular subpopulations have been purified using specific monoclonal antibodies after immunomagnetic separation. Techniques for the detection of either genomic sequences have been validated, both quantitatively and qualitatively, using synthetic templates.

*Results:* NS3-derived GBV-C sequences were detected in 36% (23:64), 21% (4:19), 15% (3:20) and 5% (3:59) of respectively IVDU (all co-infected with hepatitis C virus (HCV)), Hemophiliacs, HCV chronic carriers and non-A, non-E hepatitis patients (all with sustained elevated ALT). Detection of viral sequences using 5' NCR-derived primers was less efficient, since only 81% of patients positive using the NS3-based PCR were detected with this assay.

*Conclusions:* Prevalence of GBV-C virus appears the highest when associated with parenteral transmission, in particular in HCV-co-infected populations while prevalence of infection is very minor in cases of hepatitis from unknown etiology. Data will be presented on the cellular tropism of GBV-C viruses in the different cell populations indicated above. Clinical practice: Epidemiology (non cancer)Liver and bile ducts, 1: Hepatitis viral, diagnosis }

"Hepatitis G Virus Infection in France: Preliminary Epidemiologic Data and Analysis of Viral Tropism"

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## "P PP0 0268"PP0 0268 **HGV (GB-C) and HCV Coinfections in French Intravenous Drug Users: Prevalence and Histological Impact**

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<sup>3</sup> Hepatology Unit, Necker Hospital Paris France We have analyzed 77 anti-HCV positive intravenous drug users (IVDU) to 1) define on a large series the actual prevalence of HGV (GB-C) coinfections in this population and 2) evaluate the impact of these coinfections on liver biological tests and histology. *Patients and methods:* 77 anti-HCV positive French IVDU (63 males and 14 females), aged 32 – 5 years, including 24 anti-HIV positive. Serum HCV RNA was tested by PCR in 5{\a2}NCR and HGV (GB-C) RNA was tested by PCR with NS3 (GB-C) and NS5 (HGV) sequences. *Results:HCV:* HCV RNA was detected in 67/77 and HCV typing showed genotypes 1a (22), 1b (9), 3a (16) and 4/5 (15). *HGV (GB-C):* HGV (GB-C) RNA was detected in 16/77 (20.7%), 14 males and 2 women. Four of these 16 were infected by HIV. HGV (GB-C) RNA positive and negative individuals showed similar duration of drug abuse (11.5 and 10.2 years, respectively). There was no significant differences between HGV (GB-C) RNA positive and negative patients for ALAT/AST and GGT levels nor histology Knodell scores (5.1 – 3.2 vs. 5.2 – 3.2) (NS), respectively. Finally HCV genotypes distribution did not differ in the 2 groups. *Conclusions:* Our study 1) demonstrates a high prevalence of HCV/HGV (GB-C) coinfections in French IVDU, whether or not coinfecting by HIV1 and 2) shows no evidence for worsening of liver lesions due to these coinfections. Liver and bile ducts, 1: Hepatitis viral, diagnosis }

"HGV (GB-C) and HCV Coinfections in French Intravenous Drug Users: Prevalence and Histological Impact"

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"P PP0 0269"PP0 0269 **Is Interferon Alpha Atherogenic?** P. Kuder, A. Abergel, P. Jouanel<sup>1</sup>, C. Bonny, J. Boulant, C. Henquell<sup>2</sup>, H. Brun, H. Lafeuille<sup>2</sup>, M. Dapoigny, G. Bommelaer

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<sup>2</sup> Laboratoire de Virologie, Clermont Ferrand Interferon- $\alpha$  (IFN) is the treatment of choice for Chronic Hepatitis C (CHC). Recent report has suggested that serum triglycerides (TG), cholesterol (XOL), cardiac risk indexes (XOL-LDL/XOL-HDL, Apo B/Apo A1) increased during IFN therapy (Malaguarnera M., *Hepatology* 1995, A50). *Aim:* This study was performed to determine the effect of IFN on serum TG, XOL, XOL-HDL, XOL-LDL, Apo A1 and Apo B in adults with CHC. *Methods:* 33 patients were evaluated (mean age 48 + 2.8 years; 46% were male). All had (+) anti-HCV by third generation antibody assay and RIBA-4, ({} -) serologies for all other causes of chronic hepatitis, and liver histology compatible with CHC. All patients were treated with 3–6 MU of IFN TIW for six months. The following parameters were determined and monitored using routine laboratory tests before and during treatment (3 to 6 months): Serum XOL, TG, XOL-HDL. XOL-LDL was determined by Friedwald's formula; Apo A1 and Apo B using the nephelometric method. The Apo B/Apo A1, XOL-LDL/XOL-HDL ratios were considered. Statistical analysis was conducted using Student's test for paired data. *Results:* Mean serum Apo A1 and HDL decreased from respectively 1.30 – 0.2 g/l to 1.11 – 0.18 g/l ( $p < 0.001$ ) and 1.26 – 0.3 mmol/l to 1.02 – 0.22 mmol/l ( $p < 0.001$ ). No statistical difference was found for serum Apo B, XOL, XOL-LDL. Mean serum TG increased from 1.11 – 0.50 to 1.93 – 2.8 mmol/l ( $p = 0.06$  NS). Apo B/Apo A1 and XOL-LDL/XOL-HDL cardiac risk indexes increased respectively from 0.71 – 0.26 to 0.85 – 0.24 ( $p < 0.005$ ) and from 2.63 – 1.1 to 3.1 – 1.1 ( $p < 0.005$ ). *Conclusion:* 1) Serum TG increase and Apo A1 decrease during IFN therapy, the mechanism of which is unknown. 2) Three hypothesis should be explored: A) *inhibition of endothelial lipolysis by reduction of lipoprotein-lipase (LPL) activity.* A) *an increase of TG hepatic synthesis by IFN and/or C) a decrease of Apo A1 hepatic synthesis* 4) *In the future patients with basal increase of cardiac risk index must be considered carefully regarding IFN therapy.* Liver and bile ducts, 1: Hepatitis, viral, treatment Nutrition: Metabolism } "Is Interferon Alpha Atherogenic?"

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"P PP0 0272"PP0 0272 **Can Preoperative Variables Predict Symptomatic Outcome after Cholecystectomy?**I.B. Andersen, L. Bardram, L. Borly, E. Christensen, H. Kehlet, L. Paloheimo,

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Cholecystectomy for symptomatic gallstone disease results in pain relief in most of the patients, but for 20–30% abdominal pain is present also after the operation, as the so-called postcholecystectomy syndrome. *The aim* of this study was to investigate whether preoperative variables could predict the symptomatic outcome after cholecystectomy. *Methods*: 102 patients were referred to elective cholecystectomy in a two year prospective study. Median age was 45 years, range 20–81. A preoperative questionnaire on pain, symptoms, history etc. was completed, and the questions on pain and symptoms were repeated postoperatively after 6 weeks and one year. Preoperative cholecintigraphy and sonography evaluated gallbladder motility, gallstones and gallbladder volume. CCK-profile was measured after meal stimulation. Bile, gallbladder and stones were analysed after the operation. Preoperative variables in patients with or without pain were compared statistically and significant variables were combined in a logistic regression model to predict the postoperative outcome. *Results*: 80 patients completed all questionnaires. Of the 80 patients 21 had abdominal pain after the operation, whereas 59 had no pain postoperatively. Patients with pain one year after cholecystectomy were characterized by preoperative presence of a high dyspepsia score, "irritating" abdominal pain and an introvert personality. Further by absence of "agonizing" pain and absence of symptoms coinciding with pain.  $\chi^2 = 47$ , d.f. 5,  $p < 0.000001$ . Of 18 patients predicted as having postoperative pain, 15 had this (PV<sub>pos</sub> = 0.83). Of 62 patients predicted as having no pain postoperatively, 56 had this (PV<sub>neg</sub> = 0.90). Overall 88.7% of the patients were classified correctly according to this reclassification. *Conclusion*: In this prospective study on postoperative outcome after cholecystectomy preoperative symptoms were able to predict abdominal pain after cholecystectomy. Since reclassification gives too optimistic results, the model should be validated in independent patients. } "Can Preoperative Variables Predict Symptomatic Outcome after Cholecystectomy?"

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## "P PP0 0274"PP0 0274 A New Multimodal Therapy to Extend the Resectability of Advanced Klatskin-Tumors

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*Therapeutic concept and aim of the study:* 1. Endoscopic decompression of the tumorfree lobe of the liver by internal drainage. 2. Embolisation of the tumor-invaded lobe of the liver for its degeneration and at the same time compensatory hyperplasia of the tumorfree part of the liver. 3. Hemihepatectomy of the embolised part of the liver.

*Material and Methods:* In this prospective randomised study 12 patients with primary inoperable Klatskin-tumors of the classification III of Bismuth were included. The mean age of the patients was 61 years, 4 male, 8 female. In 6 patients initially due to a filiforme tumorstenosis on both sides with obstructive jaundice an endoscopic decompression of tumorfree parts of the liver by endoscopic drainage was indicated. In all 12 patients preoperatively an embolisation was performed. 4 to 12 coils with a diameter up to 5 mm with a length of 35 to 55 mm were used. Pre- and post embolisation the volume of the whole liver and of the left lobe of the liver was measured with spiral computed tomography.

*Results:* In 6 out of 12 patients existed a highgrade obstructive jaundice due to tumorgrowth. As first step of therapy in these patients an internal drainage in tumorfree areas of the liver lobe contralateral to the lobe with the main tumor mass could be placed successfully. In those as well as the 6 without obstructive jaundice an embolisation of the liver lobe with the main tumor mass was performed, thereof 11 arterial, 1 venous via portal vein. 11 of the 12 patients in the mean after 44 days (min 27 – max 75 days) underwent abdominal surgery: 9 patients could be hemihepatectomised after embolisation. Volumetric follow-up observations with imaging techniques showed in the following weeks a reduction of the tumor infiltrated liver lobe of 10% (min 2 – max 33%) and an augmentation of the drained resp. tumorfree liver lobe of 37% (min 11 – max 68%).

*Conclusions:* The first results of our study demonstrate that primary technical inoperable Klatskin-tumors can be changed to a status for resective surgery. This is possible by preoperative decompression of the lobe that will be preserved and embolisation of the contralateral tumor invaded liver lobe that will be resected.

*Clinical practice:* Management strategy Oncology, specific: Liver, biliary Endoscopy, specific: Biliary }

"A New Multimodal Therapy to Extend the Resectability of Advanced Klatskin-Tumors"

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## "P PP0 0277"PP0 0277 Transforming Growth Factor $\beta$ 1 (TGF $\beta$ 1) and Epidermal Growth Factor (EGF) in Caerulein-Induced Pancreatitis in Rat

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<sup>1</sup> Inst. Physiol. Jagiell. Univ. Med. Sch. Krakow, Poland **Background:** TGF $\beta$ 1 is considered as the multifunctional cytokine which modulates the expression of several constituents of extracellular matrix (ECM) resulting in the formation of fibrosis and tissue repair. EGF was shown to promote cellular growth and the regeneration of pancreatic tissue but the influence of TGF $\beta$ 1 and EGF on the course of acute pancreatitis has not been studied. In the present study we investigated the changes TGF $\beta$ 1 and EGF gene expression as well DNA synthesis, pancreatic blood flow (PBF), protein content and plasma amylase concentration in the course of hormonally induced acute pancreatitis. **Methods:** Wistar rats weighing 200–250 g were infused with supramaximal dose of caerulein (10 mg/kg/h s.c.) for 5 h to induce pancreatitis. Rats infused with saline served as a control. Animals were killed at 1, 2, 3, 4 and 5 h after the start of infusion. The PBF was measured using laser Doppler flowmeter and blood was collected to determine serum amylase concentration. The pancreatic tissue was removed and biopsy samples were taken for measurement of the protein content, DNA synthesis (by incorporation of <sup>3</sup>H thymidine) and histological assessment of pancreatitis. Expression of TGF $\beta$ 1 and EGF mRNA was studied by reverse-transcriptase polymerase chain reaction (RT-PCR) and assessed semiquantitatively as undetectable (–), minimally expressed (+) or strongly expressed (++).

**Results:** Caerulein infused at 1, 2, 3, 4 and 5 h caused a time-dependent decrease in DNA synthesis as compared to vehicle-controls, by 11%, 15%, 45%, 49%, and 54%, respectively. This was accompanied by gradual decrease of PBF by 29%, 36%, 43%, 50%, and by 54% respectively, and a significant increase in pancreatic weight reaching after 3–5 h, 157%, 163% and 173% of control value, respectively. The protein content and plasma amylase concentration showed progressive increase with the peak achieved after 5 h of cerulein infusion. Histology revealed oedema of pancreatic tissue, strong cell vacuolisation and prominent leukocyte infiltration starting after 3 of caerulein infusion. Following the development of pancreatitis, TGF $\beta$ 1 mRNA was strongly expressed at each time interval beginning from the 1 h after the start of cerulein infusion. By contrast, EGF mRNA was first detected at 5 h after induction of pancreatitis. **Conclusions:** 1) During the development of pancreatitis is observed an inhibition of pancreatic tissue growth and PBF accompanied by enhanced expression of TGF $\beta$ 1. 2) The expression of EGF at the end of the pancreatitis development may indicate the initiation of pancreatic repair. 3) TGF $\beta$ 1 seems to lead to sequential induction of EGF that stimulates the regeneration of injured pancreas.

**Pancreas: Pancreatitis experimental**  
**Hormones and receptors: Growth factors** } "Transforming Growth Factor  $\beta$ 1 (TGF $\beta$ 1) and Epidermal Growth Factor (EGF) in Caerulein-Induced Pancreatitis in Rat"

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## "P PP0 0278"PP0 0278 The Role of TGF- $\beta$ 1 and IL-6 in Pancreas Regeneration

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Some reports suggest that low doses of cholecystokinin octapeptide (CCK-8) promote the regeneration of the pancreas. We aimed to investigate whether changes occur in the serum TGF- $\beta$ 1 and IL-6 levels during the regeneration, and whether there is a connection between their levels and the rate of regeneration in rats. *Methods.* Distal pancreas resection (75%) was performed. CCK-8 was administered subcutaneously in a dose of 250 ng/kg 3 times per day to the investigated group, while the control animals received the same amount of saline. The rats were examined 3, 7, 14 and 28 days after the first injection. Serum TGF- $\beta$ 1 levels were determined by ELISA, IL-6 levels by bioassay, DNA content by Giles & Meyers method. *Results.* The weights of the residual pancreas were increased in both groups on day 3. At subsequent times the weights decreased in the controls but increased continuously in the CCK-8-treated group. There was significant difference between the two groups on day 14. The pancreas weight almost doubled in the CCK-8 group, whereas it decreased to the normal level in the controls on day 28. The DNA contents of the pancreas were higher in the treated than in the control group, but the difference proved to be significant only on day 28 (1800 – 350 vs. 780 – 240 { g}/pancreas). The protein content reached its highest level on day 28 in the CCK-8-treated group, but the levels did not differ significantly to those of controls. A significantly higher level of IL-6 was measured on day 7 vs. the control (250 – 70 vs. 50 – 30 pg/ml). Significantly different TGF- $\beta$ 1 levels were measured in the treated group on day 7 and 14 (290 – 40 vs. 275 – 10 vs. 180 – 65 ng/ml, respectively). Both cytokines returned to the normal level by day 28. No significant changes in the amylase levels were observed; they remained at a normal level (4.8 – 0.8 U/ml). This indicates that the increase in the pancreas weight was not caused by pancreatitis. *Conclusion.* Our results reveal that regular low dose of CCK-8 resulted in pancreas regeneration following 75% distal resection. This was indicated by increases in the pancreas weight, and in the DNA and protein contents of the pancreas. Significantly elevated serum TGF- $\beta$ 1 and IL-6 levels were also detected up to day 14. These data suggest that TGF- $\beta$ 1 and IL-6 might play a stimulatory effect in the process of pancreas regeneration. This work was supported by grants from the National Scientific Research Fund (T-017235) and the Ministry of Social Welfare 609/1993/02. Pancreas: Secretion, regulation Pancreas: Pancreatitis experimental } "The Role of TGF- $\beta$ 1 and IL-6 in Pancreas Regeneration"

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"P PP0 0282"PP0 0282 **RET Proto-Oncogene and Endothelin B Receptor (EDNRB) Gene Mutation in Hirschsprung Disease**

\*R. Salomon, J. Amiel, T. Atti, A. Munnich, S. Lyonnet, C. Ricour, Nihoul C. F.

Hospital des Enfants Malades, 149 rue de Sévres 75743 Paris Cedex 15 Hirschsprung disease (HSCR) is a common congenital malformation, regarded as a multigenic neurocristopathy. Two susceptibility loci have been identified in HSCR namely the *RET* proto-oncogene and the endothelin B receptor (*EDNRB*) gene. We have studied the prevalence of the *RET* and *EDNRB* mutations in a large series of HSCR patients. The mutations were detected by a combination of denaturing gradient gel electrophoresis (DGGE) and single strand conformation polymorphism (SSCP), after extraction of the DNA from blood samples. Mutant genotypes at the *RET* locus were identified in 50% of the familial forms as compared to 17% in sporadic cases, with a large proportion of *de novo* mutations. Regarding the length of the aganglionic segment, we found no phenotype-genotype correlation. Finally the penetrance of *RET* mutant alleles in familial HSCR was significantly higher in males (72%) than in females (51%). On the other hand, homozygous mutations of the *EDNRB* gene have been identified in consanguineous HSCR families presenting with other malformations of neural-crest derived cells (Shah-Waardenburg syndrome). In our series, we have identified heterozygous *EDNRB* mutations in only 4 isolated HSCR patients. Thus, genetic heterogeneity of HSCR is confirmed by the presence of mutations on *RET* and *EDNRB* gene, with a higher frequency for *RET* mutants. However, the mutations of *RET* and *EDNRB* account for a minority of the patients studied. While mutations in the non coding regions of *RET* and *EDNRB* have not yet been studied, our data suggest that other genes are involved in HSCR. Motility, general: Innervation Motility, specific: Colon, anorectum } "RET Proto-Oncogene and Endothelin B Receptor (EDNRB) Gene Mutation in Hirschsprung Disease"

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## "P PP0 0283"PP0 0283 **Overexpression of ICAM-1, VCAM-1 and ELAM-1 in Colorectal Carcinomas**

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<sup>1</sup> Dept. of Medicine and Biological Chemistry, University of California, Irvine, USA *Purpose of the Study:* The pathogenesis of colorectal cancer and the mechanisms which contribute to metastases are still poorly understood. Adhesion molecules are cell-surface-bound glycoproteins which are important in cell-to-cell attachment. Changes in the expression of adhesion molecules may increase the risk for local invasion and hematogenous metastases of colonic cancer cells. *Patients and Methods:* Cancerous tissue samples were obtained from 5 female and 19 male patients with a mean age of 67 years (range 46–84 years) undergoing colonic resection due to carcinoma of the colon or rectum. Tumors were classified according to the TNM-system (UICC): 5 stage I, 10 stage II, 1 stage III and 8 stage IV. Normal colonic tissues from the same patients served as controls. Tissues destined for RNA extraction were frozen in liquid nitrogen immediately upon surgical removal. In addition, freshly removed tissue samples were fixed in Bouin solution and paraffin embedded for histological analysis. Expression of ICAM-1, VCAM-1 and ELAM-1 was analyzed by Northern blot analysis using specific cRNA probes. In addition, immunohistochemical analysis using specific monoclonal antibodies was performed. *Results:* By Northern blot analysis ICAM-1, VCAM-1 and ELAM-1 mRNA were increased in 16/24 (67%), 12/21 (57%) and 15/24 (63%) carcinomas, respectively in comparison with the normal tissue samples. Densitometric analysis of the Northern blots revealed a 2.1-fold increase of ICAM-1 ( $p < 0.006$ ), a 3.4-fold increase of VCAM-1 ( $p < 0.02$ ) and a 2.2-fold increase of ELAM-1 ( $p < 0.002$ ) in cancerous tissues compared to controls. Linear regression analysis showed co-expression between ICAM-1 and VCAM-1 ( $r = 0.8$ ) and ICAM-1 and ELAM-1 ( $r = 0.7$ ). Immunohistochemical analysis revealed enhanced ICAM-1-, VCAM-1- and ELAM-1-immunoreactivity in endothelial cells of cancer blood vessels. Furthermore, the intercellular matrix of cancer samples exhibited more intense ICAM-1-immunostaining than the stroma of controls. *Conclusion:* Our findings suggest a role of adhesion molecules in tumor pathogenesis and disease progression. The overexpression of these factors might increase the ability of colonic cancer cells to attach in blood vessels and distant organs and thereby contribute to tumor invasion and metastasis. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics } "Overexpression of ICAM-1, VCAM-1 and ELAM-1 in Colorectal Carcinomas"

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**"P PP0 0284"PP0 0284 Overexpression of Cyclin D1 is a Common, Important and Early Event in Gastrointestinal Tumorigenesis Process**

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<sup>5</sup> Div. of Medicine, St. Luke's-Roosevelt Hospital Center, Columbia University, New York, NY  
Cyclin D1 is a cell cycle regulator essential for G1 phase progression. Our laboratory has shown that: a. Cyclin D1 is amplified in about 30% of esophageal squamous cell carcinomas, b. A cyclin D1 antisense construct introduced into human esophageal and colon cancer cell lines reduced their tumorigenesis. To further determine the importance of cyclin D1 in gastrointestinal carcinogenesis cyclin D1 expression was determined from nuclear immunoreactivity in 719 samples. Organ Normal Inflammation Adenoma Carcinoma Esophagus 0/94<sup>@</sup> 0/39 31/69 (46)\* 26/37 (67)<sup>#</sup> Stomach 0/87 0/32 – 16/33 (48) Small bowel 0/61 – 10/28 (36) 14/31 (45) Large bowel 0/88 – 12/35 (34) 8/27 (30) Pancreas 0/35 0/15 – 6/17 (35)<sup>@</sup> Number of positive/total (%), \*Barrett's esophagus, <sup>#</sup>Both squamous and adenocarcinomas. Cyclin D1 immunoreactivity was not seen in hyperplastic polyps nor in inflammatory tissues and did not correlate with the mitotic index; implying that cyclin D1 expression is not merely a marker of increased proliferation. Cytoplasmic immunostaining was seen in about 25% of the tissues, sometimes without nuclear staining, possibly representing a novel role of cyclin D1. Increased expression was associated with advanced age, well differentiated tumors and smoking status. Cyclin D1 overexpression was found in 70% of the intestinal type of gastric cancers and only 8% of the diffuse type. It was also significantly higher in the left colon than the right colon (48% and 11% respectively). We conclude that increased nuclear expression of cyclin D1 occurs in many gastrointestinal tumors; as an early event during the multistage process of carcinogenesis since it was also seen in adenomatous polyps and Barrett's esophagus. Increased expression of cyclin D1 may perturb cell cycle control and thereby enhance tumor progression. These findings suggest that cyclin D1 may be a useful target in cancer therapy. Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis } "Overexpression of Cyclin D1 is a Common, Important and Early Event in Gastrointestinal Tumorigenesis Process"

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**"P PP0 0285"PP0 0285 Increased Retinoblastoma Protein (pRb) Expression Occurs Throughout the Adeno-Carcinoma Sequence in the Colon, and is Associated with, but does Not Parallel Increased Proliferation**

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In colonic mucosa, as in other normal tissues, pRb expression in G0 and G1 is believed to mediate growth inhibition. In tumors, deregulation is typically associated with a decrease in pRb expression. In colorectal carcinomas (CRC) pRb expression is increased. We investigated the hypothesis that pre-invasive adenoma epithelium is associated with increased pRb expression, thus confirming increased pRb expression as a feature of the entire adenoma-carcinoma sequence in CRC. To evaluate pRb expression in colorectal adenomas and correlate this with proliferation. Normal colorectal mucosa, 11 hyperplastic polyps, 52 adenomas (31 low grade dysplasia (LGD), 21 high grade dysplasia (HGD), (30 tubular, 22 villous)) were immunostained using monoclonal antibodies to pRb and PCNA, by standard immunoperoxidase techniques. In normal mucosa, pRb and PCNA expression is confined to the proliferative compartments of colonic crypts (< 10% cells staining). In hyperplastic polyps 10/11 (91%) showed < 10% pRb expression in a pattern resembling that seen in normal crypts. 45/52 (87%) of adenomas showed increased pRb expression throughout the epithelium, (mean 45, { s } 25, range 10–90%). 32–52 (62%) of adenomas showed increased PCNA expression throughout the epithelium, (mean 50, { s } 22 range 10–90%). In individual adenomas, pRb expression did not correlate with increased PCNA expression and discordant percentage of expression was seen in 46/52 (89%) cases. Increased pRb expression does correlate with the grade of dysplasia, but does not correlate with growth patterns. Increased pRb expression (1) occurs in the earliest stages and throughout the adenoma-carcinoma sequence in CRC from tubular adenomas to large villous adenomas; (2) is not a feature of hyperplastic polyps; (3) shows increased pRb expression in HGD compared with LGD; (4) is associated with, but does not parallel increased proliferation. Oncology, general: Molecular biology, genetics  
Oncology, general: Proliferation, carcinogenesis } "Increased Retinoblastoma Protein (pRb) Expression Occurs Throughout the Adeno-Carcinoma Sequence in the Colon, and is Associated with, but does Not Parallel Increased Proliferation"

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## "P PP0 0286"PP0 0286 **Deregulated Apoptosis Contributes to the Developments of Human Colon Cancer**

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<sup>1</sup> Dept. of Anat. Pathol., Ajou Inst. for Medical Science, Ajou University School of Medicine, Suwon, Korea It has been shown that cells of the luminal surface epithelium exhibit fragmentation of their DNA, suggesting that programmed cell death, apoptosis, is involved in the superficial loss of intestinal cells. Normal tissue homeostasis requires the physiologic deletion of cells by activation of apoptosis. Inhibition of apoptosis by the deregulation of certain oncogenes results in clonal expansion. The progressive accumulation of genetic alterations (e.g., APC, p53, DCC, MCC, and Ras) governs the transition of normal colorectal epithelium to adenoma or carcinoma. This study was designed to know the contribution of apoptosis mechanism in preventing the accumulation of abnormal, deranged cells in colon carcinogenesis. Apoptotic cells were detected *in situ* by TdT-mediated biotin-dUTP nick end-labelling (TUNEL) in histopathological section of colorectal tissue. Immunohistochemical analysis of bcl-2 protein expression was done in normal colonic mucosa, colonic polyp, and colorectal carcinoma. The sections were incubated with monoclonal mouse antihuman Bcl-2 (DAKO 124, USA). Western analysis of bcl-2 and p53 proteins were also performed using bcl-2 Ab and p53 (Transduction Laboratories, USA). Detection of genomic fragmentation by TUNEL resulted in an intense nuclear staining of apoptotic cells and apoptotic bodies. Distinct patterns of apoptotic cell death emerged in normal mucosa mostly, whereas rarely in some polyps and colon cancers. Bcl-2 expressions were more prominent in homogenates of colon cancer as compared to normal colonic mucosa. The expressions of bcl-2 in colonic polyp were intermediate between normal and colon cancer. Immunohistochemical staining of bcl-2 showed intense increment in the whole layer of colonic tumors whereas positive staining was noted in the base of normal colonic crypts. It seems to be that progressive inhibition of apoptosis will relate to the development of colorectal cancer by the accumulation of abnormal and mutated cells. Oncology, general: Proliferation, carcinogenesis } "Deregulated Apoptosis Contributes to the Developments of Human Colon Cancer"

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"P PP0 0287"PP0 0287 ***In Vivo* Imaging of Liver-Directed Gene Transfer of Human LDL-Receptor in the Rabbit Model of LDL-Receptor Deficiency**

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Familial hypercholesterolemia (FH) is associated with early death due to myocardial infarction. The underlying defect is the deficiency of the LDL-receptor, which is primarily found within the liver. Therefore FH is an excellent model for developing liver-directed gene therapy strategies. To monitor the gene transfer of the LDL-receptor, we developed an external *in vivo* scanning technique. Gene transfer was performed using Adenovirus containing the human CMV promoter and the human LDL-receptor. Adenovirus containing  $\beta$ -galactosidase served as the negative control. The low density lipoprotein (LDL) fraction was isolated from human, radiolabelled with Indium, and injected into Watanabe Heritable Hyperlipidemic rabbits (the animal model of FH). Scans were obtained at different time points before and after gene transfer (human LDL-receptor versus  $\beta$ -galactosidase). The increased uptake of human LDL after transfer of the human LDL-receptor was easily detectable with our scans. We confirmed the successful gene transfer by measuring total cholesterol in plasma and performing human LDL turnover studies before and after gene transfer. In addition we were able to confirm the specific uptake of LDL by hepatocytes in contrast to non-parenchymal liver cells using cell separation techniques. *In conclusion*, we have developed an extremely sensitive external imaging technique to monitor the gene transfer of the LDL-receptor in the animal model of FH. This powerful method may also be used in humans to monitor cell membrane receptor mediated gene transfer. In addition it may serve as a new diagnostic tool to detect LDL-receptor deficiency in human. Hormones and receptors: Receptor characterization  
Radiology and ultrasound: Diagnosis  
Radiology and ultrasound: Therapy } "*In Vivo* Imaging of Liver-Directed Gene Transfer of Human LDL-Receptor in the Rabbit Model of LDL-Receptor Deficiency"

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"P PP0 0288"PP0 0288 **Effect of Octreotide Acetate and 5-Fluorouracil on the Human Rectal Neuroendocrine Carcinoma (Adenocarcinoid) Xenograft in Nude Mice**

\*N. Tanaka, M. Onda, T. Seya, Y. Kanazawa, K. Furukawa, K. Higuchi, H. Takasaki, K. Yoshimura, S. Yokoyama, H. Kan, H. Maruyama, H. Sasabe, T. Yamada, Z. Naitou<sup>1</sup>, G. Asano<sup>1</sup>

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Colorectal neuroendocrine carcinoma (NEC) is unusual and its biological behavior is still unclear. This tumor has clinically aggressive characteristics and its prognosis is poor. At the 4th UEGW (1995), we have reported the establishment of human rectal adenocarcinoid in nude mice xenograft. Here we examined the effect of a somatostatin analog, octreotide acetate (OA), and 5-fluorouracil (5-FU) on the growth of this tumor. *Materials and Method:* Tumors of a 3 mm cube were implanted bilaterally into the flank of nude mice. Mice were randomly divided into 4 groups (n = 10 mice/group) and agents were intraperitoneally administered for 2 weeks as followed; group 1: saline, group 2: OA (300 μg/kg), group 3: 5-Fu (10 mg/kg), group 4: OA + 5-Fu (OA 300 μg/kg + 5-Fu 10 mg/kg). The bodyweight of mice and tumor size were measured weekly. *Results:* 1) Both OA and 5-Fu, administered as single agents, inhibited the tumor growth compared with control group, and 5-Fu was more effective than OA; however, after stopped administration of these agents, tumors had grown as well as the control group. 2) OA and 5-Fu treated in combination, most significantly inhibited tumor growth, and inhibition continued to the time of killing. 3) There were no difference in body weight of mice between the experimental groups and control group. *Conclusion:* OA and 5-Fu inhibited growth of NEC in nude mice. This tumor will be a useful experimental model to elucidate the biological behavior of human NEC and further study of various therapeutic agents on this tumor is important. *Oncology, general: Therapy* Oncology, specific: Colon, rectum } "Effect of Octreotide Acetate and 5-Fluorouracil on the Human Rectal Neuroendocrine Carcinoma (Adenocarcinoid) Xenograft in Nude Mice"

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## "P PP0 0289"PP0 0289 Importance of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) in Duodenal Secretion

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<sup>1</sup> Dept. of Gastroenterology, Odense University, Denmark

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Surface epithelial bicarbonate is an important factor in preventing acid-peptic injury, as well as facilitating pancreatic enzyme function.  $\text{HCO}_3^-$  is likely transported with  $\text{Cl}^-$  by CFTR. However, the role of CFTR in duodenal secretion has been ignored. Thus, our aims were to determine if CFTR regulates basal and acid-stimulated  $\text{HCO}_3^-$  transport, as well as cAMP- and  $\text{Ca}^{2+}$ -mediated secretion. The cystic fibrosis (CF) murine model (*cftr*<sup>m1UNC</sup>) was used with genotyping confirmed by PCR. Normal littermates (25–46 d, 17–3 g) were compared to CF [CFTR (-/-)] mice (22–39 d, 13–3 g). Anesthesia was induced and maintained with hypnorm/midazolam (i.p.); animals (37°C) were hydrated with saline. The proximal duodenum (4–7 mm) was cannulated and perfused with 154 mM NaCl (0.17 ml/min). Stimulation was accomplished with either intrasegmental perfusion of HCl (10 mM, 5 min),  $\text{PGE}_2$  ( $10^{-6}$ – $10^{-4}$  M), forskolin ( $10^{-6}$ – $10^{-4}$  M), carbachol ( $10^{-6}$ – $10^{-3}$  M), or VIP (5 pmol/g, i.p.) to activate either cAMP- or  $\text{Ca}^{2+}$ -stimulated secretion; N = 4 for each series.  $[\text{HCO}_3^-]$  was measured by a validated micro-back titration method. Initial studies demonstrated that animals could be maintained under these conditions for > 3 h (stable basal  $\text{HCO}_3^-$  secretion, respiration rate, plasma  $[\text{HCO}_3^-]$ ). Basal  $\text{HCO}_3^-$  secretion was diminished significantly ( $P < 0.001$ ) in CFTR (-/-) vs. normal, 2.8–1.1 vs. 5.1–1.6 μmol/cm-h. Moreover, in CFTR (-/-),  $\text{HCO}_3^-$  secretion was significantly ( $P < 0.01$ ) impaired in response to all secretagogues (Figs). Furthermore, normal littermates demonstrated net fluid secretion during basal which increased in response to stimulation, whereas CFTR (-/-) expressed net absorption ( $P < 0.05$  vs. normal) and was largely unresponsive to agonists. We conclude that CFTR plays a key role in regulating epithelial bicarbonate transport, as well as duodenal secretion, processes likely mediated by cAMP.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic  
Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation  
Intestinal disorders, absorption: Epithelial transport  
} "Importance of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) in Duodenal Secretion"

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## "P P 12 0290" P 12 0290 **Pantoprazole Versus Famotidine in the Treatment of Acute Duodenal Ulcer Disease**

\*E.G. Hahn, H.G. Dammann, G. Adler, M. Schlander

Erlangen, Hamburg, Ulm and Konstanz, Germany *Objective:* Pantoprazole is a new, precise proton pump inhibitor. It was the aim of the present clinical study was to compare the efficacy and tolerability of pantoprazole (40 mg) and famotidine (40 mg) in outpatients with acute duodenal ulcer under the conditions of routine gastroenterological practice. *Methods and patients:* Open, 2:1 randomized, controlled, multicenter study. 456 Outpatients with acute and uncomplicated duodenal ulcer (diameter 3–20 mm) were recruited by 72 investigators to receive either pantoprazole (n = 307) 40 mg o.a.d. (morning) or famotidine (n = 149) 40 mg o.a.d. (evening) for 2 weeks, or 4 weeks if endoscopic healing was incomplete by 2 weeks. Demographic data and ulcer size were comparable in both treatment groups. *Results:* Endoscopically proven healing rates (primary study end-point, *intent-to-treat* analysis [per protocol]): 2 weeks 4 weeks Pantoprazole 82% [87%] 93% [98%] Famotidine 68% [76%] 88% [94%]  $p < 0.001$  [ $p < 0.05$ ]  $p = 0.07$  [ $p = 0.07$ ] Among the patients with pain prior to treatment, complete freedom of pain after 2 weeks was achieved in 87% of the patients in the pantoprazole group and in 72% of the patients in the famotidine group ( $p < 0.01$ ). Both drugs were well tolerated. *Conclusions:* Pantoprazole (40 mg o.a.d.) was highly effective and well tolerated in the acute treatment of duodenal ulcer. Clinically relevant superiority of pantoprazole over famotidine was achieved with respect to healing and pain relief, while the tolerability of both drugs was comparable. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Pantoprazole Versus Famotidine in the Treatment of Acute Duodenal Ulcer Disease"

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## "P P 12 0291" P 12 0291 Comparison of Pantoprazole and Ranitidine in Acid-Related Diseases

\*D.-H. von Kleist, H. Bosseckert, T. Scholten, M. Schlander

Berlin, Jena, Hagen and Konstanz, Germany *Objective:* It was the aim of this phase-IV clinical trial program to assess the efficacy and safety of pantoprazole in the acute treatment of acid-related diseases in outpatients under the conditions of routine gastroenterological practice. *Methods:* 3 open, 2:1 randomized, controlled, multicenter trials (duodenal ulcer [DU]: 73 centers; gastric ulcer [GU]: 56 centers; reflux esophagitis [GERD] grade II/III according to Savary-Miller: 130 centers) were performed. Pantoprazole (P) 40 mg o.a.d. (morning) was compared to ranitidine (R) 300 mg o.a.d. (evening) for 4 weeks (DU: 2 weeks), or 8 weeks (DU: 4 weeks) if endoscopic healing was incomplete after 4 weeks (DU: 2 weeks). *Patients:* In total 1473 patients with uncomplicated disease were enrolled (DU: n = 476; GU: n = 274; GERD: n = 723). 991 patients were treated with P and 482 received R. For each of the three clinical trials, baseline and demographic data were comparable for patient groups treated with P and R, respectively. *Results:* Endoscopically proven healing rates (intention-to-treat analysis; \* = p < 0.05, \*\*\* = p < 0.001): Indication P vs. R at 4 weeks P vs. R at 8 weeks (DU: 2 weeks) (DU: 4 weeks) DU 87% vs. 67% \*\*\* 96% vs. 91% (p = 0.06) GU 82% vs. 70%\* 91% vs. 82%\* GERD 75% vs. 54% \*\*\* 87% vs. 66% \*\*\* P provided better pain relief compared to R. Both treatments were very well tolerated, without any relevant differences in the frequency or severity of reported adverse events. *Conclusion:* Pantoprazole (40 mg) was significantly more effective than ranitidine (300 mg) in terms of healing rates as well as pain relief in patients with an acid-related disease, confirming the results from previous phase-III trials. Both treatments were well tolerated. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Comparison of Pantoprazole and Ranitidine in Acid-Related Diseases"

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## "P P 12 0292" P 12 0292 Clinical Tolerability of Pantoprazole Compared to Ranitidine and Famotidine

\*T. Scholten, G. Adler, H. Bosseckert, H.G. Dammann, E.G. Hahn, D.-H. von Kleist, M. Schlander

Hagen, Ulm, Jena, Hamburg, Erlangen, Berlin & Konstanz, Germany *Objective:* The German pantoprazole phase-IV clinical trial program was designed to assess not only the efficacy but also the safety of pantoprazole in acute treatment of acid-related diseases in outpatients. *Methods:* Six open, 2:1 randomized, controlled, multicenter trials (duodenal ulcer [DU]: 145 centers; gastric ulcer [GU]: 96 centers; reflux esophagitis [GERD] grade II and III: 259 centers) were performed comparing pantoprazole (P) 40 mg o.a.d. (morning) with ranitidine (R) 300 mg o.a.d. (evening) or famotidine (F) 40 mg o.a.d. (evening). Treatments were for 4 weeks (DU: 2 weeks), or 8 weeks (DU: 4 weeks) if endoscopic healing was incomplete after 4 weeks (DU: 2 weeks). *Patients:* In total 2842 patients were enrolled (DU: n = 932; GU: n = 453; GERD: n = 1457). 1915 patients received P, 482 received R and 445 received F. *Results:* Most frequently reported adverse events (cut-off incidence: 0.4%, overall safety analysis of the six studies, intention-to-treat): Pantoprazole Ranitidine Famotidine symptom % symptom % symptom % Headache 0.8 Headache 1.5 Headache 1.1 Abdominal 0.7 GPT/GOT 1.0 Hyperlip./ 0.7 pain increase hyperchol. Dizziness 0.7 Pruritus 0.8 Dizziness 0.4 Diarrhea 0.6 Hiarrhea 0.6 Constipation 0.4 Nausea/ 0.6 Asthenia 0.4 Pain in 0.4 vomiting extremity Hyperlip./ 0.5 Sleep 0.4 Dry mouth 0.4 hyperchol. disturbance GPT/GOT 0.4 Nausea/ 0.4 increase vomiting *Conclusion:* Pantoprazole (40 mg), ranitidine (300 mg) and famotidine (40 mg) were found to be equally well tolerated in the collective of 2842 patients studied. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Clinical Tolerability of Pantoprazole Compared to Ranitidine and Famotidine"

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"P P 12 0293" P 12 0293 **Pantoprazole in Long-Term Management of H<sub>2</sub>-Blocker Refractory Acid-Peptic Disease**

\*G. Brunner, U. Harke, A. Schneider<sup>1</sup>, R. Fischer<sup>1</sup>

Medical University, Hanover, FRG

<sup>1</sup> Byk Gulden, Constance, FRG *Aim:* The efficacy and tolerability of the H<sup>+</sup>,K<sup>+</sup>-ATPase inhibitor pantoprazole (PAN) in H<sub>2</sub>-blocker refractory acid-peptic disease was investigated. *Methods:* Patients with acute reflux esophagitis or peptic ulcer refractory to extended high-dose H<sub>2</sub>-blockers were treated with 40–120 mg PAN daily for 4–12 weeks, depending on healing, in an open-label trial. Healed patients were admitted to maintenance treatment for up to 5 years. Upper GI endoscopy was performed at admission, every 4 weeks during the healing phase, and every 6 months during long-term treatment. Intermediate results are presented. *Results:* Healing of the acute lesions was achieved in 129/141 patients (91.5%) after 4 weeks and 140 (99.3%) after 12 weeks. In one patient with severe esophagitis, the lesion took more than 6 months to heal. By the time of this analysis, 115 patients were on maintenance treatment for at least one year, 89 for 2 years, 60 for 3 years, 27 for 4 years, and 9 for 5 years. Most patients were kept in remission with 40–80 mg PAN daily; 20 patients required higher doses up to 320 mg. Most frequent possibly treatment-related adverse events were pruritus and tiredness (in two patients each). Four patients with reflux disease and full-blown liver cirrhosis tolerated this treatment without any side-effects up to five years. Routine laboratory tests remained without significant changes throughout the entire period of treatment. Median serum gastrin levels were already elevated at baseline due to pretreatment with H<sub>2</sub>-blockers (72 pg/ml, 68% range 41–191) and increased to 120.0 pg/ml (68–280) after one year of maintenance treatment without any further consistent increase thereafter. Median ECL cell density in the oxyntic mucosa increased slightly from 0.3% to 0.5% after 3 years. *Conclusions:* The data demonstrate that pantoprazole is highly effective and safe in acute healing and long-term treatment of H<sub>2</sub>-blocker refractory peptic ulcer and reflux esophagitis and also in patients with advanced liver disease. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Pantoprazole in Long-Term Management of H<sub>2</sub>-Blocker Refractory Acid-Peptic Disease"

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"P P 12 0294" P 12 0294 **No Pharmacokinetic and Pharmacodynamic Interaction between Pantoprazole and Glibenclamide**. Walter-Sack, H. Bliesath, F. Stiefel, R. Huber<sup>1</sup>, V.W. Steinijans<sup>1</sup>, W. Wurst<sup>1</sup>

University Heidelberg

<sup>1</sup> Byk Gulden Konstanz, FRG The new H<sup>+</sup>/K<sup>+</sup>-ATPase inhibitor pantoprazole is metabolized in the liver by CYP2C19 and CYP3A4. As substituted benzimidazoles can interact with the cytochrome P450 system, the interaction between pantoprazole and the sulfonyl urea glibenclamide was investigated. Glibenclamide is used in the treatment of diabetes mellitus and is metabolized in the liver by CYP3A. 20 healthy male volunteers completed a randomized single-blind cross-over study. They received 40 mg pantoprazole (Test) or placebo (Reference) *sid* for 5 days and concomitantly 3.5 mg glibenclamide on day 5. Glibenclamide, pantoprazole, glucose and insulin serum concentrations were measured on day 5 of each period. Lack of interaction was considered as an equivalence problem. The following pharmacokinetic characteristics were observed: Parameters Test: Ref.: Eq. Ratio (Test/Ref.) Geometric mean Point est. 90% CI Glibenclamide (G) with P without PAUC (ng h/l) 616 588 1.05 0.98–1.12 C<sub>max</sub> (ng/l) 193 185 1.04 0.89–1.22 Pantoprazole (P) with G without GAUC (mg h/l) 4.23 4.29 0.98 0.93–1.04 C<sub>max</sub> (mg/l) 4.62 4.78 0.97 0.89–1.06 The 90%-confidence intervals (CI) of the ratios of AUC and C<sub>max</sub> were entirely within the equivalence range of 0.8–1.25. Additionally, the pharmacodynamic profiles of glucose and insulin were comparable in both periods. No interaction between pantoprazole and glibenclamide was concluded. No dose adjustment is required during concomitant treatment. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Oesophageal gastric duodenal disorders: EG Reflux } "No Pharmacokinetic and Pharmacodynamic Interaction between Pantoprazole and Glibenclamide"

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## "P P 12 0295" P 12 0295 Rabeprazole Effectively Inhibits 24 Hr H<sup>+</sup> Activity and Nocturnal Acid Secretion in Healthy Subjects

\*H.G. Dammann<sup>1</sup>, F. Burkhardt<sup>1</sup>, N.E. Bell<sup>2</sup>, T. Bjaaland<sup>2</sup>

<sup>1</sup> Institute for Clinical Research, Hamburg, Germany

<sup>2</sup> Eisai Europe, London, UK In humans rabeprazole has produced a dose-dependent, potent and long lasting inhibition of acid secretion. No significant incremental effect was noted with doses greater than 20 mg. *Purpose:* The purpose of this study was to determine the effect of an oral dose of rabeprazole 20 mg on 24 hr intragastric pH, 24 hr H<sup>+</sup> activity and nocturnal acid secretion in healthy subjects following a 14 day dosing period. *Methods:* 12 young healthy male subjects (mean age 27.5 Yrs) were investigated in this single centre, double-blind, randomised, 2-period-crossover comparison of rabeprazole 20 mg and placebo given orally once in the morning for 14 days. On Day 7 24 hr intragastric pH was monitored and nocturnal acid secretion measured by continuous aspiration (00.00 to 06.00 hrs) and titration of gastric contents. The pH measurements were extended for a 72 hr period after the last dose of medication (Days 14, 15 and 16). pH measurements were collected using a Synectics Mk II system and a nasogastric tube with pH electrode. *Results:* In comparison to placebo, rabeprazole 20 mg significantly inhibited 24 hr H<sup>+</sup> activity (table) and nocturnal acid secretion (36.6 – 6 vs 6 – 2 mmol/00.00–06.00 hrs). 24 hr H<sup>+</sup> activity (AUC<sub>0–24</sub>) mmol.h/L (means – SE) Placebo Rabeprazole Inhibition (%) Day 7 503 – 71 72 – 27 86 Day 14 343 – 102 44 – 12 87 Day 15 501 – 121 126 – 31 75 Day 16 379 – 74 146 – 29 61 *Conclusions:* Rabeprazole 20 mg produced a significant and long lasting inhibition of acid secretion. Inhibition of up to 87% was observed. The half-life for recovery of acid secretion was longer than 72 hours. Based on published data rabeprazole 20 mg appears to be at least as potent and as long acting as omeprazole and lansoprazole. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Rabeprazole Effectively Inhibits 24 Hr H<sup>+</sup> Activity and Nocturnal Acid Secretion in Healthy Subjects"

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**"P P 12 0296" P 12 0296 Tolerability and Safety Profile of Pantoprazole Based on 71906 Patients. Results of a German Post Marketing Surveillance Program E.G. Hahn<sup>1</sup>, H. Bosseckert<sup>2</sup>,**

**\*H.G. Dammann<sup>3</sup>, M. Schlander<sup>4</sup>**

<sup>1</sup> Erlangen, FRG

<sup>2</sup> Berlin, FRG

<sup>3</sup> Hamburg, FRG

<sup>4</sup> Konstanz, FRG *Purpose:* Pantoprazole is a novel proton pump inhibitor (PPI) with precisely defined pharmacological properties, profound antisecretory capacity and high clinical efficacy in the treatment of acid related diseases. This PMS program was designed to determine the tolerability and safety profile of pantoprazole. *Methods and patients:* Between October 1994 and December 1995 71.906 patients (female 38.3%, male 61.7%) were enrolled in this PMS program (DU 40.9%, GU 22.2%, refluxoesophagitis 28.7%, other 8.2%). The majority of patients presented with a first episode of their disease (56.5%). 88.9% of patients received pantoprazole in the recommended daily dose of 40 mg for a mean treatment period of 22.75 days (SD – 14.08). *Results:* The DU, GU and refluxoesophagitis healing rates according to endoscopy (35.5%), x-ray (3.3%) and clinical symptoms (63.3%) were 95.1%, 91.3% and 86.0% respectively. Efficacy, complete relief of pain, and tolerability were rated as excellent/very good by 82.4%, 79.2 and 85.3% of the participating practitioners (n = 10838). 627 patients (0.87%) reported on 992 adverse events (AEs). The most frequently reported AEs are given in the table. All other AEs showed an incidence of 0.05–0.001%. Adverse events n % Diarrhea 136 0.19 Nausea 132 0.18 Headache 112 0.16 Dizziness 93 0.13 Gastrointestinal 65 0.09 Exanthema/Urticaria 52 0.07 *Conclusion:* The pantoprazole PMS program proves the favourable tolerability and safety profile of this novel PPI. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } " "Tolerability and Safety Profile of Pantoprazole Based on 71906 Patients. Results of a German Post Marketing Surveillance Program"

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## "P P 12 0297" P 12 0297 Drug-Drug Interaction Evaluation of Rabeprazole Sodium: A Clean/Expected Slate?

\*T.J. Humphries, R.V. Nardi, J.D. Lazar, S.A. Spanyers

Eisai Corporation of North America, Teaneck, NJ, USA

Pharmaco International, Austin, TX, USAAs was the case with the early members of the family of H<sub>2</sub> receptor antagonist, drug-drug interactions mediated by CYP-450 isoenzymes were demonstrated with omeprazole the first proton pump inhibitor (PPI) as were interactions based on the profound antisecretory effect of the PPI class with drugs for which absorption is dependent on intragastric pH. The potential for rabeprazole sodium (RAB) to interact with co-administered diazepam, theophylline, phenytoin, warfarin, ketoconazole and digoxin has been evaluated. The diazepam interaction was studied in Japanese patients (high incidence of PM) while all other studies were conducted in US subjects. Standard PK parameters, including C<sub>max</sub>, T<sub>max</sub>, T<sub>1/2</sub> and AUC were measured. The results of this group of studies are shown in the table below:

Drug Interaction	Diazepam	No	Theophylline	No	Phenytoin	No	Warfarin	No	Ketoconazole
Yes (AUC and C <sub>max</sub> )	Yes								
Digoxin Yes (AUC, C <sub>max</sub> , and T <sub>1/2</sub> )	Yes								

**Conclusions:** Based on an extensive battery of studies, RAB shows no potential for major CYP-450 interactions, and predictably effects blood levels of ketoconazole and digoxin based on its antisecretory effect. When planning to co-administer ketoconazole with RAB, consideration should be given to discontinue RAB. With respect to digoxin, although co-administered RAB results in a modest (20%) increase in trough digoxin levels, monitoring of digoxin levels is suggested when RAB therapy is initiated in patients taking digoxin. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Clinical practice: Management strategy } "Drug-Drug Interaction Evaluation of Rabeprazole Sodium: A Clean/Expected Slate?"

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"P P 12 0299" P 12 0299 **The Effects of Rabeprazole on 24-Hour Intra-gastric Acidity and Plasma Gastrin Concentration in Healthy Subjects**

\*C. Blanshard, C. Millson, J. Sercombe, R.E. Pounder

University Department of Medicine, Royal Free Hospital School of Medicine, London NW3 2PF, England

*Aim:* To observe the effects of rabeprazole, a H<sup>+</sup>, K<sup>+</sup> ATPase inhibitor, on 24-hour intra-gastric acidity and plasma gastrin concentration in healthy subjects, in a placebo-controlled double-blind study. *Methods:* 24 healthy male subjects (2 *Helicobacter pylori* positive as assessed by a <sup>13</sup>C-urea breath test) were studied on the 7th day of dosing with either placebo, rabeprazole 10 mg, 20 mg or 40 mg taken in the morning. 24-hour intra-gastric acidity was measured from 8 am using the Royal Free Hospital protocol, with gastric aspirations at hourly intervals for 24-hours, and venous blood samples at hourly intervals until midnight and at 2-hourly intervals thereafter. *Results:* The study was well tolerated by all subjects, and no serious adverse events were reported. Mean 24-hour Mean 24-hour plasma intra-gastric acidity gastrin concentration (mmol.h/L) (pmol.h/L) Placebo 679 296 Rabeprazole 10 mg 156\*

1676\* Rabeprazole 20 mg 131\* 1936\* Rabeprazole 40 mg 86\* 2403\*\* p < 0.001 vs

placebo Dosing with rabeprazole resulted in significant decreases of 24-hour intra-gastric acidity compared with placebo, there was no significant difference between the three doses. Dosing with rabeprazole resulted in a significant dose-related increase of mean 24-hour plasma gastrin — the differences between the 10 and 40 mg doses, and the 20 and 40 mg doses, being significant (p = 0.002 and 0.037, respectively). *Conclusion:* Rabeprazole is a potent gastric acid antisecretory drug: a single daily dose (10 mg, 20 mg or 40 mg) causes a significant decrease of 24-hour intra-gastric acidity with reciprocal rise of plasma gastrin concentration. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "The Effects of Rabeprazole on 24-Hour Intra-gastric Acidity and Plasma Gastrin Concentration in Healthy Subjects"

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"P P 12 0300" P 12 0300 **PD-136,450: A CCK-B (Gastrin) Receptor Antagonist with a Novel Spectrum of Antiulcer Activity**

\*S.M.A. Bastaki, M.Y. Hasan, I. Chandranath, A. Garner

Faculty of Medicine & Health Sciences, United Arab Emirates University, Al Ain, U.A.E. *Purpose:* PD-136,450 is a selective ligand for the CCK-B receptor in vitro with binding affinity for mouse cortex – 500-fold greater than for rat pancreatic CCK-A receptors. This study characterises gastric acid and pancreatic bicarbonate secretions together with anxiolytic activity of PD-136,450 in the rat. *Methods:* Gastric and pancreatic secretions were measured by titration at 10 min intervals. Basal acid output and secretion stimulated by s.c. injection of 32  $\mu\text{g/kg}$  gastrin-17 or 10 mg/kg dimaprit were determined in anaesthetised rats or conscious animals fitted with indwelling fistulae. Pancreatic secretions were collected via a catheter inserted into the main duct of anaesthetised rats. Anxiolytic activity was assessed by a standard black and white two-compartment activity assay. *Results:* As anticipated, PD-136,450 inhibited gastrin-stimulated acid output in anaesthetised or conscious rats (IC<sub>50</sub> of 1 mg/kg s.c.). Doses up to 10-fold higher had no effect on dimaprit-induced acid output (255  $\mu\text{mol/hr}$  before and 243  $\mu\text{mol/hr}$  after PD 136,450). Of note, PD-136,450 increased pancreatic secretion. At a dose of 4.5 mg/kg it showed similar efficacy to CCK-8 with bicarbonate output rising from 36 to 207  $\mu\text{mol/hr}$  60 min after s.c. dosing and remaining elevated for > 3 hr. This action was inhibited by 75% after pretreatment with the CCK-B antagonist L-364,718 (bicarbonate output 55  $\mu\text{mol/hr}$ ) but was not effected by the CCK-B antagonist L-365,60 (output 211  $\mu\text{mol/hr}$ ). Time spent in the dark compartment by rats pretreated with 10 mg/kg PD-136,450 was reduced 36% compared with control ( $p < 0.01$ ,  $n = 6$ ). This response was similar to the effect of 5 mg/kg diazepam (41% inhibition). Latency for movement from the light to the dark compartments increased similarly with PD-136,450 and diazepam. *Conclusions:* PD-136,450 is a selective inhibitor of gastrin-stimulated acid secretion in vivo. The drug also stimulates pancreatic bicarbonate secretion and displays anxiolytic activity comparable to diazepam. While PD-136,450 has weak antisecretory activity compared with H<sub>2</sub> blockers or PPIs, it may have utility as an adjunct therapy in peptic ulcer disease by countering the actions of gastrin and increasing acid neutralization. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Pancreas: Secretion, regulation } "PD-136,450: A CCK-B (Gastrin) Receptor Antagonist with a Novel Spectrum of Antiulcer Activity"

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## "P P 12 0301" P 12 0301 Evaluation of the Antisecretory Activity of Pantoprazole in Duodenal Ulcer Patients by Continuous 24-Hour pH Monitoring

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<sup>1</sup> Byk Gulden Italia, Cormano (Mi), Italy The extent and duration of acid suppression are considered of critical importance for healing of acid-related disorders and optimizing activity of antimicrobial drugs in *H. pylori* eradication. Pantoprazole (Pan) is a novel proton pump inhibitor, acting by selective binding to H<sup>+</sup>/K<sup>+</sup>-ATPase of gastric parietal cells. Its main distinctive features are represented by minimized potential for interactions with human cytochrome P450 enzyme system, the stability and lack of activation in neutral environment and a predictable pharmacokinetic profile. The aim of our study was to evaluate the effects of Pan on 24-h intragastric acidity in duodenal ulcer (DU). Pan 40 mg mane was orally administered for 5–7 days to 20 patients with DU in clinical remission. 18 out of them were *H. pylori* positive. Continuous 24-h intragastric pH-metry was performed in basal conditions and after treatment, according to well established procedures. Mean 24-h, nighttime and daytime pH values, and mean times spent above pH thresholds of 3.0, 4.0 and 5.0 have been evaluated as acidity indexes. Two-way ANOVA was used for statistical analysis. A significant reduction of gastric acidity was induced by Pan compared to basal levels ( $p < 0.001$ ), in terms of both mean pH in the different time intervals and times spent above several pH thresholds (see Table). Basal Pan 40 mg Mean (SD) 24-hour pH (17:00–16:59) 1.34 (0.22) 5.13 (1.11) Nighttime pH (20:00–07:59) 1.16 (0.25) 4.80 (1.35) Daytime pH (08:00–19:59) 1.53 (0.30) 5.47 (1.12) Mean (SD) hrs. > pH 3.0 1:33 (1:02) 19:20 (4:43) pH 4.0 0:40 (0:30) 17:30 (5:29) pH 5.0 0:10 (0:14) 14:43 (6:04) Our results show that pantoprazole represents an optimal antisecretory treatment in acid-related diseases inducing a pronounced and long-lasting suppression of acid secretion. The pharmacodynamic effect is more evident during the daytime than during the nighttime and this confirms a peculiar feature of proton pump inhibitors. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Management strategy } "Evaluation of the Antisecretory Activity of Pantoprazole in Duodenal Ulcer Patients by Continuous 24-Hour pH Monitoring"

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"P P 12 0302" P 12 0302 **Comparison of Intravenous Famotidine and Ranitidine in Suppressing Gastric Acid Secretion in Reflux Esophagitis and Duodenal Ulcer Bleeding**

\*M. Tuncer, A. Dobrucali, I. Yurdakul, C. Davutoglu, N. Bagatur, F. Hamsioglu, A. \c7elik, E. Oktay

Gastroenterology Department of Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey *Purpose:* We investigated the efficacy of H<sub>2</sub>-receptor blockers in raising gastric pH to above 4 in patients with Reflux esophagitis and duodenal ulcer bleeding and we compared the efficacy of intravenous famotidine and ranitidine in this subject. *Methods:* 44 patients with endoscopically proven Reflux esophagitis (grade II, III Savary-Miller classification) and duodenal ulcer bleeding, 44 patients (28 males, 16 female, 28–68 yrs) were assigned randomly to receive intravenous bolus doses of either famotidine 20 mg every 12 hours (n = 22) or ranitidine 50 mg every 8 hours (n = 22) for mean 5 days. Gastric juice was aspirated before the start of treatment (base-line) and six times during each 24 hour period; pH was measured by a pH meter. *Results:* Measured base-line pH was not significantly different between the two groups. Famotidine raised gastric pH to higher level than did ranitidine, reaching statistical significance (p < 0.05) for 28 of 44 collection periods. *In Conclusion;* When given by intermittent intravenous bolus, famotidine 20 mg every 12 hours is more effective than ranitidine 50 mg every 8 hours in raising gastric pH to above 4 in reflux esophagitis and duodenal ulcer bleeding. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation }"  
"Comparison of Intravenous Famotidine and Ranitidine in Suppressing Gastric Acid Secretion in Reflux Esophagitis and Duodenal Ulcer Bleeding"

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"P P 12 0303" P 12 0303 **Efficacy of Ebrotidine vs Ranitidine in the Treatment of Benign Gastric Ulcer** R. Ar<sup>1</sup>, A. Gracia<sup>2</sup>, E. Lac<sup>3</sup>, A. L<sup>1</sup>, R. Lozano<sup>2</sup>,

\*M. Papo<sup>4</sup>, J.C. Quer<sup>4</sup>, M. Rodrigo<sup>3</sup>, L. San-Jos<sup>5</sup>

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<sup>3</sup> Hospital Virgen de las Nieves, Granada, Spain

<sup>4</sup> Hospital Juan XXIII, Tarragona, Spain

<sup>5</sup> Hospital Cruz Roja, Barcelona, Spain *Purpose.* To assess the efficacy of Ebrotidine 400 mg compared with Ranitidine 300 mg nocte, in the treatment of benign gastric ulcer. *Methods.* A randomized phase III parallel double-blind trial. 104 patients from 4 hospitals were enrolled in the study. 98 of them (94.23%) completed the treatment and were evaluated. Patients gathering the entry criteria were randomized to receive Ebrotidine or Ranitidine until the endoscopic cure of ulcer, or until a maximum of 12 weeks of treatment. Basal endoscopy was repeated after 6 9 and 12 weeks of treatment. The chi-square test was used to compare the number of patients with a complete remission of the ulcer, and the ANCOVA test was used to compare reduction in the size of the ulcer. *Results.* Both groups were homogeneous and without differences for the basal parameters studied. In the intention to treat analysis Ebrotidine was effective in 88.2% of the patients and Ranitidine in 78.7% (N.S). There were significant differences ( $p = 0.017$ ) concerning the size of the ulcer at six weeks of treatment (95% CI, 0.5589 mm to 1.8724 mm for Ebrotidine and 1.6337 mm to 4.9621 mm for Ranitidine). Adverse events were absent in both groups of patients. *Conclusions.* Ebrotidine appears to be significantly faster than Ranitidine in the healing of the benign gastric ulcer. Ebrotidine is a new drug with anti-secretory profile, anti-H2 and gastroprotective activity, thus conferring a significant advantage versus Ranitidine and possibly versus other types of antiseptors drugs. *Clinical practice: Management strategy* Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Efficacy of Ebrotidine vs Ranitidine in the Treatment of Benign Gastric Ulcer"

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"P P 12 0304" P 12 0304A **Comparison of Intra-gastric Acidity Following Low Doses of Ranitidine and Cimetidine** M.R. Hamilton<sup>1</sup>, J. Sercombe<sup>1</sup>,

\*R.E. Pounder<sup>1</sup>, C.C.L. Snell<sup>2</sup>

<sup>1</sup> Royal Free Hospital School of Medicine, London NW3, UK

<sup>2</sup> Glaxo Wellcome Research & Development, Middlesex, UK This randomised, 3-way, crossover study compared the effects of low doses of ranitidine and cimetidine on intra-gastric pH. *Methods:* Thirty healthy subjects (18 male, 12 female) took part in the study. On three separate occasions single oral doses of placebo, ranitidine 75 mg (one Zantac 75' tablet) and cimetidine 200 mg (two Tagamet 100' tablets) were taken after lunch at 12.30 h. The pH of gastric aspirates was measured for 20 hours after the dose (Day: 12.30–22.30 h, night: 22.30–08.30 h). Subjects ate standard meals (lunch and supper) and snacks on each study day. *Results:* The decrease in intra-gastric acidity, relative to placebo, was 58.7% after ranitidine and 35.4% after cimetidine during the day and 18.3% and 2.0%, respectively, during the night. The decrease in acidity after ranitidine was significantly greater than cimetidine during the day and night. Both study drugs were well tolerated. Only one event (itchy rash) was considered related to study drug (cimetidine). Parameter Placebo Ranitidine Cimetidine 75 mg 200 mg H<sup>+</sup> AUC (mmol/L) Day 37.62 17.21<sup>\*\*\*</sup> 25.06<sup>\*\*</sup> Night 34.37 29.06<sup>+</sup> 33.85 Time pH > 4 (mins) Day 35.51 79.73<sup>\*</sup> 44.76 Night 33.53 67.59<sup>\*</sup> 35.00<sup>\*\*</sup> p {\a3} 0.001, \*p {\a3} 0.05 versus placebo. <sup>++</sup>p {\a3} 0.001, <sup>+</sup>p {\a3} 0.05 ranitidine versus cimetidine *Conclusions:* The decrease of acidity after ranitidine was significantly greater in magnitude and of longer duration than that following cimetidine. A lunchtime dose of ranitidine 75 mg caused a significant decrease of nocturnal acidity. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation }" "A Comparison of Intra-gastric Acidity Following Low Doses of Ranitidine and Cimetidine"

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"P P 12 0305" P 12 0305 **Trough Plasma Bismuth Concentrations during Long-Term Treatment with Ranitidine Bismuth Citrate**

\*J.C. Douglas, N. Lotay, L. Kler, L.F. Lacey

Glaxo Wellcome Research and Development, Greenford, UK Ranitidine bismuth citrate (RBC, *PYLORID*®) is used for the healing of duodenal and gastric ulcers and, when co-prescribed with certain antibiotics, for the eradication of *Helicobacter pylori* (*H. pylori*). In acute studies, bismuth absorption was found to be of no clinical concern. In this 6 month study, trough plasma bismuth concentrations (i.e. approximately 12 hours after dosing) were monitored as a measure of chronic bismuth exposure. Bismuth concentrations were determined in 190 symptomatic *H. pylori*-positive patients randomised to receive RBC 400 mg bd or comparator (ranitidine 150 mg bd), by inductively coupled plasma mass spectroscopy. Median, 95 percentile and maximum plasma bismuth concentrations (ng/mL) in the RBC group were: Week of dosing 4 13 26 No of patients 91 80 77 Bismuth concentration (ng/mL) Median 3.07 5.14 5.65 95 percentile 10.57 20.80 20.49 Maximum 22.81 54.20 74.49 Median bismuth concentrations for patients receiving ranitidine were below quantification limit (< 0.2 ng/mL). Long-term administration (6 months) of RBC 400 mg bd resulted in extremely low trough plasma bismuth concentrations. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Trough Plasma Bismuth Concentrations during Long-Term Treatment with Ranitidine Bismuth Citrate"

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"P P 12 0306" P 12 0306 **Role of  $\beta$ -Adrenoceptors and Nitric Oxide in the Circulatory, Metabolic and Protective Effects of Epidermal Growth Factor (EGF) in the Stomach**

\*W.W. Pawlik, R. Sendur, K. Czarnobilski, J. Biernat, T. Brzozowski, S.J. Konturek

Univ. Med. Sch. Inst. Physiol. CMUJ Krakow, Poland EGF is considered to play an important role in the maintenance of gastrointestinal mucosal integrity. The evidence existed has pointed to the trophic and vascular effects of EGF in the mechanism of its gastroprotective activity. The aim of this study was to investigate the involvement of betha adrenergic receptors in the vascular and protective actions of EGF in the stomach. Two series of dogs and rats were performed. In anesthetized dogs with fundic flap preparation, total gastric blood flow (GBF) was determined ultrasonically and mucosal blood flow (MBF by laser Doppler flowmetry. Gastric oxygen consumption ( $GVO_2$ ) and systemic arterial pressure (AP) were also determined. EGF administered i.a. at dose 2.0 mg/kg increased GBF, MBF,  $GVO_2$  by 58 – 9, 123 – 16 and 37 – 8% respectively, not change AP. Pretreatment with propranolol (5 mg/kg i.v.) significantly reduced above and metabolic responses induced by EGF. In rats acute gastric lesions were induced by 100% ethanol. Mucosal blood flow (LDF) was measured by laser Doppler technique area was also determined in mm. Ethanol induced mean lesion was 110 – 12 mm and reduction in LDF by 75%. Pretreatment with EGF (100 mg/kg-h s.c.) decreased the lesion area by 86 – 10% ( $p < 0.05$ ) and increased LDF by 72 – 8% ( $p < 0.05$ ). Pretreatment of animals with propranolol (5 mg/kg i.p.) abolished the protective effect of EGF. Propranolol alone was without any effect on the ethanol induced gastric damage. These data provide evidence that EGF is a potent vasodilator of gastric circulation and modulator of gastric tissue oxygenation. This peptide possess also protective properties which, at least in part, may depend on its dilatory activity. Both, vascular and protective effects of EGF appear to be mediated by betha adrenergic receptors. Hormones and receptors: Receptor characterization Intestinal disorders: Splanchnic circulation, ischemia } "Role of  $\beta$ -Adrenoceptors and Nitric Oxide in the Circulatory, Metabolic and Protective Effects of Epidermal Growth Factor (EGF) in the Stomach"

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"P P 12 0307" P 12 0307 **Inhibition of the Gastric H,K ATPase and Acid Secretion by a New Anti-Ulcer Drug**

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<sup>1</sup> UCLA, Los Angeles, USA *Background:* A new anti-ulcer drug, the imidazo 1,2{ a } pyridine BY841, that inhibits gastric acid secretion, is in clinical trial for treatment of acid related diseases. *Aims:* To correlate the binding of the drug with inhibition of the gastric H,K ATPase and to determine the relative efficacy of this inhibitor compared to a H2 receptor antagonist. *Methods:* Purified hog gastric vesicles were used to compare inhibition of the ATPase with binding of <sup>3</sup>H-BY841 and determine K competition with BY841. Isolated rabbit gastric glands were used to compare the effects of ranitidine and BY841. *Results:* The K<sub>i</sub> for inhibition of the ATPase by BY841 was 6 nM and the K<sub>d</sub> for binding was 4.4 nM. K displaced BY841 in intact cytoplasmic side out gastric vesicles only when K was able to penetrate the vesicle interior by the H,K exchange ionophore, nigericin, with a K<sub>app</sub> of 1 mM, similar to the concentration required for ATPase activation. The IC<sub>50</sub> value for inhibition of acid secretion in gastric glands by BY841 was 60 nM compared to 3 \b5M for ranitidine and BY841 inhibited basal as well as stimulated aminopyrine accumulation, in contrast to ranitidine. *Conclusions:* BY841 is a potent and effective inhibitor of gastric acid secretion by the parietal cell by binding to an extracytoplasmic site on the gastric H,K ATPase in a K competitive manner. Its mode of action and efficacy in vitro translates into effective inhibition of gastric acid secretion in vivo. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Hormones and receptors: Molecular biology }" "Inhibition of the Gastric H,K ATPase and Acid Secretion by a New Anti-Ulcer Drug"

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## "P P 12 0308" P 12 0308 Deposition of Bismuth from Different Compounds. An Advantage in Using Ranitidine Bismuth Citrate (RBC)?

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Clínica Universitária de Medicina Interna e Gastroenterologia, Hospital de Pulido Valente, Lisbon, Portugal

**Purpose:** To determine if treatment of rats with bismuth compounds can lead to its deposition in several organs after therapy, 30 days after stopping treatment and to see if this is affected by gastric pH.

**Methods:** 48 male wistar rats were gavaged twice daily, during 15 days, with placebo (PL, n = 14), bismuth subcitrate alone (B, n = 14)-13.7 mg/Kg/day, or in association with ranitidine (8.6 mg/Kg/day)-(BR, n = 8) and with RBC, (n = 12)-22.8 mg/Kg/day. After 2 weeks 8 rats of PL, B, BR and 6 of RBC groups were euthanized and samples of blood, liver, kidney, brain and lung were removed. After 30 days, remaining rats were killed and organs were collected. Intra-gastric pH was assessed at the 10th day with a glass electrode connected to a pH measuring device. Bismuth was assessed by Particle Induced X-ray Emission and concentrations are expressed in  $\mu\text{g/g}$  of dry weight.

**Results:** Intra-gastric pH levels were: PL-1.7 – 0.2, B-2.3 – 0.1, BR-3.6 – 0.2, RBC-3.5 – 0.1. In PL group all analysed samples had bismuth levels below detection limit ( $2 \mu\text{g/g}$ ). After 15 days bismuth concentration was: B BR RCBBrain 4.77 – 0.97 (50%) 3.12 – 1.31 (100%)  $< 2 \mu\text{g/g}$  (100%)Lung 4.07 – 1.92 (100%) 2.95 – 0.66 (100%) 3.20 – 0.39 (33%)Liver 2.36 – 0.29 (100%) 2.38 – 0.37 (100%) 2.17 – 0.63 (33%)Kidney 30.81 – 8.59 (100%) 32.44 – 13.1 (100%) 4.24 – 1.75 (100%)\*\*  $p < 0.001$  (t-student). Blood values above  $2 \mu\text{g/g}$  were found in 75% of B group, in 35.7% of BR group and in 83% of RBC group. After 30 days all rats had values below  $2 \mu\text{g/g}$ .

**Conclusions:** Treatment with bismuth can lead to its deposition in several organs and it is not influenced by gastric pH. Bismuth deposition was lower in brain and blood levels correlate poorly with organ deposition. One month after stopping therapy bismuth deposition was not detectable. There is a clear advantage in using RBC as far as organ deposition is concerned. }

"Deposition of Bismuth from Different Compounds. An Advantage in Using Ranitidine Bismuth Citrate (RBC)?"

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## "P P 12 0309" P 12 0309 Safety and Efficacy on Symptom Relief of Pantoprazole: Interim Analysis of a French Prospective Study

\*H. Licht, G. Giret-d'Orsay, R. Samoyeau, Eupantol study group

H\ 'f4p. Delafontaine 93 St Denis-Lab. Byk France 77 Le M\ 'e9e/Seine *Objective:* Pantoprazole is a potent inhibitor of acid secretion which binds precisely to the key cysteins of the gastric H<sup>+</sup>/K<sup>+</sup>-ATPase. This trial was conducted to assess the safety and efficacy on symptoms relief of pantoprazole 40 mg/day given for the acute treatment of acid-related diseases. *Methods:* Open, prospective, multicentric trial. The general practitioners (n = 900) selected the patients and the gastroenterologists (n = 300) included them after the endoscopic evidence of ulcer or esophagitis. Patients were treated for 1 or 2 months. *Results:* In duodenal ulcer patients (n = 166), the most frequently reported symptoms at entrance were characteristic ulcer pain (70%) and nausea and vomiting (46%). 89% of patients with characteristic ulcer pain and 97% of patients with nausea and vomiting were free of symptoms at day 7. Smokers, age under 50 and male gender seem to be predictive factors for rapid symptom relief. Gerd patients (n = 620) were classified as follows: stage I: 56%, stage II: 30%, stage III: 8%, stage IV: 6%. The most frequently reported symptoms at entrance were: heartburn (78%), acid regurgitations (73%), non characteristic epigastric pain (35%), dysphagia (23%). 87% of patients with characteristic Gerd symptoms were asymptomatic at day 7. The median time to be free of symptoms without intake of antacid was 4 days independently of the original stage. Non smoker status, age over 50, and the male gender seem to be predictive factors for a rapid pain relief. Safety was analysed on 1020 patients. The adverse events possibly or certainly related to the test medication were: diarrhea (2.4%), headache (2.3%), abdominal pain (1.8%), dizziness, asthenia. These rates correspond to those described with the other PPIs. *Conclusion:* On a large population representative of acid-related disease patients, pantoprazole is effective on symptoms relief. The tolerability was excellent. These results have to be confirmed by the final analysis. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Safety and Efficacy on Symptom Relief of Pantoprazole: Interim Analysis of a French Prospective Study"

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## "P P 12 0310" P 12 0310 Influence of the H<sup>+</sup>,K<sup>+</sup>-ATPase Inhibitor Pantoprazole on Blood Ethanol Levels in Healthy Humans

\*S. Teysse, M.V. Singer, H. Heinze<sup>1</sup>, R. Pflücker, H. Harder, R. Huber<sup>1</sup>, F. Stephan, A. Schneider, R. Fischer<sup>1</sup>

Dept. of Med. IV, Univ. Hosp. of Heidelberg at Mannheim, Germany

<sup>1</sup> Byk Gulden, Constance, Germany *Background:* Alteration in gastric first pass metabolism of ethanol during administration of several H<sub>2</sub> receptor antagonists has been previously reported. In the H<sup>+</sup>,K<sup>+</sup>-ATPase inhibitor omeprazole interaction was not detected. *Aim:* To study the effect of the H<sup>+</sup>,K<sup>+</sup>-ATPase inhibitor pantoprazole on blood ethanol levels after taking a moderate dose of ethanol in healthy humans. *Methods:* 16 healthy volunteers (12 male, 4 female; mean age 27 years) received either 40 mg pantoprazole or placebo orally at 8.00 AM for seven days in a double blind, randomized cross over design, separated by a 14 day wash out. On day 7 a standardized breakfast was given at 8.00 AM, directly after administration of pantoprazole. At 10.00 AM, 200 ml of orange juice, containing 0.5 g/kg body weight pure ethanol, were given within 5 min. Blood samples were taken at 10–30 min intervals for 4 h and then hourly until 6.00 PM. Ethanol concentrations were determined by a modified ADH enzymatic assay (ALC, Du Pont). For confirmative analysis the area under the curve (AUC) of blood ethanol levels over 8 hours (10.00 AM–6.00 PM) was calculated. Lack of interaction was handled as an equivalence problem (Steinijans et al. 1991). *Results:* The seven day administration of pantoprazole caused no significant change in peak ethanol concentration (C<sub>max</sub>, %) and in 8 h integrated (AUC) blood ethanol levels (% {\'b4} h) after ingestion of 0.5 mg/kg ethanol as compared to placebo. Independent from the sequence of treatment regimens, no side effects were reported. *Table:* Peak ethanol concentration (C<sub>max</sub>, %) and 8 h integrated (AUC) blood ethanol levels (% {\'b4} h) after ingestion of 0.5 mg/kg ethanol. 

	Pantoprazole	Placebo
AUC (% {\'b4} h)	1.127 (0.855–1.485)	1.113 (0.862–1.436)
C <sub>max</sub> (%)	0.435 (0.339–0.558)	0.427 (0.322–0.565)

 Values are geometric means and 68% ranges; the 90% confidence intervals of the pantoprazole/placebo ratio (AUC: 0.91–1.12; C<sub>max</sub>: 0.94–1.11) were within the equivalence range (0.8–1.25). *Conclusions:* 1.) A therapeutic dose of pantoprazole does not alter the pharmacokinetics of orally administered pure ethanol (0.5 g/kg body weight). 2.) Sporadic intake of ethanol does not influence the safety and tolerability of pantoprazole when concomitantly taken. Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Influence of the H<sup>+</sup>,K<sup>+</sup>-ATPase Inhibitor Pantoprazole on Blood Ethanol Levels in Healthy Humans"

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"P P 13 0311" P 13 0311 **Activity of  $\gamma$ -Glutamyl-Transferase ( $\gamma$ -GT) in Blood Serum and Mucosa in Helicobacter Pylori Infected Subjects** Grazyna Klupinska

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$\gamma$ -Glutamyl -transferase ( $\gamma$ -GT) is a heterogenic enzyme. In physiologic environment hepatic fractions (iso-enzymes) make only about 40% of the whole activity of this enzyme and the remaining part comes from other organs. The increase  $\gamma$ -GT is assumed to be a sensitive factor of tissue damage and neoplasia. The purpose of his study was estimation of  $\gamma$ -GT activity in serum and gastric mucosa in Hp-infected subjects. The studies were performed in 26 men, aged 42–66 years, whose histopathological diagnosis showed active, chronic gastritis. Hp infection was confirmed by microscopy and enzymatic examination (urease test). Other diseases particularly of liver and pancreas were excluded. The patients were not administered any drugs or alcohol. Before and six weeks after treatment (famotidine + amoxycyline + metronidazol)  $\gamma$ -GT was determined in serum according to kinetic method and in fundic and atrial mucosa – by method of Cormay  $\gamma$ -GT – TRIS no cat. 1-033 acc. to F. Hoffmann-La Roche. The following results were obtained:

	Before treatment	After treatment
Serum (U/l)	77.8 – 7.3	61.3 – 8.2
Stomach (mU/mg protein) – fundic	14.3 – 5.2	9.1 – 5.4
– antrum	16.7 – 8.0	10.4 – 5.9

It has been concluded that, Hp infection is the reason of the increase of  $\gamma$ -GT activity in gastric mucosa and serum. The role of Hp infection in gastritis pathogenesis also proves the necessity of antibacterial treatment. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Activity of  $\gamma$ -Glutamyl-Transferase ( $\gamma$ -GT) in Blood Serum and Mucosa in Helicobacter Pylori Infected Subjects"

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**"P P 13 0312" P 13 0312 Proliferative Response to Helicobacter Pylori (Hp) CagA Protein of Gastric Vein Blood Lymphocytes from Infected Subjects A. Tricerri,**

\*M.E. Riccioni<sup>1</sup>, L. Guidi, D. Frasca<sup>2</sup>, M. Vangeli, S. Ciletti<sup>1</sup>, M. Costanzo, C. Bartoloni, R. Coppola<sup>1</sup>, G. Doria<sup>2</sup>, G. Gasbarrini

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<sup>1</sup> Patologia Chirurgica, Universit  Cattolica, Roma, Italy

<sup>2</sup> Laboratorio di Immunologia ENEA-CRE. Roma, Italy In organ specific infections the significance of local immune reactivity can be different from that of peripheral blood lymphocytes (PBL). The organ draining blood could represent an intermediate compartment between the mucosa associated and the systemic immunity. Aim of our study was to investigate if the PBL were able to proliferate to Hp CagA protein and if this assay had any specificity in Hp infected patients. Moreover we compared the data with those obtained testing the lymphocytes isolated from gastric vein blood (GVBL). Patients supposed to undergo abdominal surgery (not for neoplastic diseases) underwent a thorough study for Hp infection. During the surgical intervention blood samples were obtained by puncture of the gastric draining veins and the antecubital vein. Lymphocytes were purified and cultured in the presence of several mitogenic stimuli (anti-CD3, anti-CD28, PHA, Hp CagA protein) and the proliferative response was measured by means of tritiated thymidine uptake. Hp CagA protein induced lymphocyte proliferative response in a high percentage of Hp infected subjects (71.5% GVBL and 57% PBL) while it did not in the Hp negative patients. Comparing the Hp positive and negative groups the mean lymphocyte proliferative response to CagA was significantly higher in the GVBL ( $p < 0.05$ ) while no difference was detected for the other mitogenic stimuli. Analysing the patients as a whole, GVBL showed a significantly higher response to PHA than PBL. It is known that the Hp CagA protein can induce a humoral immune response. We have detected a different functional behaviour of GVBL compared to PBL. We have demonstrated that T lymphocytes from Hp infected subjects specifically proliferate when challenged with this antigen and that GVBL of such patients show a more frequent and higher response. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Host defense mechanisms Immunology and microbiology: GI infections in adults } "Proliferative Response to Helicobacter Pylori (Hp) CagA Protein of Gastric Vein Blood Lymphocytes from Infected Subjects"

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"P P 13 0313" P 13 0313 **Detection of Cytotoxin Associated Gene a (*CagA*) as Serodiagnostic Marker in Diagnosis and Treatment of Duodenal Ulcer (DU) and Non-Ulcer Dyspepsia (NUD)**

\*E. Karczewska, A. Bobrzynski, S.J. Konturek, H. Keanthous

Inst Physiol, Univ Sch Med, Krakow, Poland

OraVax Inc, Cambridge, MA, USA *Purpose:* It has been proposed that about 60% of *Helicobacter pylori* (Hp) isolates express *CagA* and that this protein induces serum IgG antibodies. Infection with Hp expressing *CagA* was suggested to increase the risk of DU but no comparative studies have been made regarding the expression of *CagA* in DU and NUD during anti-Hp therapy. *Methods:* This study included 50 Hp-positive (by <sup>14</sup>C-UBT, CLO, histology and culture of gastric biopsy) DU patients with active ulcers, 50 symptomatic NUD patients and 25 Hp-negative healthy control. Serum samples were obtained at day of initial endoscopy, 2 wk after triple therapy (omeprazole 20 mg bd, amoxicillin 750 mg bd and metronidazole 500 mg bd) and 4 wk after completion of this therapy. The presence of serum IgG antibodies to Hp was determined by ELISA using EIAGEN HP IgG test. Antibodies to *CagA* sera were detected by ELISA using recombinant *CagA* (ORV220) as antigen. *Summary of results:* All tested Hp-positive DU and NUD patients but none of healthy controls had positive serology for IgG. Serum IgG antibodies to *CagA* were positive in 80% of DU, in 40% of NUD but in none of healthy controls. After 2 and 6 wk of anti-Hp therapy, which succeeded in 95% eradication of Hp both in DU and NUD and complete ulcer healing in DU, there was significantly gradual decrease in IgG and *CagA* titre both in DU and NUD, reaching – 80% of patients. *Conclusions:* 1. Expression of *CagA* is strongly associated with Hp infection and is about twice higher in DU than in NUD patients suggesting that *CagA* expression increases the risk of DU and may serve as serodiagnostic marker to implement anti-Hp therapy, 2. gradual decrease in serum IgG and *CagA* titre may be useful in documentation of the progress in DU healing. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Immunology and microbiology: GI infections in adults } "Detection of Cytotoxin Associated Gene a (*CagA*) as Serodiagnostic Marker in Diagnosis and Treatment of Duodenal Ulcer (DU) and Non-Ulcer Dyspepsia (NUD)"

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"P P 13 0314" P 13 0314 **Suppression by Sulglycotide of H. Pylori Protease Activity towards PDGF and TGF{ b}**

\*B.L. Slomiany, J. Piotrowski, J. Majka, E. Piotrowski, A. Slomiany

Res Ctr., UMDNJ, Newark, NJ USA Sulglycotide, a chemically sulfated derivative of duodenal mucin, is a potent cytoprotective agent also recognized for its remarkable inhibitory activity towards *Helicobacter pylori* (HP). Since, HP is known to undermine the gastric mucosal integrity through a variety of enzymes capable of rapid destruction of gastric mucosal defense potential, in this study we assessed the effect of sulglycotide on the susceptibility of PDGF and TGF{ b} to HP protease. The experiments were carried out with HP, strain ATCC 43504. The plates with grown colonies were washed with 0.9% NaCl, filtered (0.2 μm) to retain the bacteria, and the filtrate was used as an enzyme source. The incubation mixtures for HP protease assays consisted of <sup>125</sup>I-labeled PDGF or TGF{ b}, enzyme protein (50–100 μg), sulglycotide (0–100 μg) and 0.22 ml phosphate buffer, pH 7.0. After 1 h incubation at 37°C, the incubates were chromatographed on a Bio-Gel P-2 column and the produced <sup>125</sup>I-labeled peptide fragments were measured in a gamma counter. The results of analysis of the eluted fragments revealed that HP protease caused extensive degradation of growth factors. Under the assay conditions HP protease evoked a 61.7% degradation of PDGF and a 62.3% degradation of TGF{ b}. Introduction of sulglycotide to the reaction assay system caused a dose dependent inhibition in PDGF and TGF{ b} proteolysis by HP enzyme. The maximal inhibitory effect was obtained with sulglycotide at 100 μg/ml, at which dose an 84.4% decrease in PDGF and 88.3% decrease in TGF{ b} degradation was achieved. These results demonstrate that sulglycotide by exerting a strong inhibitory activity on the HP protease towards PDGF and TGF{ b} is capable of promoting the proliferative action of these peptides in mucosal repair process. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Hormones and receptors: Growth factors Hormones and receptors: Molecular biology } "Suppression by Sulglycotide of H. Pylori Protease Activity towards PDGF and TGFβ"

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"P P 13 0315" P 13 0315 **Mucosal Levels of Prostaglandins E<sub>2</sub> (PGE<sub>2</sub>) and F<sub>2α</sub> (PGF<sub>2α</sub>) in Helicobacter Pylori (HP) — Positive Chronic Gastritis (CG)** P. Grigoriev, L. Korobeinikova, E. Yakovenko, A. Yakovenko, E. Chtcherbina, V. Gorodinskaya

Russian State Medical University, Moscow, Russia The interaction between mucosal levels of PGF<sub>2</sub> and PGF<sub>2α</sub> and histological features of CG HP-positive still remain to be elucidated. *Aim:* to assess the relationship between the CG HP-positive activity and concentration of PGE<sub>2</sub>, PGF<sub>2α</sub> in the gastric mucosa. *Methods:* 73 patients (pts) with CG HP-positive (22 men, 51 women age 43.7 years) were randomized into three groups. Group 1 (n=21) – pts with histological features of superficial gastritis and neutrophil polymorph infiltration (active gastritis). Group 2 (n=33) and group 3 (n=19) – without polymorph infiltration (non-active gastritis), but with temperate and severe mucosal atrophy conformity. Group 4 – control (n=20) included healthy volunteers. Multiple gastric antral and corpus biopsies were performed in every subject. HP was sought by histology and biopsy urease test. PGE<sub>2</sub> and PGF<sub>2α</sub> concentrations were investigated by R.I.A. Our results are presented in the table: Concentration PG (ng/mg) Group E<sub>2</sub> F<sub>2α</sub> antrum corpus antrum corpus 1 1.54 – 0.5<sup>\*4</sup> 1.88 – 0.6<sup>\*4</sup> 6.4 – 0.8<sup>\*2,3,4</sup> 9.52 – 1.2<sup>\*2,3,4</sup> 2 1.64 – 0.5<sup>\*4</sup> 1.18 – 0.3<sup>\*4</sup> 3.97 – 0.4<sup>\*1,3</sup> 3.72 – 0.4<sup>\*1,3</sup> 3 1.02 – 0.3<sup>\*4</sup> 1.1 – 0.5<sup>\*4</sup> 1.41 – 0.4<sup>\*1,2,4</sup> 1.71 – 0.5<sup>\*1,2,4</sup> 4 6.02 – 1.1<sup>\*1,2,3</sup> 6.17 – 1.2<sup>\*1,2,3</sup> 3.46 – 0.1<sup>\*1,3</sup> 3.0 – 0.5<sup>\*1,3</sup> \*p < 0.05 with above mentioned groups *Conclusion:* The found disbalance between concentration of PGE<sub>2</sub> and PGF<sub>2α</sub> may be very important in the pathogenesis of CG-associated with HP. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Mucosal Levels of Prostaglandins E<sub>2</sub> (PGE<sub>2</sub>) and F<sub>2α</sub> (PGF<sub>2α</sub>) in Helicobacter Pylori (HP) / Positive Chronic Gastritis (CG)"

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"P P 13 0316" P 13 0316 **Emerging Patterns of Helicobacter Pylori (*H. Pylori*) Antimicrobial Susceptibility in Europe - Q.N. Karim<sup>1</sup>, R.P.H. Logan<sup>2</sup>, GlaxoWellcome *H. pylori* Study Group**

<sup>1</sup> St Mary's Hospital, Paddington

<sup>2</sup> University Hospital, Nottingham *Introduction:* *H. pylori* antimicrobial susceptibility is an important determinant of the efficacy of eradication therapies [1]. The prevalence of antimicrobial resistance varies within Europe and is likely to increase given the diverse number of regimens and dosages currently used. This multicentre study assesses the prevalence of *H. pylori* antimicrobial resistance in the United Kingdom. *Methods:* *H. pylori* was isolated from antral biopsies of patients undergoing routine endoscopy and cultured according to standard microbiological methods (blood/chocolate agar in a microaerophilic environment, incubated for up to 10 days). Antimicrobial resistance was determined using "E-tests" or disc tests (tinidazole only) and breakpoints were taken from previous studies. *Results:* *H. pylori* has been isolated from 32% (1222/3823) of biopsies and antimicrobial susceptibility determined in 90% (1077/1222) of isolates. The percentage national average resistances (and ranges) for the most widely used antimicrobials are as shown in the table below: Metronidazole Tinidazole Clarithromycin Tetracycline 38.6 (14.6–65.2) 28.2 (7.2–41.5) 4.8 (1.3–12.5) 2.2 (0.7–6.3) The prevalence of resistance to metronidazole was greater in isolates from inner city centres (45.1%, n = 488) compared with rural centres (17.7%, n = 273). The same was shown with resistance to clarithromycin (4.8% vs. 1.7%). Nineteen isolates showed resistance to both clarithromycin and metronidazole. Multiple resistance was therefore seen in 5.3% of isolates. *Discussion/Conclusion:* The results demonstrate the wide variation of antimicrobial resistance to *H. pylori*. In the UK metronidazole resistant *H. pylori* is endemic. Multiple antimicrobial resistance seen in approximately 5% of *H. pylori* positive isolates, underlines the importance of establishing local patterns of antimicrobial resistance.

Reference: Penston JG. Aliment. Pharmacol. Ther 1994; 8: 369–389 Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Epidemiology (non cancer) }  
"Emerging Patterns of Helicobacter Pylori (*H. Pylori*) Antimicrobial Susceptibility in Europe -"

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"P P 13 0317" P 13 0317 **Nitric Oxide Synthase Activity in Gastric Mucosa: Influence of Helicobacter Pylori Colonization and NSAID Administration** J. Esteban<sup>1</sup>,

\*M.A. Rodr'edguez<sup>1</sup>, P. Hergueta<sup>2</sup>, F. Pellicer<sup>2</sup>, D. Delgado<sup>2</sup>, J.M. Herrer\edas<sup>2</sup>

<sup>1</sup> Servicio Central de Investigaci\fn en Ciencias de la Salud. Universidad de C\el diz

<sup>2</sup> Servicio de Aparato Digestivo. Hospital Universitario ""Virgen Macarena"", Universidad de Sevilla  
*Purpose:* Nitric oxide (NO) is related to several gastric processes including protective and aggressive effects. In this sense, NO synthesized by constitutive enzyme has protective effects such as an increase of mucus production and a major proliferative index of epithelial cells. These effects are mediated by cGMP. As opposed to this, NO released by inducible enzyme is related to appearance and maintenance of inflammatory processes. On the other hand, Helicobacter pylori (Hp) and NSAID administration have the ability to induce gastric damage by different mechanisms: Hp increases aggressive factors and NSAID decreases protective effects. In this sense, we have studied the influence of Hp colonization and NSAID administration on the NOS activity and the cGMP levels in gastric mucosa. *Methods:* Determination of NOSi and NOSc activity by measuring <sup>14</sup>C-L-citrulline formation (pmol.g of tissue<sup>-1</sup>}.min<sup>-1</sup> } and cGMP levels (pmol.g of tissue<sup>-1</sup> } in gastric biopsies of 78 patients of Gastroenterological Service of Virgen Macarena Hospital, Sevilla. The sample studied was composed by 11 normal subject, 7 patients with NSAID-induced gastric damage, 35 with gastritis Hp+, 6 patients with gastritis Hp{ -}, and 19 patients Hp+ and with duodenal ulcer. *Results:* NOS activity, both constitutive and inducible are not significantly different when normal, and gastritic patients (Hp+ and Hp{ -}) were contrasted (normal NOSc: 17.21 – 4.24 and NOSi: 20.89 – 3.81; gastritic patients Hp+ NOSc: 13.42 – 5.16 and NOSi: 35.67 – 12.26 and gastritic patients Hp{ -} NOSc: 14.34 – 11.23 and NOSi: 31.24 – 6.27). Similarly there were no significant differences when cGMP gastric levels were compared (normal: 100.55 – 27.35; gastritic patients Hp+: 76.59 – 21.85; and gastritic patients Hp{ -}: 81.57 – 14.28). On the contrary, the NOSi activity in patients with duodenal ulcers was significantly increased in comparison with normal and gastritic patients (NOSi: 67.34 – 15.43). The cGMP concentration is similar to normal. In patients with NSAID-induced gastric damage, the NOSc activity is significantly lower than normal (NOSc: 2.75 – 1.27). The same result was observed when cGMP was determined (22.08 – 5.24). *Conclusions:* NO can be related to gastrolesive ability of Hp through the NOSi activation and perpetuation of inflammatory processes. On the contrary, the NSAID-induced gastric injury can be related with a fall in NOSc activity and decrease of cGMP levels in gastric mucosa. This last results is in concordance with others experimental results obtained in rats. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Nitric Oxide Synthase Activity in Gastric Mucosa: Influence of Helicobacter Pylori Colonization and NSAID Administration"

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"P P 13 0318" P 13 0318 **Effect of Helicobacter Pylori Infection on Gastric Endocrine Cell Behavior of Duodenal Ulcer Patients**

\*Hagiwara Eitirou, Kashiwagi Hideyuki, Chen Gang, Ishibashi Yoshirou, Omura Nobuo, Moriya Yusuke, Aoki Teruaki

Department of Surgery (II), The Jikei University School of Medicine, Tokyo, Japan *Aim.* This study investigated the influence of H. pylori infection on gastrin-immunoreactive cell (G-cell) and histamine-immunoreactive cell numbers in stomachs of duodenal ulcer patients. *Method.* Endoscopic biopsy specimens from antrums of 22 duodenal ulcer patients were fixed by Carnoy's fluid and immuno-stained using antibodies of gastrin and H. pylori. Another specimens from gastric bodies were fixed by 4% [1-ethyl-3 (3-dimethyl-amino-propyl) carbodimide] (EDCDI) and 4% paraformaldehyde (PEA), and they were immuno-stained using antibodies of histamine. The numbers of gastrin cell and histamine cell were counted. The degree of H. pylori infection was classified to three groups according to the ratio of the numbers of gastric pits where H. pylori exist in 50 pits at random. *Result.* The G-cell numbers in middle-infected group were more than those in low-infected groups, but they were significantly decreased in high-infected group. The histamine cell numbers had a tendency to increase according to the degree of H. pylori infection. *Conclusion.* This result suggests that H. pylori infections has a stimulatory effect on gastrin cell numbers, but the severe infection in antrum seemed to induce the damage and decrease of gastrin cells. And histamine cell numbers were also increased according to the degree of H. pylori infection. The increase of histamine-immunostained cell in gastric body should be considered not only the increase of enterochromaffine-like cells but also those of mucosal mast cell. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Effect of Helicobacter Pylori Infection on Gastric Endocrine Cell Behavior of Duodenal Ulcer Patients"

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"P P 13 0319" P 13 0319 **Induction of Gastric Epithelial Apoptosis by H. Pylori Lipopolysaccharide and Its Suppression by Sucralfate**. J. Piotrowski, E. Piotrowski, D. Skrodzka, A. Slomiany,

\*B.L. Slomiany

Res. Ctr., UMDNJ, Newark, NJ USA The preservation of gastric mucosal homeostasis is a highly complex biological process that involves the programmed cell death. Under normal physiological conditions the mucosal integrity is maintained by a dynamic equilibrium of cell loss by apoptosis with that of cellular proliferation, while the enhanced cell apoptosis is a prominent feature in HP-associated gastritis. In this study we assessed the effect of HP lipopolysaccharide (LPS) on the induction of gastric epithelial cell apoptosis. The experiments were conducted with rats subjected to intragastric surface epithelial treatment with a dose of 50 µg HP LPS or LPS preincubated with 100 µg sucralfate. The animals were sacrificed 2 days following the treatment and their stomachs subjected to quantification of apoptotic epithelial cells. The cells undergoing apoptosis were identified using terminal deoxynucleotidyl transferase-mediated dUTP-digoxigenin nick end labeling assay. The slides were developed with diaminobenzene reagent and counterstained with methyl green. The sections were subjected to counting and the number of positive cells was expressed as the apoptotic index (AI %). The results of microscopic assessment revealed only occasional presence of apoptotic cells in the surface epithelium from the control group (AI 2.6%), while in the LPS group a numerous apoptotic cells were identified not only in the superficial epithelium but also deeper in the glands (AI 51.5%). Preincubation of HP LPS with sucralfate prior to animal treatment led to a marked reduction in the epithelial cell apoptosis (AI 4.9%). The findings demonstrate that HP induces apoptosis through its cell wall LPS and that sucralfate is capable of suppressing this untoward effect of HP. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Proliferation, carcinogenesis Hormones and receptors: Molecular biology } "Induction of Gastric Epithelial Apoptosis by H. Pylori Lipopolysaccharide and Its Suppression by Sucralfate"

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"P P 13 0320" P 13 0320 **Corporal Lymphoid Follicles (LF) Do Not Discriminate Autoimmune or H. Pylori Related Chronic Atrophic Gastritis (CAG)**

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Dept. Gastroenterology, University "La Sapienza" Roma, Italy

<sup>1</sup> Dept. Pathology, University "La Sapienza" Parma, Italy CAG is a condition characterized by atrophy of oxyntic mucosa hypo/achlorhydria and fasting hypergastrinemia. It has been considered an autoimmune condition, usually associated with latent or overt pernicious anemia (PA), but it has recently been observed that a small proportion of CAG patients are Hp infected. However, since the progression of corporal gastritis is accompanied by disappearance of H. pylori, the persistence of immunological memory, expressed by the presence of IgG to Hp, could indicate past exposure to the bacterium. Presence of LF in gastric biopsy specimens have been described as a constant feature of H. pylori-associated gastritis. Aim of this study was to investigate in a consecutive series of newly diagnosed CAG patients, the prevalence of present or past infection and the presence of LF as a histological marker of H. pylori infection. 104 consecutive hypergastrinemic CAG patients (84 F, 20 M aged 22–81) were divided in three groups as follows: Histo{ - } = histology, culture, IgG negative. Histo+ = histology, culture, Ig G; at least two of these tests positive. IgG+ = histology and culture negative, only IgG positive (> 40 U/l; Elisa, Biorad). Corporal atrophy was defined as focal or complete replacement of oxyntic glands by metaplastic pyloric or intestinal glands. LF were defined as intramucosal, basally located lymphoid aggregates with or without germinal centers. % Positive lymphoid follicles CAG groups Antrum Corpus Histo{ - } (n = 58; 55.8%) 16.7 52.8 Histo+ (n = 25; 24%) 50\* 70 IgG+ (n = 21; 20.2%) 5.9 61.9 *Results:* In a consecutive, newly diagnosed series of CAG patients, autoimmunity accounts for 55.8%, whereas active or past H. pylori infection for 44.2%. Corporal LF are widely present but do not discriminate the two different etiologic causes. In the antrum of Histo+ pts, LF are present in the 50%, being significantly higher than the other two groups (\* Fisher test p < 0.005) *Conclusions:* These data show that 44.2% of CAG pts have been infected H. pylori and that corporal LF are not exclusive markers for the presence of the infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Corporal Lymphoid Follicles (LF) Do Not Discriminate Autoimmune or H. Pylori Related Chronic Atrophic Gastritis (CAG)"

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"P P 13 0321" P 13 0321 **Helicobacter Pylori Biotypes in Patients with Peptic Ulcers**

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<sup>1</sup> Department of Gastroenterology, Hachioji Medical Hospital, Tokyo Medical College

<sup>2</sup> The Fourth Department of Internal Medicine, Tokyo Medical College *Objectives:* We isolated *Helicobacter pylori* from the collected gastric mucosa in patients with peptic ulcers. The obtained strains were classified into biotypes according to the presence or absence of activity of some enzymes, and the differences of these biotypes among peptic ulcers was investigated. *Methods:* The subjects were 164 patients with peptic ulcers, who had undergone endoscopic examination including *H. pylori*. They consisted of 82 with gastric ulcer, 61 with duodenal ulcer and 21 with gastroduodenal ulcer. In upper gastrointestinal endoscopy, gastric mucosal samples were collected from the greater curvatures of the antrum and the gastric body incubated under microaerophilic conditions (5% O<sub>2</sub>, 10% CO<sub>2</sub> and 85% N<sub>2</sub>) for 5–7 days. The produced colonies were allowed to grow with blood agar medium for 3–7 days. A bacterial solution was used for experiments using API ZYM Kit (Bio Merieux S.A., France) for determination of *H. pylori* biotype. *H. pylori* was classified into biotypes I, II and III according to Kung's classification. *Results:* Investigation of the clinical isolates from 164 patients with peptic ulcers showed that 154 (94%) were positive for incubation (with Squiraud medium). Biotypes I, II and III were revealed in 7, 48 and 46 cases, respectively. There were some patients who showed different biotypes in the antrum and the gastric body of the same patient. This type was designated as mixed type. The patients who showed such mixed types consisted of one with mixed type I + II, one with mixed type I + N.D. (non-differentiated), and 18 patients with mixed type II + III. As a result of assessment of biotypes according to each disease, the frequencies of biotypes II and III were high in each peptic ulcer. There was no significant difference between disease and biotype using the chi-square test of independence. *Conclusions:* The frequencies of Kung's types II and III were high on the evaluation of *H. pylori* biotypes in patients with peptic ulcers. There were some patients who showed different *H. pylori* biotypes in the stomach of the same patient. There were no significant relationships between various peptic ulcers and biotypes. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } " *Helicobacter Pylori Biotypes in Patients with Peptic Ulcers*"

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"P P 13 0322" P 13 0322 **Enhanced Cellular Proliferation and P53 Accumulation in Gastric Mucosa Chronically Infected with *Helicobacter Pylori***

\*K. Hibi, W. Koizumi, S. Tanabe, H. Imaizumi, S. Noguchi, M. Kida, M. Ohida, T. Mitsuhashi, K. Saigenji<sup>1</sup>, H. Mitomi, S. Kuwao, I. Okayasu<sup>2</sup>

<sup>1</sup> Department of Internal Medicine, Kitasato University, Sagamihara, Kanagawa, Japan

<sup>2</sup> Department of Pathology, Kitasato University, Sagamihara, Kanagawa, Japan *Aims:* The purpose is to evaluate whether the increased risk of gastric carcinoma development due to *Helicobacter pylori* (*H. pylori*) infection might be linked with elevated cell proliferative activity and oncoprotein overexpression. *Subjects:* Forty-eight patient undergoing therapy for *H. pylori* positive gastroduodenal ulcer were separated into not eradicated (NE;23 cases) and eradicated (E;25 cases) group 6 months after the treatment. *Methods:* Histological change in the gastric corpus and the antrum, assessed according to modified Sydney System, as well as epithelial cell kinetics (mitosis, Ki 67, PCNA), and expression of oncoproteins (p53, *bcl-2*) were examined before and at 3 months and 6 months after treatment for *H. pylori*. *Results:* Chronic persistent *H. pylori* infection was associated with increased inflammation and activity score, as well as elevated proliferation, as evidenced by the Ki67 and PCNA labeling indices and the mitotic index in NE group. Overexpression of p53 protein continued to be observed in the NE group after treatment but was significantly decreased in the E cases. *Conclusions:* Persistent *H. pylori* infection causes gastritis, with epithelial degeneration and regeneration that result in accentuation of epithelial cell proliferation and overexpression of p53 protein, this presumably heightening the risk of gastric carcinoma development. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Proliferation, carcinogenesis } "Enhanced Cellular Proliferation and P53 Accumulation in Gastric Mucosa Chronically Infected with Helicobacter Pylori"

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"P P 13 0323" P 13 0323 **Effect of Helicobacter Pylori (HP) Infection on Oxygen Metabolism in Gastric Mucosa** Grazyna Klupinska

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In pathogenesis of gastrointestinal tract diseases more and more often the role of active forms of oxygen is taken into consideration especially as they cause the direct damage to mucosa. The overproduction of free oxygen radicals is stimulated by many pathologic factors which include also Hp infection. The aim of this study was the estimation of selected parameters of aerobic metabolism in subjects with Hp dependent gastritis before and after infection eradication. Investigations were carried out in 30 subjects, aged 38–73 years, with histopathological diagnosis of chronic gastritis. Hp infection was confirmed by urease test and histological examination. In gastric mucosa biopsate frozen to  $-70^{\circ}\text{C}$ , there were determined: – malonic dialdehyde (MDA) – by Yagi method; – glutathione peroxidase (Gpx) -by Paglia and Valentine method; superoxide dismutase (SOD) -by Minami and Joshicara method. The tests were performed before and six weeks after the successful anti-bacterial treatment (famotidine + amoxycyline + metronidazol). The following results were obtained: Before treatment After eradication MDA (nmol/mg protein) 0.976 – 0.239 0.985 – 0.250 Gpx (U/mg protein) 0.0369 – 0.0173 0.0249 – 0.024 SOD (U/mg protein) 6.61 – 2.11 4.29 – 1.25

**Conclusions:-** the decrease in SOD activity in gastric mucosa after Hp eradication indicates the bacterial origin this enzyme- lack of simultaneous significant decrease in MDA activity proves that short-term treatment may result in clinical improvement but does not restore metabolic balance- after Hp eradication the anti-inflammatory treatment ought to be continued, particullary in its antioxidant form, in order to decrease oxygen radicals generation. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Effect of Helicobacter Pylori (HP) Infection on Oxygen Metabolism in Gastric Mucosa"

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"P P 13 0324" P 13 0324 **Helicobacter Pylori (Hp), Gastric Mucus and Endocrine Cells in Duodenal Ulcer**

\*E.V. Bespalova, Y.A. Gaidar, E.V. Stepanova

Ukrainian Scientific Research Institute of Gastroenterology, Dnepropetrovsk, Ukraine  
The aim of the study was to investigate the interrelation between Hp and gastric mucus-producing, gastrin- and somatostat in producing cells in patients with duodenal ulcer (DU). *Material and Methods:* 94 patients with DU were observed. Hp-infection was revealed in 86% cases. The estimate of gastric mucus production based on quantitative and qualitative analysis of intracellular mucus in surface epithelium and mucus in gastric juice using biochemical, histochemical and morphometric methods. The condition of G- and D-cells was determined by immunomorphologic method and electron microscopy. The generally accepted methods of statistic analysis were used. *Results:* It was determined, that persistence of Hp in patients with DU was accompanied by considerable decrease of intracellular mucus quantity in surface epithelium ( $p < 0.01$ ) with simultaneous increase of mucoprotein concentration in basal gastric juice ( $p < 0.03$ ). That testified to intensive mucus exstrusion. These changes were increased in correlation with the increase of Hp-infection degree ( $r = 0.62$ ). The considerable decrease of fucose and sialic acids testified to qualitative changes of mucus. The morphologic confirmation of direct contact of Hp with G-cells was received. The different degree of G-cells hyperplasia accompanied with D-cells hyperplasia was noted in 23% patients with DU associated with Hp. *Conclusion:* The obtained data testify to the modulating action of Hp on protective mechanisms and neuroendocrine function of the stomach in DU. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Helicobacter Pylori (Hp), Gastric Mucus and Endocrine Cells in Duodenal Ulcer"

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"P P 13 0325" P 13 0325 **Immunohistochemical Study in Gastric Mucosa of *Helicobacter Pylori*-Positive Duodenal Ulcer**

\*T. Shimizu, T. Ando, T. Yamaguchi, M. Sakakibara, M. Shinoda, T. Konagaya, K. Kyokane, M. Ohsuga, N. Kasuga, K. Kusugami

First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan  
**Purpose:** In *Helicobacter pylori* (*H. pylori*) infected gastric mucosa, there is an increase in the number of polymorphonuclear neutrophils (PMN) and mononuclear cells (MNC). *H. pylori* is known to stimulate the production of chemokines involved in recruitment of PMN and MNC. This study aimed to evaluate infiltrating cells and chemokine activity (IL-8 and GRO- $\alpha$ ) in *H. pylori* infected gastric mucosa.  
**Materials and Method:** Ten duodenal ulcer patients were studied before and after 1 week eradication therapy with omeprazole, metronidazole, and clarithromycin. *H. pylori* infection was confirmed by bacterial culture, histology, CLO, and urea breath test before the treatment. Three mucosal biopsies were taken from the antrum and body, respectively: one was for immunohistochemical staining with the antibody against *H. pylori*, myeloperoxidase (MPO), CD11b, CD68, IL-8, and GRO- $\alpha$ , one for HE staining to assess according to the Sydney system, and one for 24-hr organ cultures.  
**Results:** *H. pylori* eradication was achieved in all 10 cases (100%). Before eradication, there was a significant increase of mucosal PMN and MNC especially in the antrum. Most MPO-positive PMN were also positive for CD11b. After eradication, the number of MPO-positive PMN (antrum, 108.4 – 25.2 vs. 5.1 – 2.0/mm<sup>2</sup>; body, 56.8 – 23.1 vs. 1.0 – 1.0/mm<sup>2</sup>) and MNC was significantly decreased. The infiltrating IL-8 and GRO- $\alpha$ -positive cells were mostly CD68-positive macrophages and their number decreased after eradication (IL-8, 59.6 – 12.8 vs. 14.7 – 6.9/mm<sup>2</sup>; GRO- $\alpha$ , 43.4 – 9.2 vs. 10.6 – 5.3/mm<sup>2</sup> in the antrum). Before eradication, the gastric epithelial cells were also positive for IL-8 and GRO- $\alpha$ . In the organ culture supernatant, IL-8 and GRO- $\alpha$  activity decreased significantly after eradication.  
**Conclusion:** Mucosal chemokines may play an important role in the pathogenesis of *H. pylori*-infected gastric mucosa. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: Inflammation } "Immunohistochemical Study in Gastric Mucosa of *Helicobacter Pylori*-Positive Duodenal Ulcer"

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"P P 13 0326" P 13 0326 **Salivary and Gastric Epidermal Growth Factor (EGF) and Gastric Mucosal EGF Expression in Duodenal Ulcer (DU) Patients before and after Eradication of Helicobacter Pylori (Hp)**

\*P.C. Konturek<sup>1</sup>, A. Bobrzynski<sup>2</sup>, H. Ernst, S.J. Konturek<sup>2</sup>, G. Faller<sup>3</sup>, Ch. Klingler<sup>1</sup>, T. Kirchner<sup>3</sup>, E.G. Hahn<sup>1</sup>

Dept. Med. I, Univ. Erlangen, Germany

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<sup>1</sup> Dept. Med. I and Inst. Pathol., Univ. Erlangen, Germany

<sup>2</sup> Inst. Physiol. Jagiell. Univ. Med. Sch. Krakow, Poland EGF is released mainly by salivary glands and promotes gastric mucosal growth and repair but the influence of Hp infection on EGF release and its mucosal expression have not been evaluated. In this study, basal and pentagastrin-induced salivary and gastric luminal release of EGF (radioimmunoassay) as well as gastric mucosal expression of EGF (immunohistochemistry and RT-PCR) have been examined. 10 Hp-negative (by <sup>14</sup>C-urea breath test) controls and 20 Hp-positive active duodenal ulcer (DU) patients were tested before and 4 weeks after 2 week triple therapy (amoxicillin 500 mg qd, metronidazole 500 mg bd and omeprazole 20 mg bd). There was no difference in basal salivary and gastric luminal EGF contents between healthy controls and DU patients. Infusion of pentagastrin (2 mg/kg-h) raised by 3 folds salivary and gastric luminal concentrations and outputs of EGF both in control and DU subjects but following successful eradication of gastric Hp (confirmed by histology and culture of endoscopic biopsy samples) and complete healing of DU, there was 3–4 fold higher gastric EGF release in basal state and after pentagastrin than before the triple therapy. Salivary basal and pentagastrin-stimulated EGF was not significantly affected by the triple therapy and Hp was detected in gingival pockets in 18 out of 20 DU patients using Hp culture and PCR technique. Gastric mucosal EGF expression was negligible in healthy controls but was 2–4 times higher in DU patients and triple therapy had no influence on this enhanced expression. We conclude that (1) the stomach itself is capable to release large amounts of EGF that is augmented by pentagastrin, (2) gastric Hp eradication by triple therapy results in DU healing and further increase in gastric luminal EGF release and mucosal EGF expression but does not affect salivary EGF release possibly due to the failure to eradicate oral Hp. Oesophageal gastric duodenal disorders: Helicobacter Pylori Hormones and receptors: Growth factors } "Salivary and Gastric Epidermal Growth Factor (EGF) and Gastric Mucosal EGF Expression in Duodenal Ulcer (DU) Patients before and after Eradication of Helicobacter Pylori (Hp)"

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"P P 13 0327" P 13 0327 **Is there a Correlation between the Mean Values of IgG and IgA Specific Antibodies Against *H. Pylori* and Severity of Chronic Active Gastritis?**

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Gastroenterology and Pathology Departments, ""Ram\fn y Cajal"" Hospital, Madrid, Spain  
**Aim:** To evaluate the correlation between specific IgG and IgA values to *H. pylori* according to the severity of chronic active gastritis.  
**Methods:** A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum, gastric body, and gastric fundus were obtained for histology and *H. pylori* culture. The severity of chronic active gastritis was graded as mild, moderate and severe on the basis of polymorphonuclear leukocyte infiltration of gastric mucosa. It was not possible to determine the severity of chronic active gastritis in 7 patients. At endoscopy serum samples were obtained for serological testing. Specific IgG and IgA antibodies against *H. pylori* were determined by a quantitative commercial IgG ELISA (Helico G, Porton, Cambridge, UK) and a semiquantitative commercial IgA ELISA (G.A.P. Test IgA, Bio-Rad, Italy), respectively. *H. pylori* infection was diagnosed if culture was positive in at least one of the biopsy samples obtained.  
**Results:** 355 out of 400 (89%) patients were diagnosed with histological chronic gastritis involving some of the portion stomach. A total of 337 out of 355 (95%) patients with histological chronic gastritis were infected by *H. pylori* (demonstrated by culture). Mean values of IgG and IgA specific antibodies against *H. pylori* in relationship to the chronic gastritis activity and the severity of gastritis in patients with gastritis yielded the following results: Chronic gastritis IgG (U/ml) IgA (U/ml) Without activity 69 – 38.6\* 19 – 13.4 Mild activity 77.4 – 44.5\* 20.5 – 10.5 Moderate activity 89 – 38.1 27.8 – 22.3 Severe activity 105.8 – 30.8 53 – 69.1  $p < 0.05$  in all comparisons between the different groups, with the exception of the comparison signed with ""\*"". **Conclusions:** IgG and IgA specific antibodies against *H. pylori* mean values are clearly higher in patients with chronic gastritis with moderate and severe activity than those with chronic gastritis without activity. Moreover, mean values of IgG and particularly IgA specific antibodies against *H. pylori* *H. pylori* infection increased with increasing severity of chronic gastritis. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Immunology and microbiology: Inflammation }" "Is there a Correlation between the Mean Values of IgG and IgA Specific Antibodies Against *H. Pylori* and Severity of Chronic Active Gastritis?"

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"P P 13 0328" P 13 0328 **Correlation between Helicobacter Pylori Gastric Infection and Plasma Levels of Fibrinogen, Plasminogen Activator Inhibitor (PAI) and Von Willebrand Factor (vWF) Antigen** L. Bierti,

\*C. Cernuschi, C. Abbiati, G. Beccari, R. Di Battista, R. Marchi, A. Federici<sup>1</sup>, B. Bottasso<sup>1</sup>, N. Di Rocco<sup>1</sup>, R. de Franchis, P.M. Mannucci<sup>1</sup>

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There is evidence suggesting that patients at risk for coronary heart disease (CHD) are more likely to suffer from Helicobacter Pylori (HP) gastric infection than controls. In addition, preliminary data suggest that patients with HP infection may have high levels of plasma fibrinogen. *Aim:* to determine whether HP infection is associated with increased plasma levels of fibrinogen and other risk factors for CHD such as PAI and vWF antigen. *Methods:* consecutive patients undergoing upper gastrointestinal endoscopy at our Institute were studied. HP infection was diagnosed by the histological (modified Giemsa) and biochemical (CLO-test) methods. Concomitant inflammatory conditions were excluded by clinical examination and by measuring ESR, WBC, PCR, alpha-1-acid-glicoprotein. Fibrinogen levels were measured by Clauss' technique, while vWF antigen and PAI were assayed by ELISA. Statistical analysis was carried out by means of Student's t test. *Results:* 130 patients (66 HP positive and 64 HP negative) were enrolled. There was no difference between the two groups in sex, age, smoking history, hormonal therapy in females, arterial hypertension, dyslipidaemia, values of acute phase reactants, family history of CHD. Plasma fibrinogen levels (mg/dl) were 318 – 76 in the HP+ group vs 291 – 65 in the HP{ -} group; plasma PAI levels (ng/dl) were 41.2 – 29 in the HP+ and 35.8 – 24 in the HP{ -} patients; vWF antigen levels (U/dl) were 138 – 53 in the HP+ group vs 114 – 52 in the HP{ -} group. Differences between the two groups were statistically significant for vWF plasma levels  $p = 0.01$  and fibrinogen plasma levels  $p = 0.037$ . *Conclusion:* Plasma levels of vWF and fibrinogen were significantly higher in HP+ than in HP{ -} patients, PAI levels were also increased in HP+ patients although the difference did not reach statistical significance. Further studies on larger patients populations are required to clarify whether HP+ patients are indeed at higher risk for CHD. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Correlation between Helicobacter Pylori Gastric Infection and Plasma Levels of Fibrinogen, Plasminogen Activator Inhibitor (PAI) and Von Willebrand Factor (vWF) Antigen"

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"P P 13 0329" P 13 0329 **Helicobacter Pylori Infection and Serum Pepsinogen I  
Concnetration**

\*S.M. Park, J.W. Park, B.C. Yoo

Dept of Med, Chung-Ang University Hospital, Seoul, Korea *Purpose:* In order to clarify the relationship between H. pylori (Hp) infection and pepsinogen I (PGI), we have compared fasting serum PGI levels before and after the eradication of Hp infection in patients with peptic ulcer. *Methods:* Serum PGI levels were measured by RIA in 511 Hp (+) and 225 Hp ({ -}) patients. 110 out of 511 Hp (+) patients were given TDB, metronidazole, ranitidine, and antacid. 97 Hp (+) and 54 Hp ({ -}) patients were treated only with ranitidine and antacid. *Results:* Fasting serum PGI levels were significantly higher in infected patients (124.3 – 46.9 vs 77.9 – 25.8 ng/ml,  $p < 0.001$ ). Hp was eradicated in all the patients who received 4-week antibacterial therapy and serum PGI were significantly decreased from 129.8 – 43.0 to 82.4 – 24.0 ng/ml ( $p < 0.001$ ). Pre- and post-eradication PGI levels of both Hp (+) patients, not receiving antibacterial therapy, (120.8 – 40.9 vs 126.3 – 40.4 ng/ml) and Hp ({ -}) patients (75.1 – 8.0 vs 77.3 – 24.5 ng/ml) were not changed. *Conclusion:* We have confirmed that Hp infection causes increased PGI secretion and eradication of Hp results in significant fall in PGI levels. }" "Helicobacter Pylori Infection and Serum Pepsinogen I Concnetration"

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"P P 13 0330" P 13 0330 **Serum *CagA* IgG Antibodies in Korean Patients with *Helicobacter Pylori* Infection and their Relation to Gastric Pathology and Serum Pepsinogen**

\*K.C. Kim, H.J. Park, K.S. Lee, S.I. Lee, I.S. Park

Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea *Purpose:* To examine serum IgG response to *CagA* protein of *Helicobacter pylori* (HP) in HP+ Korean patients with functional dyspepsia (FD) and peptic ulcer disease and evaluate its effect on gastric pathology and biochemical changes (changes of serum gastrin and pepsinogen (PG) concentrations). *Methods:* Sera from 74 patients with FD (n = 50), gastric ulcer (GU, n = 12) and duodenal ulcer (DU, n = 12), all of whom were HP+ by histology and rapid urease (CLO) test, were assayed by ELISA for *CagA* IgG antibodies using a recombinant fragment (50 kDa) of *CagA* as antigen. The cut-off level for seropositivity was determined as 2 standard deviations above the mean reactivity of Western blot negative sera. The degree of gastric inflammation was studied in patients with FD using gastric inflammatory scores (modified method of Marshall et al. and Rugger et al., total score 0–8). The serum levels of gastrin, PG I, PG II were also studied in patients with FD using radioimmunoassay kits. *Results:* Percentage *CagA* seropositivity in HP+ patients with DU, GU and FD was 92%, 83% and 77% respectively ( $p = 0.28$ ). The magnitude of *CagA* IgG response was higher in patients with DU than those with GU and FD, but the difference was not statistically significant (mean optical density (OD) ratios;  $0.41 - 0.25$  vs  $0.26 - 0.18$  vs  $0.28 - 0.21$ ,  $p = 0.12$ ). The IgG titers (OD ratios) of *CagA* in patients with FD (n = 32) correlated well with the degree of gastric inflammation ( $r = 0.6558$ ,  $p < 0.001$ ). The mean inflammatory score was  $5.67 - 1.61$  in *CagA*+ patients and  $2.25 - 2.19$  in *CagA*{ - } patients ( $p < 0.01$ ). The IgG titers of *CagA* in patients with FD (n = 48) also correlated with serum PG II level ( $r = 0.3133$ ,  $p < 0.05$ ) and PGI/II ratio ( $r = \{ - \}0.4056$ ,  $p < 0.05$ ), but not with serum levels of gastrin or PG I. *Conclusions:* Levels of *CagA* seropositivity in HP+ ulcer patients and HP+ FD patients did not differ in this Korean population and may not be useful to predict peptic ulceration. However IgG titers of *CagA* correlated well with gastric inflammation and serum PG II level. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Serum *CagA* IgG Antibodies in Korean Patients with *Helicobacter Pylori* Infection and their Relation to Gastric Pathology and Serum Pepsinogen"

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"P P 13 0333" P 13 0333 **Decrease in Basal and Stimulated Gastrin and Pepsinogen I Levels after Eradication of *H. pylori*. A One-Year Follow-Up Study**

\*J.P. Gisbert, D. Boixeda, T. Vila, A. Al-Mostafa, Mart'edn C. de Argila, F. Bermejo

Ram\ 'f3n y Cajal Hospital, Madrid, Spain *Purpose:* To demonstrate the influence of *H. pylori* eradication on basal and stimulated gastrin (G) and pepsinogen I (PG) levels in duodenal ulcer patients, at an early stage and for a one-year follow-up period. *Methods:* Twenty-six patients (81% males, mean age 51 – 12 years) with a duodenal ulcer and successful *H. pylori* eradication were studied. In all patients biopsy (H&E) and a C<sup>13</sup>-urea breath test were performed both at diagnosis and 1 month after completing therapy (triple therapy with bismuth, or omeprazole plus one or two antibiotics). Serum samples were obtained at diagnosis and at 1 month, 6 months and 1 year, to measure basal and stimulated G (10 and 20 min) and PG (30 and 60 min) levels after ingestion of beef cubes (Oxo Ltd. McColl et al, Lancet 1989) and injection of pentagastrin (6 \ 'b5gr/kg), respectively. *Results:* A significant histologic improvement both in the antrum and body ( $p < 0.001$ ) was observed after finishing treatment. Decreases in G and PG levels after eradication are summarized in the table. G 0 m G 10 m G 20 m PG 0 m PG 30 m PG 60 m Initial 45 – 12\* 94 – 48\* 92 – 40\* 101 – 30\* 108 – 33\* 118 – 36\* 1 mth 40 – 10\* 62 – 22\* 62 – 21\* 83 – 23\* 86 – 27\* 95 – 29\* 6 mth 38 – 10 60 – 26 60 – 24 75 – 24\* 77 – 25\* 86 – 26\* 1 year 39 – 80 66 – 27 62 – 22 74 – 26 77 – 27 87 – 30 m: minutes; \* $p < 0.05$  G levels decreased immediately after eradication (at 1 month), and remained unchanged afterwards (for the 1-year follow-up) (Wilcoxon test for paired data). However, decrease in PG occurred progressively during the 6 months following eradication (they fell down at 1 month, and again at 6 months). Finally, the values remained unchanged at 1 year. *Conclusions:* *H. pylori* eradication in duodenal ulcer patients was associated with a significant decrease in basal and stimulated G levels, that was detected immediately (one month) after finishing treatment, and remained unchanged for one-year. However, decrease in basal and stimulated PG levels occurred progressively during the six months following eradication, although such levels also remained unchanged afterwards. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Decrease in Basal and Stimulated Gastrin and Pepsinogen I Levels after Eradication of *H. pylori*. A One-Year Follow-Up Study"

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"P P 13 0335" P 13 0335 **Gastric Metaplasia (GM) and Helicobacter Pylori (HP) Infection in Normal Men (N) and Patients with Duodenal Ulcer Disease (DU)** A. Biad<sup>1</sup>, N. Benfenatki<sup>1</sup>, R.M. Hamladji<sup>1</sup>, A. Bouhadef<sup>2</sup>

<sup>1</sup> Internal Service

<sup>2</sup> Pathology Service, University d'Alger, Hopital Rouiba 35300, Algeria GM has been considered a necessary condition for the infection of duodenum by Helicobacter Pylori and the development of DU disease (Marshall 1988). *Purpose of the study:* To assess the prevalence of GM (Toluidine, Pas+) on median bulb N or marginal ulcer DU biopsies (n = 3), Gastric acid secretion was collected by aspiration in basal state (1 hour) and after pentagastrin stimulation 6 \b5g/kg/im (1 hour): PAO (mml/h) (titremetric method): Histological detection of bulbar and antral mucosa (biopsies = 4 = in all N and DU. *Endoscopic findings:* N DU n 20 60 M/F 15/5 15/10 Age (yr) median range 38 41.18 => 68 9 MG+ MG. 1 16 => 63 44, 16 MG+/PAO > 30, PAO < 30 1/1 19 44/36 # 44/8 \* MG { - } / PAO > 30, PAO < 30 19/6 19/13 16/4, 16/12 MG+/bulbar HP+, bulbar HP { - } 1/0 0/C 14/42 #, 44/2 \* MG+/bulbar HP+, bulbar HP { - } 19/0 0/19 16/3 #, 16/20 Antral mucosa (n°, AC, CG) 5 0, 19 0, 2, 50 MG+ Antral (n°, AC, CG) 1/0 1/0, 1/1 44/10, 44/0, 44/44 MG { - } / Antral (n°, AC, CG) 19/5 19/0, 19/14 16/0, 16/2 16/14+: presence; { - }: absence, n°: normal, AG: Acute gastritis. CG: chronic gastritis, #significative, \*p < 0.05 *Conclusion:* This study confirmed the high incidence of GM in DU (GM+ = 75%) compared to N (GM+ = 5%) and his strong link with hyperacidity (82% of GM+ = PAo > 30) bulbar HP+ (95% of GM+ = HP) and CG Antral mucosa (100% of MG++ = CG) in DU. } "Gastric Metaplasia (GM) and Helicobacter Pylori (HP) Infection in Normal Men (N) and Patients with Duodenal Ulcer Disease (DU)"

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"P P 13 0336" P 13 0336 **H. Pylori Colonization of Gastric Metaplasia in Proximal Duodenum (DGM) Is Not an Obligatory Condition for a Duodenal Ulcer (DU) Development and a Preferentially One**

\*D. Pospai, C. Vissuzaine, M. Merrouche, S. Forestier, M. Joubert-Collin, M. Mignon

Bichat, Cl. Bernard Hospital, Paris, France According to the accepted cascade of pathophysiological events in DU disease, H. pylori colonizes DGM resulting in active duodenitis and ulceration. In fact DGM is a pre-existing obligatory condition for DU development independent of any associated risk factor (Gastroenterology 1996; 110, 4: A 232). In contrast Hp is inconstantly found in DGM areas. To establish duodenal Hp prevalence and location in DGM areas, and determinants of duodenal Hp colonization, 55 active DU pts with Hp positive gastritis were evaluated prospectively. *Methods:* Duodenal Hp was detected by histology and immunohistochemistry (IHC) (antibody-DACO B0471) from multiple biopsies (4–8 quadrantic in 1st duodenum and 3 on DU margins). PAS (DGM prevalence and extent [as % of total epithelial surface measured in biopsies] and HPS [grading of gastritis (in 6 Sydney system biopsies) and duodenitis] stains were performed. *Results: Prevalence:* Duodenal Hp was detected in 17/55 (30.9%): Hp was detected by histology and IHC in 13 cases and by IHC only in 4 cases. *Location:* In all pts with Hp detected in duodenum, Hp was located on DGM areas harbouring the niches (100%) and concomitantly in DGM areas outside the ulcer in 23% only. In Hp+ve DGM areas, active duodenitis was present in 100% on ulcer margins and 50% in extra ulcer DGM areas. *Determinants* of the preferential duodenal Hp colonization: *a)* larger extent of Hp colonized DGM vs non colonized DGM: % median (range): 85 (70–100) vs 50 (10–100) respectively  $p = 0.03$ . *b)* significantly higher association with Hp pangastritis in duodenal Hp+ve (12/17) vs duodenal Hp{ - }ve (11/38) pts  $p = 0.03$ . *c)* significantly higher association with antral atrophic gastritis and intestinal metaplasia in duodenal Hp+ve (7/17) vs duodenal HP{ - }ve (5/38) pts  $p = 0.02$ . No other significant differences were observed concerning age, sex, familial history, smoking, number of relapses, location and type of ulcer or previous treatment between duodenal Hp+ve vs. Hp{ - }ve group. *Conclusion:* In DU pts Hp colonization of DGM was found in only 31%, located in the most extended areas of DGM and preferentially in patients presenting with both Hp pangastritis, antral atrophic gastritis and intestinal metaplasia. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, specific: Stomach, duodenum } "H. Pylori Colonization of Gastric Metaplasia in Proximal Duodenum (DGM) Is Not an Obligatory Condition for a Duodenal Ulcer (DU) Development and a Preferentially One"

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"P P 13 0338" P 13 0338 **Structure of Gastric Mucous Membrane When an Ulcer Disease is Present Associated with Helicobacter Pylori (HP)** M.I. Dauletbaeva, B.K. Nurgalieva

Almaty state medical institute, Almaty, Kazakhstan *The purpose:* study of the role HP colonization in progression of structural changes of gastric mucosae. *Materials and methods:* There were 162 patients observed with Ulcer disease, including 94 with gastric Ulcers and 68 with duodenal ulcers. Endoscopy with biopsy and histologic examination of gastric mucosal biopsies were performed as well as detection of HP. Cytologic smears and the presence of HP in them were studied also. *Results:* Endoscopic gastritis was diagnosed in 87% of gastric Ulcers, and 95% of duodenal ulcers. In histologic examination gastritis was found in 100% of the patients, surface gastritis in 13.6%, atrophic gastritis in 23.4%, atrophic gastritis with intestinal metaplasia in 38.8%, atrophic-hyperplastic in 6.2%, erosive gastritis 8%, diffuse gastritis in 10.5%. The cytologic picture was characterized by marked cell changes: there were signs of inflammation and proliferation in 100%, dysplasia in 85%, dystrophy in 53%, intestinal metaplasia in 65% and infiltration by lymphocytes in 38.8% of all cases. In all investigated smears, neutrophil infiltration was revealed. Cell dysplasia was characterized by expressed proliferation, illegible borders, polymorphic cells, changes of a nucleo-cytoplasmatic ratio. Dysplasia of the first degree was revealed in 9%, second degree in 55.6%, and third degree in 20.4% of all cases. The results listed above testify the significant structural changes of gastric mucosae in HP colonization. HP was detected by Standard histologic method in gastric ulcers in 66%, and in duodenal ulcers at 87% of the time. In cytologic smears HP was detected in 67% of gastric Ulcers and in 89.8% of duodenal ulcers. *Conclusions:* The degree of HP colonization correlates with structural changes of gastric mucosae. It also correlates with the length of time needed for healing from ulcer damage. Structural changes and time for healing seem to be closely related. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, specific: Stomach, duodenum } "Structure of Gastric Mucous Membrane When an Ulcer Disease is Present Associated with Helicobacter Pylori (HP)"

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## "P P 13 0339" P 13 0339 Helicobacter Pylori (HP) and Free Oxygen Radicals

\*N. Yen & N. Aksoy, M. Y. K. G. Haklar, S. Yalçın

SSK Okmeydanı Education Hospital & Marmara University Fac. of Medicine, Istanbul-Turkey Free radicals (FR) can easily intake and give out electrons from molecules around them due to the fact that they contain in the last orbit only one electron. These radicals come into the being either during normal cell functions which are toxic, or materials produced by defence cells. They cause the degeneration and death of the cell membrane or loss of organs function and tissue. The aim of our work was searching the relation between the action of HP on gastric mucosa inflammation caused by FR and to know the condition by patients given omeprazole (om.) or om. + amoxicillin (amox.) before or after treatment in the basis of FR. The study has begun with 20 female, 27 male (totally 47) patients. In our clinic with peptic complaints, who had taken no medicine for last 1 month. (Age range 16–63, average 35.9 years). Endoscopic results have shown duodenal ulcer 10, antral gastritis 25, bulbitis 7, bulbitis + gastritis 5 cases. The patients have been divided into two groups at random. *Group IA*: (n: 16), HP (+), omeprazole (omep). *Group IB*: (n: 24), HP (+), om. + amox. Another group was built up of HP (–)'s; *Group II*: (n: 7), HP (–), om. Omeprazole was given. 40 mg/day orally every morning by hungry for 1 month, amox. 500 mg/day for 10 days orally. From each case 9 biopsies have been taken from antrum on days 0 and 30. HP searched by Clo test, FR were searched through chemiluminescence method. For  $H_2O_2$ ,  $OH^{\cdot}$ , hypochlorite and peroxynitrite "*Luminal*", for  $O_2^{\cdot-}$  "*Lucigenin*" are used. The results are given as in the table

	Luminal (Cpm/mg-tissue)	Lucigenin	Day 0	Day 30
Group IA	2.25	1.57	2.40	1.61
HP (+), Omep.	p: 0.03	p: 0.008		
Group IB	1.65	0.32	1.96	0.49
HP (+), Omep + Amox.	p: < 0.001	p: < 0.001		
Group II	0.60	0.30	0.82	0.64
HP (–), Omep.	p: 0.11 (NS)	p: 0.02 (St. t test)		

**Conclusion:** \* The FR level before the treatment in both HP (+) and HP (–) were considerably high. This indicates that HP is increasing of the gastric mucosa inflammation through the FR. \* By single or combined treatment a considerable decrease of FR has been observed. (Those decreases are more obvious by the patients who take om. + amox. related to the patients who take only om. So the treatment of peptic diseases causes to decrease of FR and consequently the decreasing of destructive action of HP. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Helicobacter Pylori (HP) and Free Oxygen Radicals"

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"P P 13 0340" P 13 0340 **Condition of Hormonal System and Mucosal Immune Response of Antral Section in Women of Different Age Categories with Helicobacter Pulori: — Associated Duodenal Ulcer**

\*R.R. Gazizova, A.N. Novikova, M.A. Vinogradova, F. Kamilov, L.N. Mingazetdinova, N.A. Vinogradov, E.G. Mutalova

Bashkir Medical University, Ufa, Russia *Aim:* To investigate the relationship between the hormonal system and the local immune response of the gastric mucosa (GM) in women of the reproductive and postmenopausal age groups with duodenal ulcer (DU) associated with *Helicobacter pulori* (H.p.). *Methods:* Basal Levels of pituitary (FSH, LH, STH, ACTH, TSH) and peripheral hormones (estradiol, progesterone, testosterone, cortisol, T3, T4, gastrin, C-peptide, insulin) in 98 women with DU in both phases of their menstrual cycle plus 20 control subjects and also in 76 elderly women as well as 16 comparable controls were assessed by RIA. In antral biopsies the number of IgA, M, G-producing cells and T-helpers (T-h), and T-suppressors (T-s) — by the indirect immunofluorescent method with the aid of monoclonal antibodies. H.p. was detected according to L. Walters et al. *Results:* It has been found that DU distorts the feedback between the central and the peripheral parts of the endocrine system. The prevalence of confirmed H.p. was 98.2%, the number of H.p. bacteria in the pits was 15.44 – 0.54 against 10.29 – 0.14 in younger women (×900 magnification). Elderly women manifested a statistically reliable decline in the number of IGA-producing cells ( $p < 0.01$ ) and T-h. Their immunoregulatory index was reduced to 0.71 against 0.81 in younger women. Women of the reproductive age group had a high correlation between the amount of progesterone and IGM in the first phase of the menstrual cycle, such correlation disappeared in the second phase; in elderly women there was a positive correlation between IgG and STH and a negative correlation with the number of H.p. ( $R = 0.74$ ,  $D = 0.55$ ). *Conclusion:* Depending upon their age and phase of the menstrual cycle, women suffering from DU associated with H.p. display marked differences in the relationship between the hormonal system and the local immune response of GM. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: Inflammation }" "Condition of Hormonal System and Mucosal Immune Response of Antral Section in Women of Different Age Categories with Helicobacter Pulori: / Associated Duodenal Ulcer"

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"P P 13 0341" P 13 0341 **Gastric Mucosa Lymphoid Hiperplasia in Helicobacter Pylori (H P) Infections** C. Hajdu, G. Simu, S. Bataga<sup>1</sup>, L. Bancu<sup>1</sup>, C. Copotoiu<sup>2</sup>

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<sup>1</sup> Department of Gastroenterology, Clinical Contry Hospital Tg Mures, Romania

<sup>2</sup> Depart. of Surgery, Clinical Contry Hospital Tg Mures, Romania A long time infection with H P can evolve in some people from diffuse lymphoid hiperplasia towards malignant lymphoma, although the lymphoid tissue is not extremely abundant in the gastric mucosa. Were studied 54 surgical removed stomachs, 46 from patients with complicated gastric ulcer and 8 from patients with endoscopic aspect as lobulated, polypoid mass in the distal half of the stomach. We made slides from gastric mucus and stained them with Giemsa for HP; the removal pieces were embedded in paraffin and stained with hematoxiline eosine and PAS hematoxiline. We also applied imunohistochemic methods. 39 cronic gastric ulcers associated with cronic gastritis and H P infections have been found. In 7 cases the gastric ulcer was accompanied by a diffuse mucosal and submucosal inflamatory hiperplasia with the presence of clearly reactive germinal centers throughout the lesions. In the gastric mucus H P was present. One case was a marginal extranodal lymphoma with small cleaved cells, accompanied with cronic diffuse gastritia with active foci and a high H P infection. We found also 2 large polymorphous B cell lymphoma and 4 cases were mixed diffuse form, small and large B cell limphoma. In the 2 cases of large cell lymphoms in the gastric mucus microbial flora was polymorph and HP was absent. Interesting was the case of an undiferentiated gastric carcinoma accompanied with a high diffuse lymphoid hiperplasia, HP being also present. Our observation suggest that the H P infection could develop an important lymphoid hiperplasia, sometimes liable to turn into lymphoma. The establishment of policlonal or monoclonal nature of the lymphoid hiperplasia by imunohistochemical methods is essential in finding out the reactive or neoplastic aspect of this hiperplasia. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infections in adults Oncology, specific: Lymphoma } "Gastric Mucosa Lymphoid Hiperplasia in Helicobacter Pylori (H P) Infections"

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"P P 13 0342" P 13 0342 **DNA Fingerprinting of Helicobacter Pylori Isolated from Patients with Peptic Ulcer**

\*C.S. Shim, Y.H. Lee, Y.D. Cho, H.K. Bong, J.O. Kim, J.Y. Cho, Y.S. Kim, J.S. Lee, M.S. Lee, S.G. Hwang, S.J. Hong

Institute for Digestive Research, Division of Gastroenterology, Soon Chun Hyang University, Seoul, Korea

The gastric pathogen, *Helicobacter pylori* establishes long-term chronic infection that can lead to gastritis, peptic ulcer, and gastric cancer. Urease might allow the survival of the bacteria in an acidic environment, a prerequisite for colonization. *Helicobacter pylori* is cytotoxic to cultured human gastric epithelial cells and this toxicity is due in part to ammonia produced by hydrolysis of urea. In a previous study by Foxall et al., they suggested that Hae III digest patterns of PCR-amplified UreA and UreB genes might serve as a sensitive epidemiological tool for the typing of clinical isolates of *Helicobacter pylori*. We obtained the PCR-amplified UreA and UreB genes from the 18 clinical isolates in Korean and analyzed the Hae III digest patterns. In methods, clinical isolates of *Helicobacter pylori* were obtained by endoscopic biopsy from 18 patients with gastric or duodenal ulcer. Biopsy tissues were inoculated onto blood agar plates containing 5% horse serum and skirrow's supplement, and the plates were cultured for 3 days at 37 °C under microaerobic conditions. Chromosomal DNA of *Helicobacter pylori* were extracted from harvested colonies and PCR amplification were performed to amplify the urease structural subunit genes, UreA and UreB (Labigne A, et al. J. Bacteriology, 1991). PCR products, digested with Hae III, were run on 1.5% agarose gels. In results, the 2.4 kb PCR products were amplified from all 18 *Helicobacter pylori* isolates. From the restriction enzyme digestion of these PCR products, we could classify on the basis of RFLP patterns by Hae III restriction endonuclease digestion produced 11 distinct patterns on agarose gel, with five patterns occurring within two or three isolates. In conclusion, the urease genes of *Helicobacter pylori* had genetic heterogeneity, therefore it could be of considerable tool for epidemiological studies.

Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: GI infections in adults } "DNA Fingerprinting of *Helicobacter Pylori* Isolated from Patients with Peptic Ulcer"

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"P P 13 0343" P 13 0343 **Low Gastric Glutathione and Glutathione S-Transferase Levels in Patients Infected with Helicobacter Pylori**

\*M.L. Verhulst, A.H.A.M. v Oijen, H.M.J. Roelofs, W.H.M. Peters, J.B.M.J. Jansen

Department of Gastroenterology, University Hospital Nijmegen. The Netherlands *Introduction:* Infection with Helicobacter pylori (HP) is strongly associated with peptic ulcer disease. In addition, chronic infection with HP may increase the risk of gastric cancer. The mechanism of carcinogenesis, however, is not yet clarified. Glutathione (GSH) and glutathione S-transferases (GSTs) represent an important detoxification system in epithelial cells of the gastrointestinal tract. Toxins or carcinogens are inactivated by conjugation with GSH, catalyzed by GSTs. High levels of GSH and GST have been correlated with a low risk of developing gastrointestinal cancers. *Methods:* GST and GSH levels were measured in biopsies taken from the gastric antrum of 1) patients with gastric complaints without HP infection (n = 57; age 43.1 – 13.5 yrs), 2) patients who became HP negative after eradication of HP (n = 22; age 49.4 – 2.3 yrs) and 3) patients with proven HP infection (n = 24; age 49.5 – 2.6 yrs). Results are given as means – SD and were tested for significant differences with the Wilcoxon rank sum test. *Results:* GSH and GST levels in both groups of patients negative for HP (groups 1 and 2) did not differ and were 32.8 – 10.8 vs. 27.2 – 11.1 nmol/mg protein, and 775 – 291 vs. 860 – 208 nmol/min. mg protein, respectively. GSH and GST values in the HP positive patients (11.6 – 11.8 nmol/mg protein and 591 – 176 nmol/min. mg protein, respectively) were significantly lower as compared to values in both groups of HP negative patients (all p-values < 0.01). *Conclusion:* The antral mucosa of patients infected with HP contains significantly lower amounts of GSH and GST, which results in a decreased capacity to detoxify toxins and carcinogens. This finding may contribute to the increased risk of development of adenocarcinomas in these patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach } "Low Gastric Glutathione and Glutathione S-Transferase Levels in Patients Infected with Helicobacter Pylori"

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"P P 13 0344" P 13 0344 **Short-Chain Fatty Acids Produced by *Helicobacter Pylori***

\*T. Ohkusa, K. Shimoi, K. Ariake, I. Takashimizu, K. Fujiki, A. Araki, K. Honda, Y. Enomoto, T. Sakurazawa, T. Horiuchi, S. Suzuki, K. Ishii, S. Endo, H. Hosoi, S. Tokoi, N. Sasaki

First Department of Internal Medicine, Tokyo Medical and Dental University School of Medicine, Tokyo, Japan Short-chain fatty acids (SCFA) are produced by various bacteria and principle fermentation products are different depending on individual groups of bacteria. There have been few studies which demonstrate what kinds of short-chain fatty acids to be produced by *Helicobacter pylori* (*Hp*). Therefore, we analysed the short-chain fatty acids produced by *Hp*. **Methods:** The five strains of *Hp* which had been isolated from the mucosa of gastric ulcer patients were cultured in burcella broth supplemented with 10% horse serum under a microaerophilic atmosphere without antibiotics, at 37°C for 7 days. After incubation, the cells were removed from the cultured broth by centrifugation and filtration. The supernatant was analysed by HPLC. **Results:** SCFA Amount (mean – SD, μmol/L) Malic acid 0.458 – 0.034 Succinic acid 1.95 – 0.407 Lactic acid 4.97 – 0.911 Formic acid 2.65 – 0.747 Acetic acid 17.4 – 12.8 Levulic acid 1.01 – 0.065 Propionic acid 12.9 – 4.14 i-Butyric acid 1.62 – 0.555 n-Butyric acid 3.27 – 2.96 i-Valeric acid 3.04 – 1.96 TOTAL 50.5 – 19.6 Citric and pyruvic acids were not detected. **Conclusion:** Acetic acid and propionic acid were the principal SCFA produced by *Hp*. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Nutrition: Metabolism } "Short-Chain Fatty Acids Produced by *Helicobacter Pylori*"

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## "P P 13 0345" P 13 0345 Degradation of Growth Factors by Helicobacter Pylori: Effect of Sucralfate

\*B.L. Slomiany, J. Piotrowski, A. Slomiany

Res. Ctr., UMDNJ, Newark, NJ USA Infection with *Helicobacter pylori* (HP) is now recognized as a major factor in the pathogenesis of gastric disease, and the bacterium is known to elaborate a number of enzymes capable of rapid compromise of gastric mucosal homeostasis and the repair mechanisms. Among the factors implicated in the control of mucosal repair are bioactive peptides that exert their effects by activating specific cell surface receptors which often contain an intrinsic tyrosine kinase activity. The purpose of this study was to assess the susceptibility of EGF, bFGF, TGF $\beta$  and PDGF to degradation by HP protease. The effect of an antiulcer agent, sucralfate on this pathogenic activity of HP was also investigated. The experiments were carried out with HP protease obtained from the filtrates of saline washes of the bacterium cultures. The incubation assays for growth factors susceptibility to HP protease consisted of  $^{125}\text{I}$ -labeled EGF, bFGF, TGF $\beta$  or PDGF, enzyme protein (50  $\mu\text{g}$ ), sucralfate (0–200  $\mu\text{g}$ ), and 0.22 ml of phosphate buffer, pH 7.0. The reaction mixtures were maintained at 37 $^{\circ}\text{C}$  for 1 h, and then subjected to chromatography on Bio-Gel P-2 column and the produced  $^{125}\text{I}$ -labeled peptide fragments were quantitated by counting in a gamma counter. The results established that under the assay conditions HP caused only 5–7% degradation of EGF and bFGF. However, the HP protease evoked a 61.7% degradation of PDGF and a 62.3% degradation of TGF $\beta$ . Introduction of sucralfate to the assay system caused the inhibition in the extent of growth factors proteolysis by HP enzyme. This inhibitory effect of sucralfate was dose dependent and reached a maximum value at 200  $\mu\text{g}/\text{ml}$  sucralfate, at which concentration a 79.7% decrease in PDGF and 82.7% decrease in TGF $\beta$  degradation occurred. The results provide strong evidence for the effectiveness of sucralfate in the protection of gastric mucosal growth factor pool against degradation by HP. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Hormones and receptors: Growth factors Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Degradation of Growth Factors by *Helicobacter Pylori*: Effect of Sucralfate"

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"P P 13 0346" P 13 0346 **Increasing Surface Hydrophobicity in Transformation to the Coccoid Form of Helicobacter Pylori. A Pathogenic Factor?** D. Risberg, H. Enroth, L. Engstrand, A. Uribe

Department of Medicine, Karolinska Institute, Danderyd Hospital, Stockholm, Sweden

Department of Microbiology, University Hospital, Uppsala, Sweden It has been suggested that the coccoid form of *H. pylori* facilitate the survival of the microorganism in the stomach. This may contribute to the relapses of infection following eradication therapy. Our aim was to examine the contact angles during transformation of *H. pylori* to the coccoid form, to estimate potential changes in surface hydrophobicity which could affect bacterial attachment and the protection of the microorganism in an acidic environment. *Methods:* *H. pylori* strains 88–23, A5 and knock-out mutants lacking vac A cytotoxic protein (A5 vac A), the urease-negative strain 4, and the mutant strain 69 A lacking flagellae were investigated. All strains were cultured on agar from 2 up to 15 days. Samples of viable bacteria were obtained at regular intervals, and evenly spread on glass covers. After 30 minutes of drying, a droplet of saline was applied and the contact angle was measured using a goniometer. *Results:* In all examined strains the contact angle was significantly increased from day 2–3 and on, compared to control values ( $p < 0.001$ ). Thus, the contact angle of the strain 88–23 was 50% higher after 14 days, the maximal increment for the urease negative strain was 46.15% and for the flagellae-negative mutant 28.3%, respectively. Similarly, an increment in contact angle of 37% and 21.5% were observed in the A5 and the A5 vac A strains, respectively. *Conclusions:* Development of coccoid forms of *H. pylori* is associated with increased surface hydrophobicity, which may facilitate the attachment of the microorganism to the gastric mucosa. Possibly, it may also act as a protective mechanism against hydrophylic agents such as gastric acid. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infections in adults Immunology and microbiology: Host defense mechanisms } "Increasing Surface Hydrophobicity in Transformation to the Coccoid Form of Helicobacter Pylori. A Pathogenic Factor?"

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"P P 13 0347" P 13 0347 **Gastric Production of Inflammatory Cytokines in Patients with Helicobacter Pylori Infection with and without Duodenal Ulcer**

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Institute of Internal Medicine, University of Milan, Milan, Italy

<sup>1</sup> Institute of Medical Sciences, University of Milan, Italy

IRCCS Ospedale Policlinico, Milan, Italy An enhanced mucosal production of interleukins 8 (IL-8) and 6 (IL-6) has been observed in Helicobacter pylori (Hp) infection, while fewer data are available on interferon gamma ( $\gamma$ INF) and IL-4. However, the correlation between cytokines levels and presence of duodenal ulcer (DU) is unknown. *Aim:* to study gastric mucosal production of IL-8, IL-6, IL-4 and  $\gamma$ INF in patients with Hp infection with DU or nonulcer dyspepsia (NUD). *Methods:* we studied 13 patients with Hp+ DU, 8 with Hp+ NUD and 4 with Hp{ - } NUD. 10 DU patients underwent repeat endoscopy after treatment. Hp was assayed by rapid urease test and histology. IL-8, IL-6, IL-4 and  $\gamma$ INF concentrations were measured in the homogenate supernatant of 2 antral biopsies by commercially available ELISA kits. *Results:* (see table) IL-8 was detectable in 0/4 patients with Hp{ - } NUD, in 5/8 Hp+ NUD and in 12/13 untreated DU. IL-8 levels were higher in Hp+ than in Hp{ - } patients ( $p = 0.013$ ). After treatment, IL-8 was detectable in 0/4 eradicated and in 5/6 noneradicated DU patients. IL-6 was detectable in 7/13 untreated DU but in 0/12 NUD, regardless of Hp status ( $p = 0.026$ ), and remained detectable in most DU patients after ulcer healing and/or Hp eradication.  $\gamma$ INF levels were higher in Hp+ NUD and UD than in Hp{ - } NUD, reaching statistical significance ( $p = 0.046$ ) only for Hp+ NUD; IL-4 was detected only in 1 patient with DU. Cytokine Hp+ Hp{ - } Hp + DU DU after treatment mean NUD NUD Baseline healed Hp{ - } healed Hp+ unhealed (pg/mg)  $n = 8$   $n = 4$   $n = 13$   $n = 4$   $n = 2$   $n = 4$  IL-8 26.7 0 39.8 0 21.0 18.8 IL-6 0 0 1.4 2.0 0 0.8  $\gamma$ INF 10.0 0 7.1 3.1 0 0 *Conclusions:* Our data confirm a strong correlation between IL-8 production and Hp infection, regardless of the presence of DU. A weaker correlation exists between Hp positivity and  $\gamma$ INF levels. IL-6, by contrast, appears to be produced only in patients with DU, either active or healed. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Inflammation } "Gastric Production of Inflammatory Cytokines in Patients with Helicobacter Pylori Infection with and without Duodenal Ulcer"

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"P P 13 0348" P 13 0348 **Antral G-Cell and D-Cell Numbers in Helicobacter Pylori Infection**

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<sup>1</sup> Dept of Pathology, National Medical Center, Seoul, Korea *Purpose:* It has been recognized that H. pylori infection induced abnormal regulation of serum gastrin secretion. We examined whether there was a relationship between H. pylori infection and G- and D-cell numbers. *Methods:* The numbers of antral G- and D-cells and serum gastrin levels were compared between 37 peptic ulcer patients infected with H. pylori and 33 patients without infection. G- and D-cells in antral mucosa were examined immunohistochemically using antibodies specific for the gastrin and somatostatin. *Results:* While the number of G-cells per gastric gland was similar in infected and uninfected patients (7.1 – 3.1 vs 7.3 – 3.9), that of D-cells was significantly less in infected patients (1.3 – 0.4 vs 2.5 – 1.6,  $p < 0.001$ , G/D-cell ratio: 5.7 – 2.7/1.0 vs 3.5 – 19./1.0,  $p < 0.001$ ). Serum gastrin level was also significantly higher in infected patients (80.3 – 23.5 vs 47.6 – 14.1 ng/ml,  $p < 0.001$ ). *Conclusion:* These results suggest that H. pylori-associated increased secretion of gastrin appear to be related to relative G-cell hyperfunction resulted from reduced number of D-cells. } " Antral G-Cell and D-Cell Numbers in Helicobacter Pylori Infection"

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## "P P 13 0349" P 13 0349 **Helicobacter Pylori (Hp) and Domestic Cats**

\*D. Bets, J. Ferwerda, W. Dekker

Department of internal medicine, EG Haarlem and Comprehensive Cancer Centre Amsterdam, The Netherlands Handt et al isolated (*Infection and Immunity* 62: 2376–2374) *Helicobacter pylori* from domestic cats in 1994. Because the exact mode of transmission is not fully understood we speculated that patients who had been living in close contact with cats in child- and/or adulthood may have a higher infection rate of Hp. From 200 consecutive patients who attended the endoscopy unit for diagnostic oral endoscopy 5 biopsies were taken from their stomach, independent of whatever endoscopic diagnosis was made. Two from antrum and corpus for histology and one for the CLO-test from antrum to determine if they were infected with Hp. These patients were asked if they had been in close contact with cats in child- and/or adulthood and whether they were born and lived in the Netherlands. The same questionnaire was handed out to patients who visited the department for colonoscopy. Excluded from this study were patients who were treated recently for eradication of Hp, had undergone gastric surgery, were suffering from bleeding during examination or came for an acute endoscopy. We decided that a patient was Hp positive if both CLO-test and histology turned out to be positive. Likewise a patient was free of Hp if both assays didn't show Hp. In a period of 4 months 185 patients were enrolled in this study. In 25 of the cases the CLO-test outcome was not equal to histology. From the remaining 160 patients 38 were Hp positive (23.8%) and 122 negative. From the 40 patients who never had cats 11 (28%) were contaminated with Hp. The "ever" group is a combination of people who had cats all their lives 10.7% (3/28) or only in child- or adulthood resp. 28.1% (9/32) and 22.2% (6/27) were Hp positive. The overall Hp positive status of Dutch patients in our study turned out to be 22.8% (29/127). The patients who came for colonoscopy showed an equal behavior in owning cats as the gastroscopy group. With only 22.8% of our patients suffering from Hp, the incidence in our patient group is low compared to the 30–50% which is the average nation-wide. In our material we didn't find over-presentation of Hp positive patients whom were in close contact compared to the "never" group. Although the group of people who were in close contact with cats all their lives is small with only 28 patients, this group shows a remarkable low percentage of 10.7% infected patients. So in our patient group we couldn't find support for our speculation that owning a cat leads to a higher rate of Hp. Clinical practice: Epidemiology (non cancer) } "Helicobacter Pylori (Hp) and Domestic Cats"

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"P P 13 0350" P 13 0350 **Inhibition of Gastric Mucosal Somatostatin Receptor by H. Pylori Lipopolysaccharide: Effect of Ebrotidine**. J. Piotrowski, A. Slomiany,

\*B.L. Slomiany

Res. Ctr., UMDNJ, Newark, NJ USA Among the consequences of Helicobacter pylori (HP) infection is the loss of inhibition of gastrin release and subsequent hypergastrinemia. This apparent pathological effect of HP has been linked to the impairment in feedback inhibition by somatostatin. Recently, we provided evidence that HP through its cell wall lipopolysaccharide inhibits the binding of somatostatin to its mucosal cell membrane receptor (Biochem. Mol. Biol. Int. 1995: 36; 491). The purpose of this study was to assess whether an antiulcer agent, ebrotidine, is capable of countering this untoward effect of HP. The study was conducted with rat gastric mucosa. The somatostatin receptor was prepared from the solubilized gastric epithelial cell membranes by affinity chromatography on a column consisting of covalently coupled D-Tryp<sup>8</sup>-SRIF-14 to Affi-Gel 10. The receptor protein displayed on SDS-PAGE a band of 61 kDa and showed specific affinity towards <sup>125</sup>I-labeled somatostatin. The binding of somatostatin to the isolated mucosal somatostatin receptor was inhibited by HP lipopolysaccharide and reached a maximum of 94.1% inhibition at 50 μg/ml. Preincubation of HP lipopolysaccharide with ebrotidine caused a dose-dependent reversal of HP inhibitory effect, and at the optimal concentration of 20 μg/ml ebrotidine produced an 84% restoration in somatostatin-mucosal receptor binding. The interference by HP lipopolysaccharide with the receptor binding site for somatostatin could account for the observed deficiency of negative feedback from D-cells to G-cells with HP infection. Further, our results demonstrate that ebrotidine possesses the ability to counteract HP interference with somatostatin acid secretion regulatory effects. Hence, ebrotidine offers a new potent choice in ulcer therapy. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Hormones and receptors: Receptor characterization } "Inhibition of Gastric Mucosal Somatostatin Receptor by H. Pylori Lipopolysaccharide: Effect of Ebrotidine"

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"P P 13 0351" P 13 0351 **Inducible Nitric Oxide (NO) Synthase in *Helicobacter Pylori* Associated Gastritis in Duodenal Ulcer Patients**

\*J. Stachura, J.W. Konturek, E. Karczewska, W. Domschke, S.J. Konturek

Inst Physiol & Pathomorphol Univ Sch Med Krakow

Dept Med B, Univ Muenster, FRG *Purpose:* Previous studies showed the presence of constitutive NO synthase (NOS) in gastric epithelial and endothelial cells and NO was found to mediate mild irritant-induced gastroprotection and mucosal hyperemia in rats but no study was undertaken to identify the role of inducible NOS (iNOS) in mucosal damage associated with *Helicobacter pylori* (Hp) infection in men. *Methods:* The immunohistochemistry, which selectively stains iNOS has been used to detect the iNOS in the antral mucosa obtained by endoscopic biopsy from Hp positive (<sup>14</sup>C-urea breath test, histology and culture) duodenal ulcer (DU) patients and in the Hp isolated from the culture of antral mucosa. These bacteria were checked that they are members of the group of Gram-negative, spirally curved microaerophilic, oxidase-positive rods. A sterile swab harvested all culture from previously prepared subculture plates. The density of bacteria suspended in saline was  $10^9$  colony forming units and 30  $\mu$ l of this suspension was smeared on glass and air dried. The immunoreactivity of iNOS was examined using primary antibody (Santa Cruz Biotechnology Inc, Santa Cruz, CA) diluted at 1:50. The reaction was completed with APAAP Dako kit (Dako, Copenhagen) using fast red as chromogen. *Summary of results:* The iNOS immunoreactivity was found in the antral mucosa obtained during gastroscopy from 50 active DU patients who were Hp-positive (with <sup>14</sup>C-urea breath test, CLO-test and culture). The iNOS was detected in histiocytic cells and in mucosal microvessel cells. The epithelial cells in the pits and glands were negative. The isolated bacteria from these DU patients were strongly stained by the antibody used in all tested samples. *Conclusions:* Hp is capable of expressing iNOS and NO produced in excess in gastric mucosa by this enzyme may contribute to the pathogenesis of Hp-associated gastritis Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Inducible Nitric Oxide (NO) Synthase in Helicobacter Pylori Associated Gastritis in Duodenal Ulcer Patients"

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## "P P 13 0352" P 13 0352 Helicobacter Pylori (Hp) and Gastrin-Somatostatin (S-S) Link in Duodenal Ulcer (DU) Patients

\*J.W. Konturek, W. Bielanski, S.J. Konturek, W. Domschke

Dept. of Medicine, University of Münster, Münster, Germany

Institute of Physiology, Jagiellonian University School of Medicine, Kraków, Poland Hp infection is associated with DU in over 90% of patients and accompanied by increased release of gastrin and deficiency of S-S but the mechanisms of these changes in patients after eradication of Hp have little been studied. Cholecystokinin (CCK) has been implicated in the feedback control of gastric acid secretion in healthy subjects but its contribution to secretory disorders and delay of ulcer healing in DU patients have not much been examined. This study, therefore, investigated whether CCK participates in the impairment of postprandial gastrin release and gastric acid secretion in active DU patients. Tests were undertaken in 10 DU patients without or with elimination of the action of endogenous CCK using loxiglumide (LOX), a selective CCK-A receptor antagonist, before and 4 wks after eradication of Hp with triple therapy (omeprazole, amoxicillin and bismuth). In Hp positive DU patients, the postprandial acid secretion (measured by continuous intragastric pH monitoring) was accompanied by a pronounced increment in plasma gastrin with negligible increase of intraluminal release of S-S. The administration of LOX in these patients did not affect significantly the postprandial pH profile and the rise in plasma gastrin. After eradication of Hp the median postprandial intragastric pH increased to about 4.3 (compared to 3.5 before Hp eradication); the postprandial gastrin concentration was reduced by about 40%, while luminal release of S-S was increased about 2 fold. The administration of LOX resulted in significantly greater decrease in median pH (3.1) and higher rise in postprandial plasma gastrin in these patients. Also the postprandial plasma S-S showed a small, but significant decline (by about 25%) as compared to that in placebo treated patients. This study provides evidence that: (1) Hp infection in DU patients is accompanied by enhanced gastrin release and reduction in luminal release of S-S; (2) The failure of LOX to affect gastric secretion and plasma gastrin in Hp infected DU patients could be attributed, at least in part, to the failure of endogenous CCK to control gastric acid secretion via release of S-S; (3) Hp infected patients appear to exhibit a deficiency of S-S release that can be reversed by the eradication of Hp indicating that both CCK and S-S may contribute to the acceleration of ulcer healing following Hp eradication in DU patients; (4) Testing with LOX and gastric luminal S-S assay may be useful in identification of Hp positive DU patients with CCK-mediated impaired feedback control of gastric secretion and deficiency of S-S caused by Hp infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Helicobacter Pylori (Hp) and Gastrin-Somatostatin (S-S) Link in Duodenal Ulcer (DU) Patients"

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"P P 13 0353" P 13 0353 **Health Care Workers and *Helicobacter Pylori* Infection**

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An oral-to-oral route of transmission of *H. pylori* infection has been postulated, which is supported by the observation that *H. pylori* is present in saliva, gastric juice and dental plaque. On the basis of this assumption, an increased risk for *H. pylori* infection among health care workers was postulated.  
**Aim:** To determine the prevalence of *H. pylori* infection among a wide group of health care workers compared with a control group and its possible relationship with inherent endoscopy risks.  
**Materials and Methods:** A group of 224 medical workers (48 females; mean age: 41. – 8 yrs; range: 25–70 yrs) and a control group of 84 persons (36 females; mean age: 36.3 – 10.4 yrs; range: 19–62 yrs) -not working in health area- were studied. Subjects with history of previous peptic ulcer or digestive disease were excluded. All health care workers were asked for their relationship with gastroenterology and endoscopy activities. In all subjects *H. pylori* status was assessed by the <sup>13</sup>C-urea breath test following the European Standard Protocol. A positive result was defined as an excess of { d }<sup>13</sup>CO<sub>2</sub> excretion > 5%.  
**Results:** The overall (medical and non health care workers) *H. pylori* prevalence was 50%. The measurement of <sup>13</sup>C-urea breath test in different groups yielded the following distribution: Control group 37/84 (44%) Medical workers 118/224 (53%) Non Gastroenterologists 22/44 (50%) p > 0.05 Gastroenterologists 96/180 (53%) Endoscopists 23/43 (55%) p > 0.05 Non endoscopists 73/137 (53%) No significant differences were observed comparing *H. pylori* prevalence in the control group with other groups.  
**Conclusions:** 1) The overall *H. pylori* prevalence was in agreement with that observed in other western countries. 2) Health care workers had not a higher prevalence of *H. pylori* infection than the control group. 3) Performing gastrointestinal endoscopies and the gastroenterology specialty itself are not associated with a higher risk for developing *H. pylori* infection in Spain. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Clinical practice: Epidemiology (non cancer) } "Health Care Workers and *Helicobacter Pylori* Infection"

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"P P 13 0354" P 13 0354 **Does Helicobacter Pylori Infection Have a Role in Primary Sjögren's Syndrome?** N. Erdem, G. Ersöz,

\*A. Aydin, U.S. Akarca, E. Doganavsargil, B. Çelikkale, T. Akalin, Y. Batur

Rheumatology, Gastroenterology, Microbiology and Pathology Depts, Ege University, Izmir, Turkey To investigate a possible relationship between primary Sjögren's syndrome (pSs), an autoimmune disease of unknown etiology, and Helicobacter pylori (Hp) infection 14 patients with pSs (13 women and 1 men, mean age: 48 – 13.2) were studied. The diagnosis of pSs was based on Sen Diego criteria. Hp infection was assessed by histology, urease test and culture of gastric biopsies and detection of IgG antibodies for Hp. All cases were treated with omeprazole 20 mg b.i.d. for 1 month and amoxicillin 1 g b.i.d, and tinidazole 500 mg b.i.d. between 16–30 days. Clinic and endoscopic examinations were repeated one month after completion of the therapy. Hp eradication was defined by negativity of all these tests, except anti-Hp IgG. Active Hp infection was diagnosed in 11 (78.4%) cases. In 2 (14.3%) patients anti-Hp IgG was positive alone. Hp eradication was achieved in all cases. After Hp eradication xerostomia disappeared in 8 (57.1%). But, xerostomia was not improved in any of 3 Hp (–) cases, given the same therapy. Mean serum IgG level decreased from 2036.5 – 726.2 mg/dl to 1817.9 – 597.6 (p = 0.06) and Chisholm score, showing the degree of mononuclear cell infiltration on lip mucosal biopsy, from 3.45 – 0.9 to 2.7 – 1.3 (p = 0.1). Shrimmer's test improved from 6.0 – 5.4 mm to 13.9 – 9.4 (p = 0.0006). In Hp (–) 3 cases, given the same therapy, mean IgG level changed from 2584.6 – 1084.2 mg/dl to 2023.6 – 896.7 and Chisholm score from 3.0 – 1.7 to 2.3 – 1.5. Shrimmer's test also increased from 11.3 – 8.1 mm to 14.0 – 7.9 (Because of small number of patients statistical evaluation could not be performed). *Conclusions:* 1. The prevalence of Hp is high in patients with pSs. 2. Hp eradication results in a significant improvement in the signs and symptoms of pSs. 3. It seems that Hp infection may have a role in the pathogenesis of pSs. 4. Probable beneficial effect of the therapy should be tried in more Hp (–) patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Does Helicobacter Pylori Infection Have a Role in Primary Sjögren's Syndrome?"

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"P P 13 0355" P 13 0355 **Different Topical Duodenal and Gastric Mucosal Production of Interleukin-1 Beta, Interleukin-6, Interleukin-8, Tumor Necrosis Factor Alfa and Interleukin-2-Soluble Receptor in Helicobacter Pylori Positive and Negative Patients. A Pilot Study**

\*S. Rejchrt, L. Pl'edskov'e1, J. Bures, P. Zivn'fd, M. Sirok'fd, V. Palicka

Charles University Teaching Hospital, Hradec Kr'el'lov'e9, Czech Republic *Purpose of the study* was to evaluate topical differences of mucosal cytokine production in Helicobacter pylori [HP] positive and negative patients. *Methods.* Seventeen patients [6 men, 11 women, aged 21–74] entered the study. Five biopsy specimens for *in vitro* culture were taken from each person during routine gastroscopy: from duodenal bulb [DB], distal *antrum* [DA], proximal *antrum*, gastric *corpus* and *fundus* [GF]. HP positive status (7 patients) had both histology and CLO-testing positive, and *vice versa* in HP negative one (10 patients). Biopsy specimens were cultivated in RPMI medium for 23 hours. Cytokines were measured in homogenate supernatants by means of ""sandwich"" EIA using Quantikine kits [R + D Systems] and kit of Immunotech: interleukin-1{ b} [IL-1{ b}], interleukin-6 [IL-6], interleukin-8 [IL-8], tumor necrosis factor-*a* [TNF-*a*] and interleukin-2-soluble receptor [sIL-2R]. Data were statistically treated [t-test, Mann-Whitney, Student-Newman-Keuls tests, PM ANOVA and Pearson Correlation] using Jandel Scientific. *Results* are given as median (in pg/ml, except sIL-2R in pM, \* significance  $p = 0.015$ ). HP IL-1{ b} IL-6 IL-8 TNF-*a* sIL-2R DB pos 7.59 22.40 22.11 1.580 7.63 DB neg 4.75 9.12 0.00 1.560 11.70 DA pos 23.35 19.90 371.40 4.065 3.44 DA neg 7.97 20.70 222.00 0.720 3.39 GF pos 11.19 50.50\* 19.60 0.945 3.19 GF neg 9.79 5.54 4.21 1.540 5.34 There was a correlation between antral IL-1{ b} and IL-6 ( $p < 0.0001$ ), IL-1{ b} and TNF-*a* ( $p < 0.0001$ ), IL-6 and IL-8 ( $p = 0.0076$ ). There was a correlation between fundal IL-6 and IL-8 ( $p = 0.0009$ ). Duodenal sIL-2R production was significantly higher than antral one ( $p = 0.0038$ ). *Conclusions.* A great deviation of values (both personal and topical difference) suggests the significance of several factors (including HP) influencing the consequent local inflammatory reaction. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation } "Different Topical Duodenal and Gastric Mucosal Production of Interleukin-1 Beta, Interleukin-6, Interleukin-8, Tumor Necrosis Factor Alfa and Interleukin-2-Soluble Receptor in Helicobacter Pylori Posi"

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"P P 13 0356" P 13 0356 **DNA Typing of HLA Class II Genes in Japanese Patients with Helicobacter Pylori Infection**

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<sup>1</sup> First Department of Internal Medicine, Fukuoka Univ.

<sup>2</sup> Department of Genetics, Medical Institute of Bioregulation, Kyushu Univ. *Purpose:* The aim of this study is to investigate the HLA-linked genetic predisposing factors in *H. pylori* infection. *Subjects and Methods:* The study group consisted of 58 Japanese patients with *H. pylori* positive gastric ulcer and 44 Japanese patients with *H. pylori* positive duodenal ulcer and 44 Japanese patients with *H. pylori* positive gastritis. Control subjects were 36 without *H. pylori* infection. The biopsy specimens taken from the antrum and the body were used for the bacterial culture. We compared HLA class II genes between control and patients groups. HLA class II genes was analyzed by the PCR-SSOP typing of each group. *Results:* 1) The allele frequencies of DRB1\*1502, DPA1\*0201 and DPB1\*0901 were significantly higher in *H. pylori* positive gastric ulcer patients than in controls, whereas those of DRB1\*1501, DQA1\*01021 and DQB1\*0601 were significantly lower in *H. pylori* positive gastric ulcer patients than in controls. The same results were observed between *H. pylori* positive gastritis patients and controls, except for DPA1\*0201. 2) The allele frequencies of DRB1\*0405 and DQB1\*0401 were significantly higher in *H. pylori* positive duodenal ulcer patients than controls, whereas those of DRB1\*1501, DQA1\*01021 and DQB1\*0601 were significantly lower in *H. pylori* positive duodenal ulcer patients than in controls. 3) There were no significant differences in the allele frequencies between *H. pylori* positive gastric ulcer patients and *H. pylori* positive gastritis patients. 4) The allele frequency of DRB1\*0901 was significantly lower in *H. pylori* positive duodenal ulcer patients than in *H. pylori* positive gastritis patients. *Conclusions:* These observations suggest that *H. pylori* infection is associated with HLA class II genes and the HLA class II genes are involved in the pathogenesis of peptic ulcer and gastritis via different mechanisms. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Host defense mechanisms } "DNA Typing of HLA Class II Genes in Japanese Patients with Helicobacter Pylori Infection"

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"P P 13 0357" P 13 0357 ***Helicobacter Pylori* and *Borrelia Burgdorferi* Infections in Forestry Workers**

\*V. Presecki, M. Katicic, S. Bolanca, V. Babus, M. Marusic, M. Prskalo

Medical School University of Zagreb, Zagreb, Croatia Aim of this study was to evaluate the seroprevalence of *H. pylori* and *B. burgdorferi* in different professions of forestry workers. A group of 288 healthy forestry workers was studied. Subjects with history of previous ulcer or digestive disease were excluded. All positive for *B. burgdorferi* were tested for antibodies to *T. pallidum* to exclude syphilis. Specific antibodies to *H. pylori* were investigated with complement fixation (CF) and ELISA methods (CF positive: titers {\'b3} 1:40, ELISA index IgG {\'b3} 40%) and to *B. burgdorferi* with indirect immunofluorescent antibody (IFA) assay, enzyme immunoassay (EIA) and Dot Blot G test (IFA positive titers {\'b3} 1:64, EIA corrected absorbance > 0.16, Dot Blot G test positive with Borrelia extract, HMV, flagellin p41, p39, Osp C). The measurement of IgG specific antibodies against *H. pylori* and *B. burgdorferi* yielded the following distribution: Profession Total (%) *H. pylori* +ve (%) *B. burgdorferi* +ve (%) Foresters 31 (10.7) 14 (45) 6 (19) Forestry 164 (56.9) 82 (50) 42 (26) workers Drivers 35 (12.1) 21 (60) 10 (29) Technicians 58 (20.1) 26 (45) 16 (28) Two forestry workers had IFA weak positive *B. burgdorferi* IgG titer 1:64, EIA corrected absorbance < 0.12 (non reactive) and Dot Blot G test positive only *B. burgdorferi* flagellin (p41) and significant seropositiveness to *H. pylori* (CF titer > 1:60; ELISA index IgG > 90%). **Conclusions:** Among professionals with a lower socioeconomic status (drivers, forestry workers) prevalence of *H. pylori* infection was higher. Cross-reactions *H. pylori* +ve sera and *B. burgdorferi* flagellin (p41) are possible; cross-reactions of fixed *B. burgdorferi* cells and flagellin have limited the reliability of *B. burgdorferi* serology tests. Clinical practice: Epidemiology (non cancer) Immunology and microbiology: GI infections in adults } " *Helicobacter Pylori* and *Borrelia Burgdorferi* Infections in Forestry Workers "

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## "P P 13 0358" P 13 0358 Cytokines Gene Expression on Helicobacter Pylori Infected Gastric Epithelial Cells

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<sup>1</sup> Dept. of Medicine, Nihon University School of Medicine, Tokyo, Japan

<sup>2</sup> Dept. of Medicine, Tokyo Women's Medical College, Tokyo, Japan

Infection of *Helicobacter pylori* (*H. pylori*) activates infectious response on gastric epithelial mucosa by monocytes and neutrophils. This cellular response probably represents a primary immune defense mechanism against a microbial pathogen. *H. pylori* produces various factors which will attract or activate neutrophils. Infection with *H. pylori* also results in increased gastric mucosal production of cytokines, interleukin-6 and -8, which is a potent activator and chemotactic agent for neutrophils. As gastric epithelial cells express interleukin-6 and -8, they may have an important role in regulating primary host defense mechanisms and be functionally involved in the neutrophils response to *H. pylori* infection. In this study, we analyzed IL-6 and -8 gene expression by reverse transcription-PCR of human gastric epithelial cells, Kato-III, to *H. pylori* infection with special reference to neutrophil modification. Human IL-6 and -8 specific mRNA was detected when Kato-III cells were incubated with neutrophils or *H. pylori*. *H. pylori* itself did not express IL-6 and -8 mRNA, whereas Kato-III cells and neutrophils showed expression of IL-6 and -8 mRNAs. IL-8 mRNA expression by Kato-III cells was further enhanced when they were co-incubated with both *H. pylori* and neutrophils compared to those with neutrophils only. We conclude that human gastric epithelial cells, Kato-III expresses IL-6 and -8 mRNA which can be further enhanced by neutrophils. These results indicate that neutrophil may upregulate IL-8 mRNA expression in *H. pylori*-infected gastric epithelial cells. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infections in adults } "Cytokines Gene Expression on Helicobacter Pylori Infected Gastric Epithelial Cells"

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"P P 14 0359" P 14 0359 **Familial Occurrence of Helicobacter Pylori Infections- Contribution to the Studies of Treatment Failures** K. Wasowska-Kr'f3likowska, E. Toporowska-Kowalska, E. Kowalska

I Children Clinic, Medical University of L'f3dz, Poland In children with persistent complains associated with the alimentary tract it is necessary to look for Helicobacter pylori (Hp) infection, also in their family environment. The study was carried out in a group of 50 children with suspected inflammation of the upper alimentary tract mucosa. *Methods:* 1/Endoscopic examination of upper portion of the alimentary tract; 2/Histopathological evaluation of mucous membrane of the stomach and duodenum (according to the Sydney Classification); 3/Quantitative determination of anti-Hp antibodies performed by means of immunoenzymatic tests (Boehring) in all the children and members of the families of patients with Hp infection confirmed by means of histopathological or immunological techniques. In the investigated group it was demonstrated that among 50 children with suspected inflammation of the upper alimentary tract mucosa on the basis of endoscopy suggesting Hp etiology the coincidence was confirmed histopathological in 44 children. In 26/50 children there was a positive result demonstrating the anti-Hp antibodies (range 24–245); simultaneous presence of serological and histopathological markers of Hp infection were observed in 22 out of 50 patients. In the investigated group infection markers were present in 34 family environments, including 16 cases in which anti-Hp antibodies were detected in more than one member of the family, more frequently in parents than in brothers or sisters.). The above observations may indicate horizontal transmission in the family environment and make a contribution to the studies of the causes of failures of the currently recommended alternatives of the therapy in the infected patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Endoscopy: children } "Familial Occurrence of Helicobacter Pylori Infections- Contribution to the Studies of Treatment Failures"

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"P P 14 0360" P 14 0360 **The Seroprevalence of Helicobacter Pylori in Instituted Intellectually Disabled and Employees** C.J.M. B\'f6hmer, E.C. Klinkenberg-Knol<sup>2</sup>, M.C. Niezen-de Boer<sup>1</sup>, H. Schreuder<sup>3</sup>, S.G.M. Meuwissen<sup>2</sup>

<sup>1</sup> Bartim\`e9us, Zeist, the Netherlands

<sup>2</sup> Free Univ Hosp, Amsterdam, the Netherlands

<sup>3</sup> Hosp. Eemland, Amersfoort, the Netherlands In instituted intellectually disabled an acquisition rate of *Helicobacter pylori* infection (HpI) of 60%–75% is indicated (Berkowitz, 1987/Lambert 1995), while in the normal Dutch population a prevalence from 5–50% is found. Therefore we analysed the seroprevalence of HpI in 2 institutes with 1997 inhabitants and 1404 employees. Randomly, in 338 intellectually disabled HpI was assessed by retrospective analysis of sera with an EIA-g test (Orion), and after voluntary venapunction in 254 employees. A level of > 300 IU was defined as evidence of HpI. Subjects with HpI were defined as patients and compared with the total Dutch population evaluated by Loffeld (thesis 1989). In 280 (82.8%, mean age 51 yrs) intellectually disabled HpI was found, compared with 51.4% in the total normal intellectual Dutch population (mean age: 55 yrs;  $p < 0.0001$ ). Riskfactors in intellectually disabled for developing HpI were: male gender, the duration of institutionalisation, an IQ < 50, rumination, and a history of upper abdominal symptoms. 75 (29.5%, mean age: 29.5 yrs) employees showed HpI, compared with 25% (mean age: 30.5 yrs) in the total Dutch population (ns). Employees with intensive physical contact with the intellectually disabled, with a long duration of employment, and with upper abdominal symptoms had HpI more frequently. *In conclusion:* instituted intellectually disabled have a higher frequency of HpI, especially if they are male, with a long stay in an institute, with an IQ < 50, with rumination or with a history of upper abdominal symptoms. Employees with intensive physical contact with intellectually disabled, and after longer duration of employment are at higher risk for HpI. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "The Seroprevalence of Helicobacter Pylori in Instituted Intellectually Disabled and Employees"

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"P P 14 0361" P 14 0361 **H. Pylori Gastritis and Intestinal Metaplasia in Polynesian and European Inhabitants of New Zealand**

\*J.R. Jass, S.-L. Peng, A.G. Fraser

University of Auckland, School of Medicine, Auckland, New Zealand  
There is up to a fivefold excess of gastric cancer in Polynesian (Maori and Pacific Island) versus European inhabitants of New Zealand (NZ). The aim of the study was to determine the frequency of *H. pylori* (HP) gastritis and intestinal metaplasia (IM) within these ethnic groups. A prospective series of 92 Polynesians (mean age 51.6 years) and 66 Europeans (mean age 59.5 years) was referred for routine gastroscopy and showed the following distribution of endoscopic diagnoses: gastric ulcer (18.4%), duodenal ulcer (21.5%), oesophagitis (11.4%), gastric carcinoma (0.6%) and normal (48.1%). HP gastritis was diagnosed when two of the following were positive: histology, CLO test and urease breath test. Six biopsies were obtained from prepylorus (2), antrum (2) and body (2). HP gastritis was detected in 88% of Polynesians (mean age 51 years) and 47% Europeans (mean age 61 years) ( $p = 0.0001$ ). IM was found in 60% Polynesians (mean age 53 years) and 29% Europeans (mean age 65 years) ( $p = 0.0006$ ). IM was more extensive and inflammation more severe in Polynesians. Eight Polynesians (8.7%) had type III IM at a mean age of 51 years. Three Europeans (4.5%) had type III IM at a mean age of 72 years. No dysplasia was seen. These data suggest that Polynesians develop HP gastritis, IM and type III IM with greater frequency and/or severity and at an earlier age than European inhabitants of NZ. The findings are consistent with the view that HP gastritis is a major risk factor in the aetiology of gastric cancer. Oncology, specific: Stomach; Oncology, general: Epidemiology; Endoscopy, specific: Stomach, duodenum }  
"H. Pylori Gastritis and Intestinal Metaplasia in Polynesian and European Inhabitants of New Zealand"

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"P P 14 0362" P 14 0362 **Is Helicobacter Pylori Infection an Occupational Hazard for Medical Staff?**

\*R. Kosik, H. Kordecki, D. Pilecka

Dept. of Gastroenterology, M. Curie Hospital, Szczecin, Poland  
The epidemiology and the way of transmission of Helicobacter pylori (H.p.) are still unclear. The way from person to person is generally accepted. In this way of transmission helical bacillary forms play an essential role. But because besides of these forms also coccoidal forms of H.p. have been discovered the way of transmission through secretions and excretions could be also possible. *The aim* of our study was to analyse if medical personnel who are in contact with human excretions and secretions are at higher risk to acquire H.p. infection. We analysed the incidence rate of H.p. antibodies in medical and laboratory staff. We diagnosed it by using "Helisal" test produced by "Cortecs Diagnostics UK". This method evaluates IgG antibodies in diluted capillary blood. We examined 14 persons who work in Endoscopic Unit in our department and perform endoscopic examinations (endoscopists and nurses), 14 persons who work in the Department of Cardiology and 15 persons who work in the Laboratory in our hospital. These groups were similar according to age and dyspeptic symptoms. *Results:* No. of pers. % of H.p. positive % of H.p. negative  
Endoscopical pers. 14 86% 14%  
Cardiological pers. 14 36% 64%  
Laboratory person. 15 80% 20%  
*Conclusions:* 1. H.p. infection appears more frequently in persons working in Endoscopic Unit and Laboratory who are in contact with human secretions and excretions as compared with those carrying out cardiological treatment. 2. Due to high frequency of H.p. antibodies in these groups of medical personnel this infection should be considered as occupational hazard. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Complications } "Is Helicobacter Pylori Infection an Occupational Hazard for Medical Staff?"

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"P P 14 0363" P 14 0363 **Role of *Helicobacter Pylori* in the Pathogenesis of Gastroduodenal Lesions in Patients with Cirrhosis: A Prospective Evaluation**

\*L. Prigent-Delecourt, D. Lamarque, F. Roudot-Thoraval, R. Akremi, M.T. Chaumette, J.P. Richardet, J.C. Delchier

Hopital Henri Mondor, 94000 Cr\`eteil, France Although gastroduodenal ulcerated mucosal lesions in patients with cirrhosis are common, their pathogenesis remains unclear. The aim of this prospective study was to determine the pathogenic factors associated with gastroduodenal mucosal lesions in patients with cirrhosis and especially to assess the role of *Helicobacter pylori* (*Hp*). Patients with histologically proven cirrhosis and not recently treated by antibiotics, antisecretory or anti-inflammatory drugs, were enrolled and referred for upper gastrointestinal endoscopy. Upper digestive tract bleeding within the last week was an exclusion criteria. Age, gender, smoking habit, recent alcohol intake, etiology of cirrhosis, Child-Pugh grade were recorded and basal gastrinemia was determined. Esophageal varices were graded from 0 to 3. Severity of hypertensive gastropathy in the body and the antrum was graded from 0 to 3 for erythema, edema and snake-skin mosaic pattern (maximum score: 18). *Helicobacter pylori* status was determined from rapid urease test and histology on biopsy samples or 13-C urea breath test when biopsies were impossible. Sixty four patients were included. There were 52 males and 12 females, mean age – SD: 55 – 11 years. Cirrhosis was alcoholic in 47, grade A, B and C in the Child-Pugh classification in 19, 21 and 24 respectively. Thirty five (55%) were *Hp* positive. One or several mucosal lesions were present in 24 patients (37%): gastric ulcer in 8, duodenal ulcer in 7, gastric erosions in 9, duodenal erosions in 4. Univariate analysis showed that mucosal lesions were not significantly related with age, gender, smoking habit, etiology of cirrhosis, Child-Pugh grade, esophageal varices grade, *Hp* positivity (12/24 vs 23/40,  $p = 0.74$ ), and basal gastrinemia. Univariate and multivariate analysis showed that they were significantly related to a recent alcohol ingestion (62.5% vs 27.5%,  $p < 0.006$ ) and to a high hypertensive gastropathy score (10.9 – 4.4 vs 7.4 – 5.3,  $p < 0.02$ ). **Conclusion:** Ulcerated lesions in cirrhotics are unrelated to *Hp* despite high prevalence of infection. They are significantly and independently related to recent ingestion of alcohol and to hypertensive gastropathy severity. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Liver and bile ducts, 1: Cirrhosis: portal hypertension }" "Role of *Helicobacter Pylori* in the Pathogenesis of Gastroduodenal Lesions in Patients with Cirrhosis: A Prospective Evaluation"

"P P 14 0364" P 14 0364 **Variation in Immunoblot Patterns According to Geographical Origin of Patients Infected by *Helicobacter Pylori* (Hp)**

\*D. Lamarque<sup>1</sup>, T. Gilbert<sup>1</sup>, F. Roudot-Thoraval<sup>1</sup>, L. Deforges<sup>1</sup>, R. Ferrero<sup>2</sup>, A. Labigne<sup>2</sup>, J.C. Delchier<sup>1</sup>

<sup>1</sup> CHU H. Mondor, Cr\`e9teil, Paris

<sup>2</sup> INSERM U389, Institut Pasteur, Paris Hp infection is generally acquired early in childhood. The antigenic pattern of Hp may be related to the geographical area of origin. The aim of this study was to compare, by using Hp serological test by Western Blot (Helico Blot 2.0<sup>®</sup>, Genelabs), the different antibodies present in patients according to the area of birth and childhood. Hp infection was found in 136 patients by mean of positive culture, histology or 13C urea breath-test and positive Hp Elisa serological test. Country and rural/urban area at birth and childhood were recorded. Countries were distinguished as France and Southern country (Southern Europe and Africa). By using Western Blot serology, the presence of antibodies against different molecular weight antigens (19.5, 26.5, 30 or 35 kD) or against VacA (89 kD) and CagA (116 kD) was compared in the different groups. Fifty-eight percent of patients were born or spent their childhood in France and 30% in rural area. Antibodies against antigens of 19.5, 26.5, 30, 35, 89, 116 kD were found in 46, 88, 61, 63, 45 and 67% respectively. Antigens of 26.5, 35 kD were significantly more frequent in patient born or who spent their childhood in Southern country than in France (97% vs 81%; P < 0.03; and 74% vs 53%; P < 0.05, respectively). By contrast, 89 kD (Vac-A) was more frequent in patient born in France (53% vs 25%; P < 0.03). Antibodies against antigens of 19.5 and 89 kD (Vac-A) were more frequent in patients issued from urban area (51% vs 28%, P < 0.02 and 49% vs 32%, P < 0.05 respectively). Cag-A was found similarly whatever the patient origin (66% in France vs 61%; 67% in urban area vs 68%). Western Blot patterns suggest that the antibodies directed against antigens of 26.5, 35 kD are more frequent in South of Europe and in Africa than in France. By contrast Vac A seems more frequent in France and in urban areas. These results evoke that differences in Hp strain are associated with geographical origin of patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Variation in Immunoblot Patterns According to Geographical Origin of Patients Infected by Helicobacter Pylori (Hp)"

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"P P 14 0365" P 14 0365 **Serological Assessment H. Pylori Infection in Children and Adults with Chronic Gastritis and Gastroduodenitis**

\*E. Czkwianianc, M. Chmiela, M. Lawnik, T. Rechcinski, L. Bak-Romaniszyn, I. Planeta-Malecka, W. Rudnicka

Dep. of Pediatrics, Polish Mother's Memorial Hospital, Military Medical University, Dep. of Infectioctious Biology, University, Dep. of Internal Medicine, K. Jonsher's Hospital, L\`f3dz, Poland Despite of available commercial serologic tests for H. pylori (Hp.) the diagnostic value of this method is still controversial. The aim of the study was to assess the serologic exponents of Hp. in children and adults. 27 and 23 dyspetic children and adults with chronic gastritis or gastroduodenitis (diagnosed endoscopically and pathomorfologically according to ""Sydney System"" ) with Hp. infection (confirmed by urease test, histologic and microbiologic methods) and 14 adult volunteers as well as 13 children excluded of Hp. were examined by serologic methods. The sera were tested for presence of IgG, IgM and IgA specific antibodies to the surface acid-glycine extract (GE) obtained from cells of the reference Hp. strain (CCUG 17874) and cagA antigen of Hp. In 70% of children and in all adults with Hp. but only in 9% of uninfected children and in 40% of adult volunteers IgG antiGE antibodies were found. In contrast anticagA IgG were detected only in 30% infected children and in 55% adults with Hp. The highest frequency of IgM antiGE was found in infected adults (70%), but anticagA IgM only in 25% individuals of this group were seen. IgA antibodies were detected only in 2 (7%) children, while in adults they were present in 52% with Hp. and in 30% of the volunteers. Also titres of these antibodies were much higher in adults. The presence of IgG antibodies (in high titres) against the surface extract antigens of Hp. in both infected groups irrespective of age was seen. Lower frequency of the antibodies to cagA suggests the possibility of cross reactions with other bacterial antigens and rather exludes monitoring Hp. infection by only serologic tests alone. Serologic test IgA of Hp. has no much usefulness in children. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infection, children } "Serological Assessment H. Pylori Infection in Children and Adults with Chronic Gastritis and Gastroduodenitis"

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"P P 14 0366" P 14 0366 **An Audit of the Management of *Helicobacter Pylori* Infection in a District General Hospital**

\*N. Coleman, C. Grimley, P. Ramsell, C. Nwokolo, D. Loft

Department of Gastroenterology, Walsgrave NHS Trust, Clifford Bridge Road,

Coventry Carefully controlled clinical trials indicate *Helicobacter pylori* (HP) eradication rates of 80–90% but it is important to know whether these rates are translated to clinical practice on an intention to treat basis. *Aims of Audit:* 1. Is HP eradication being used appropriately? 2. What method is used for HP diagnosis pre-treatment. 3. Which treatment regimes are being used and evaluate their efficacy. 4. To check the timing of follow up breath tests. *Method:* Information was collected prospectively over a 14 month period. Subjects who attended for a post eradication <sup>13</sup>C UBT to confirm the success of eradication were included. The original diagnosis, the initial method used to confirm HP infection, the HP eradication regime used and the timing to the follow-up breath test after completing eradication therapy were noted. *Results:* There were 92 post-eradication breath tests in the study period in 85 patients. The overall eradication rate was 85%. The initial diagnosis was gastric or duodenal ulcer in 91% of cases but eradication was also offered to subjects with NUD (5%), oesophagitis (1%) and gastritis (1%). The CLO test was used most frequently to make the diagnosis of HP infection pre-treatment. Five eradication regimes were used in the period. The best results were obtained with omeprazole (O) 20 mg bd, Clarithromycin (C) 250 mg bd and metronidazole 400 mg bd with an eradication rate of 96% (n = 25). Dual therapy with O 20 mg bd and C 250 mg tds was second at 93% (n = 27) and traditional triple therapy regimes gave a rate of 80% (n = 25). 96% of post eradication breath tests were done more than 4 weeks after completing treatment. *Conclusion:* In the DGH setting on the basis of intention to treat with no exclusion criteria, eradication rates were comparable to those of randomised controlled trials. Most patients received HP eradication for PUD but 7% were treated inappropriately. The best results were achieved with low dose OCM (cost 29.88 \a3). The CLO test was used most frequently to make the initial diagnosis and the timing of a follow-up breath test was appropriate in 96% of cases. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "An Audit of the Management of *Helicobacter Pylori* Infection in a District General Hospital"

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"P P 14 0367" P 14 0367 **Seroconversion of Helicobacter Pylori: A Five Years Follow-Up in Asymptomatic Donors Living in a Western Country**

\*M. Menegatti, F. Landi, D. Palli, B. Massardi, C. Ricci, J. Holton, A. Al'ec, S. Farinelli, F. Mucci, C. Saieva, M. Miglioli, D. Vaira

Ist Medical Clinic, Bologna, Center for Oncology Study and Prevention, Florence, Italy

Microbiology Dept, University College London Hospital, London, UK *Purpose:* Infection rate for Helicobacter pylori (H pylori) in Western countries is reported to be very low: 0.5–2%/year. We aimed to assess the infection rate, as determined by seroconversion from H pylori IgG seronegative to H pylori IgG seropositive, in asymptomatic blood donors resident in an urban area in the North of Italy over a follow-up period of 5 years (1990–95). *Methods:* From a blood donors population screened for H pylori in 1990–91 (N = 1010; M/F: 556/454, age: range 18–65, mean 44 years) a total of 588 (58%) tested as seronegative and were invited for a new IgG antibodies assessment in 1995–96. Specific anti-H pylori antibody were evaluated in duplicate by an "in house" ELISA assay validated in endoscoped patients (sensitivity and specificity of 94%). For each participant a repeat ELISA on the original serum sample (stored at { - }20\°C) was also carried out. *Results:* Until now 324 donors have been re-evaluated (M/F: 191/133, age: range 23–65, mean 42 years). At the repeat assessment of original serum a total of 19/324 (6%) were found to be seropositive, and confirmed seropositive at follow-up. The remaining 305/324 (94%) were confirmed as seronegative. A total of 5/305 (1.6%) were found to have seroconverted to seropositive at the follow-up sample. The table shows the results at repeated assay compared to previous results (+/{ - }ve = positive/negative). 1995: +ve 1995: { - }ve 1990: +ve (n = 19) 19 –1990: { - }ve (n = 305) 5 300 Assuming the seroconversion at mid point of the considered period, for the 305 seronegative donors have been considered more than 1500 years-person of follow-up, the mean follow-up period was 5.2 years (range 4.9–5.8 years) with a seroconversion rate of 0.33%/year (95% CI = 0.1–0.8). *Conclusion:* Our preliminary results confirm an extremely low seroconversion rate for H pylori infection in asymptomatic populations living in a Western country. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Seroconversion of Helicobacter Pylori: A Five Years Follow-Up in Asymptomatic Donors Living in a Western Country"

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"P P 14 0368" P 14 0368 **Household Members and *Helicobacter Pylori* Infected Patients**

\*C. Mart\edn de Argila, D. Boixeda, R. Cant\fn, N. Valdezate, F. Bermejo, J.P. Gisbert, A. Garc\edaPlaza

Gastroenterology and Microbiology Departments, "Ram\fn y Cajal" Hospital, Madrid, Spain Reports on the epidemiology of *Helicobacter pylori* infection are scarce, and the source and spread of this organism are still relevant unanswered questions. *Aim:* The aim of this study was to evaluate *Helicobacter pylori* infection among first- and second- degree relatives and spouses of duodenal ulcer patients with previously demonstrated *Helicobacter pylori* infection to provide further information on the potential spread of this microorganism mediated by a close personal contact. *Materials and Methods:* Sixty-two close personal contacts of 19 patients with duodenal ulcer in whom *Helicobacter pylori* had been cultured from gastric biopsies (18 spouses, 11 siblings, 29 children, and 4 parents) and 272 controls from the same environment and with similar age were studied. *Helicobacter pylori*-specific IgG antibodies were detected by an enzyme-linked immunosorbent assay (ELISA). Subjects were considered positive when titers were > 10 U/ml. *Results:* The antibodies were positive in 81% of the household contacts of the index patients and in 49% of the controls ( $p < 0.001$ ). In all families there was at least one member infected. Parents (100%) and siblings (100%) were more likely to be infected than spouses (78%) and children (72%) ( $p < 0.001$ ). *Conclusions:* Clustering of *Helicobacter pylori* infection within household contacts suggests that a person-to-person spread of these microorganisms or a common source exposure. This fact might account for some therapeutic failures in patients living together with infected household contacts. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Clinical practice: Epidemiology (non cancer) }"  
"Household Members and *Helicobacter Pylori* Infected Patients"

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## "P P 14 0369" P 14 0369 Infection of Partners: Is It a Risk Factor for Helicobacter Pylori Reinfection?

\*J.P. Gisbert, D. Boixeda, C. Mart'edn de Argila, R. B'e1rcena, T. P'e9rez, L. Moreno, A. Garc'eda Plaza

""Ram\ 'f3n v Cajal"" Hospital, Madrid, Spain *Purpose:* At present it is unknown whether *H. pylori* status of spouses plays a role in reinfection after successful eradication. Our purpose was to study the incidence of reinfection in a one-year follow-up period after eradication of *H. pylori* and to describe the prevalence of infection in spouses of these patients. *Methods:* Thirty-three patients (mean age: 49 – 12 yrs, 79% males) with duodenal ulcer in whom *H. pylori* had been successfully eradicated (with bismuth triple therapy, or omeprazol plus one or two antibiotics) were prospectively studied. Endoscopy with biopsies (H & E), and C<sup>13</sup>-urea breath test were performed 1 month after completing therapy. Eradication was defined as the absence of *H. pylori* by both methods. C<sup>13</sup>-urea breath was repeated at 6 and 12 months. At the 1-year follow-up visit, a breath test was also performed to respective partners. *Results:* At the 6-month control, all patients were *H. pylori*-negative. At 1-year, two patients become reinfected (52 and 63 years old, respectively), which represents an incidence of reinfection of 6% (CI95%: 1.7–20%). The mean age of spouses was 49 – 13 yrs, and their prevalence of *H. pylori* infection was 82% (n = 27) (higher than the corresponding prevalence in similar age-population), with a mean { d } <sup>13</sup>CO<sub>2</sub> level of 35 – 27. The mean time of living together was 24 – 1 yrs. None had a previous history of peptic ulcer, and only two (6%) complained from ulcer-like symptoms. Reinfection occurred in 7.4% (2.1–23%) of patients when the spouse was infected, and in 0% if the spouse was *H. pylori*-negative (a non-significant difference; the power of the study was only 10%). Thus, even if the spouse is infected, 92.6% of patients persist uninfected one year after eradication. *Conclusion:* These preliminary results suggest that further studies are needed to assess a possible role of spouses infection in the reinfection rate after *H. pylori* eradication. It seems that reinfection is uncommon even if partners are *H. pylori*+. However, if a role is demonstrated, therapy against the organism could be recommended also in infected spouses. Oesophageal gastric duodenal disorders: EGD disorders in children Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Epidemiology (non cancer) } " Infection of Partners: Is It a Risk Factor for Helicobacter Pylori Reinfection?"

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## "P P 14 0370" P 14 0370 **Reinfection Rate of Helicobacter Pylori Infection in Türkiye, a Developing Country**

\*Ahmet Aydin, Galip Ersöz, Dömer Öztemiz, Mehmet Tunçel, Hanefi Çavusoglu

Depts. of Gastroenterology and Pathology, Ege University, Izmir, Türkiye Eradication of Helicobacter pylori (Hp) leads to regression of gastric inflammation, and reduction of ulcer recurrence. But, reinfection is thought to be a serious problem, especially in developing countries where the sanitation conditions are inadequate. To investigate the reinfection rate of Hp infection in Türkiye, a developing country, 59 cases (31 women and 28 men, with a mean age of 41.4 – 11.5 yr) in whom Hp was eradicated 12–36 (14.2 – 6.2) months ago were studied. Pretreatment diagnoses were duodenal ulcer (DU) and non ulcer dyspepsia (NUD) in 18 and 41 of them, respectively. All cases underwent upper GI endoscopy and 6 gastric biopsies (2 for histologic examination and 1 for urease test from both antrum and corpus) were taken. A case was regarded as Hp negative, if all of the biopsies were found to be negative on both the diagnostic methods. Only 2 (3.4%) of the cases (1 DU and 1 NUD) were found to be Hp positive. In both cases, histological findings of active chronic gastritis were also present. Histological examination showed normal gastric mucosa in 50 (87.7%), focal inflammatory cell infiltration in 3 (5.3%), chronic only gastritis in 2 (3.5%), and chronic atrophic gastritis in 2 (3.5%) cases. None of the DU cases who remained Hp negative described any symptoms suggesting an ulcer recurrence. Their endoscopic examinations also showed no ulcer recurrence. But, the symptoms of the DU patient who was found Hp (+) were going on. Her endoscopic examination also demonstrated the presence of a DU. The result of this study shows that, reinfection rate of Hp infection is not high in Türkiye. Low reinfection rate, despite the high prevalence of Hp infection in our population, suggests that Hp colonization is not common in adulthood. It seems more reasonable to think that the infection is generally acquired in early ages when gastric acid production is inadequate due to immaturity of the parietal cells. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Reinfection Rate of Helicobacter Pylori Infection in Türkiye, a Developing Country"

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## "P P 14 0371" P 14 0371 H. Pylori Gastritis in the Cardia Region & Clinical Correlates

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<sup>1</sup> Dept. of Pathology, University of Magdeburg, Germany *Aim:* Helicobacter pylori (HP) according to current knowledge predilects colonization of the gastric antrum. As the cardiac glands resemble pyloric glands a similar colonization pattern could be expected. We investigated the prevalence of HP colonization (HPC) and gastritis in the cardia (CA) in relation to gastric antrum (A) and corpus (CO) in a sample of unselected<sup>+</sup> patients. *Methods:* Two biopsies of each A, CO and CA (within 1 cm below squamocolumnar junction) from 269 consecutive pats. without previous attempts at H. pylori eradication, or esophageal varices<sup>+</sup> were obtained. In addition a rapid-urease test (HUT-Test, Astra) was performed. Histologic gastritis grading followed the Sydney system (modif. Giemsa, if necessary Warthin-Starry). We used a 4 pt. scale (0 to 3) for activity (ACT), degree (DG), HPC, intestinal metaplasia (IM) and atrophy (AT). Mean rank gradings were compared for A, CO and CA (Friedman two way ANOVA, SPSS,  $p < 0.05$ ). Expression of gastritis in the CA for different clinical diagnoses was evaluated. *Results:* Endoscopy revealed the following diagnoses: Normal aspect: 9.3%, signs of gastritis 45%, DU 14.6%, GU 6%, GERD 8.6%, others 16.5%. 132 pats (49.1% of the sample) showed HP+ve active gastritis in histology and/or urease-test. 120 pats. (90.1%) thereof had HP+ve gastritis in A, 112 pats (84.5%) in CO, 93 pats (70.4%) in CA. The table gives mean rank gradings only for HP+ve pats. No correlation of the macroscopic diagnoses with HP+ve gastritis in the Cardia was found.  $n = 132$

	ACT	DG	HPC	IM	AT
Antrum	1.47	2.05	1.31	0.21	0.20
Corpus	1.22	1.68	1.27	0.14	0.11
Cardia	1.15	1.69	0.98	0.19	0.05
A/CA	$p = ** < 0.01$	$*** < 0.001$	$*** < 0.001$	0.855	0.345

*Conclusion:* About 70% of pats. with HP detected in A have HPC of the cardia region also. However ACT and DG of cardia gastritis are lower compared to the antrum. HP+ve gastritis in the cardia region shows no positive correlation to patients clinical diagnoses. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "H. Pylori Gastritis in the Cardia Region & Clinical Correlates"

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## "P P 14 0372" P 14 0372 Chronic *Helicobacter Pylori* Gastritis: A Lifelong Progressive Inflammation?

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**Aim:** *Helicobacter pylori* (HP) gastritis is a lifelong infection of the gastric mucosa, mostly acquired in childhood, predominantly in the antrum and expanding in a pylorocardial direction over decades. If so, we suspect there could be a different histological expression of gastritis in antrum, corpus and cardia in different age groups. We therefore investigated the age dependence of the histological features of gastritis.  
**Methods:** 218 carefully selected patients with mere gastritis, (no circumscribed lesions) were included. Two biopsies of each antral, corpus and cardiac gastric mucosa were obtained for histology. In addition a rapid urease test (HUT test, Astra) was performed. Histology was graded by the Sydney system with modified Giemsa- and if necessary Warthin-Starry. A four point scale (0–3) was used for grading of activity (A), degree (D), HP-colonization (HPC), intestinal metaplasia (IM) and mucosal atrophy (AT). According to patients age quartiles were formed (I- 21–43 ys, II-44–55 ys, III-56–64 ys, IV- 65–85 ys). Statistical tests (T-test, ANOVA) were performed (SPSS, 6.1).  
**Results:** 107 pats. showed HP+ve gastritis; only their data are reported herein. Means of histological A and D only showed an increase from age group I to II in the antrum and cardia (\*p < 0.05), but not in the corpus. In contrast a slight continuous increase in HPC showed in the antrum and cardia for all age groups, but was expressed significantly\* only in the corpus mucosa. No age dependent differences for AT were shown. IM decreased significantly\* in antral mucosa from age group II to III, but remained stable in corpus and cardiac mucosa.  
**Conclusion:** The data suggest, that the inflammatory responses to HP infection and intestinal metaplasia in the antrum are marked in younger and middle-aged subjects but decrease in the elderly. This happens in spite of a trend towards higher HPC with age.  
Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: GD disorders, acid peptic  
Clinical practice: Epidemiology (non cancer) } "Chronic *Helicobacter Pylori* Gastritis: A Lifelong Progressive Inflammation?"

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"P P 14 0373" P 14 0373 **Helicobacter Pylori Antibodies Against CAG A and VAC A in Patients with Chronic Gastritis, Duodenal and Gastric Ulcer** M. Nilius, G. Illies, U. Platzer, U. Schmidt-Wittig, A. Hackelsberger, P. Malfertheiner

Dept. Gastroenterology, Hepatology and Infect. Diseases Otto-von-Guericke-University Magdeburg, Germany **Background:** Serological studies have shown that Cag A producing strains of *H. pylori* are associated with duodenal ulcer. Antibody titers against Cag A correlate with severity of disease. Vac A always is coexpressed with Cag A. Aim of the study was to investigate the antibody reaction against Cag A and Vac A of patients with chronic gastritis (CG) and gastric (GU) and duodenal ulcer (DU). **Methods:** 133 patients undergoing upper gastrointestinal endoscopy were included. *H. pylori* infection was determined by urease test (HUT), histology and IgG-ELISA (Bio Whittaker). Patients were considered *HP*-positive if they were positive in 2 of these reference methods. Antibody response to specific *H. pylori* antigens was tested by a commercially available Immunoblot-System (BAG-Pylori-Blot). **Results:** 116 from 133 patients had a positive Immunoblot (DU: 21/28 (75%); GU: 23/32 (71.9%); CG: 72/73 (98.6%). Antibody reactions against the different antigens are summarized in the following table: Antigen DU GU CG 116 kd (Cag A) 23/28 (82.1%) 24/32 (75%) 53/72 (73.6%) 89 kd (Vac A) 11/28 (39.2%) 12/32 (37.5%) 38/72 (52.8%) 30 kd (Ure A) 17/28 (60.7%) 17/32 (53.1%) 45/72 (62.5%) 26.5 kd 24/28 (85.7%) 17/32 (53.1%) 56/72 (77.8%) 19.5 kd 13/28 (46.4%) 15/32 (46.9%) 33/72 (35.8%) **Conclusion:** Whereas the serological profile to CagA and all other antigens was not significantly different between DU, GU and CG patients, serological profile to VacA was significantly associated with CG. } "Helicobacter Pylori Antibodies Against CAG A and VAC A in Patients with Chronic Gastritis, Duodenal and Gastric Ulcer"

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"P P 14 0374" P 14 0374 **Helicobacter Pylori, Gastric Ulcer and Non-Steroidal Anti-Inflammatory Drugs**. Boixeda,

\*J.P. Gisbert, F. Bermejo, Baleriola I. Alvarez, R. Cantón, R. Aller, Martín C. de Argila

"Ramón y Cajal" Hospital, Madrid, Spain *Purpose:* To describe the prevalence of *H. pylori* infection in gastric ulcer (GU) patients and to study its relationship with non-steroidal anti-inflammatory drug (NSAID) administration. *Methods:* 161 patients with active GU were studied (mean age: 54 years, 70% males). In all patients 3 biopsy specimens were taken from both gastric antrum and body (H&E stain, Gram stain and culture). *Results:* *H. pylori* was found in 83% (95% CI = 77–89%) of patients. In non-NSAID users *H. pylori* infection reached 87% (95% CI = 81–93%), while in NSAID users the corresponding figure was 63% (CI = 43–79%) ( $p = 0.008$ ). The percentage of GU patients without *H. pylori* infection not taking NSAIDs was 11% (CI = 6–16%). In multiple logistic regression analysis NSAID administration was the only variable which correlated with *H. pylori* infection (odds ratio = 0.25; 95% CI = 0.09–0.66;  $\chi^2$  model = 7.27;  $p = 0.007$ ). Additional variables (age, sex, smoking, alcohol, and GU location) were not correlated with *H. pylori* infection. Chronic gastritis percentages were higher in *H. pylori*+ than in *H. pylori*{ - } patients (97% vs 67% at antrum, and 78% vs 42% at body) ( $p < 0.001$ ). *Conclusion:* The overall prevalence of *H. pylori* infection in GU patients was 83%; this prevalence increased up to 87% when only non-NSAID users were considered. The percentage of GU patients without *H. pylori* infection not taking NSAIDs was only 11%, which suggests that both factors (*H. pylori* and NSAIDs) are the most relevant in GU disease, the emergence of GU without them being uncommon. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Helicobacter Pylori, Gastric Ulcer and Non-Steroidal Anti-Inflammatory Drugs"

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"P P 14 0375" P 14 0375A Survey on Management of *H. Pylori* by Dutch Specialists in 1995

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In order to conduct a survey of the management of *Helicobacter pylori* infection by Dutch specialists a postal questionnaire was sent to 420 members of the Dutch Society of Gastroenterology in June 1995. Of the 226 respondents (response rate 54%) all but two treated patients for *H. pylori* infection. From the survey it could be estimated that at least one out of thousand Dutch inhabitants was treated for *H. pylori* infection in 1995. Accepted indications for treatment of *H. pylori* infection were duodenal ulcer (98%), gastric ulcer (91%), low-grade B cell MALT lymphoma (56%), pre-malignant gastric mucosal changes (33%), non-ulcer dyspepsia (32%), and chronic use of proton pump inhibitors (30%). The diagnostic methods mainly used by the respondents were histology (93%), urease test (60%), and culture (46%). Most physicians (82%) used a combination of tests to detect *H. pylori*. Non-invasive diagnostic tests were only used by a minority of respondents. Triple therapy was used for treatment by 54% of the respondents but the "classical" bismuth triple therapy (14%) has been surpassed as the treatment of choice by proton pump inhibitor based triple therapy combinations (40%). The relatively new quadruple therapy combinations were already used by 26% of the respondents. After treatment the eradication of *H. pylori* was routinely confirmed by diagnostic tests by 42% of the respondents, while 48% only did so when confirmation of eradication was considered clinically relevant. Confirmation of eradication was assessed at least 4 weeks after treatment. 72% of the respondents waited 8–12 weeks before testing for eradication. It was concluded that, medio 1995, treatment of *H. pylori* was almost generally accepted by Dutch specialists in case of associated ulcer disease. An association of *H. pylori* with other upper gastrointestinal diseases was not unanimously accepted. Biopsy-based diagnostic methods were generally preferred. Treatment regimens differed widely. Sponsored by the Dutch Society of Gastroenterology  
Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Clinical practice: Management strategy } "A Survey on Management of *H. Pylori* by Dutch Specialists in 1995"

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"P P 14 0376" P 14 0376 **Serum Lipids, Body-Indices, Age at Menarche, and Helicobacter Pylori Infection in 1,756 Danish Women**

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Dept. of Surgery K, Bispebjerg Hospital, the Copenhagen Hospital Corporation, the Glostrup Population Studies, University of Copenhagen, 2400 NV Denmark *Aim:* To assess the association between the seroprevalence of IgG antibodies to *H. pylori*, serum lipids, body-indices, and age at menarche in women. *Methods:* A random sample of 3,589 adult Danes entered a population study in 1982–1983. A total of 1,756 women were eligible for the present study. Seroprevalences of circulating IgG antibodies to *H. pylori* were assessed with an in-house ELISA assay. IgG antibody levels were categorized as sero-negative, border-line, or sero-positive. Information on life-style factors and age at menarche was ascertained from a questionnaire. Height and weight was measured and body mass index (BMI) calculated. High-density-lipoprotein (HDL), triglyceride, and cholesterol levels in serum were measured. Age, life-style factors, and socioeconomic status was included as possible confounders in multivariate logistic regression analyses using IgG seropositivity as the dependent variable. *Results:* The likelihood of seropositivity for IgG antibodies to *H. pylori* was increased in women with upper quartile HDL values (OR 1.7 [1.1–2.6]), upper quartile weights (OR 1.6 [1.1–2.3]), and upper quartile BMIs (OR 1.4 [0.9–2.0]). Women with upper quartile heights (OR 0.7 [0.5–1.0]) were less likely than women with lower quartile heights to be seropositive for IgG antibodies to *H. pylori*. The likelihood of *H. pylori* infection increased with age at menarche with 12 per cent/year (OR 1.12 [1.02–1.20]). Serum triglyceride and serum cholesterol levels were not associated with *H. pylori* infection. *Conclusion:* *Helicobacter pylori* infection relates to late menarche in Danish women. This finding may explain the relationship between decreased height in women in this study and the association with impaired pubertal growth spurt earlier reported. Increased HDL values may be found more often in women with *H. pylori* infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Epidemiology (non cancer) } "Serum Lipids, Body-Indices, Age at Menarche, and Helicobacter Pylori Infection in 1,756 Danish Women"

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"P P 14 0377" P 14 0377 **CagA Hp Infection: Its Association with Gastroduodenal Disease**.  
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<sup>1</sup> IRIS, Siena, Italy Helicobacter Pylori (Hp) is believed to have a pathophysiologic role in chronic active gastritis and peptic ulcer disease. *Aim:* To investigate whether these alterations might be related with specific Hp strains, expressing the cytotoxin associated gene product (CagA). *Methods:* We recruited 135 Hp+ve subjects: 42 non ulcer dyspepsia (NUD), 65 duodenal ulcer (DU) and 28 gastric ulcer (GU). All patients were assessed by histology and rapid urease test. Sera from these subjects were assayed by anti-Hp ELISA and EIA for CagA-IgG. *Results:* A high prevalence of anti-CagA was found associated with DU (56/65, 86.1%) and GU (27/28, 96.4%) patients, while NUD patients showed anti-CagA seropositivity in 22/42 (52.4%). No significant difference was observed in seropositivity rates between DU and GU patients. Besides, in chronic active gastritis patients (CAG), 76/102 (74.5%) were anti-CagA+ve. The prevalence raised to 95% (19/20) in patients with chronic active atrophic gastritis (CAAG) and was 76.9% (10/13) in subjects with CAAG +intestinal metaplasia (IM). Among CAG, a high prevalence of anti-CagA was found associated with DU (46/53, 86.8%) and with GU (13/14, 92.8%), while NUD patients showed anti-CagA in 17/35 (48.6%). *Conclusions:* 1) Anti-CagA seropositivity is strongly associated with peptic ulcer disease but there is no significant difference between DU and GU. 2) The presence of endoscopic lesions in a small number of anti-CagA { - }ve patients suggests that CagA is not essential for the development of the ulcer disease. On the other side, the evidence of a marked number of NUD anti-CagA+ve patients implies that CagA is not sufficient to induce ulcerative lesions. 3) Anti-CagA seropositivity is strongly correlated with all the forms of chronic gastritis, although the absence of anti-CagA in a reasonable number of NUD with CAG suggests that some Hp strains induce CAG independently from the production of CagA. Immunology and microbiology: GI infections in adults } "CagA Hp Infection: Its Association with Gastroduodenal Disease"

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"P P 14 0378" P 14 0378 **High Incidence of H Pylori Seropositivity in Young Patients with Coronary Artery Disease** S.D.H. Malnick, K. Adlan, S. Goland, D.D. Bass,

\*M. Beergabel, A. Fink, D. Geltner, O. Eisenberg, M. Fogel, A. Caspi, Z.M. Stoeger

Division of Internal Medicine, Kaplan Hospital, Rehovot, Israel H pylori infection is now clearly linked with peptic ulcer disease. In addition H pylori infection appears to be associated with gastric carcinoma and MALT-lymphoma of the stomach. Peptic ulcer disease has been shown to be associated with coronary artery disease (CAD) and evidence is accumulating linking H pylori infection with CAD. We investigated young (< 50 years) patients who were survivors of a myocardial infarction or who had angiographically-proven CAD. H pylori seropositivity was determined by a 2nd generation ELISA (Roche) in sera from the study patients and an age- and gender-matched control population. 43 patients have been examined, 32 males and 6 females. The mean age is 45 – 6.15 years. 31 (81.6%) patients were H pylori seropositive and 7 (18.4%) seronegative. Of the 31 seropositive patients 28 were male and 3 female and of the 7 seronegative patients 4 were male and 3 female. In 33 control patients H pylori seropositivity was seen in 21 (63.6%) and 12 (37.4%) were seronegative (χ<sup>2</sup> test, p < 0.001). Anti-cardiolipin antibodies (ACA), which have been linked to CAD, were also examined by a solid-phase ELISA. ACA were detected in 2 of 38 (5.3%) study patients and in none of the control patients. In summary, we have shown a high (81.6%) incidence of H pylori seropositivity in young patients with CAD. This is much higher than seen in a control population and also much higher than the incidence of ACA. Further work is needed to investigate whether this relationship is causal and if there is an effect of H pylori eradication on these patients. (Supported by a grant from Abic Ltd.) Oesophageal gastric duodenal disorders: Helicobacter Pylori } "High Incidence of H Pylori Seropositivity in Young Patients with Coronary Artery Disease"

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"P P 14 0379" P 14 0379 **High Prevalence of *Helicobacter Pylori* Infection in Coronary Heart Disease Demonstrated by the <sup>13</sup>C-Urea Breath Test**

\*C. Mart\edn de Argila, D. Boixeda, A. Fuertes, R. Aller, C. Arocena, J.P. Gisbert, R. Cant\f3n, A. Garc\eda Plaza

Gastroenterology and Cardiology Departments, "Ram\f3n y Cajal" Hospital, Madrid, Spain Previous studies have reported an association between coronary heart disease (CHD) and *H. pylori* infection, but all of them have used serological tests to confirm infection. *Aim:* To determine the prevalence of *H. pylori* infection in a large group patients with CHD and its relationship with different conventional CHD risk factors. *Materials and Methods:* One hundred and twelve consecutive patients (95 males and 17 females, Mean age: 59.1 – 11.9 yrs) were studied with documented CHD admitted at the Coronary Care Unit in our Hospital. Patients with previous history of peptic ulcer disease or digestive conditions were excluded. Information was inquired on the presence of conventional risk factors for cardiovascular disease (diabetes, hyperlipidemia, smoking, and arterial hypertension). Eighty-three healthy persons (24 males and 59 females; mean age: 51.5 – 10.7 yrs) comprised the control group. IgG antibodies to *H. pylori* were measured in all persons by means of a serological ELISA method (Helico-G, Porton, Cambridge, UK). All persons with CHD underwent also a <sup>13</sup>C-urea breath test (<sup>13</sup>C-UBT) to study *H. pylori* infection. *Results:* Ninety-one (81.3%) of 112 patients with CHD had a positive serology for *H. pylori* (> 10 U/ml) compared with 53 (63.8%) persons out of the 83 in the control group (p < 0.01). In 90/112 (80.4%) of patients with CHD the <sup>13</sup>C-UBT was positive (dCO<sub>2</sub> > 5/1000). No association was observed between *H. pylori* infection and the different risk factors for CHD: Characteristic Yes No history of: *H. pylori* + *H. pylori* { - } *H. pylori* + *H. pylori* { - } Smoking 43 (82.7) 9 (17.3) 47 (78.3) 13 (21.7) Hyperlipidemia 33 (76.7) 10 (23.3) 57 (82.6) 12 (17.4) Diabetes 19 (82.6) 4 (17.4) 71 (79.8) 18 (20.2) Hypertension 40 (76.9) 12 (23) 50 (83.3) 10 (16.7) p > 0.05 in all comparisons between the different groups. *Conclusions:* Patients with CHD had a high prevalence of *H. pylori* infection, significantly higher than that observed among healthy persons. The absence of an association between conventional risk factors for CHD and *H. pylori* infection suggests an independent action of *H. pylori* in its possible involvement in CHD. Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Epidemiology (non cancer) } "High Prevalence of Helicobacter Pylori Infection in Coronary Heart Disease Demonstrated by the 13C-Urea Breath Test"

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"P P 14 0380" P 14 0380 **Lack of Association between *Helicobacter Pylori* Infection and Angiographically Documented Coronary Heart Disease** F. Maier, A. Auricchio<sup>1</sup>, M. Nilius, J.-E. Dominguez-Munoz, H. Klein<sup>1</sup>, P. Malfertheiner

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<sup>1</sup> Dept. Cardiology, Angiology and Pulmonology, Otto-von-Guericke-University Magdeburg, Germany **Background:** Recent data have linked chronic infection with *Helicobacter pylori* (HP) to coronary heart disease (CHD). Since symptoms like angina, palpitation or chest pain as well as non-invasive testing are less sensitive and specific for detection of CHD, the gold standard for assessing CHD remains coronary angiography. The aim of this study was to evaluate the incidence of HP infection in patients undergoing routine coronary angiography. **Methods:** 257 consecutive patients undergoing routine coronary angiography with known or suspected CHD, valvular defects or electrophysiological abnormalities were screened for antibodies by HP-IgG-ELISA. Laboratory investigations for well known risk factors of CHD, such as arterial hypertension, diabetes mellitus, adipositas, cholesterol, triglycerides uric acid, fibrinogen as well as acute phase reactants (C-reactive protein, ESR, WBC) were performed. Further, smoking history, family history, sex, age and history of gastric symptoms has been investigated. Patients were divided in a group with angiographically documented CHD and in a second group without morphological evidence of CHD. Statistical analysis was performed with unconditional multivariate stepwise logistic regression analysis. **Results:** The patient groups were comparable in age and sex. No significant difference was seen in prevalence of *H. pylori* infection and between men and women in patients with and without CHD. Both groups had a comparable mean age (61.88 (CHD+) vs. 58.04 (CHD{ - })). Whereas no significant correlation for CHD was found with HP infection, multivariable analysis resulted in a very significant correlation with well known risk factors like cholesterol, triglyceride concentration, smoking and age. **Conclusion:** The results of our study clearly show that there is no significant link between CHD and *H. pylori* infection as hypothesized by others. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Lack of Association between Helicobacter Pylori Infection and Angiographically Documented Coronary Heart Disease"

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"P P 14 0381" P 14 0381 **Relation between *H. Pylori*-Gastritis and GERD**

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<sup>1</sup> Dept. of Pathology, University of Magdeburg, Germany *Aim:* Few data on the relation between chronic *H. pylori* (HP)-gastritis and gastroesophageal reflux (GERD) exist. We compared the histologic pattern of gastritis in the cardia from patients with erosive GERD to that of patients with chronic gastritis. *Methods:* Two endoscopic biopsies of antrum, body and cardia mucosa (within 1 cm below the squamocolumnar junction) were obtained in 450 consecutive pats. Gastritis (modified Giemsa, HE, AB-PAS) was graded by the Sydney System on four pt. scale (0 to 3) for activity, degree, HP colonization (HPC), atrophy and intestinal metaplasia (IM). To assess HP-status histology and rapid urease test, if necessary additional Warthin Starry stain, 13-CUBT, culture, and serology were performed. At endoscopy 61 pats showed erosive lesions in the esophagus, forming the GERD group. As controls 212 pats. with mere gastritis, without ulcers, erosive lesions and GERD symptoms were selected. Mean gastritis gradings were compared (SPSS, win 6.1: Mann-Whitney-U-test, Wilcoxon rank sum test) *Results:* 26 out of 61 GERD pats. were HP+ve (42%), 35 were HP{-}ve (58%). Of 212 pats. with gastritis 104 were HP+ve (49.1%), 108 were HP{-}ve (50.9%). Age and sex were equally distributed. No differences were found between GERD and gastritis in HP{-}ve pats. Histology in gastric antrum and corpus did not differ between HP+ve GERD and gastritis patients. activity degree HP-C atrophy IMHP+ve GERDCardia 0.846 1.538 0.538 0.077 0.154HP+ve GastritisCardia 1.135\* 1.731 0.99 \*\* 0.058 0.173 p < 0.05 p < 0.01 *Conclusion:* A causal link between chronic HP+ve gastritis and GERD is unlikely. Reflux may however create a hostile environment for HP, as the activity of gastritis and density of HPC in the cardia are decreased in HP+ve pats. with GERD. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: EG Reflux }" "Relation between *H. Pylori*-Gastritis and GERD"

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"P P 14 0382" P 14 0382 **Delayed Gastric Emptying Unchanged after Cure of H. Pylori Infection (HP) in Functional Dyspepsia (FD)**

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Elisabeth Hospital, Essen, Germany

<sup>1</sup> INFAI, Bochum, Germany

<sup>2</sup> Institute of Pathology, Bayreuth, Germany *Purpose:* There seems to be a smaller subgroup of HP infected FD patients profiting of HP cure. The influence of HP cure on FD symptoms and gastric emptying is investigated in this study. *Methods:* 18 patients with FD have been enrolled. HP infection was assessed pretherapeutically by consisting results of culture and histology from gastric biopsies. The infection was cured in all patients by a one-week triple therapy comprising omeprazole, clarithromycin and amoxicillin as determined 4 weeks and 6 months posttherapeutically by urea breath test. Gastric emptying was measured by a previously validated <sup>13</sup>C-octanoic acid breath test pre- as well as 4–8 weeks and 6–7 months posttherapeutically. *Results:* 4–8 weeks (resp. 6–7 months) after HP cure, there was a major symptom relief stated by 9 (6) patients, a slight relief in 5 (8), no change in 3 (3) and worsening of symptoms in 1 (1) cases. Gastric half-emptying time (t1/2, min) data are given in the following table: Parameter: t1/2 Pre 4–8 weeks 6–7 months Mean: 117.6 108.8 117.6 Median: 115 114 120 SD 35.1 33.3 33.3 Minimum 64 56 72 Maximum 181 163 200 The differences were not significant in Wilcoxon test (p = 0.42 after 4–8 weeks, p = 0.97 after 6–7 months). *Conclusions:* Gastric emptying was delayed in FD patients with a wide interindividual variation. HP cure did not change consistently the t1/2 in the short or long term. Also, change of t1/2 was not closely related to symptom relief. Motility, specific: Stomach/Oesophageal/gastric/duodenal disorders: Helicobacter Pylori } "Delayed Gastric Emptying Unchanged after Cure of H. Pylori Infection (HP) in Functional Dyspepsia (FD)"

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"P P 14 0383" P 14 0383 **Chronic Dyspepsia and H. Pylori Infection**

\*I. Jovanovic, T. Milosavljevic, M. Krstic, M. Micev, M. Ugljesic, D. Miletic, D. Popovic, P. Dugalic, R. Krstic, M. Bulajic

Institute of Digestive Diseases, Clinical Center of Serbia, Belgrade, Yugoslavia  
Chronic dyspepsia was defined as a presence of one or more upper gastrointestinal symptoms over the preceding 6 months. Due to the present disputes over Helicobacter pylori infection causing chronic dyspeptic symptoms, we compared the prevalence of H. pylori infection in the patients with the upper gastrointestinal symptoms. Upper abdominal symptoms: epigastric pain, nausea, bloating, pyrosis, vomiting and belching were assessed by a questionnaire from 52 patients, (29 females and 23 males; mean age 48, range from 20 to 72) on a visual analog scale. The severity of each symptom was scored on a linear scale from 0 (absent) to 3 (unbearable). Patients taking NSAID and antibiotics or with the history of gastrointestinal disease, such as duodenal and gastric ulcers were excluded from the study group as well as patients with hepatobiliary or pancreatic diseases. In all patients we performed upper endoscopy. Macroscopic findings ranged from complete normal to focal redness and swollen mucosa of the stomach antrum. The presence of the H. pylori infection was diagnosed both with light microscopic examination and rapid ureasa test samples from stomach antral and body mucosa. H. pylori was found in 60% subject expressing dyspeptic symptoms since in 40% H. pylori was absent. According to the used scale, the severity of the symptoms in patients with and without H. pylori infection was equal. H. pylori infection was significantly associated with histological abnormalities, mainly superficial chronic gastritis and chronic atrophic gastritis. In the Yugoslav population, H. pylori infection is an important cause of dyspeptic symptoms in non-ulcer patients (60%). On the other hand, the severity of the symptoms does not differ in H. pylori positive and negative patients with dyspepsia. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Motility, general: Functional GI disorders }  
"Chronic Dyspepsia and H. Pylori Infection"

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"P P 14 0384" P 14 0384 **The Density of Gastric H. Pylori Colonization is not Associated with the Occurrence of Dyspepsia**

\*B. Braden, W.F. Caspary, B. Lembcke

Dpt. of Gastroenterology, University hospital Frankfurt Main, Germany *Purpose:* In most studies, the prevalence of *Helicobacter pylori* infection in patients with functional dyspepsia does not clearly differ from the prevalence in asymptomatic controls. However, the degree of *H. pylori* colonization might play a role for the occurrence and severity of dyspeptic symptoms. *Methods:* Between August, 1993, and July, 1994, we tested 1500 apparently healthy volunteers (1036 m, 464 w, 42 – 12 years) for *H. pylori* infection using the <sup>13</sup>C-urea breath test. The non-invasive urea breath test enables a semiquantitative assessment of the extent of *H. pylori* colonization in the stomach (Gastroenterology 1994; 106: A48; Z Gastroenterology 1993; 31: 312). *Results:* 526 (35.1%) of the 1500 volunteers complained about occasionally or frequently occurring dyspeptic symptoms. No difference was observed in the *H. pylori* prevalence between asymptomatic subjects (35.5%) and those with dyspeptic symptoms (35.9%; p > 0.95). A high density of *H. pylori* colonization in the gastric mucosa indicated by strongly increased { d}% values in the <sup>13</sup>C-urea breath test was not associated with a higher frequency of dyspepsia (p > 0.80). HP-negative. HP-positive < 5 { d}% 5–10 { d}% 10–20 { d}% > 20 { d}% Age [years] 40 – 12 44 – 13 45 – 12 45 – 14 n 965 201 223 111 Dyspepsia never 628 135 140 71 n = 974 (65.1%) (67.2%) (62.8%) (64.0%) rarely 303 55 69 30 n = 457 (31.4%) (27.4%) (30.9%) (27.0%) frequently 34 11 14 10 n = 69 (3.5%) (5.5%) (6.3%) (9.0%) *Conclusion:* According to these findings an eradication therapy on the basis of dyspeptic symptoms alone can not be recommended as *H. pylori* is not a proven etiology of dyspepsia. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori Motility, general: Functional GI disorders } "The Density of Gastric H. Pylori Colonization is not Associated with the Occurrence of Dyspepsia"

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"P P 14 0385" P 14 0385 **H. Pylori Infection-Gastritis-Dyspepsia, Any Relation?**

\*A. Goldis, N. Tudose, C. Vernic, V. Cleescu, R. Strain

Dept. of Gastroenterology, University of Medicine Timisoara, Romania The purpose of our study was to investigate the relation between H. Pylori (HP) infection-chronic gastritis-dyspepsia and some possible risk factors. *Methods:* We prospectively investigated a batch of 59 NUD patients (37 F, 22 M) with a mean age of 39.3 years (17–68). HP was evidenced by bacteriology and histology (2 biopsies each from the antrum, corpus and duodenum). Gradings from 0–3 were made for HP infection, chronic gastritis and its activity. Each patient was questioned for personal data, dyspeptic complaints (epigastric pain, heartburn, belching/burping, nausea) and some possible risk factors. *Results:* HP was positive in 39 (66.1%) patients by bacteriology and in 41 (69.4%) by histology (95.1% concordance). In this study we considered the histology HP results and compared the mean values for the following parameters (Student test) for the HP+/HP{ - } subjects: age-41.5 – 13.1/34.2 – 11.8 years ( $p = 0.0790$ -marginally significant), educational level-2.9/3.2 ( $p = \text{NS}$ ), duration of dyspepsia-4.1/3.6 years ( $p = \text{NS}$ ), dyspeptic symptoms (mean of the scores of the symptoms)-17.2/14.1 ( $p = \text{NS}$ ), stress level-5.1/4.5 ( $p = \text{NS}$ ), chronic gastritis-4.45 – 1.86/1.64 – 1.55 ( $p < 0.0001$ ). From the 41 HP+ patients, we compared those with low, with those with high HP infection scores, but for age, educational level, dyspepsia duration and symptoms, stress level and chronic gastritis, the comparison of the mean values of these parameters in the 2 batches revealed  $p = \text{NS}$ . *Conclusions:* In our study only chronic gastritis was significantly correlated to HP infection ( $p < 0.0001$ ). Age, educational level, duration and symptoms of Dyspepsia, as well as stress level did not correlate with HP infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "H. Pylori Infection-Gastritis-Dyspepsia, Any Relation?"

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"P P 14 0386" P 14 0386 **Gastroduodenal Lesions and Gastritis are Correlated with Infection of CagA+ H. Pylori Strains in Dyspeptic Patients** P. Rossi, O.A. Paoluzi, S. Bernardi<sup>1</sup>, O.P. Marchione<sup>1</sup>, A. Mastracchio<sup>2</sup>, F. Nardi<sup>2</sup>, P. Paoluzi

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<sup>2</sup> Cattedra di Anatomia Patologica, Universit\ 'e0 \lquoteLa Sapienza\rquote, Rome, Italy *H. Pylori* (HP) strains encoding the immunogenic antigen called CagA seem to correlate with a more severe peptic disease. *Aim:* to investigate in a population of dyspeptic patients the incidence of CagA<sup>+ve</sup> HP strains and the relationship with mucosal lesions. *Patients & Methods:* 80 pts, with a mean age (\ 'b1 SD) of 53 yrs (\ 'b1 14), undergone upper GI endoscopy for ulcer-like dyspepsia and found HP<sup>+ve</sup> by rapid urease test, histology (Giemsa stain) and polymerase chain reaction (PCR), were assessed for CagA status by PCR. Inflammatory changes of mucosa were classified according to Sydney's classification. *Results:* 25 pts (21%) showed no mucosal lesions (endoscopic negative dyspepsia-END), 61 pts (54%) active duodenal ulcer (DU) and 28 pts (25%) gastric erosions and/or ulcers (GL). CagA positivity for the three groups of pts is shown in the Table. Incidence of CagA<sup>+ve</sup> strains resulted to be significantly higher in pts with UD + GL than in END pts ( $p < 0.03$ ). Inflammatory changes of mucosa were found in 77/80 pts (96%), 44 pts with superficial chronic gastritis (SCG) and 33 pts with atrophic chronic gastritis (ACG). CagA<sup>+ve</sup> strains appear significantly ( $p < 0.05$ ) higher in the moderate/severe active ACG than in inactive/mild forms. parameters CagA<sup>+ve</sup> n n (%) END 14 8 57 DU 49 42 86 GL 17 14 82 SCG (a + mi/mo + s)\* 26/18 19/17 73/94 ACG (a + mi/mo + s) 19/14 14/14 73/100 \*activity of gastritis: a = absent; mi = mild; mo = moderate; s = severe. *Conclusions:* CagA + HP strains appear to be involved in the development of both gastroduodenal lesions and more severe inflammatory changes. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Gastroduodenal Lesions and Gastritis are Correlated with Infection of CagA+ H. Pylori Strains in Dyspeptic Patients"

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"P P 14 0387" P 14 0387 **Gastroduodenal Lesions and Gastritis Are Correlated with Infection of CagA+ H. Pylori Strains in Dyspeptic Patients** P. Rossi, O.A. Paoluzi, S. Bernardi<sup>1</sup>, O.P. Marchione<sup>1</sup>, A. Mastracchio<sup>2</sup>, F. Nardi<sup>2</sup>, P. Paoluzi

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<sup>2</sup> Cattedra di Anatomia Patologica, Universit\ 'e0 \lquoteLa Sapienza\rquote, Rome, Italy *H. Pylori* (HP) strains encoding the immunogenic antigen called CagA seem to correlate with a more severe peptic disease. *Aim:* to investigate in a population of dyspeptic patients the incidence of CagA<sup>+ve</sup> HP strains and the relationship with mucosal lesions. *Patients & Methods:* 80 pts, with a mean age (\ 'b1 SD) of 53 yrs (\ 'b1 14), undergone upper GI endoscopy for ulcer-like dyspepsia and found HP<sup>+ve</sup> by rapid urease test, histology (Giemsa stain) and polymerase chain reaction (PCR), were assessed for CagA status by PCR. Inflammatory changes of mucosa were classified according to Sydney's classification. *Results:* 25 pts (21%) showed no mucosal lesions (endoscopic negative dyspepsia-END), 61 pts (54%) active duodenal ulcer (DU) and 28 pts (25%) gastric erosions and/or ulcers (GL). CagA positivity for the three groups of pts is shown in the Table. Incidence of CagA<sup>+ve</sup> strains resulted to be significantly higher in pts with UD + GL than in END pts ( $p < 0.03$ ). Inflammatory changes of mucosa were found in 77/80 pts (96%), 44 pts with superficial chronic gastritis (SCG) and 33 pts with atrophic chronic gastritis (ACG). CagA<sup>+ve</sup> strains appear significantly ( $p < 0.05$ ) higher in the moderate/severe active ACG than in inactive/mild forms. parameters CagA<sup>+ve</sup> n n (%) END 14 8 57 DU 49 42 86 GL 17 14 82 SCG (a + mi/mo + s)\* 26/18 19/17 73/94 ACG (a + mi/mo + s) 19/14 14/14 73/100 \*activity of gastritis: a = absent; mi = mild; mo = moderate; s = severe. *Conclusions:* CagA + HP strains appear to be involved in the development of both gastroduodenal lesions and more severe inflammatory changes. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: EGD disorders in children } "Gastroduodenal Lesions and Gastritis Are Correlated with Infection of CagA+ H. Pylori Strains in Dyspeptic Patients"

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"P P 14 0389" P 14 0389 **Relationship between Helicobacter Pylori Infection and NSAID-Related Gastropathy in the Elderly**

\*A. Pilotto, G. Leandro<sup>1</sup>, L. Bozzola<sup>2</sup>, M. Franceschi, F. Di Mario<sup>3</sup>, S. Meli<sup>2</sup>, G. Valerio

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<sup>1</sup> Dept. of Gastroenterology, Castellana Grotte (BA)

<sup>3</sup> Dept. of Gastroenterology, University of Padova, Italy With the *aim* to evaluate the role of Hp infection on the prevalence and severity of NSAID-related upper G.I. lesions in the elderly we studied endoscopically 154 subjects NSAID-users with upper GI symptoms (62 males, 92 females; mean age: 80 years, range: 67–98). Patients were defined as "NSAID-users" if they took a drug of this class any time in the 7 days prior to endoscopy and by different use patterns they were separated in Occasional Users, Acute Users or Chronic Users. In 128 subjects HP infection was studied by histology (2 antral and 2 body gastric biopsies, Giemsa and H&E stains) and by the rapid urease test. Statistical analysis was performed by means of Student t test for unpaired data and the X<sup>2</sup> test. *Results:* 127/154 subjects (82.4%) presented gastro-duodenal damage: 6 pts (3.9%) were affected with erosive oesophagitis (OE), 46 pts (29.9%) with gastric ulcer (GU), 48 pts (31.1%) with duodenal ulcer (DU), 5 pts (3.2%) with both GU and DU and 22 pts (14.3%) with erosive gastritis (EG). 64/154 pts (41.55%) were affected with a bleeding lesion. 74/128 pts (57.8%) resulted HP-positive. HP-positive pts presented a statistically significant higher percentage of GU (68.4% vs 31.6%,  $p < 0.0001$ ) and DU (67.4% vs 32.6%,  $p < 0.0001$ ) and a lower percentage of oesophagitis (33.3% vs 66.7%,  $p < 0.05$ ) and non gastro-duodenal lesions (38.1% vs 61.9%,  $p = 0.01$ ). No significant differences were found between HP-negative (46%) and HP-positive (54%) subjects as regards bleeding lesions. No significant differences were observed as regards NSAID use patterns between HP-positive and HP-negative subjects: respectively occasional users: 55.4% vs 51.8%, acute users: 12.1% vs 14.2%, chronic users: 32.4% vs 35.1%. In *conclusion* 1) HP infection was associated with higher NSAID-related GU and DU in the elderly; 2) HP infection was not associated with a higher risk of bleeding in elderly NSAID-users. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Relationship between Helicobacter Pylori Infection and NSAID-Related Gastropathy in the Elderly"

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"P P 14 0390" P 14 0390 **High Prevalence of H. Pylori Infection among Patients with Functional Dyspepsia. Assessment with C<sub>13</sub>-Urea Breath Test** T. Pin<sup>1</sup>,

\*M. Barenys<sup>2</sup>

<sup>1</sup> CAP 2 Cerdanyola, L'Alian<sup>e</sup>7a de Sabadell, Barcelona

<sup>2</sup> Hospital de Viladecans, Barcelona

*Introduction* Up to date, the majority of previous studies about the prevalence of H.P. infection were done by gastric mucosal biopsy (urease or culture) or by serologic tests. Breath urea tests, reported for the first time by Graham in 1987, are known to be highly specific and sensitive for the detection of active H. pylori infection, both almost 100%. This type of tests are based in H. pylori's efficient hydrolysis of urea. In this test the urea labeled with a carbon isotope is administered orally, and in infected individuals metabolized to ammonia and labeled carbon dioxide, that can be quantified in the breath. Because their sensitivity, specificity and simplicity breath tests are becoming the preferred method for the assessment of H. pylori infection in epidemiologic studies.

*Aim of the Study:* To evaluate the prevalence of H. Pylori infection in patients with functional dyspepsia using <sup>13</sup>C-urea breath test.

*Methods:* We studied 67 consecutive patients with symptoms of dyspepsia with a duration longer than six months. None of them had a previous history of peptic ulcer disease or treatment with pump proton inhibitors. An upper gastrointestinal endoscopy was performed in all of them and if negative, we indicated a <sup>13</sup>C-urea breath test. We employed the European Standard Method for the Urea Breath Test, which uses 4.2 gr of citric acid as a meal to delay gastric emptying and an oral dosage of urea of 75 mgr.

*Results:* 26 patients (38.8%) were and 41 (61.2%) female. Mean age of the patients with FD was 43.2 years. The <sup>13</sup>C-urea breath test showed positivity in 50 patients and negative results were found in 19 patients. So, the presence of h. pylori infection is proved in 72.4% of the patients with functional dyspepsia. Mean age of H. pylori positive subjects was 44.16 – 15.65 and 40.35 – 13.15 for H. pylori negative subjects. (p = 0.372)

*Remarks* *Conclusions:* Our study shows that patients with functional dyspepsia in our area have H. pylori infection in 72.4% of cases. These results are similar to figures found in patients with gastric ulcer (70–80%) and slightly inferior to prevalence of infection in the duodenal ulcer group (90–95%). In our opinion this high percentage of positive values in a functional dyspepsia group of patients, higher than that reported with other methods, may suggest minor pathogenetic relevance of H. pylori infection in peptic ulcer disease.

Oesophageal gastric duodenal disorders: Helicobacter Pylori Motility, general: Functional GI disorders }

"High Prevalence of H. Pylori Infection among Patients with Functional Dyspepsia. Assessment with C<sub>13</sub>-Urea Breath Test"

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"P P 14 0391" P 14 0391 **Helicobacter Pylori (HP) Antibodies Against CAG A Protein in Bleeding and Non-bleeding Gastric and Duodenal Ulcers** G. Illies, M. Nilius, J.E. Dominguez-Munoz, A. Hackelsberger, B. Pepperkok<sup>1</sup>, P. Malfertheiner

Dept. Gastroenterology, Hepatology and Infect. Diseases, Otto-von-Guericke-University Magdeburg, Medical Laboratory Dr. Limbach, Germany

**Background:** Cag A is a recognized indicator for increased *H. pylori* virulence and is more frequently detected in strains from patients with ulcer disease and gastric malignancy. The prevalence of CagA producing *H. pylori* strains in bleeding ulcers is unknown. Aim of the study was therefore to evaluate the frequency of Cag A-antibodies in patients with bleeding and non-bleeding ulcers and chronic gastritis.

**Methods:** 100 patients, 30 patients with non-bleeding, 30 patients with bleeding gastric (GU) and duodenal ulcer (DU) and 40 patients with active chronic gastritis (CG) were included. All patients were examined for HP-infection by urease-test (HUT), histology, <sup>13</sup>C-UBT and serology. HP-serology was performed by a commercially available ELISA (BioWhittaker). Cag A determination was investigated by an ELISA, coated with recombinant Cag A protein (viva diagnostika) and by a commercial Western Blot (BAG-pylori-Blot).

**Results:** 87/100 (87%) were HP-positive by at least 3 tests. HP-antibodies were detected in 81/100 (81%) of the patients, 61/100 (61%) had also CagA antibodies in the CagA-ELISA. 80/100 (80%) had a positive Western-Blot result. The profile of CagA and VacA antibodies within the three different patient groups is summarized in the following table:

Antibody	BU	NBU	CG
Cag A	22/30 (73.3%)	23/30 (76.7%)	27/40 (67.5%)
Vac A	11/30 (36.7%)	11/30 (36.7%)	19/40 (47.5%)
CagA-ELISA	22/30 (73.3%)	20/30 (66.7%)	19/40 (47.5%)

**Conclusion:** CagA-antibodies are detectable in about 2/3 of patients and are present as frequently in bleeding and non-bleeding ulcers and chronic gastritis. Antibodies against VacA seem to be higher in CG. However CagA as well as VacA are not useful indicators for predicting ulcer complications. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Helicobacter Pylori (HP) Antibodies Against CAG A Protein in Bleeding and Non-bleeding Gastric and Duodenal Ulcers"

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"P P 14 0392" P 14 0392 **The Relation of Malt with Helicobacter Pylori Associated Gastritis in Patients with Ulcer and Non-Ulcer Dyspepsia**

\*N.Y. Bagatur, A.F. Celik, C. Davutoglu, A. Dobrucali, F. Hamsioglu, K. Bal, M. Tuncer, S. Goksel, A. Dirican, I. Yurdakul, H. Uzunismail, E. Oktay

University of Istanbul, Cerrahpasa Medical Faculty, Internal Medicine and Pathology Department, Turkey *Aim:* To determine the prevalence of mucosa associated lymphoid tissue (MALT) and its relation with age, sex, ulcer, non-ulcer dyspepsia, activity of gastritis and density of H. pylori in H. pylori positive patients. *Methods:* 110 consecutive, previously untreated patients underwent endoscopic examination and two biopsies were taken from both antrum and corpus. Only histologically H. pylori positive patients were included (only three patients out of 110 were H pylori negative). In grading the gastric biopsy specimens, Sydney system classification was used. *Results:* MALT was positive in 39 (35.5% – 19 females, 20 males, mean age: 41.3 + 3.1) and negative in 71 (64.5% – 45 females, 26 males, mean age: 40.1 + 3.1) patients and found more often in antral mucosa (89.7%) than in corpus (20.5%) ( $p < 0.0001$ )<sup>\*\*\*</sup>. When both malt positive and negative patients were divided into groups by decades of age, the correspondent groups in malt positive and negative patients included similar percentage of individuals ( $p < 0.05$ ).<sup>\*\*</sup> Sex distribution, prevalence of duodenal ulcer, gastric ulcer, gastritis, gastroduodenitis and intestinal metaplasia were not different in MALT positive and negative groups ( $p < 0.05$ )<sup>\*\*</sup>. There were also no significant differences with respect to both the severity of activity of gastritis (Mild, Moderate, Severe) and the density of H. pylori (Mild, Moderate, Severe) between MALT positive and negative groups ( $p < 0.05$ )<sup>\*\*</sup>. *Conclusion:* Our results suggest that additional factors such as bacterial or host related ones are responsible for MALT rather than the severity of the activity of gastritis or the density of H. pylori. Comparisons made by using independent samples t-test<sup>\*</sup>, chi-square<sup>\*\*</sup> or fisher.<sup>\*\*\*</sup> Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oncology, specific: Lymphoma }" "The Relation of Malt with Helicobacter Pylori Associated Gastritis in Patients with Ulcer and Non-Ulcer Dyspepsia"

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"P P 14 0393" P 14 0393 **The Helicobacter Pylori Colonization in Gastroduodenal Mucosa and Immune Response in Patients with Acne Rosacea: Aspects of Etiopathogenesis and Treatment** L.E. Abrahamovych

Medical Institute, Lviv, Ukraine The aim of our study was to determine Helicobacter pylori (H.P.) prevalence in gastroduodenal mucosa and its role in immune response and etiopathogenesis of acne rosacea (A.R.) and gastroduodenal pathology. The study was based on 160 patients (pts) with A.R. (64.4% women, 35.6% men; mean age 41.6 – 1.7 years). All pts underwent upper gastroduodenal endoscopy and biopsy samples were taken and studied for H.P. by both methods: microscopic – Giemsa staining and CLO – rapid diagnosis urease test. The cellular and humoral immune response was analysed by WHO demanded tests constellation (1981). The beginning of skin changes has been observed 3–4 years after the symptoms of the gastroduodenal pathology (Gastroduodenitis – 68.2%, duodenal ulcer – 30.6%) in 98.8% pts with A.R. The H.P. positive test was found in the majority of examined pts, among them 92.5% in the antrum, 93.28% in the duodenum, as well as immune inflammation in gastroduodenal mucosa. The extent of H.P. colonization in gastroduodenal mucosa was compared with cellular and humoral immune response in pts with A.R. Changes of immunology reactivity parameters were analogous in 4 stages of A.R. which is typical for hyperreactive T- and B-immunity systems dysbalance. High level of total T-E lymphocytes was accompanied by low level of active T-A lymphocytes with resulting low effector T-A/T-E index ( $p < 0.01$ ). High receptor activity of T-E lymphocytes, T-A lymphocytes and T-helpers ( $p < 0.001$ ) with concomitant high immunoregulatory index (T-H/T-S;  $p < 0.01$ ), increased O-lymphocytes and leucocyte/O-lymphocyte index ( $p < 0.001$ ), reflecting inflammation component of internal organs involvement, high receptor activity of B-lymphocytes ( $p < 0.001$ ) and increased total circulatory immune complexes was also revealed. Thus, profound autoaggressive disorders of cellular and humoral immunity are baseful mechanisms for A.R. and gastroduodenal pathology development. The treatment by antihelicobacterial and immunoregulatory drugs gave the positive clinical results of gastroduodenal and cutaneous pathology in 99.37% pts (recovery in 66.25%, uncomplete clinical remission in 33.12%) with eradication of H.P. colonization. *Conclusions:* The established changes indicate the importance of H.P. infection with the autoaggressive immune response in the etiopathogenesis of acne rosacea as well as gastroduodenal pathology with corresponding treatment approaches. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Immunology and microbiology: Host defense mechanisms } "The Helicobacter Pylori Colonization in Gastroduodenal Mucosa and Immune Response in Patients with Acne Rosacea: Aspects of Etiopathogenesis and Treatment"

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"P P 14 0394" P 14 0394 **Helicobacter Pylori (H.P.) Infection in Gastric Stump Mucosa and Immunoreactivity in Patients (Pts) with Postgastroresectional Disease (PGRD): Aspects of Pathogenesis**

\*O.O. Abrahamovych, M.P. Pavlovsky, E.S. Abrahamovych, M.O. Abrahamovych

Medical Institute, Lviv, Ukraine The aim of our study was to determine H.P. prevalence in pts in late terms (5–33 years) after partial gastrectomy for gastroduodenal ulcer (GDU), and its role in immunoreactivity and PGRD pathogenesis. The study was based on 250 pts (96% men, 4% women; aged range 31–74 years) who underwent gastric resection by Billroth-I (B-I; 48%) and Billroth-II (B-II; 52%) mode. Thirty pts with GDU, without gastric surgery, were used as control. All pts underwent upper gastrointestinal endoscopy and biopsy samples were taken and studied for H.P. by CLO – urease test. The cellular and humoral immunoreactivity was analysed by WHO demanded tests (1981). The H.P. positive test was found in 56% examined pts totally, among them in 24% in both gastric stump body (GSB) and anastomosis (A), in 28% – only in the GSB and in 4% – only in the A, compared with 28 (93.5%) of 30 pts with GDU without gastric surgery ( $p < 0.01$ ), as well as duodeno (jejuno) gastric reflux – in 97.1%, versus – 66.7% ( $p < 0.01$ ). More often H.P. occurred after partial gastrectomy by B-II than by B-I mode (1.2:1.0), after 1/2 gastric resection than 2/3 one (2.1:1.0), in pts who suffered from duodenal than gastric ulcer (1.7:1.0). Thus, H.P. prevalence in pts with partial gastrectomy is lower than in GDU pts without gastric surgery, indicating a potential inhibitory role of bile reflux on the development of the microorganism. The extent of H.P. colonization in gastric stump mucosa was compared with cellular and humoral immunoreactivity. The hyperreactive (autoaggressive) type of T- and B-immune systems was established. Blood T-lymphocytes were increased (59.7 – 0.9%,  $p < 0.01$ ), effector index (T-A/T-E) -decreased (0.28 – 0.02,  $p < 0.001$ ), immunoregulatory index (T-helpers/T-suppressors) – increased (5.52 – 1.19,  $p < 0.001$ ), leucocytes/T-E index – increased (9.31 – 0.42,  $p < 0.001$ ), reflecting inflammation component of internal organs involvement. B-lymphocytes were decreased (16.06 – 0.64,  $p < 0.001$ ) with concomitant tendency to Ig and circulatory immunocomplexes (CIC) increase (total CIC – 392.6 – 19.7 IU,  $p < 0.001$ ; small CIC – 548.45 – 33.5 IU,  $p < 0.05$ ), pointing to activation of antibody formation by decreased number of B-lymphocytes, hyperreactivity of humoral immunity and autoimmune processes in pts with PGRD. Thus, the established changes indicate the importance of H.P. infection in gastric stump mucosa with the autoaggressive immune response in the PGRD pathogenesis, which must be taken into account in diagnostics, evaluation treatment results by antihelicobacterial and immunoregulatory drugs, and prognosis. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Host defense mechanisms Oesophageal gastric duodenal disorders: GD disorders, acid peptic } " Helicobacter Pylori (H.P.) Infection in Gastric Stump Mucosa and Immunoreactivity in Patients (Pts) with Postgastroresectional Disease (PGRD): Aspects of Pathogenesis"

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"P P 14 0395" P 14 0395 **Helicobacter Pylori in Patients with Resected Stomach**

\*A. Nagorni, J. Milonovic, T. Tasic, V. Katic, V. Brzacki, S. Petrovic-Nagorni, I. Stamenkovic, V. Zivkovic

Clinic for gastroenterology and Clinic for pathology Faculty of Medicine Nis, Yugoslavia Chronic gastritis and dysplasia of the resected stomach (adenomatous, cystic, microglandular, globoid, mixed) are common findings, especially ten and more years after gastric resection. These findings are more frequent after Billroth II resection. The aim of our study was to evaluate *Helicobacter pylori* (*H. pylori*) prevalence in patients after partial gastric resection for duodenal ulcer. We studied 42 partially resected patients, 30 men and 12 women, mean age 59.1 years, range 31 to 75 years. Twenty nine patients were with Billroth II procedure and 13 patients with Billroth I procedure. The mean time interval between the gastric resection and our study was 15.2 years (range 5 to 24 years) in Billroth II procedure group and 6.3 years (range 1 to 11 years) in Billroth I procedure group. All patients were underwent to proximal gastrointestinal endoscopy. Biopsy samples were taken from the mucosa in the surroundings of anastomosis. Biopsy samples were studied for histology and *H. pylori* by rapid urease test (bramio test). Forty patients with duodenal ulcer were used as a control group for *H. pylori* evaluation. Chronic gastritis of various types and stages of dysplasia was diagnosed in all patients with resected stomach. *H. pylori* was present in 13 (44.8%) patients of Billroth II group and in 8 (61.5%) patients of Billroth I group, compared with 34 (85%) patients of duodenal ulcer group ( $p < 0.05$ ). *Conclusion:* The prevalence of *H. pylori* in patients with Billroth II resection is lower than in patients with Billroth I procedure, probably because of inhibitory role of bile reflux on the development of *H. pylori* infection. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Endoscopy, specific: Stomach, duodenum } "Helicobacter Pylori in Patients with Resected Stomach"

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"P P 14 0396" P 14 0396 ***Helicobacter Pylori* Colonization and Ulcer Recurrence after Gastric Surgery in Duodenal Ulcer (DU) Patients**

\*S.J. Konturek, E. Sito, T. Popiela

Inst Physiol and Dept Surg, Univ Sch Med, Krakow, Poland *Purpose:* The eradication of *Helicobacter pylori* (Hp) is known to reduce remarkably the recurrence of DU similarly as does gastrectomy but it is not clear what is the prevalence of Hp in DU patients undergoing gastrectomy or vagotomy. The purpose of this study was to evaluate the influence of gastrectomy or selective vagotomy with pyloroplasty on the prevalence of Hp. *Material:* 79 patients (35–73 yrs old) just before and 6–8 months after surgical interventions were included. <sup>14</sup>C-urea breath test and CLO-test and culture of Hp in the biopsy samples of antral mucosa obtained during endoscopy were used to detect Hp. *Summary of results:* Hp infection was detected in all patients before the surgery. Following distal gastric resection (antrectomy) with Billroth II anastomosis (N = 32) due to ulcer resistance to conservative therapy (N = 26) or pyloric stenosis (N = 6), Hp was only in 3 out of 32 operated patients) and no ulcer recurrence was observed. Following selective vagotomy and pyloroplasty (N = 43) or simple closure of perforated ulcer in DU patients (N = 4), Hp was found in all (100%) cases and ulcer relapse occurred in 7 vagotomized patients (16%). *Conclusions:* (1) disappearance of Hp is probably the major factor responsible for low ulcer recurrence after gastrectomy and (2) vagotomy should be avoided as the method of treatment of DU because of the high Hp prevalence rate and high ulcer recurrence after this procedure. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } " *Helicobacter Pylori* Colonization and Ulcer Recurrence after Gastric Surgery in Duodenal Ulcer (DU) Patients"

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"P P 14 0397" P 14 0397 **Epithelial Cells Proliferation in *Helicobacter Pylori* (HP) Associated Gastritis and in Operated Stomach**

\*V.A. Isakov, L.E. Gurevitch, A.R. Zlatkina

Moscow Regional Research Clinical Institute (MONIKI), Moscow, Russia

The increase of epithelial proliferation rate in HP-positive gastritis is considered as one of the initial steps in gastric carcinogenesis. The increased PCNA labeling index was reported in HP gastritis comparing with health controls. On the other hand, operated stomach, which usually lacks HP, is one of independent risk factors for the development of gastric carcinoma. The aim of the study was to evaluate epithelial proliferation rate in gastric mucosa of the patients with HP-gastritis and in patients with operated stomach using proliferating cell nuclear antigen labeling index (PCNA-LI). Multiple formalin-fixed gastric biopsies taken from the body of the stomach of 6 HP-negative patients (2–10 yrs after Billroth-II operation because of peptic ulceration) and from the body and antrum of the stomach of 4 patients with HP-positive gastritis were routinely stained with H&E and toluidine blue for the assessment of HP-status. PCNA was revealed by PAP immunostaining with PC-10 murine anti-PCNA monoclonal antibody, using microwave pretreatment technique for better antigen retrieval. *Results:* All 6 operated patients have type C gastritis with moderate/severe mucosal atrophy, five of them have focal incomplete intestinal metaplasia. All HP-positive patients have pangastritis with mild/moderate atrophy in antrum and corpus mucosa and two of them have intestinal metaplasia. Mean PCNA-LI of 6 operated patients was significantly higher (22.31 – 1.86) than in HP-positive patients (17.62 – 1.75) ( $p < 0.01$ ). It indicates that in operated stomach epithelial cells experienced other proliferative stimuli, than in HP gastritis. In conclusion, there are at least two different ways for stimulation of epithelial cell's proliferation in the stomach that can independently induce the development of gastric carcinoma in HP associated gastritis and in operated stomach. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach } "Epithelial Cells Proliferation in *Helicobacter Pylori* (HP) Associated Gastritis and in Operated Stomach"

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"P P 15 0398" P 15 0398 **Gastric Carcinoma (GC) Strains of *H. Pylori* (HP) Presents *vacA* Sequence that Allows to Differentiate Them from Duodenal Ulcer (DU) and Chronic Gastritis (CG) Strains**

\*D.M.M. Queiroz, E.N. Mendes, G.A. Rocha, A.M.R. Oliveira, S.B. Moura, G.F. Lima Jr., C.A. Oliveira

Lab. Research in Bacteriology/FM/UFMG, Brazil HP is the major cause of human CG and is now considered a significant risk factor for the development of peptic ulcer and GC. The vacuolating cytotoxin, encoded by *vacA*, is an important virulence factor, being more frequently produced by HP strains associated with DU. Patients with GC also present antibodies to cytotoxin. Despite *vacA* can be detected in almost all strains, only about 50% of them induce vacuolation *in vitro*. It was demonstrated that *vacA* presents 3 signal (s1a and s1b, which are closely related, and s2) and 2 mid region sequences (m1 and m2). It was also observed that HP strains isolated from DU patients are more frequently type s1/m1, a sequence associated to cytotoxin and *cagA* positivity. We investigated the distribution of *vacA* genotypes in HP strains isolated from GC patients to verify if it is possible to differentiate them from CG and DU strains. We studied 48 HP isolates from GC, 33 from DU and 37 from CG patients. DNA was extracted by a phenol-chloroform method. Primers used for *vacA* homologues detection were previously published by Atherton *et al* (1995). GC patients presented 38 (79.1%) s1/m1, 9 (18.8%) s1/m2 and one (2.1%) s2/m2 strain. Most strains isolated from DU patients were also s1 (31 { - } 93.9%), but they were more frequently m2 (12 { - } 36.4%) than those isolated from GC patients ( $p = 0.06$ ). On the other hand, 18 (48.6%) patients with CG presented s2/m2 strains, 9 (24.3%) s1/m1 and 10 (27.1%) s1/m2. In regard to signal sequences s1 and s2, there were significant differences between GC and CG isolates ( $p < 10^{-6}$ ) and DU and CG strains ( $p < 10^{-3}$ ) but no difference was observed between GC and DU isolates ( $p = 0.56$ ). GC patients have also type m1 strains more frequently than CG patients ( $p < 10^{-6}$ ). To better differentiate GC from DU strains we employed other primers to identify s1a and s1b signal sequences and we observed that 93.5% (29/31) strains from GC patients were type s1b and 80.0% (16/20) strains from DU patients were type s1a ( $p < 10^{-8}$ ). In conclusion, GC patients present more frequently type s1b/m1 strains, DU patients types s1a/m1 and s1a/m2 strains and CG patients types s2/m2 and s1b/m2 strains. Supported by: CNPq, FINEP and FAPEMIG/Brazil. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach } "Gastric Carcinoma (GC) Strains of *H. Pylori* (HP) Presents *vacA* Sequence that Allows to Differentiate Them from Duodenal Ulcer (DU) and Chronic Gastritis (CG) Strains"

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**"P P 15 0399" P 15 0399 Comparing the Presence of H. Pylori on the Unchanged Gastric Mucus Layer and within the Tumor Tissue in Patients with Gastric Carcinoma**

\*T. Milosavljevic, M. Micev, M. Krstic, M. Ugljesic, I. Jovanovic, R. Krstic, P. Dugalic, V. Antic, D. Popovic, M. Bulajic

Institute of Digestive Diseases, Clinical Center of Serbia, Belgrade, Yugoslavia One of the most controversial discussions in the recent studies has been the possible association between H. pylori infection and gastric cancer. The risk of the gastric cancer is 6 times increased by the presence of H. pylori, accounting for about a half of all the gastric cancers. The complicated interaction between gastric H. pylori infection, gastric acid secretion and gastric histology remains unraveled. The aim of our present study was to compare the presence of H. pylori in the tumor tissue and on the unchanged stomach mucosa surrounding the carcinoma. During the last two years we investigated 99 patients with endoscopically and histologically confirmed stomach carcinoma (55 males and 44 females, age between 46 and 80). After the operation, we examined H. pylori presence in tumor tissue and surrounding stomach mucosa. In the 55 (55%) persons we found H. pylori in the surrounding mucosa, but in 13 patients we also found H. pylori in the tumor tissue (23.60% of all cases of gastric cancer). Majority of all patients with presence of H. pylori were males (12). Histologically, the intestinal type of cancer was the most frequent one, counted 12 cases: macroscopically, the vegetant type was present in 9 cases and superficial, infiltrative and early cancer counted one case each. In addition to still present enigma of H. pylori infection role in gastric cancer pathogenesis, we conclude that Helicobacter pylori is not present on the surrounding mucus layer only. It can also be detected in tumor tissue in about 25% of patients with gastric cancer and concomitant H. pylori infection. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach } "Comparing the Presence of H. Pylori on the Unchanged Gastric Mucus Layer and within the Tumor Tissue in Patients with Gastric Carcinoma"

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## "P P 15 0400" P 15 0400 Helicobacter Pylori Cag-A Prevalence in Patients with Gastric Cancer

\*M. Menegatti, C. Ricci, J. Holton, F. Landi, N. Figura, A. Al'ec, B. Massardi, S. Farinelli, R. Gusmaroli, F. Milesi, A. Casadei, P. Maiolo, F. Mucci, M. Miglioli, D. Vaira

Ist Medical Clinic Bologna, GI Section Treviglio, GB Morgagni Hospital, Forl\ec, Italy

Dept. of Microbiology, University College, London, UK *Purpose:* To evaluate Helicobacter pylori (H pylori) IgG and Cag-A seroprevalence in a gastric cancer (GC) compared to 1 non ulcer dyspepsia (NUD) population. *Methods:* In a 40 months period 531 (M/F: 312/219, age: range 19–95, mean 69 years) patients with a gastric malignancy (site: 313 antrum, 62 fundus, 156 corpus) (histology: 368 intestinal, 138 diffuse and 25 lymphomas) were screened for H pylori by IgG serology with an in house ELISA technique (previously validated in endoscoped patients with sensitivity and specificity of 94%). A first series of 78 gastric cancer patients (56 H pylori IgG positive) was also assessed for Cag-A presence by Western Blotting. As control group 52 consecutive non ulcer dyspepsia patients (25 H pylori IgG positive) (M/F: 28/24, age: range 21–80, mean 47.3 yrs), selected among a total of 1601 (M/F: 825/776, age: 18–89, mean 46.1 yrs) (H pylori IgG +ve 1055/1601: 66%) patients referred to upper GI endoscopy to our unit in the same study period, were also assessed for Cag-A. *Results:* The overall seroprevalence of H pylori infection in gastric cancer patients was 437/531 (82%) with no significant differences according to both site or histology of malignancy. The table shows the Cag-A positivity in the two population according to IgG serology. GC IgG+ GC IgG{ -} NUD IgG+ NUD IgG{ -} Cag-A+ 51/56\* (91%) 7/22 (32%) 14/25 (56%) 2/27 (7%)\*P < 0.001 vs NUD IgG+ *Conclusions:* 1. We confirm an high seroprevalence of H pylori infection in gastric cancer; 2. The prevalence of Cag-A positivity is significantly higher in gastric cancer compared to non ulcer dyspepsia patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Screening, prevention Oncology, general: Epidemiology } " Helicobacter Pylori Cag-A Prevalence in Patients with Gastric Cancer "

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"P P 15 0401" P 15 0401 **Gastric Epithelial Cell Proliferation and Helicobacter Pylori CagA-Positive Strains: Immunohistochemical Study in a High Gastric Cancer Risk Population**

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<sup>3</sup> Dept. Int. Med., Catholic University, Rome, Italy Recently, *Helicobacter pylori* was classified as Type I carcinogen. Many evidences in literature show that an increased cell proliferation can be an important step in carcinogenesis. The role of *H. pylori* on gastric epithelial cell proliferation is still debated. High prevalence of *H. pylori* CagA positive (Hp CagA+ve) strains was found in a representative sample of a population at high risk for gastric cancer (San Marino Study I – GUT 1995). *Aim:* to evaluate, in this population, the gastric epithelial cell proliferation, in order to find possible correlations with Hp infection and CagA-status. *Methods:* Thirty-six patients were studied, subdivided into 4 groups: Hp CagA+ve gastritis, Hp CagA { - } ve gastritis, Hp { - } ve gastritis and controls. Antral mucosal biopsies were incubated with PC 10 monoclonal antibody for the immunohistochemical detection of PCNA (avidin-biotin peroxidase technique). The following parameters were blindly evaluated by computerized image analysis system: Proliferative Zone index (PZ = number of cell included between the uppermost and lowest labelled cell), and Labelling index (LI = percentage ratio between total number of labelled cells and total number of cells in proliferative zone). *Statistics:* data were analysed with T-Student's test and linear regression. *Results:* Hp+ve gastritis shows a significant higher LI (33 – 8) and PZ index (70 – 9) with respect to normal mucosa (23 – 15; 50 – 16) and Hp { - } ve gastritis (13 – 3; 41 – 10). LI and PZ index are directly correlated with anti-CagA antibodies (p < 0.01). *Conclusions:* These data indicate that CagA+ve *Hp* strains induce a higher gastric cell proliferation, and support the role of this infection in gastric carcinogenesis. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oncology, general: Proliferation, carcinogenesis }"  
"Gastric Epithelial Cell Proliferation and Helicobacter Pylori CagA-Positive Strains: Immunohistochemical Study in a High Gastric Cancer Risk Population"

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"P P 15 0402" P 15 0402 ***Helicobacter Pylori* and Intestinal Type of Gastric Cancer**

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Gastroenterology, Pathology and Microbiology Departments, "Ram\fn y Cajal" Hospital, Madrid, Spain Epidemiological studies have consistently shown an association between infection with *H. pylori* and gastric cancer but different conclusions have been reported regarding its association with the intestinal and diffuse histologic types. *Aim:* To determine whether there is an association between *H. pylori* infection and gastric adenocarcinoma and its relationship with two histologic gastric cancer types: intestinal and diffuse. *Materials and Methods:* 48 (17 females; mean age: 68.7 – 11.5 yrs; range: 39–88 yrs) patients with histologically confirmed gastric adenocarcinoma were studied. No patient had received blood or blood derivatives. Gastric cancers were histologically classified as intestinal or diffuse type following Lauren classification. *H. pylori* infection status was assessed by determining IgG antibodies to this organism using an ELISA assay commercial kit (Helico-G, Porton, Cambridge, UK). Titers > 10 U/ml were considered positive. *Results:* 31 (65%) of gastric cancers were classified as intestinal type, 12 (25%) as diffuse type and 5 unknown. Age and male/female distribution were similar in both groups. The overall *H. pylori* seroprevalence was 85.4%. *H. pylori* was found in 29 (93.5%) of the 31 intestinal-type cancer cases compared with 8 (66.7%) of the 12 diffuse-type cancer cases ( $p < 0.05$ ). *Conclusions:* The overall *H. pylori* prevalence in cancer gastric patients was clearly higher than that reported in healthy people in Western developed countries. The prevalence of *H. pylori* in intestinal-type gastric cancer exceeded by far the prevalence of *H. pylori* in diffuse disease, thus suggesting that *H. pylori* may be a cofactor for the development of this histologic gastric cancer type. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach Oncology, general: Epidemiology } "Helicobacter Pylori and Intestinal Type of Gastric Cancer"

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"P P 15 0403" P 15 0403 **Gastric Adenocarcinoma Location and *Helicobacter Pylori* Infection**

\*C. Mart\edn de Argila, D. Boixeda, C. Redondo, L. de Rafael, J.P. Gisbert, E.S. Villalobos, F. Hernandez Ranz

Gastroenterology, Pathology and Microbiology Departments, "Ram\fn y Cajal" Hospital Madrid, Spain. *H. pylori* infection is recognized as a risk factor for gastric adenocarcinoma. **Aim:** To determine if there is an association between *H. pylori* infection and gastric cancer and its relationship according to tumor location. **Materials and Methods:** 48 (17 females; mean age: 68.7 – 11.5 yrs; range: 39–88 yrs) patients with histologically confirmed gastric adenocarcinoma were studied. None of patients had received blood or blood derivatives. Gastric cancers were assigned to the following groups according its location: antrum, corpus, and gastric fundus (near to cardia). *H. pylori* infection status was assessed by determining IgG antibodies to this organism using an ELISA assay commercial kit (Helico-G, Porton, Cambridge, UK). Titers > 10 U/ml were considered positive. **Results:** 13 (27%) of gastric cancers were located at gastric antrum, 12 (25%) at gastric corpus, and 5 (10.4%) at gastric fundus. In 18 (37.5%) patients the tumor extended to more than one of the described locations, thus preventing to accurately know the origin of the neoplasm. The overall *H. pylori* seroprevalence was 85.4%. *H. pylori* infection according tumor location yielded the following distribution: Tumor location *H. pylori* + *H. pylori* { - } Total Antrum 13 (100%) 0 13 Corpus 11 (91.7%)\* 1 (8.3%) 12 Fundus 2 (40%)\*@ 3 (60%) 5 \*p < 0.05 (compared with "antrum"); @p = 0.052, almost significant (compared with "corpus"). **Conclusions:** These results confirm the high prevalence of *H. pylori* infection in patients with gastric adenocarcinoma, much higher than that observed in healthy people in Western developed countries. The higher *H. pylori* prevalence observed in patients with antrum and corpus gastric adenocarcinoma supports a relationship between *H. pylori* infection and the noncardia gastric adenocarcinoma. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach Oncology, general: Epidemiology } "Gastric Adenocarcinoma Location and Helicobacter Pylori Infection"

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"P P 15 0404" P 15 0404 **Gastric Cancer and Helicobacter Pylori Infection**

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Fundeni Clinic Hospital, Bucharest, Romania *Background:* Helicobacter pylori has been implicated as a possible factor in gastric cancer. This study aimed to examine the association between Helicobacter pylori, histological gastritis, and intestinal metaplasia in gastric cancers of different histological types. *Methods:* In total 154 cases of gastric cancer were studied: 92 (59.74%) intestinal; 40 (25.97%) diffuse; and 22 (14.28%) unclassified. As a control group, 147 patients with non malignant disorders were selected (54 patients with gastric ulcer, 23 with peptic ulcer, 39 with chronic superficial gastritis, 31 with chronic atrophic gastritis), who were frequency matched with respect to age and sex. *Results:* A) Presence of Helicobacter pylori related to the histological type of gastric cancer diagnosis in the control group: Diagnostic H. pylori-positive cases *Gastric cancer type* Intestinal 78 of 92 (84.78%) Diffuse 23 of 40 (57.50%)\*Unclassified 12 of 22 (54.54%)\* *Controls* Gastric ulcers 34 of 54 (62.96%) Peptic ulcer 11 of 23 (47.82%) Chronic superficial gastritis 27 of 39 (69.23%) Chronic atrophic gastritis 12 of 31 (38.70%)\*  $p < 0.05$  versus intestinal-type gastric cancer. B) Presence of Helicobacter pylori related to the histological type of intestinal metaplasia Cases H. pylori-positive cases Type I 29 (61.53%) Type II 19 (70.37%) Type III 5 (38.46%) Total 79 of 154 (51.29%) 53 of 79 (67.08%) *Conclusions:* These findings suggest that there is a possible association between the intestinal type of gastric cancer and H. pylori infection. H. pylori was not colonized in the gastric tumor tissue. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach } "Gastric Cancer and Helicobacter Pylori Infection"

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"P P 15 0405" P 15 0405 **Low-Grade Malt Lymphoma of the Stomach, Associated with *Helicobacter Pylori*: Russian Experience**

\*V.A. Isakov, L.E. Gurevitch

Moscow Regional Research Clinical Institute (MONIKI), Moscow, Russia During the last two years we have followed-up 6 patients with low-grade MALToma of the stomach. There were 5 women and 1 man, the mean age was 51.8 years. There were one polypoid-like lesion, four ulcerated and one was presented as a bulk infiltration of 1/3 of the stomach with ulceration. The diagnosis was confirmed by histology and monoclonality of tumor cells was confirmed by immunohistochemistry with  $\{k\}$  and  $\{l\}$  light chains antibodies. All patients received triple therapy that consisted of CBS (De-nol) 120 mg qid, ampicillin 500 mg qid and methronidazole 250 mg qid during 14 days, one patient because of allergy for penicillins received tetracycline 500 mg qid instead of ampicillin. *H. pylori* was eradicated in 5 patients. In all these patients the regression of MALToma was progressively noted. It started with the decrease of density of infiltrate in lamina propria of gastric mucosa, then lympho-epithelial lesions disappeared. Nevertheless, at that period of time and up to the 8 month after treatment monoclonality of cells infiltrating lamina propria was revealed by immunohistochemistry with anti- $\{k\}$ -antibodies in two patients. Nine months after the cessation of the therapy the biological remission of low grade MALToma was achieved in all 5 patients in whom the *H. pylori* was successfully eradicated. During the follow-up period one patient relapsed after 8 months of biological remission with *H. pylori* reinfection and showed reappearance of all features of low-grade MALToma including lympho-epithelial lesions and mucosal ulceration. After the repetition of the triple therapy *H. pylori* was eradicated again and after 6 mo biological remission of MALToma was achieved. *In conclusion:* Eradication of *H. pylori* leads to histological and biological remission of low-grade MALToma of the stomach. Reinfection of *H. pylori* followed by rapid relapse of MALToma. Oncology, specific: Lymphoma Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "**Low-Grade Malt Lymphoma of the Stomach, Associated with *Helicobacter Pylori*: Russian Experience**"

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"P P 15 0406" P 15 0406 **Sequential Histological and Molecular Follow Up of Low Grade Gastric Malt Lymphoma after Eradication Therapy for *Helicobacter Pylori***

\*D. Boixeda, C. Montalban, A. Manzanal, J.L. Calleja, M.G. Montero, C. Martin de Argila, I. Alvaez Baleriola, C. Bellas

Departments of Internal Medicine, Pathology, Gastroenterology, "Ramón y Cajal" Hospital and Hematology, "Severo Ochoa" Hospital, Madrid, Spain. *H. pylori* infection is associated with low grade gastric MALT lymphoma, and available data support that the eradication of *H. pylori* can cause lymphoma regression. In this study, 10 untreated patients with low grade gastric MALT lymphoma were treated with amoxicillin, metronidazole and omeprazol for 14 days. In order to assess the response to *H. pylori* eradication and the evolution of the histological and molecular responses, patients were followed up with sequential endoscopy, mapping gastric biopsies and molecular studies with amplification of the IgH gene by PCR with Fr2 and Fr3 V-region primers with nested primers directed to the J-region. *H. pylori* was eradicated in all patients and reinfections were non demonstrated. In 8 of the 10 patients the lymphoma regressed both endoscopically and histologically; another patient achieved a partial histological regression. In 4 of the 8 histologically cured patients no clonal band was detected by PCR; in the remaining 4 patients, PCR demonstrated a clonal band, that disappeared in all patients after a mean of 7.2 – 6 months. All 8 patients have a persistent clinical and histological remission after a median follow up of 12.5 – 6 months. **Conclusions:** 1) *H. pylori* eradication can produce histological regression of low grade gastric MALT lymphoma. 2) *H. pylori* should be the initial therapy for stage I low grade gastric MALT lymphoma. 3) Despite histological regression of the lymphoma, a clonal population may persist in some cases. 4) The disappearance of this clonal population may be delayed for months. 5) Patients with histological regression of the lymphoma but with a persistent clonal population should no be treated unless a relapse can be histologically demonstrated. These observations suggests that gastric lymphoma can be effectively cured; still, long-term follow up studies are necessary to assess the ultimate outcome of these patients. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oncology, specific: Stomach } "Sequential Histological and Molecular Follow Up of Low Grade Gastric Malt Lymphoma after Eradication Therapy for *Helicobacter Pylori*"

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"P P 15 0407" P 15 0407 **Precancerous Lesions in Patients HP Positive and Gastric Cancer Risk Index**

\*E. Masci, E. Viale, M. Freschi, A. Tittobello

S. Raffaele Hospital, University of Milan, Italy *Background:* the follow-up of precancerous gastric lesions (PGL) is a controversial problem, because only few patients with chronic atrophic gastritis (CAG) and intestinal metaplasia (IM) develop cancer. Recently a simple score has been proposed to detect Hp infected patients with an increased risk for gastric cancer (GC). In this risk index histological criteria were evaluated in early gastric cancer patients in comparison with duodenal ulcer (DU) patients [1]. *Aim:* to compare two groups of patients, with DU and with CAG with type III IM, a well know PGL, both characterized by Hp infection and to assess if the only difference of lymphocytes/plasmacells and neutrophiles infiltration in corpus and antrum without considering metaplasia to discriminate the two groups of patients with different cancer risk. *Materials and methods:* we have drawn two biopsies from the antrum and two from the corpus of 41 patients with DU and 25 subjects with CAG and type III IM. The samples were histologically examined. *Results:* in subjects with CAG and type III IM samples from the gastric corpus, compared to those from the antrum, showed higher infiltration of lymphocytes and plasmacells. In addition, when compared with DU patients, they showed higher lymphocytic and neutrofiles, considered as 1 point of the score: DU type III IM pLymphocytes/plasmacells 14.63% (6) 40% (10) < 0.020 Neutrophiles 14.63% (6) 44% (11) < 0.0082 vs 0 points: Odds – ratio = 5.71; 95% CI = 1.49–21.84 *Conclusions:* in our preliminary study the degree of Hp gastritis and the activity, in the corpus, is more pronounced in subjects with CAG and type III IM than in DU patients. However, the overlapping of the results in the two groups of patients need further data in large group to confirm the usefulness of considering the two histological features in corpus as a predicting factor of risk of cancer, independently of IM.

Reference: Meining A. et al.: Gastric carcinoma risk index in patients infected with Hp. Arg. Gastroenterol. Clin (suppl. 6) 8: Settembre 1995 (abs). Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Screening, prevention } "Precancerous Lesions in Patients HP Positive and Gastric Cancer Risk Index"

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"P P 16 0409" P 16 0409 **Comparative Cytopathologic and Histologic Study of Benign Nonspecific Inflammation and Infections of Upper Alimentary Tract in Childhood**

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The aim of the study was to review the role of cytological abrasive biopsy in children upper endoscopy for establishing changes in gastric and esophageal epithelium & for detecting infectious agent (*Helicobacter pylori*-H.p.). In 1994/95 the examination covered 113 children and adolescents (57 girls and 56 boys) aged 6–18 years with upper dyspeptic syndrome. Each patient underwent gastroscopy with brush biopsy. Smears of 108 patients were stained with Giemsa. Sixty three of them was examined histologically and 26 with urease test. Twenty five patients with endoscopic diagnosis gastritis were examined for cytological changes of gastric epithelium & 5 patients with endoscopic diagnosis esophagitis – of epithelium of esophagus. H.p. was found in smears in 50.9%. *Gastrospirillum hominis* in 1.9% & *Candida albicans* in 0.9%. For detection of H.p. cytological method had (in comparison with histological) sensitivity 91%, specificity 46%, accuracy 62%, positive predictive value 48% and negative predictive value 91%. In comparison with histological and urease test, cytology had sensitivity 93%, specificity 92% and accuracy 92%, positive predictive value 93% and negative predictive value 92%. In patients with endoscopic gastritis cytological examination revealed minimal cell atypia 9/25, increased cellular exfoliation 7/25 and nuclear hyperchromatism 9/25. Histological activity of gastritis was related with increased nuclear hyperchromatism & cellular exfoliation. Inflammatory cells and cells undergone intestinal metaplasia were not found cytologically. Established cytological changes in patients with endoscopic esophagitis were increased cellular exfoliation 2/5, minimal cellular atypia, inflammatory cells and *Candida albicans* – 1/5. In conclusion brush biopsy in childhood is a rapid and simple method for detection of H.p. infection. Cytological changes may suggest to inflammation of gastric and oesophageal mucosa. Endoscopy, general: Endoscopy: children Oesophageal gastric duodenal disorders: EGD disorders in children Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Comparative Cytopathologic and Histologic Study of Benign Nonspecific Inflammation and Infections of Upper Alimentary Tract in Childhood"

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"P P 16 0410" P 16 0410 **Recurrent Abdominal Pain (RAP) and Helicobacter (HP) Infection in Children: Effectiveness of Eradication Therapy** A. Carroccio, F. Cavataio, C. Acierno,

\*G. Montalto, G. Li Voti, M. Soresi, S. Ippolito, P. Campagna, C. Magliarisi, G. Iacono

Cattedra di Med. Int. and Chir. Ped. Univ. di Palermo II Div. Ped., Osp. "Di Cristina" Palermo (Italy) A relationship between HP infection and RAP in children has been suggested but not clearly demonstrated. We evaluated the effectiveness of eradication treatment for HP infection in patients with RAP, selected from over 4,000 children in the general population. 180/4,000 subjects presented RAP, defined according to Apley's criteria. 77/180 were positive for serum anti-HP antibodies. After esophagogastrosopy (EGDS), 65 patients were randomly assigned to 3 treatment groups: Group A (omeprazole + clarithromycin), Group B (clarithromycin + bismuth citrate), Group C (amoxicillin + bismuth citrate), each including 23, 22 and 20 patients respectively. 35 HP-negative RAP patients were selected as controls and treated with placebo. A RAP severity score was determined at study entry and at 3 and 12 months after treatment. In the 3 eradication treatment groups, symptoms scores were significantly lower both at 3 and 12 months after treatment than at the entry. The percentage of completely cured patients at 3 months was significantly higher in Group A (22/23 subjects) than in Group B (13/22) and in Group C (10/20); At 12 months the number of cured patients was 17/23 in Group A, 12/22 in Group B and 9/20 in Group C. In general the frequency of cured RAP was significantly higher in the HP-positive patients than in controls both at 3 and at 12 months. Post treatment EGDS showed persistent HP in 14/20 patients who were still symptomatic after treatment and in 0/15 subjects considered cured ( $p < 0.0001$ ). Eradication percentages were significantly higher in the subjects of Group A than in the other 2 treatment groups. We conclude that more than 1/3 of the RAP patients also have HP infection and that the eradication treatment is useful in curing RAP. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Management strategy } "Recurrent Abdominal Pain (RAP) and Helicobacter (HP) Infection in Children: Effectiveness of Eradication Therapy"

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## "P P 16 0411" P 16 0411 Gastric Mucous Inflammation at Childhood Upper Gut Disease

\*K. Marakhovsky, A. Zarubov, S. Zuk, Y. Marakhovsky

Minsk Diagnostic Centre for Child, Republican Gastroenterology Centre, Minsk, Belarus Inflammatory reactions of the gastric mucous are accompanied with many upper gastrointestinal diseases. On the other hand, such widespread infectious factor, as *H. pylori* colonised gastric mucous and it associated with the mucous inflammation which has the adverse prognosis, especially in children. However, the frequency and feature of gastric mucous inflammatory reactions at the children are investigated not reasonably. *Aim of the study* Evaluate of gastric mucous inflammatory reactions (GMIR) at the various diseases of upper gastrointestinal tract and at different level of *H. pylori* colonisation in children's age. *Methods.* 2594 patients (pts) (F – 1413, M – 1181) in age from 2 to 15 years old was examined by upper endoscopy and mucous lesions was assessment by the OMED standards. Biopsies from antrum was evaluated by a degree of lymphoplasmacytic (LPC), polymorphonuclear (PMN) reactions and *H.p.* colonisation (HpCo) on Sydney system following for the descriptions of the histological parameters. *Results.* Group I – 1273 pts (49.07%) had gastritis with total HpCo-61.2%; group II – 69 (2.66%) pts had duodenal ulcer and *H.p* positive in 81.8%; group III – 154 (5.94%) pts with flat lesions of duodenal bulb mucous and HpCo-66.0%; group IV – 195 (7.52%) pts with flat stomach lesions and HpCo-67.7%. Following GMIR was detected: middle LPC > PMN in 29.3% from all cases; low grade LPC = PMN in 39.7%; LPC < PMN was found in only 21 cases (0.8%). High and middle HpCo is associated with severe GMIR in 68.7% pts. *Conclusion:* 1. Childhood upper gastrointestinal diseases are provided with predominated chronic gastric mucous inflammatory reactions type. Severe grade of gastric mucous inflammatory reactions correlated with high gastric mucous *H. pylori* colonisation rate. Oesophageal gastric duodenal disorders: EGD disorders in children Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Endoscopy, general: Endoscopy: children } "Gastric Mucous Inflammation at Childhood Upper Gut Disease"

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"P P 16 0412" P 16 0412 **The <sup>13</sup>C-Urea Breath Test for the Diagnosis of Helicobacter Pylori Infection in Children** **The Bologna <sup>13</sup>C-Urea Breath Test User Group,**

\*F. Bazzoli, L. Cecchini<sup>1</sup>, L. Corvaglia, M. Dall'Antonia<sup>6</sup>, M. Dalla Libera<sup>2</sup>, C. De Giacomo<sup>4</sup>, S. Fossi, P. Garisio<sup>5</sup>, L. Gobbio Casali<sup>3</sup>, S. Gullini<sup>2</sup>, R. Lazzari, G. Leggeri<sup>3</sup>, P. Lerro<sup>5</sup>, F. Lizzoli<sup>4</sup>, G. Mandrioli<sup>2</sup>, M. Marani<sup>1</sup>, P. Martelli<sup>5</sup>, A. Miano<sup>1</sup>, C. Mwangemi, G. Oderda<sup>5</sup>, A. Pasetti, P. Pazzi<sup>2</sup>, P. Pozzato, L. Ricciardiello, E. Roda, P. Simoni, S. Sottili, G. Torre<sup>6</sup>, L. Urso<sup>6</sup>, R.M. Zagari

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<sup>6</sup> Trieste *Background.* The <sup>13</sup>C-Urea Breath Test (<sup>13</sup>C-UBT) is a simple non invasive highly accurate test for the detection of Helicobacter (H.) pylori infection in adults. Although the use of <sup>13</sup>C-labelled urea renders this test absolutely safe and thus undoubtedly suitable for the detection of H. pylori infection in children, as yet a standardized <sup>13</sup>C-UBT protocol for children has not been formulated. In particular we have no information on the three fundamental components of the <sup>13</sup>C-UBT: the number of and time intervals for breath sample collection, the appropriate test meals to delay gastric emptying and doses of <sup>13</sup>C-Urea. *Purpose.* The aim of our study was to evaluate the accuracy of the <sup>13</sup>C-UBT in children using different types of test meal, doses of <sup>13</sup>C-Urea and breath sampling intervals. *Methods.* 98 children, recruited in our study (51 males, 47 females; age (yrs) range 2–16, mean – SE: 10.1 – 0.3; body surface area (m<sup>2</sup>) range 0.5–1.7, mean – SE: 1.2 – 0.03) underwent routine upper GI endoscopy. 3 antral and 2 corpus-fundus biopsy specimens were taken for histological evaluation for the presence of H. pylori infection (Haematoxylin/Eosin; GIEMSA) and the quick Urease-test was performed. The <sup>13</sup>C-UBT was performed in each child after undergoing endoscopy, and was then repeated within three days modifying the test meal or the dose of the <sup>13</sup>C-Urea. 62 children were given a fatty test meal, Pulmocare (Abbott) 100 ml, and two different doses of <sup>13</sup>C-Urea, 100 and 50 mg respectively. 36 children were given the same dose of <sup>13</sup>C-Urea, 50 mg, but two different types of test meal, Pumocare 100 ml and 10 gr at 10% of Polycose (polymer of glucose) respectively. Breath samples were collected every 10 minutes for 60 minutes and analyzed by an Automated Breath <sup>13</sup>C Analyzer (ABCA Europa Scientific). The "gold standard" for the detection of H. pylori infection was defined as a concordant result on histology and quick urease-test. The cut-off value was calculated taking the mean of H. pylori { - }ve subjects – 3 SD and using a ROC curve. *Results.* According to the "gold standard" 48 children were considered H. pylori +ve and 44 H. pylori { - }ve. 100 mg Urea + Pulmocare 50 mg Urea + Pulmocare 50 mg Urea + Polycose T10 T20 T30 T40 T50 T60 T10 T20 T30 T40 T50 T60 Sens (%) 96.3 100

100 100 100 100 91.3 95.6 100 100 100 97.8 94.4 89.9 83.3 88.9 88.9 88.9Spec (%) 92.0 96.0  
100 100 100 96.0 94.9 97.4 100 100 97.4 100 100 100 100 100 100Accur (%) 94.2 98.1 100  
100 100 98.1 92.2 96.5 100 100 98.8 98.8 97.0 93.9 90.9 93.9 93.9 93.9Conclusions. The <sup>13</sup>C-  
UBT is a simple, non invasive test that can be used as the "gold standard" for the detection of  
H. pylori infection. Administering 50 mg of <sup>13</sup>C-Urea, a fatty test meal and a single breath  
sample at T30 makes it ideal even in children. Oesophageal gastric duodenal disorders:  
Helicobacter PyloriOesophageal gastric duodenal disorders: EGD disorders in children } "The  
13C-Urea Breath Test for the Diagnosis of Helicobacter Pylori Infection in Children"

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## "P P 16 0413" P 16 0413 Upper Gastrointestinal Mucosal Lesions Caused by Intensive Cytostatic Therapy in Children

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<sup>2</sup> Department of Pathology, University Hospital, Fin-90220 Oulu, Finland To assess the degenerative effects of intensive cytostatic therapy on the upper gastrointestinal mucosa, we enrolled all new cases of children with malignant diseases older than 1 year of age in a six-week follow-up study with upper gastrointestinal endoscopy performed at four weeks. Eleven patients (7 males, 4 females, median age 6 yrs, range 1–15 years) were monitored clinically, and nine of them consented to endoscopy. – Five patients complained of mouth pains during eating and two developed mucosal ulcerations. Abdominal cramps, mostly during the first three weeks, were reported by three patients and two developed diarrhoea. A positive lactose challenge test (increment > 20 ppm) was found in three patients out of the nine who were able to do a breath test. Macroscopic findings at endoscopy were observed in five out of the nine patients, the most prominent feature being esophagitis. All the duodenal samples showed histological alterations (increased eosinophils in 5, crypt hyperplasia in 5 and mild villous atrophy in 3). Only one patient had inflammation of the antral mucosa and two others excessive lymphocytes in their esophageal samples. *Conclusion:* The most prominent histological changes attributable to cytostatic therapy are in the jejunum, while the ventricle and esophagus are less affected. Oesophageal gastric duodenal disorders: EGD disorders in children Endoscopy, general: Endoscopy: children Immunology and microbiology: Inflammation } "Upper Gastrointestinal Mucosal Lesions Caused by Intensive Cytostatic Therapy in Children"

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## "P P 16 0415" P 16 0415 **Beta-Endorphin Levels in Children with Gastroduodenitis**

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Department of Pediatrics, Endocrinology and Adolescent Diseases, Medical Academy, Lublin, Poland

The experimental investigation indicates that opioid can regain a protective field in gastric and duodenal mucosa lesion prevention. In the group of 50 children (10–16 years old) suffering from chronic gastritis and duodenitis, which were confirmed by endoscopic examination, beta-endorphin ( $\beta$ -E) levels in serum (RIA Kit Incstar Corp.) were determined. Afterwards, the results were compared to values of control group. In group of healthy children level was mean  $8.43 \pm 1.41$  pmol/L, however in group of sick children was significantly lower ( $p < 0.01$ ) and it was mean  $6.47 \pm 1.02$  pmol/L. In group of 20 children,  $\beta$ -E level before and after monthly dietetic and drug treatment (Venter or Ventrisol) was determined. According to our data, mean beta-endorphin level before treatment  $\beta$ -E =  $5.85 \pm 1.77$  pmol/L was significantly lower ( $p < 0.05$ ) than beta-endorphin level after the therapy  $\beta$ -E =  $7.2 \pm 1.82$  pmol/L. We also found, that in group of children, where ulcer formation were presented,  $\beta$ -E level was the lowest  $\beta$ -E =  $4.2 \pm 1.2$  pmol/L and increased after the treatment up to  $\beta$ -E =  $6.5 \pm 1.6$  pmol/L. Our conclusion is that in children with gastritis and duodenitis, particularly in such cases where ulcer is accompanied, lowered opioid activity was observed. We paid attention to increased tendency during the therapy. Oesophageal gastric duodenal disorders: EGD disorders in children } "Beta-Endorphin Levels in Children with Gastroduodenitis"

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"P P 16 0416" P 16 0416 **Serum Cholinesterase and Acetylcholinesterase Activity in Children with Gastroduodenitis** L. Szewczyk, S. Zbaranska, H. Lozowska,

\*D. Witkowski

Department of Pediatrics, Endocrinology and Adolescent Diseases Medical Academy, Lublin, Poland  
Though its role has not been very well defined yet, serum cholinesterase (ChE) is said to play a role similar to acetylcholinesterase (AChE) in cholinergic activity regulation. Our investigation involved 35 healthy children and 35 children (25 girls and 10 boys aged 9.6–16.3) with gastroduodenitis treated with Venter or Ventrisol. These children underwent endoscopy examinations because of epigastric pains. Urease test and histopathological examinations in 13 children confirmed *Helicobacter pylori* (Hp) infections; in 22 children these results were negative. In these children the AChE (colorimetric meth. f. Chemed) and ChE (Weber kinetic meth.) activity test was conducted twice. *Results:* ChE activity in children with digestive tract pathological changes (mean = 6129.16 – 1333 IU/L) was significantly lower ( $t = 2.34$ ,  $p < 0.05$ ) than in healthy children (mean = 6825.08 – 1135 IU/L). There were differences in ChE activity between children with positive and negative results of confirmed Hp presence investigations. Namely, the ChE activity in children with Hp infection (mean 5245 – 1118 IU/L) was significantly lower ( $t = 2.73$ ,  $p < 0.01$ ) than in children with negative bacteriological tests. (mean 6617.19 – 1607 IU/L). AChE levels behaved in the same way. AChE and ChE activity decrease may prolong acetylcholine action and cause secretory and motile changes in the upper part of digestive tract. This situation facilitates the bacterial factor penetration. Oesophageal gastric duodenal disorders: EGD disorders in children Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Serum Cholinesterase and Acetylcholinesterase Activity in Children with Gastroduodenitis"

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## "P P 16 0417" P 16 0417 Salivary Diagnosis of *Helicobacter Pylori* Infection in Children: A Multicenter Study

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<sup>3</sup> Servizio di Anatomia Patologia, Ospedale Pugliese, Catanzaro, Italy **Background/Aim:** Epidemiological studies suggest that in most populations *H. pylori* infection is commonly acquired in childhood. Serology is a sensitive and specific indicator of *H. pylori* infection also in pediatric population, provided that children's sera are used to standardize the assay. We have recently shown that salivary IgG to *H. pylori* paralleled specific circulating IgG and accurately detected *H. pylori* infection in adults (Am J Gastro 1995). In this study we validated our salivary test to diagnose *H. pylori* infection in children. **Methods:** 112 consecutive patients (55 M; median age: 11 yrs, range 2–18) attending for upper GI endoscopy were available for the study. Two antral and corpus biopsy specimens were taken for histology (Giemsa staining) and one antral biopsy for urease quick test. Assessments were made blinded to the final diagnosis. Where both evaluations were concordant this was taken as the gold standard *H. pylori* status for that patient. 1–2 ml of unstimulated saliva were collected from each patient before endoscopy and stored at  $-20^{\circ}\text{C}$  until tested. Saliva samples (working dilution 1:2) were assayed for *H. pylori* IgG by an in-house ELISA using a sonicate of a whole *H. pylori* strain as antigen. All samples were run in duplicate in the same assay. A cut-off of 2 SD above the mean of a standard reference pool of histologically *H. pylori* negative children's saliva was chosen. Results were expressed as mean optical density (OD) – SD. 95% CI were given. **Results:** *H. pylori* was identified in 57 (51%) patients. Salivary *H. pylori* IgG were significantly higher in *H. pylori* positive than negative patients (0.495 – 0.292 vs 0.150 – 0.131,  $p < 0.001$ ). Based on a cut-off of 0.200 OD, we found that 4 *H. pylori* positive patients were saliva negative and 10 *H. pylori* negative were saliva positive. The sensitivity and specificity of salivary *H. pylori* IgG were 93% (83–98%) and 82% (70–91%) with positive and negative predictive values of 84% (73–92%) and 92% (80–98%), respectively, with an accuracy of 87.5% (80–93%). **Conclusion:** Salivary *H. pylori* IgG is an accurate indicator of gastric *H. pylori* colonization in pediatric population. It may offer practical advantages in children in both clinical and investigational settings. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Stomach, duodenum } "Salivary Diagnosis of Helicobacter Pylori Infection in Children: A Multicenter Study"

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"P P 16 0418" P 16 0418 **Immune Response to *Helicobacter Pylori* in Duodenal Ulcer in Children**

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The study evaluates the frequency of *Helicobacter pylori* (*H. pylori*) infection, as well as systemic cellular immune response to *H. pylori* in duodenal ulcer (DU) in children. The study group comprised 60 children with DU, aged 6–17 (mean 13.3 – 2.5). *H. pylori* detection was based on urease test, histology, culture and serologic tests. Endoscopic and morphologic findings were analysed according to Sydney System criteria. In 16 children from the overmentioned group subsets of blood lymphocytes B and T (CD3, CD4, CD8, CD3/DR, CD19) and NK cells, some neutrophils functions (phagocytosis, chemiluminescence), phagocytes receptors (CD11B, Fc{ g} IIIIRa), components C4, CH50 before and one month after *H. pylori* triple treatment were investigated. *H. pylori* infection was detected in 56 (93%) of the investigated children. In addition, pathologic examination revealed chronic gastritis and chronic duodenitis in 91% of them. In immunosystemic examination decreased percentage of CD8 lymphocytes, NK cells, increased CD4/CD8 ratio, decreased mitogen-induced response and changes of function and receptor expression of neutrophils were found. In addition the decrease of components C4, CH50 were found. After *H. pylori* eradication normalisation of immune parameters in children were shown. The results of our investigation indicate, that *H. pylori* infection and the changes in host immune response may play an important role in the pathogenesis of duodenal ulcer in children.

Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: GI infection, children Oesophageal gastric duodenal disorders: EGD disorders in children }

"Immune Response to *Helicobacter Pylori* in Duodenal Ulcer in Children"

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## "P P 16 0419" P 16 0419 **The Role of Endoscopy Procedures in Upper Gastrointestinal Anomalies Treatment in Infants**

\*E. Czkwianianc, A. Chilarski, S. Nowak, E. Chruslinska

Deps. of Pediatrics, Pediatric Surgery, Intensive Neonatal Care, Pediatric Intensive Care, Polish Mother's Memorial Hospital, L\ 'f3dz The aim of the paper is to assess the role of interventioned endoscopy in upper gastrointestinal anomalies treatment in newborn and infants, as a supplementary method to the surgical procedures. Dilatation of anastomotic strictures jkin two children, operated previously for different esophageal anomalies were performed, with Savary-Gilliard's method. The children underwent the dilatation procedures with different size of bougies used till the nr 6 (11 mm in diameter) several times at five days intervals. First case was a newborn with a congenital esophageal atresia. Because the distance between both ends of esophagus was very long (more than 4 cm) one step operation was impossible and the several steps treatment was applied. At the begining the upper esophageal end has been elongated under the endoscopy control, then by plastic probe. Under radiologic control both, upper and lower parts of esophagus were brought close to each other: upper end by probe and lower one endoscopically. As the proper condition for surgical treatment was confirmed, anastomosis was performed. No complications in the postoperative course were observed. Two months later the symptoms of esophageal stricture were seen clinically and were confirmed radilologically. After several dilatation procedures the significant improvement was seen. Next case was an infant with a slight esophageal stricture after the GERD surgical treatment. The dilatation procedures were performed and the symptoms of dysphagia were relived. In the third case, of a newborn with a single esophagotracheal fistula (so-called H-fistula), we tried to close it endoscopically using the submucosal fibrin adhesion technique. In the first stage the occlusion of the fistula was achieved, but the fistula reccurented seven months later. This time a successful surgical operation was performed. The sealing procedure with the fibrin glue allowed delay of the operation and to perform it in older child with better anatomical and physiological conditions. Those are some new possibilities of application of endoscopy procedures in congenital esophageal malformations in infants. Oesophageal gastric duodenal disorders: EGD disorders in children Endoscopy, general: Instrumentation, therapy Endoscopy, general: Endoscopy: children } "The Role of Endoscopy Procedures in Upper Gastrointestinal Anomalies Treatment in Infants"

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"P P 16 0420" P 16 0420 **Triple Therapy with Omeprazole and Two Antibiotics in Children with *Helicobacter Pylori* Gastritis** G. Oderda, P. Lerro, P. Caristo, M. Kuvidi, M. Forni, N. Ansaldi, P. Martelli, E. Chiroboli, G. Monga, G. Bona

Pediatric Gastroenterology, University of Turin & Novara, Italy In children with *Helicobacter pylori* (*Hp*) gastritis dual therapy regimens with antibiotics with or without bismuth salts usually reach eradication rates ranging from 70 to 80% and triple therapy has seldom been tried. *Aim:* to evaluate efficacy of triple therapy in childhood *Hp* gastritis with Omeprazole plus Clarithromycin and Amoxicillin or Metronidazole for one or two weeks. *Patients & Methods:* *Hp* gastritis was diagnosed by urease test and histology (*Giemsa* stain) in 79 children (M/F 44/35) median age 11 yrs (range 5 { - } 15). They were divided in two groups: a first one (*group A*: 45 children) was treated with a 2-week course of Omeprazole (1 mg/kg bid) + Clarithromycin (15 mg/kg bid) + Amoxicillin (50 mg/kg bid) a second one (*group B*: 34 children) was treated with an 1-week course of Omeprazole (0.5 mg/kg mane) + Clarithromycin (15 mg/kg bid) + Metronidazole (20 mg/kg bid). Six weeks after stopping treatment endoscopy was repeated and eradication proven by urease test, histology of both the antrum and the gastric corpus biopsies and <sup>13</sup>C-Urea breath test (UBT). *Results:* Six children refused repeated endoscopy and eradication was evaluated by UBT only. *Hp* was eradicated in 35 children of group A (77.7%) in 23 of group B (67.6%). Compliance was poor in 5 children of group A, and in 4 of group B. *Conclusions:* Triple therapy for 1 or 2 weeks, with Omeprazole given one or two times a day does not reach a better eradication rate than the average obtained with dual therapy for a poor patient compliance. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Triple Therapy with Omeprazole and Two Antibiotics in Children with *Helicobacter Pylori* Gastritis"

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"P P 16 0421" P 16 0421 **Trace Elements (TE) and Metallothionein (MT) in Duodenal Mucosa of Wilson's Disease (WD)**

\*C. Mestriner, R. D'Inc\ 'e0, P. Irato<sup>1</sup>, M. Minotto, R. Naccarato, G.C. Sturniolo

Division of Gastroenterology, University of Padua, Italy

<sup>1</sup> Dept. of Biology, University of Padua, Italy Wilson Disease is due to an inherited disorder in copper (Cu) metabolism. Cu absorption involves intracellular carriers known as metallothionein (MT). Zinc (Zn) is the most relevant competitive antagonist for MT-dependent Cu absorption and storage. MT synthesis can be experimentally induced in duodenal mucosa by Zn administration. We measured MT and TE (Zn, Cu, Fe) in the duodenal mucosa of 6 WD patients (3 F, 3 M, range of age 26–31 years) and 8 controls (5 F, 3 M, range of age 28–34 years). 5 WD patients were on Zinc sulphate (ZnSO<sub>4</sub> 220 mg po tid) and Cu-deficient diet (less than 1.5 mg/day). One patient was examined any at diagnosis before treatment. Controls had negative endoscopy and did not take any drug. MT concentration was measured in the duodenal mucosa by the Ag-saturation haemolysate method. TE were assayed by Atomic Absorption Spectrophotometry (AAS). *Results:* Patients with WD treated with ZnSO<sub>4</sub> had significantly higher tissue levels of MT (434.4 – 337 ug/g wet wt) with respect to controls (41.56 – 16) (p < 0.05). The newly diagnosed WD patient before treatment had MT concentrations similar to controls (54.3 ug/g wet wt). Mucosal Zn concentrations were higher in WD patients than in controls (513 – 160 vs 119.5 – 64 ug/g dry weight) as were Iron (Fe) concentrations (202.34 – 67.5 vs 80.6 – 33.7 ug/g dry weight). Cu concentration was undetectable in the duodenal mucosa of both patients and controls. *Conclusion:* Zinc therapy increases Zn and MT concentrations in the duodenal mucosa. MT induction may bind Cu within the intestinal cells blocking its absorption although we did not find a direct evidence of increased Cu in the duodenal mucosa. Increased Fe concentration in the duodenal mucosa may also derive from MT induction. Liver and bile ducts, 1: Hepatotoxicity, ethanol }" "Trace Elements (TE) and Metallothionein (MT) in Duodenal Mucosa of Wilson's Disease (WD)"

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## "P P 17 0422" P 17 0422 **Indefinite Dysplasia in Ulcerative Colitis: Clinical Significance and Possible Relation to p53 Protein**

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Gastroenterology Dept., "Tzaneion" General Hospital, Piraeus, Greece

<sup>1</sup> Pathology Dept., "Tzaneion" General Hospital, Piraeus, Greece High-grade and persistent low-grade dysplasia in ulcerative colitis (UC) are well established predisposing conditions for colorectal cancer, but the significance of indefinite dysplasia has not been completely clarified. Changes in p53 gene have been observed early in the histological progression of neoplasia in UC. The aim of this study was to evaluate the clinical significance of indefinite dysplasia in UC and its possible relation to p53 protein accumulation. Between January 1989 and December 1995, indefinite dysplasia was diagnosed in colon biopsies of 20 UC patients [12 M/8 F, mean age: 42 (range: 21–81) years]. Patients with indefinite probably negative dysplasia or with indefinite dysplasia not confirmed by both pathologists were excluded. Five (25%) patients had total and 15 (75%) left-sided UC and the duration of disease was longer than 8 years in 5 patients with left-sided colitis (13, 17, 18, 20 and 23 years) and less than 8 years in the remaining cases. Paraffin embedded microwaved tissue sections with indefinite dysplasia were retrospectively examined for p53 protein accumulation using the commercially available monoclonal antibody DO-7 (Biogenex). p53 Protein overexpression was not detected in any of the sections tested. The patients have been followed for a median of 26 (range: 10–40) months. Colon cancer has not been developed in any of the 20 patients. Ten of the patients underwent a second total colonoscopy approximately two years after the initial examination, where multiple biopsies were taken (2–3 specimens from each 10–15 cm of the total colon). Dysplasia was not detected in any of the last specimens. Our data support that indefinite dysplasia in UC: 1. is not a high risk condition for colon cancer and 2. is not related to p53 protein accumulation. Intestinal disorders: IBD diagnosis, monitoring Oncology, general: Screening, prevention } "Indefinite Dysplasia in Ulcerative Colitis: Clinical Significance and Possible Relation to p53 Protein"

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## "P P 17 0423" P 17 0423 **Aminoterminal Propeptide of Type III Procollagen (PIIINP) and Hepatobiliary Dysfunction in Ulcerative Colitis**

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The aim of the study was to determine the circulating concentrations of the aminoterminal propeptide of type III procollagen (S-PIIINP) in ulcerative colitis and associated hepatobiliary diseases and to estimate the usefulness of S-PIIINP in the screening for hepatobiliary diseases in patients with ulcerative colitis. S-PIIINP was measured in three patient groups: 69 patients with ulcerative colitis only, 14 with ulcerative colitis and elevated serum alkaline phosphatases but no radiological findings consistent with primary sclerosing cholangitis, and 20 patients with ulcerative colitis and primary sclerosing cholangitis. The median serum concentration of PIIINP was 3.1 µg/l in UC only, 4.3 µg/l in the patients with ulcerative colitis and minor hepatobiliary dysfunction and 8.9 µg/l in those with ulcerative colitis and primary sclerosing cholangitis (reference interval 1.7–4.2 µg/l). When the S-PIIINP cut off level was set at 5 µg/l, 5% of the patients with ulcerative colitis only, 21% of those with minor hepatobiliary dysfunction, and 90% of the patients with primary sclerosing cholangitis had S-PIIINP values above that level. In conclusion, S-PIIINP above 5 µg/l in a patient with ulcerative colitis strongly suggests concomitant primary sclerosing cholangitis. Intestinal disorders: IBD diagnosis, monitoring Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Aminoterminal Propeptide of Type III Procollagen (PIIINP) and Hepatobiliary Dysfunction in Ulcerative Colitis"

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"P P 17 0424" P 17 0424 **Primary Sclerosing Cholangitis and Colorectal Neoplasia in Ulcerative Colitis**

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The aim of the study was to evaluate, if the risk of colorectal dysplasia and carcinoma in ulcerative colitis (UC) is accentuated by concomitant primary sclerosing cholangitis (PSC). Thirty-two PSC patients with UC for 7 years or longer were examined for colorectal dysplasia and carcinoma in a case-control study. They were pair-matched with controls with extensive, longstanding UC but without PSC or even a history of elevated liver function tests. The matching factors included sex, the age at the onset of UC and the duration of UC. Also, if a PSC patient was operated on because of the intractable UC, we tried to find a control with the same history when possible. Biopsy specimens for assessing dysplasia and carcinoma were obtained in colonoscopy and/or colectomy. The median duration of UC was 16.5 years in PSC patients and 18.5 years in controls. Twelve PSC cases (38%) had colorectal neoplasia: 4 had carcinoma, 3 high grade dysplasia (HGD) and 5 had low grade dysplasia (LGD). Three controls with UC alone (9%) had neoplasia: one had carcinoma, one LGD and one HGD. Our results indicate that PSC is an additional risk factor for the development of colorectal dysplasia and carcinoma in UC. Intestinal disorders: IBD diagnosis, monitoring  
Oncology, general: Screening, prevention  
Oncology, specific: Colon, rectum } "Primary Sclerosing Cholangitis and Colorectal Neoplasia in Ulcerative Colitis"

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"P P 17 0426" P 17 0426 **<sup>99m</sup>Tc-HMPAO Leukocyte Scintigraphy in the Assessment of Disease Extent in Ulcerative Colitis**

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The knowledge of the location and extent of bowel involvement is an important aspect in the management of patients with inflammatory bowel diseases. The simplest technique for imaging intestinal inflammation involves radiolabeling patients mixed white cells ex vivo with <sup>99m</sup>Tc which are then reinjected. *The purpose of the study:* to evaluate the clinical yield of <sup>99m</sup>Tc-HMPAO leukocyte scintigraphy in the estimation of inflammatory extension in patients with ulcerative colitis. *Methods:* 17 patients with active ulcerative colitis were investigated from 1993 to 1995 using total colonoscopy with stepwise biopsies and <sup>99m</sup>Tc-HMPAO leukocyte scintigraphy. The interval between colonoscopy and leukocyte scintigraphy was less than 12 (average: 5.5) days in all patients. Images were obtained at 30 min., 2 and 4 hours after injection of the labeled cells. For comparative evaluation colon was divided into 4 parts: recto-sigmoid, descending, transverse and ascending colon + caecum. 68 parts were analyzed for the extent of active inflammation. For comparison histology was used as reference. *Results:* By colonoscopy there were 41 true-positive, 1 false-positive, 18 true-negative, 8 false-negative by leukocyte scintigraphy 45 true-positive, 6 false-positive, 13 true-negative and 4 false-negative cases. *Conclusion:* <sup>99m</sup>Tc HMPAO leukocyte scintigraphy a simple non-invasive test is an excellent technique for the assessment of diseases extent in ulcerative colitis, and is useful when total or partial colonoscopy can not be performed. Intestinal disorders: IBD diagnosis, monitoring Radiology and ultrasound: Diagnosis }

"<sup>99m</sup>Tc-HMPAO Leukocyte Scintigraphy in the Assessment of Disease Extent in Ulcerative Colitis"

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## "P P 17 0427" P 17 0427 **Effect of Oral Elemental Diet on Nutritional Status, Intestinal Permeability and Disease Activity Crohn's Patients**

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Ricerca in Medicina, Bologna, Italy

II Medicina Interna, Universit\ 'e0 Cattolica, Roma, Italy Elemental diet is considered an effective primary treatment for active Crohn's disease (CD), and it is usually administered enterally. Twenty patients (12 males, median age 30 years, range 18–60) with moderately active CD were enrolled in a randomized study in which the efficacy of elemental diet administered orally was compared to high dose corticosteroids in achieving clinical and laboratory remission. Ten patients were treated by oral elemental diet (Peptamen, Clintec) and ten received corticosteroids. Both treatment regimens lasted 2 weeks. The two groups were not different with respect to age, sex, body weight, location of disease, treatment and disease activity before the study. In all patients studied simple Crohn's disease activity index (SCDAI), nutritional status (evaluated with anthropometric and bioelectric measurements, expressed as body mass index (BMI), percentage of ideal body weight (% IBW), fat mass (FM, kg and %), fat free mass (FFM, kg and %) eritrocyte sedimentation rate (ESR), interleukin-6 (IL-6), intestinal permeability (expressed as permeability index (PI), prealbumin (PA), retinol binding protein (RBP), multiskin test (Multitest IMC), were evaluated before and after treatment. After two weeks of treatment, in the diet group there was a significant improvement of SCDAI (5.6 – 0.8 vs 2 – 1.4,  $p < 0.01$ ), ESR (21.4 – 6 vs 16.7 – 6.7,  $p < 0.05$ ), PI (4.9 – 5.3 vs 2.1 – 2,  $p < 0.01$ ), BMI (18.5 – 3 vs 19.2 – 3.1,  $p < 0.02$ ), PA (22.2 – 8 vs 23.5 – 7.8,  $p < 0.01$ ), RBP (3.7 – 0.7 vs 4 – 0.8,  $p < 0.02$ ), IMC test (4.2 – 2.1 vs 5.9 – 2.3,  $p < 0.01$ ); no significant differences were found for the other parameters studied. In the corcosteroid group there was a significant improvement of SCDAI (4.5 – 0.7 vs 3.5 – 1.2,  $p < 0.04$ ) and of FFM (kg) (45.9 – 10.5 vs 47.2 – 10.7,  $p < 0.05$ ). These data suggest that, in the short term, oral elemental diet is at least as effective as steroids in inducing remission of mild-moderately active CD, but it may be more effective in improving nutritional status of these patients, probably through a more quickly restoration of intestinal permeability. Nutrition: Nutrients and gut function }" "Effect of Oral Elemental Diet on Nutritional Status, Intestinal Permeability and Disease Activity Crohn's Patients"

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"P P 17 0428" P 17 0428 **Decrease in Cortical Bone Density in Women with Ulcerative Colitis: A Controlled Study**

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Istituto di Scienze Mediche, Cattedra di Gastroenterologia, Universit\`e di Milano, Italy

<sup>1</sup> II Servizio di Radiologia, IRCCS Ospedale Maggiore, Italy *Background:* Osteoporosis has been observed in about 40% of patients with inflammatory bowel disease but the series studied were unselected. *Aim:* To determine bone mineral density and body composition in a selected series of patients with ulcerative colitis. *Patients and method:* We enrolled 31 patients (12 M, mean age 36, range 21–49, and 19 F, mean age 36, range 23–45) with ulcerative colitis followed as outpatients and not currently treated with calcium, vitamin D, calcitonin or biphosphonates. All patients underwent total body bone, lean and fat mass measurement by dual X-ray absorptiometry (Hologic QDR-1000/W). The mean time from ulcerative colitis diagnosis was 8 yr (range 2–18). Disease was confined to the rectum in 2 cases and to the rectum and sigmoid colon in 12; 7 patients had left-sided colitis, 4 substantial colitis and 6 pancolitis. Previous total steroid intake in the patients' lifetime was computed and expressed in mg prednisone-equivalent. Osteocalcin, intact parathyroid hormone and fasting urinary hydroxyproline/creatinine excretion were determined. Healthy subjects matched for sex, age and body mass index served as controls. Statistical analysis was performed using the Wilcoxon and Spearman rank correlation tests. *Results:* Mean lifetime steroid intake in men was 3764 mg (range 0–13205) and in women 1556 mg (range 0–5964). No differences were found in bone mineral density and body composition between male patients and their controls, nor was there a correlation between steroid intake and bone density. In female patients, cortical bone density was significantly reduced compared to their controls ( $p = 0.01$ ), and lean mass was significantly greater ( $p = 0.01$ ). Bone formation and resorption markers did not differ significantly in the male and female patients and healthy subjects. *Conclusion:* We observed a significant decrease in cortical bone density in a selected group of women with ulcerative colitis. This finding warrants further investigation to delucidate the pathogenesis and the possible relation to fracture risk. Intestinal disorders: IBD diagnosis, monitoring } "Decrease in Cortical Bone Density in Women with Ulcerative Colitis: A Controlled Study"

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"P P 17 0429" P 17 0429 **Ulcerative Colitis (UC): How Many Diseases?** E.A. Belousova, N.A. Morozova, L.D. Serova, A.R. Zlatkina

Moscow Regional Research Clinical Institute, Moscow, Russia The distribution of HLA antigens I and II classes (A, B, C, DR) was investigated in patients with UC in Moscow Region with 8000000 population to study HLA phenotype and genetic peculiarities and heterogeneity of the disease in UC of different extent and different age of onset. 149 patients were observed. The investigation was performed by standard method with histotypical serum kits. The positive association with HLA DR5 ( $x^2 = 10.25$ , RR = 2.36) and HLA Cw4 ( $x^2 = 3.88$ , RR = 2.4) was shown in whole UC group in compare with healthy population. The  $x^2$  criterion and RR was the highest in the group with combination of DR5 and Cw4 ( $x^2 = 37.5$ , RR = 6.5). The negative association was found in this group with HLA Aw19 ( $x^2 = 7.48$ ) and DR4 ( $x^2 = 5.94$ ). Thus, HLA Aw19 and DR4 may play a role of defense antigens. Their absence enhances the ability of HLA DR5 and Cw4 realization and increases RR (relative risk of disease) threefold. The significant correlation between HLA DR5 and large forms of UC (total and left side) was found ( $x^2 = 7.21$ , RR = 2.58), but there was no difference in HLA frequency between distal colitis and healthy population. The peculiarity of phenotype was found in young UC patients group (HLA DR5  $x^2 = 8.58$ , RR = 2.0 and Cw4  $x^2 = 12.9$ , RR = 2.15) and in elderly patients (HLA DR3  $x^2 = 16.4$ , RR = 5.64). *Conclusion:* The genetic heterogeneity of UC in Russia has been shown. Our data confirm the hypothesis about different pathogenesis of various UC forms and the possibility to exist few different UC. Intestinal disorders: IBD, etiology and genetics } "Ulcerative Colitis (UC): How Many Diseases?"

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"P P 17 0430" P 17 0430 **Variation of p-ANCA over Time in Patients with Ulcerative Colitis (UC)** G. Monteleone, R. Marasco, T. Parrello, P. Doldo, F. Lizza, F. Pallone

Dipt Med. Sper. e Clin, Univ di Reggio Calabria, Catanzaro, Italy *Background.* ANCA exhibiting an immunofluorescence perinuclear pattern (p- or x-ANCA) are a subclinical marker of UC. Variations of ANCA status have been reported. *Aim.* To examine whether in UC patients p-ANCA may vary over time and to explore whether p-ANCA status is related to disease activity, extent, treatment, duration and extraintestinal manifestations. *Methods.* 75 patients (54 M and 21 F; mean age 39.5, range 13–72) with diagnosis of UC were followed for a median time of 24 months (range 12–36). 3–6 serum samples were obtained from each patient at regular intervals (4–6 months). ANCA status was tested by ELISA (1:100 serum dilution) and confirmed by indirect immunofluorescence. Only perinuclear pattern was considered for the purposes of this study. 20 healthy subjects were also considered as negative control group. *Results.* At entry p-ANCA were detected in 43/75 (57%) patients: 38/59 (63%) with active disease and 5/16 (33.3%) with inactive disease ( $p = 0.036$ ). No relation was observed with the other disease clinical variables. Variation in the p-ANCA status occurred in 21/75 (28%) patients. 13 out of 15 sera initially p-ANCA positive became p-ANCA negative after that stable remission was achieved, whereas 7 sera initially p-ANCA negative reverted to positive during flare-up. In 1 patient ANCA status change did not seem to be apparently related to disease activity. In addition, 5/5 patients with stable remission and 11/13 with a "non aggressive course" (1–4 flares-up/1–3 years) were persistently negative for p-ANCA. In contrast, 11/11 patients with chronic active disease and 10/12 patients with aggressive course" (> 4 flares-up/year) showed a persistent p-ANCA positivity over the follow-up study. All five patients p-ANCA positive with inactive disease at entry experienced > 4 flares-up per year in the subsequent follow-up and their p-ANCA status was persistently positive. *Conclusions.* Data suggest that p-ANCA in UC may help defining subgroups of patients with a more aggressive course and that disease activity may contribute to ANCA status. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Variation of p-ANCA over Time in Patients with Ulcerative Colitis (UC)"

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"P P 17 0431" P 17 0431 **Interest of Flow Cytometry and of KI-ras Gene Mutation and p53 Gene Alteration Research in the Follow Up of Ulcerative Colitis**

\*F. Gaetan<sup>1</sup>, M.C. Gelineau<sup>2</sup>, C. Mar\`e7ais<sup>2</sup>, M. Cottier<sup>4</sup>, S. Isaac<sup>3</sup>, M. Rochet<sup>3</sup>, A. Revol<sup>2</sup>, L. Descos<sup>1</sup>

<sup>1</sup> Gastroenterology Department

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<sup>4</sup> Histology's laboratory, Hospital Nord 42000 St Etienne, France *Aim:* to evaluate the degenerative potential of ulcerative colitis (UC) by studying Ki-ras and p53 genes as well as flow cytometry. *Method:* 38 patients (average age 44 years – 14) underwent a total colonoscopy during a reactivation stage or during the follow-up. In all these cases, the ulcerative colitis had been evolving for an average of 12 years – 7. In 5 cases, there was a longstanding total colitis; two of which had lasted more than 20 years. Systematic biopsies were carried out on the whole length of the colon. All the patients were submitted to a test for Ki-ras codon 12 mutation by hybridization; 7 patients with dysplasia, cancer, or an isolated Ki-ras mutation, were checked for an overexpression of p53 protein by immunohistochemistry and 32 patients were examined for DNA ploidy by flow cytometry. *Results:* histological examinations revealed 4 cases of dysplasia (2 low grade and 2 high grade) and 1 case of adenocarcinoma. Ki-ras gene mutation was found in 7 patients, 5 cases involving histological lesions (3 times in inflammatory mucosa, once in a low grade dysplasia, once in an adenocarcinoma) and 2 cases involving healthy mucosa. An overexpression of p53 protein was observed in only 1 patient with adenocarcinoma. Only 1 patient displayed a DNA aneuploidy, on an inflammatory non dysplastic mucosa. *Conclusions:* despite the lack of hindsight and a group with a feeble risk of degeneration, we can say that, out of 38 patients, 10 cases of potentially higher degeneration risk were identified, 4 presenting the usual histological anomalies (dysplasia) whereas the other 6 cases had either a Ki-ras codon 12 mutation or a DNA aneuploidy. The regular follow up of all these patients and the systematic search for overexpression of p53 protein must be undertaken in order to evaluate, along with the histological date, which patients can be considered members of a high risk group requiring more frequent colonoscopies. Intestinal disorders: IBD, etiology and genetics Oncology, general: Molecular biology, genetics Oncology, specific: Colon, rectum }" "Interest of Flow Cytometry and of KI-ras Gene Mutation and p53 Gene Alteration Research in the Follow Up of Ulcerative Colitis"

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"P P 17 0433" P 17 0433 **Efficacy of Association of Low-Doses of CsA-Steroids in Treatment of Ulcerative Colitis**

\*G. Pia, L. Pascalis, G. Aresu

University Cagliari Italy 20 patients with endoscopically and histologically diagnosed colite ulcerosa were treated with Cyclosporin A and low doses of fluocortolone, supplementary to standard medication (mesalazin or sulfasalazin) within the framework of a therapy trial during an acute attack. Inclusion criteria for patients: a therapy refractory condition after an at least 2-weeks treatment with prednisone at a dose of 1 mg/Kg body weight, which usually corresponded to 40–70 mg. However the onset of side effects not only made it impossible to use higher doses but implicated a progressive reduction of the posology which led to a relaps of the clinical syndrome after 6–7 weeks. Cyclosporin A was administered: initial daily dose of 5 mg per Kg body weight (ideal weight in the case of overweight subjects). Blood levels of the drug were between 100 and 200 mcg/l by the third day of treatment. Fluocortolone was administered initially at a dose to control disease activity, that is, 80–70 mg/week on 5 days depending on the case, and then tapered in relation to the course of the disease down to a maintenance dose of 15–20 mg/week administered on 3 days. Fluocortolone administration was withdrawn in all patients (at 36 months) and treatment proceeded with CsA alone at dose of 5 mg/Kg per day administered 4 days a week. All patients were given a coloscopic before inclusion in the study to determine the degree of endoscopic activity according to the Rachmilewicz scoring system, and their clinical activity index (CAI) was also calculated according to the Rachmilewicz evaluation. The criterium for clinical remission was a decline in the specified indications. *Results:* All patients presented a significant improvement of the clinical picture 7–15 days after onset of treatment and total remission of symptoms after 20–30 days whilst regression of the colonscopic and histomorphologic phenomena was observed 30 days after onset of treatment. In addition, the disease activity indexes normalized and remained normal for the rest of the follow-up period (60.18 – 9.15 months, range 69–50). No renal or hepatic toxicity was observed in any patient. Nine of them presented hypertrichosis, 4 iperplasia gengivale an one nausea. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Efficacy of Association of Low-Doses of CsA-Steroids in Treatment of Ulcerative Colitis"

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"P P 17 0434" P 17 0434 **P53 Mutation Is a Genetic Marker on Ulcerative Colitis which Predicts the Clinical Responder to the Medical Treatment?**

\*S.K. Chang, J.S. Chang, J.H. Do, C. Moon, H.J. Kim, J.K. Kim, S.M. Park

Division of Gastroenterology, Dept of Medicine, Chung-Ang Univ Hospital Seoul, Korea

*Background/Purpose:* Long standing ulcerative colitis (UC) has known to increase the development of colorectal cancer. Although the molecular events demonstrate the frequent loss of p53 allele in carcinoma and their precursors dysplasia in UC, a rare incidence of p53 genetic alteration was also noted in indefinite dysplasia and long standing UC. Therefore we investigate the p53 point mutation in UC patients who did not show the evidence of dysplasia and cancer. *Methods:* Sixteen patients with UC had extensive disease of more than 8 years' duration were followed prospectively by colonoscopic surveillance using mucosal biopsy sampling. P53 gene alterations in 16 UC by polymerase chain reaction single-strand conformation polymorphism analysis (PCR-SSCP) for exon 4–8 and immunohistochemical staining (IHCS) with anti-p53 antibody. *Results:* p53 mutations were detected in 4 (25%) out of 16 by PCR-SSCP in exon 4–8: 1, 1, 0, 2, and 0 mutations in exons 4, 5, 6, 7, and 8 respectively. The positive staining by IHCS was 5 (31%) out of 16. With regards to clinical characteristics these patients with p53 point mutation showed more frequent activation of underlying colitis, and not well respond to medical treatment (5-ASA, steroid, cyclosporin A). One of four patients undertaken total colectomy. *Conclusion:* These results suggest P53 point mutation is not an infrequent event in UC patients who didn't show dysplasia and cancer, and this genetic alterations suggest that it plays a role as a possible genetic marker to evaluate the responsiveness to the medical treatment. Intestinal disorders: IBD diagnosis, monitoring Oncology, general: Molecular biology, genetics } "P53 Mutation Is a Genetic Marker on Ulcerative Colitis which Predicts the Clinical Responder to the Medical Treatment?"

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## "P P 17 0435" P 17 0435 Early Prediction of IV Steroid Treatment Failure in Ulcerative Colitis

\*S. Lindgren, L. Flood, A. Kilander, R. L'f6fberg, R. Sj'f6dahl

Departments of Gastroenterology, University hospitals of Malm'f6, Huddinge, G'f6teborg and Link'f6ping, Sweden *Purpose.* Early identification of patients with exacerbations of ulcerative colitis not responding to corticosteroids remains difficult and critical. We therefore scrutinized clinical and biochemical data in an effort to identify prognostic markers for steroid resistance and subsequent colectomy. *Methods.* The outcome of iv steroid treatment was analysed retrospectively in 97 patients with moderate and severe attacks of ulcerative colitis treated in 4 major Swedish hospitals 1988–1993. Basic clinical and biochemical data were obtained from patient record forms. Patients requiring colectomy within 30 days after admission were compared to those who did not. *Results.* Thirty days after admission 37 patients (38%) were in complete clinical and endoscopic remission while 33 (34%) had undergone colectomy. No association between steroid unresponsiveness and the extent of disease, duration of the acute exacerbation, number of previous attacks or maintenance treatment was observed. In contrast, short disease duration (mean 2.7 years vs 8.1 years,  $p = 0.0037$ ), prior steroid treatment (70% vs 42%,  $p = 0.010$ ) and particularly sustained increase of body temperature (mean 37.4' b0 vs 36.9' b0,  $p = 0.012$ ), sustained diarrhea (mean 6.8/d vs 3.6/d,  $p < 0.0001$ ), passage of blood (83% vs 42%,  $p = 0.0003$ ) and CRP elevation (36.3 mg/L vs 18.0 mg/L,  $p = 0.007$ ) after three days of treatment were identified as predictors of a poor response and a high risk for colectomy during the forthcoming month. *Conclusion.* Sustained elevation of body temperature, high stool frequency, passage of blood and increased CRP during the first three days of iv steroid treatment strongly predict steroid resistance, particularly in ulcerative colitis of short duration. In these patients more aggressive medical treatment or colectomy should be considered at an early stage. Clinical practice: Management strategy Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy } "Early Prediction of IV Steroid Treatment Failure in Ulcerative Colitis"

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"P P 17 0436" P 17 0436 **Anti-Neutrophil Cytoplasmic Antibodies (ANCA) in Sera from Patients with Ulcerative Colitis**

\*C.Z. Stachowiak, J. Zeromski, G. Dworacki, L. Hryniewiecki, K. Rzymiski, J. Hasik

Departments of Gastroenterology, Immunopathology and Radiology University of Medical Sciences, Poznan, Poland *Aim of the study:* In the current study, an attempt was made to trace a correlation between the incidence of serum autoantibodies, predominantly ANCA, in various stages of UC activity. *Background:* Antibodies reacting with cytoplasmic components of human neutrophils (ANCA) manifested as diffuse staining of cytoplasm (c-ANCA) by immunofluorescence (IMF) have been found in several vascular diseases, especially in Wegener's granulomatosis. A variant of ANCA called p-ANCA, seen in fluorescence microscopy as a perinuclear rim of staining has been described in inflammatory bowel disease and especially in ulcerative colitis (UC). *Material and methods:* The study was performed in 48 UC patients (14 women and 34 men) aged from 17 to 61 years. In 17 UC patients p-ANCA were detected while in 25 patients the test came out negative. In 6 patients c-ANCA were found. P-ANCA+ group has been shown in 100% of cases to be in active phase of disease as demonstrated by rectosigmoidoscopy. Presence of p-ANCA correlated with extent of colon involvement. There was no relationship between p-ANCA positivity and mean age and mean duration of disease. ANCA were determined by indirect IMF on cytospin sediments of human (group O Rh+) neutrophils. In addition, organ autoantibodies have been evaluated by indirect IMF on rat tissue sections. *Conclusions:* 1. Incidence of combined ANCA (p + c) in patients with UC is 68% of all cases 2. pANCA-positive group shows correlation with activity of the disease as well as the extent of colon involvement 3. No relationship could be established between pANCA positivity and mean age and mean duration of the disease 4. Prevalence of some autoantibodies (esp. antinuclear antibodies) demonstrates the correlation between pANCA and disease activity 5. Determination of pANCA may be of value in diagnosis and monitoring of UC patients

Intestinal disorders: IBD, etiology and genetics  
Intestinal disorders: IBD diagnosis, monitoring  
Intestinal disorders: IBD, therapy } "Anti-Neutrophil Cytoplasmic Antibodies (ANCA) in Sera from Patients with Ulcerative Colitis"

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"P P 17 0437" P 17 0437 ***Escherichia Coli* and Ulcerative Colitis**

\*J. Machado, L.S. Sousa, M.H. Troni, A. Pinto, T.C. Macedo, F.A. Ventura, M. P\ 'e1dua, M.G. Quina

Hospital de Pulido Valente; INSA Lisbon Portugal **Objectives:** Comparison of *Escherichia coli* strains isolated from patients (p) with Ulcerative Colitis (UC), with those isolated from healthy individuals. **Materials and Methods:** Two groups were studied and compared: a) 22 p with UC – average age 47.9 years (22–72 years), average evolution time 5.7 years (0.2–30 years), 8 of those with clinically active disease (Truelove and Witts mod.); b) 22 healthy individuals studied as a control group – average age 48.6 years (18–72 years). These groups were matched by age ( $p < 0.0045$ ). *E. coli* was isolated by stool cultures in the studied groups. The genes responsible for expression of toxins (LT, ST, VT1 and VT2) and for mucosal invasion were studied by PCR in the isolated *E. coli* strains. *E. coli* strains were also compared based on their antibiotypes and ribotypes. **Results:** *E. coli* strains were isolated in all p with clinically active UC disease ( $n = 8$ ), and all were multiresistant to  $> 2$  antibiotic groups. 4 of those strains presented pathogenicity factors. Only 7 *E. coli* strains were isolated in p with inactive disease ( $n = 14$ ), and from those only one shown pathogenicity factors, although 3 were multiresistant. 60 *E. coli* strains were isolated in the control group and only 4 were multiresistant. **Conclusions:** These results suggest the selection of multiresistant *E. coli* strains in patients with active UC. Some of these strains shown pathogenicity factors. These characteristics were not found in the control group of healthy individuals. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, therapy } "*Escherichia Coli* and Ulcerative Colitis"

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"P P 17 0438" P 17 0438 **Interleukin's Role in the Quantification of the Inflammation in Active Ulcerative Colitis**

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Department of Gastroenterology, University Hospital La Paz, Madrid, España

The importance of the interleukins as a sign of the level of inflammation in the EII is disputed because some authors find them increased in the active phase of the disease, while others don't find significant differences with the control group.

**Objectives:** To determine if the interleukin I.L-6, I.L-8 and the necrosis tumoral factor (TNF{ a}) can be used as an indicator as the grade of inflammation in the CU.

**Methods:** We have carried out a case control study with endoscopy/histology test on twenty patients with CU classified with the Floren's index in Grade I (low affection), G- II (moderated) and G- III (several) and we have compared them with ten controls. We have done a complete colonoscopy and biopsy on all the patients with a study of their 48 hour evacuations. We determined the interleukins in the sample of biopsy and the faecal for enzyme-immunological analysis (Medgenix).

**Results:** In the colonic biopsy we didn't find significant differences in I.L-6 and TNF{ a} levels between the controls; while the value of I.L-8 was clearly higher in patients with CU (120.6 ng/gr protein with a range of 4.95–433), in relation to the control group (16.3 ng/gr protein with a range of 0.5–66.2). In the faecal's study the patients with CU had a value of I.L-8 (39.523.8 gr/24 h of average with a range of 155–171.900) higher than the control group (4.204 gr/24 h with a range of 88–1.624). The determination of TNF{ a} also showed an average value distinctly higher in patients with CU (5.604 gr/24 h with a range of 884–20.526) in relation with control group, whose values were sensitively lower (774.5 gr/24 h, with a range of 44–1444).

**Conclusion:** The determination of I.L-8 and TNF{ a} in the faecal of patients with CU shows the presence of inflammation, although it doesn't appear to be of use to determine the intensity grade of inflammation or its extension, because despite of finding differences between the patients.

Immunology and microbiology: Inflammation/Intestinal disorders: IBD diagnosis, monitoring }

"Interleukin's Role in the Quantification of the Inflammation in Active Ulcerative Colitis"

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## "P P 17 0439" P 17 0439 Expression and Secretion of Annexin 1 in Biopsies of Patients with Ulcerative Colitis

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<sup>1</sup> Dept of gastroenterology, CHU Rangueil, Toulouse, France Annexin 1 is a 38-kDa protein, displaying pharmacological anti-inflammatory properties in several experimental models. We have previously shown that annexin 1 is selectively secreted in rats 1) by proximal colons inflamed by a TNBS-injection 2) by small intestine after a TNBS-treatment as well as after an infection with a nematode parasite: *Nippostrongylus brasiliensis*. Here, we studied the annexin 1 expression and secretion in biopsies of control and ulcerative colitis (UC) patients. Biopsies of inflamed tissues were collected by endoscopic examination in the colon of 10 patients (women: 4; men: 6; age: 29.8 – 10.5 years, range 19–47) with UC and 5 control patients (age 69.2 – 7.6: years, range 60–76). Using the Truelove classification, UC were divided in 3 groups (severe n = 6, moderate n = 2 and slight n = 2). In 7 UC patients (4 severe, 2 moderate and 1 slight), biopsies were also collected in unaffected parts of the colon. Five patients were treated by glucocorticoids (severe n = 3, moderate n = 2). Secretion of annexin 1 was identified by incubating colonic tissues in culture media for 30 min. at 37°C. Annexin 1 was then detected by Western-blot analysis, in both colons and culture media. No major difference in annexin 1 expression was seen in biopsies of control, slight, moderate or severe UC patients and in unaffected biopsies of UC patients. Biopsies from 1) control patients 2) slight or moderate UC patients and 3) unaffected tissues of severe UC patients did not release annexin 1 into the culture media. In contrast, annexin 1 was secreted by all the inflamed samples from patients with severe UC. The glucocorticoid treatment did not seem to influence the mechanism of secretion of annexin 1 (in the severe group, annexin 1 secretion occurs in the presence or in absence of glucocorticoid-treatment). Because annexin 1 presents anti-inflammatory extra-cellular properties, this study suggests that annexin 1 is selectively involved in severe human intestinal inflammatory processes, possibly to reduce them. Annexin 1 appears to be a marker of severity of UC. Immunology and microbiology: Inflammation Hormones and receptors: Molecular biology Intestinal disorders: IBD, etiology and genetics } "Expression and Secretion of Annexin 1 in Biopsies of Patients with Ulcerative Colitis"

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"P P 17 0440" P 17 0440 **Rifaximin in Patients with Moderate or Severe Ulcerative Colitis Resistant to Steroid-Treatment**

\*F. Rizzello, P. Gionchetti, A. Venturi, S. Peruzzo, E. Raule, C. Brignola, M. Miglioli, M. Campieri

Ist. Clinica Medica e Gastroenterologia, University of Bologna, Italy *Aim:* Aim of this study was to evaluate the efficacy and the systemic absorption of Rifaximin, a non absorbable rifamycin antibiotic, in patients with moderate to severe, steroid resistant, ulcerative colitis. *Methods:* The study was an open-controlled trial. Patients were eligible if they had an histological confirmed diagnosis of ulcerative colitis and no response after 7–10 days of intravenous corticosteroid therapy (Methylprednisolone 1 mg/kg/day). Fourteen patients with moderate to severe steroid-resistant ulcerative colitis entered in the study and received rifaximin 400 mg tablets bid for ten days, in addition to the intensive standard intravenous steroid regimen. Clinical activity of disease was defined in accordance with Truelove and Witts criteria. Before the entry to the study and on the last day of treatment, serum and urine samples were taken to determine the systemic absorption of rifaximin. *Results:* Nine of 14 treated patients (64.3%) showed a substantial clinical and endoscopic improvement with a significant decrease of clinical activity score [mean – SD (2.14 – 0.36 vs 1.57 – 0.64)( $p < 0.05$ )]. Plasma concentrations of rifaximin were undetectable and the urinary excretion at the end of treatment was negligible. *Conclusions:* This preliminary study suggest that rifaximin, being practically not absorbed after oral administration, may be useful in patients with steroid-resistant ulcerative colitis. Intestinal disorders: IBD, therapy }" "Rifaximin in Patients with Moderate or Severe Ulcerative Colitis Resistant to Steroid-Treatment"

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"P P 17 0441" P 17 0441 **Are There Parameters Likely to Predict Successful Outcome in Patients with Severe Ulcerative Colitis Receiving Cyclosporine?** A. Schmit<sup>1</sup>,

\*A. Van Gossum<sup>1</sup>, M. Adler<sup>1</sup>, C. Chioccioli<sup>2</sup>, R. Fiasse<sup>2</sup>, P. Louwagie<sup>3</sup>, G. D'Haens<sup>3</sup>, P. Rudgeerts<sup>3</sup>, M. Devos<sup>4</sup>, H. Reynaert<sup>5</sup>, G. Devis<sup>5</sup>, J. Belaiche<sup>6</sup>, M. Van Outryve<sup>7</sup>

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<sup>7</sup> Department of Gastroenterology, Erasme Hospital, UZA, Brussels, Belgium *Introduction:* Cyclosporine (CsA) has been successfully administered in patients with acute severe ulcerative colitis (UC). The aim of this multicenter Belgian study was to determine parameters which may be important to predict successful outcome of CsA therapy. *Material & methods:* The study included 32 patients (median age: 33 y. (15–77 y.); 15 females and 17 males). The median duration of the disease was 4 y. (0.3 to 33 y.). According to Truelove's clinical score, UC was severe in 30 cases and moderate in 2 cases. Before initiating CsA, patients were unresponsive to treatment including iv corticosteroid, 5-ASA or salazopyrine, azathioprine or antibiotics. The iv mean dose was 4 mg/kg/day and adapted to blood CsA level. Patients were considered as responders to CsA when immediate colectomy was avoided. The following parameters before starting CsA therapy were studied: 1. age; 2. sex ratio; 3. duration of the disease; 4. mean hemoglobin level; 5. mean erythrocyte sedimentation rate; 6. location of the disease (left colon versus total colon). *Results:* Good outcome was observed in 23 patients (72%). Thus 9 patients were referred for subsequent colectomy. Patients with higher mean hemoglobin levels, lower mean erythrocyte sedimentation rate and longer history of the disease presented better immediate outcome. However, these differences were not significant (NS). There was no trend for other parameters. *Conclusion:* In patients with steroid refractory ulcerative colitis who received CsA, immediate colectomy was avoided in 72% of the cases. Among clinical and biochemical parameters which were studied, none of them was likely to predict a successful outcome of the treatment. Intestinal disorders: IBD, therapy } "Are There Parameters Likely to Predict Successful Outcome in Patients with Severe Ulcerative Colitis Receiving Cyclosporine?"

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"P P 17 0442" P 17 0442 **Administration of Cyclosporine in Acute Severe Ulcerative Colitis: Short-Term Efficacy and Long-Term Outcome**

\*A. Van Gossum, A. Schmit, M. Adler, C. Chioccioli, R. Fiasse, P. Louwagie, G. D'haens, P. Rutgeerts, M. Devos, H. Reynaert, G. Devis, J. Belaiche, M. Van Outryve

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*Introduction:* Cyclosporine (Csa) has been proposed in the management of patients with acute ulcerative colitis (UC) who failed standard therapy and were candidates for colectomy. *Material and Methods:* Seven academic hospitals contributed to this study that included 32 patients (median age: 33 y. (15–77 y.); 13 females and 17 males). The median duration of the disease was 4 y. (0.3 to 33 y.) According to Truelove's clinical score, UC was severe in 30 cases and moderate in 2 cases. The mean level (SD) of Hb was 9.7 – 1.4 g/dl and ESR: 56 – 24 mm/H. Before initiating Csa, patients were unresponsive to treatment including – IV corticosteroid (n = 27), 5-ASA or Salazopyrine (n = 18), azathioprine (n = 3), antibiotics (n = 18), total parenteral nutrition (n = 3). The mode of Csa administration was intravenous (IV) (n = 15), IV + subsequently oral (n = 11), oral (n = 3). The IV mean dose was 4 mg/kg/day and adapted to blood Csa level. Concomitant treatment included corticosteroid (n = 27). *Results:* The mean duration of IV Csa administration was 13.2 – 8.1 days. At the end of Csa administration, a global improvement was described in 23 patients (72%) while a surgery had to be performed immediately in 8 patients (25%) because of exacerbation of symptoms (n = 7) or perforation (n = 1). One other patient died because of pneumocystis carinii infection. For the responders, maintenance therapy included: tapering dose of corticosteroid (n = 13), Azathioprine (n = 12), 5-ASA or Salazopyrine (n = 10), methotrexate (n = 1) or oral Csa (n = 11). The mean duration of follow-up was 14.3 – 12.9 months. Among the 23 responders, 9 (28%) were subsequently referred for colectomy either selectively (n = 3) or because of recurrence (n = 6). *Conclusion:* In patients with acute refractory UC who received Csa, the short-term efficacy (avoidance of immediate colectomy) was 72%. However, the overall success rate at a mean follow-up of 14 months was 44%. Intestinal disorders: IBD, therapy }" "Administration of Cyclosporine in Acute Severe Ulcerative Colitis: Short-Term Efficacy and Long-Term Outcome"

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"P P 17 0443" P 17 0443 **Low-Dose Weekly Methotrexate Therapy in Remission Maintenance in Ulcerative Colitis** M.D. Onuk,

\*S. Kaymakoglu, K. Demir, Y. Akaloglu, G. Boztas, Z. Mungan, F. Besisik, U. Evikbas<sup>1</sup>, N. Erol, R. Sezer

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<sup>1</sup> Dept. of Pathology, Istanbul Medical Faculty, Istanbul, Turkey Immunosuppressive drugs have been commonly used in refractory cases with inflammatory bowel disease in the last years. Relapse rates are relatively high (25–40%) in patients with ulcerative colitis taking sulfasalazine (SFZN) for maintenance therapy. The purpose of this study was to evaluate whether long-term use of methotrexate (MTX) concurrent SFZN in patients with remission is effective to reduce relapse rate. The presence of ulcerative colitis was previously diagnosed by appropriate combinations of clinical, endoscopic, histological and radiological criteria. All patients were maintained in full remission on oral SFZN for at least 2 months at study entry. Twenty-six patients were randomly assigned to receive either MTX (15 mg per week, orally) plus SFZN (3 g per day, orally) or SFZN alone for 12 months. Fourteen patients (8 women, mean age: 36.6 – 7.4 yr., left-sided colitis in 6, pancolitis in 8) were in MTX group, and 12 patients (10 women, mean age: 36.3 – 10.7 yr., left-sided colitis in 9, pancolitis in 3) in SFZN group. Two groups were similar in regard to age, sex and the features of the disease. Clinical, biochemical, sigmoidoscopic and histological assessments were made initially, at 3, 6, 9 and 12 months. Relapse was accepted if endoscopic inflammatory score and histological activity index were grade 2 or higher, or if symptoms were present. Three patients (25%) relapsed in SFZN group over the study period, none in MTX group. Although the difference was insignificant, the success rate of MTX plus SFZN in maintaining remission appears to be better than SFZN alone. The relapse was severe in 2, and mild in 1 patients. Patient compliance was excellent and none was withdrawn because of treatment related intolerance or adverse effects in both groups. These findings suggest that MTX may have an important adjunctive therapeutic role for remission maintenance in patients with ulcerative colitis. Intestinal disorders: IBD, therapy } "Low-Dose Weekly Methotrexate Therapy in Remission Maintenance in Ulcerative Colitis"

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"P P 17 0444" P 17 0444 **Disposition of 5-ASA by Olsalazine (Dipentum) and Mesalazine (Asacol) in Patients with Ulcerative Colitis in Remission** A. Archimandritis<sup>1</sup>, G. Hatzis<sup>1</sup>, A. Konstandinidis<sup>2</sup>, K. Paraskeva<sup>2</sup>, M. Tjivras<sup>1</sup>, N. Skandalis<sup>2</sup>

<sup>1</sup> Department of Pathophysiology, Medical School, University of Athens, Greece

<sup>2</sup> Gastroenterology Section, Laiko Gen Hospital and Gastroenterology Clinic, Gen State Hospital of Athens, Greece *Purpose:* To determine whether olsalazine (Dipentum) (1 g/d), gives a lower systemic uptake of 5-ASA and Ac-5-ASA at steady state, compared to mesalazine (Asacol) (1.2 g/d), when treating patients with ulcerative colitis in remission. *Patients and methods:* Eight male and 9 female patients, aged 19 to 69 years, with disease duration from 1–15 years were included in this open, randomized, cross-over study. Dipentum, 500 mg twice daily for 7 days or Asacol, 400 mg three times daily for 7 days, orally with food were given. Urine and plasma sampling at day 6 and 7 of each treatment period for the determination of 5-ASA and Ac-5-ASA at steady state were taken. *Results:* Nineteen patients were included and randomized to first week's treatment. Two patients withdraw from the study, one before starting treatment. Seventeen patients remained in remission, completed the study and were included into the statistical analysis. The systemic uptake of 5-ASA and Ac-5-ASA was significantly lower as reflected by urine and plasma data following treatment with Dipentum (1 g/d) compared to Asacol (1.2 g/d). Asacol showed, compared to Dipentum, 8.35 times higher levels of 5-ASA in urine. The treatment ratio (Asacol/Dipentum) was for Ac-5-ASA in plasma 3.3 with the 95% lower confidence limit equal to 2.56. One patient on olsalazine withdraw from the study due to diarrhea. No other serious adverse events were noted. *Conclusions:* This study demonstrates that mesalazine (Asacol), 1.2 g/d, causes higher levels, at steady state, compared to olsalazine (Dipentum), 1 g/d, of both 5-ASA and Ac-5-ASA in urine as well as in plasma. The low systemic load of 5-ASA provided by Dipentum thus reduces the potential risk of nephrotoxicity. Intestinal disorders: IBD, therapy } "Disposition of 5-ASA by Olsalazine (Dipentum) and Mesalazine (Asacol) in Patients with Ulcerative Colitis in Remission"

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"P P 17 0445" P 17 0445 **DNA Aneuploidy and Histologic Dysplasia in Long Standing Ulcerative Colitis: Identification of Patients at High Risk**

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The risk of colorectal cancer is increased among patients with long-standing Ulcerative Colitis (UC), therefore identification of patients at high risk is a crucial point. Thirty patients with extensive UC and at least 15 years of disease have been selected for a prospective colonoscopic surveillance program. Each patient underwent a colonoscopy with multiple biopsies. Bioptic specimens were sampled from predetermined locations of the colon and rectum at regular intervals and from macroscopical lesions, when present. In our program specimens were assessed for dysplasia by histology and for DNA aneuploidy by Flow-Cytometry (FC). For DNA Index (DI) evaluation fresh samples were stained, after mechanical disaggregation, with propidium iodide and at least 20,000 nuclei analyzed on an Epics Elite cytofluorimeter (Coulter Co). We found 23 out of 30 patients with macroscopic lesions (polypoid lesions and/or lumen narrowing). Six patients showing macroscopical lesions at endoscopy revealed aneuploidy biopsies by FC (26.1%). Among the 6 patients with aneuploid biopsy: 2 were indefinite for dysplasia, 1 had low grade dysplasia, 1 was affected by colorectal cancer and the last 2 were negative for dysplasia. We found no patients with dysplasia without aneuploidy. Our results show the close correlation between aneuploidy and dysplasia. Moreover, the changes in nuclear DNA content could be earlier than dysplasia in the neoplastic progression of the UC colorectal mucosa. For this reason we propose FC as a selection technique in colonoscopic surveillance program for long-standing UC patients. The finding of aneuploidy in 25% of patients with endoscopic lesions confirms that FC could be a useful tool to select high risk patients and could reduce costs and improve effectiveness in screening programs. Intestinal disorders: IBD diagnosis, monitoring  
Oncology, general: Proliferation, carcinogenesis  
Oncology, general: Screening, prevention } "DNA Aneuploidy and Histologic Dysplasia in Long Standing Ulcerative Colitis: Identification of Patients at High Risk"

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"P P 17 0446" P 17 0446 **Prednisolone Enemas Improve Patients with Distal/Left Sided Ulcerative Colitis More Rapidly than Butyrate Enemas**

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Leicester Royal Infirmary, Leicester, U.K. *Purpose:* Butyrate, a short chain fatty acid readily metabolised by colonocytes, has been used to treat diversion colitis and distal ulcerative colitis unresponsive to standard therapy. This study compares butyrate enemas with prednisolone enemas and with combined butyrate/prednisolone enemas. *Method:* 27 patients with active distal or left sided ulcerative colitis were randomly allocated into 3 groups of nine. The enemas (all 100 ml nocte for 6 weeks) were 20 mg prednisolone 21-phosphate, 100 mmol sodium butyrate or the same amount of prednisolone and butyrate mixed together as one enema. *Results:* After 2 weeks treatment median stool frequency fell significantly in the prednisolone group (pre-treatment: 9 stool/24 hr; 2 weeks: 3 stool/24 hr,  $p < 0.02$ ) but not in those given butyrate enemas (pre-treatment: 7 stool/24 hr, 2 weeks; 6 stool/24 hr). At 2 weeks 2 patients receiving butyrate showed no improvement in their colitis and withdrew from the trial. At 6 weeks 8 patients treated with prednisolone still had a reduction in stool frequency compared with 5 in the butyrate group. In both groups there was an improvement in urgency, incontinence, blood loss and sigmoidoscopic score, but not in histological appearance. 16 of 18 patients receiving butyrate alone or in combination complained of its unpleasant odour. *Conclusions:* Prednisolone enemas were successful in treating most patients with distal or left sided ulcerative colitis and the improvement was apparent at 2 weeks. Butyrate enemas, which were malodorous, improved some patients by 4 weeks. There was no additional advantage in combining both butyrate and prednisolone into one enema. Intestinal disorders: IBD, therapy Nutrition: Nutrients and gut function } "Prednisolone Enemas Improve Patients with Distal/Left Sided Ulcerative Colitis More Rapidly than Butyrate Enemas"

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"P P 17 0447" P 17 0447 **Combined Immune Modulation for Refractory Ulcerative Colitis. A Five-Year Study** R. Sostegni, G. Rocca, M. Pinna-Pintor<sup>1</sup>,

\*G.C. Actis, M. Rizzetto

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<sup>1</sup> Dept of Digestive Surgery, Ospedale Molinette, Turin, Italy *Background* Owing to the difficult management and the side effects, it has been recommended that the use of Cyclosporin (CsA) for refractory ulcerative colitis (UC) be restricted to tertiary care Centers. As one such Center, we have used this drug in a 5-year study. *Patients and Methods* The requirements for enrolment were the patient's eligibility for emergency colectomy after failure of his flared UC to respond to a 7-day course of full-dose parenteral steroids. On such criteria, 43 patients were enrolled in a 5-year time. There were 24 males, and 19 females, aged 17–72. They had sub-total or universal colitis, with a mean CAI score of 10 marks. In the 14-day acute phase, the steroids were tapered, and CsA was continuously infused at 2 mg/Kg/day (ref blood range 60–240 ng/ml). The responders (reducing the CAI score by 50%), received 6–8 mg/Kg/day oral CsA for the 6-month chronic phase. *Results* 14 (32%) patients worsened on IV CsA and had emergency colectomy. Further 10 (23%) although not improved avoided emergency surgery, but 7 of them had surgery in a year. The remaining 19 (44%) had a full response in 7 days and were discharged disease-free on oral CsA and tapering steroids. One of them dropped out, the remaining 18 were followed up for 1–60 months. Medication on leaving CsA included mesalamine in 12, and 1.5 mg/Kg azathioprine (AZA) in 6. Of the 12, 10 had an > 2 year follow-up. One has avoided surgery, for the other 9 the median time-to-colectomy was 23 months, with 5 keeping remission till the 3rd year; early relapse significantly ( $p = 0.05$ ) associated to previous aggressive disease. In the same follow up, none of those on aza has needed surgery ( $p = 0.02$ ). Side effects included cholestasis in the acute phase (7 cases), seizures (1 case); nephrotoxicity (2 cases). No infection was found at all. *Conclusion* Some half of the patients with severe refractory UC fully remit in one week of IV CsA; 40% of them delay surgery for > 2 years or may not need it at all after 4 years. This figure may be brought up to 60% combining aza to oral CsA. At the doses used no infection due to immune suppression was seen. We conclude that combined immune modulation for severe refractory UC is effective and safe, and its use should be encouraged at tertiary care Centers. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation Clinical practice: Management strategy } "Combined Immune Modulation for Refractory Ulcerative Colitis. A Five-Year Study"

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"P P 17 0448" P 17 0448 **Role of Different Indirect Immunofluorescence Techniques in Detecting pANCA and Antinuclear Antibodies in Ulcerative Colitis**

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<sup>1</sup> Clinica Medica I, Policlinico Umberto I, Roma, Italy A distinct subset of antineutrophils cytoplasmic antibodies showing a perinuclear staining pattern (pANCA) on ethanol fixed neutrophils (EFN) have been detected in ulcerative colitis (UC) with a prevalence ranging from 50% to 70% [1]. In most studies the typical perinuclear pattern observed by indirect immunofluorescence (IIF) on EFN is considered diagnostic for pANCA. However also antinuclear antibodies (ANA) can give a similar pattern. In order to differentiate pANCA from ANA we have used two additional IIF techniques: IIF on formalin fixed neutrophils (FFN) and IIF on Hep2 cell. Formalin fixation prevents the redistribution of granular antigens to the perinuclear space rendering the staining as a cANCA one and Hep2 cell is a highly sensitive substrate for ANA. Sera from 47 UC patients were assayed for pANCA with conventional IIF using EFN as substrate. All positive sera were retested on FFN to confirm the presence of pANCA. Sera in which pANCA were not confirmed were assayed on Hep2 cell to detect the presence of ANA. Result are shown in the figure below: IIF on EFN (screening test) IIF on FFN IIF on Hep2 Negative Positive (pANCA) (ANA) 23/47 (49%) 24/47 (51%) 17/24 (71%) 7/24 (29%)

pANCA could be confirmed in 71% of sera showing a perinuclear staining pattern on EFN; in 29% the perinuclear pattern was due to ANA. Moreover ANA were detected in 3 additional patients showing a negative IIF on EFN and the coexistence of both antibodies occurred in 5 patients. The prevalence of pANCA and ANA in UC patients was 17/47 (36%) and 15/47 (32%) respectively. The lower prevalence of pANCA as compared to other studies can be explained by the fact that IIF on EFN alone overestimates the prevalence of pANCA of about 30% and can not rule out the presence of ANA. The use of the three IIF techniques is therefore warranted in assessing the true prevalence of pANCA in IBD.

Reference: Gross WL et al Clin Exp Immunol 91 1 1993 Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Role of Different Indirect Immunofluorescence Techniques in Detecting pANCA and Antinuclear Antibodies in Ulcerative Colitis"

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"P P 17 0449" P 17 0449 **Binding of Antagonists of H<sub>1</sub> and H<sub>2</sub> Histamine Receptors to Peripheral Blood Lymphocytes in Patients with Ulcerative Colitis**

\*A. Salomon, Z. Knapik

Department and Clinic of Gastroenterol. Medical University, Wroclaw, Poland In 20 patients with ulcerative colitis and 20 healthy volunteers the binding of H<sub>1</sub>-receptor antagonist-clemastine, and H<sub>2</sub>-receptor antagonist ranitidine by lymphocytes was investigated. The lymphocytes were isolated by centrifugation and dialysed in 100 ccm of solution containing  $2.5 \times 10^{-5}$  M of clemastine or ranitidine. Using standard curves the concentration of clemastine and ranitidine in dialyzate before and after incubation was denoted. The results were expressed in umol of clemastine and ranitidine bound by  $2 \times 10^6$  lymphocytes. The results are presented in the table. Clemastine Ranitidine Ulcerative X 2.02 0.89 colitis SD 0.86 0.21 Control X 1.48 0.98 SD 0.50 0.24 p 0.05 NS The carried out investigation show that the lymphocytes in patients with ulcerative colitis bind more H<sub>1</sub>-receptor antagonist than the lymphocytes in healthy persons. It proves indirectly that H<sub>1</sub>-receptors may play some role in the pathophysiology of this disease. Intestinal disorders: Anorectal disorders Immunology and microbiology: Inflammation Hormones and receptors: Receptor characterization } "Binding of Antagonists of H<sub>1</sub> and H<sub>2</sub> Histamine Receptors to Peripheral Blood Lymphocytes in Patients with Ulcerative Colitis"

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"P P 17 0450" P 17 0450 **Prevalence of Antineutrophil Cytoplasmic Antibody (ANCA), HLA DR2 and HLA DR4 in Patients with Ulcerative Colitis and in First Degree Relatives**.  
**J. Baranda,**

\*F. Portela, H. Ribeiro, F. Cardoso, P. Amaro, M. Ferreira, P. Andrade, P. Ministro, A. Rosa, I. Pimenta, M.C. Leitão, A. Donato, D.S. Freitas

Department of Gastroenterology, Coimbra University Hospital, Coimbra, Portugal *Background:* xANCA (ANCA with perinuclear pattern but without reactivity against myeloperoxidase) is more frequent in ulcerative colitis (UC) than in other colitis and in controls. The prevalence of xANCA in first degree relatives (FDR) of patients (pts) with UC and its relationship with HLA DR2 and HLA DR4 is less well defined. *Aim:* 1) To compare the prevalence of xANCA between pts with UC and FDR. 2) To evaluate if there is preponderance of HLA DR2 in xANCA positive (pos) UC pts and if HLA DR4 is associated with xANCA negative (neg) UC. 3) To confront the frequency of HLA DR2 and HLA DR4 in UC pts and FDR with the one that occurs in a healthy population of Central Portugal (HPCP). *Methods:* xANCA, HLA DR2 and HLA DR4 status were determined in 29 UC outpatients and in 58 FDR without UC. The mean age was 44.7 – 18.1 yr; 58.6% were females. xANCA was searched by indirect immunofluorescence; myeloperoxidase was measured by an ELISA assay. HLA DR2 and HLA DR4 status were based on the microlymphotoxicity technic. Data from HPCP was given by Lusotransplante/Centro de Histocompatibilidade do Centro. Data analysis was made by  $\chi^2$  and Odds Ratio (OR) for a confidence interval (CI) of 95%. *Results:* xANCA was detected in 46.4% of UC pts and in 3.8% (2 cases) of FDR ( $p < 0.0001$ ); these 2 cases were FDR of xANCA pos UC pts. We didn't find differences in the prevalence of DR2 and DR4 status between UC pts and FDR (DR2: 25% vs 26.4%; DR4: 0% vs 3.7%;  $p$  NS). The frequency of DR2 status was 23.1% in xANCA pos UC pts and 28.6% in xANCA neg UC pts ( $p$  NS). DR4 status was never found in UC patients either xANCA pos or neg. DR2 status is slightly more prevalent in UC patients and FDR than in HPCP (25% and 26.4% vs 16.2%;  $p$  NS). There is a lower frequency of DR4 status in UC patients and FDR than in HPCP (UC – 0%; FDR – 3.8%; HPCP – 27.4%; OR = 0.067; CI: 0.016–0.28). *Conclusions:* 1) The prevalence of xANCA in FDR is no different from that expected in control groups. 2) We didn't find any association between xANCA pos UC patients and DR2 status neither between xANCA neg UC patients and DR4 status. 3) It seems to exist a strong negative association between DR4 status and UC in Central Portugal. *Intestinal disorders: IBD, etiology and genetics* } "Prevalence of Antineutrophil Cytoplasmic Antibody (ANCA), HLA DR2 and HLA DR4 in Patients with Ulcerative Colitis and in First Degree Relatives"

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P P 17 0451" P 17 0451 **Autoimmune Haemolytic Anaemia and Coombs Positivity without Haemolysis Associated with Ulcerative Colitis**

\*S. Potamianos, E. Giannadaki, M. Roussomoustakaki, A. Kapsoritakis, P. Skordilis, O.N. Manousos

Department of Gastroenterology, University Hospital of Crete, Greece *Objectives:* To estimate the frequency of autoimmune haemolytic anaemia and Coombs positivity without overt haemolysis in ulcerative colitis; to determine subsets of patients with ulcerative colitis susceptible to this complication; to assess the efficacy of the applied therapeutic modalities. *Patients:* 302 patients with ulcerative colitis treated at the University Hospital of Heraklion, Crete over a 6 years period were included. Within this group, a subgroup of 152 patients were studied prospectively for the presence of a positive direct Coombs test. *Results:* A diagnosis of autoimmune haemolytic anaemia was made in 5 of 302 patients with ulcerative colitis (1.7%). One more patient developed a Coombs positive haemolytic anaemia attributed to sulphasalazine. A positive Coombs test without evidence of haemolysis was found in 3 of 152 patients (2%). The mean age of all Coombs positive patients was 50.5 years and there was a definitive male preponderance (M/F: 2/1). In all cases autoimmune haemolytic anaemia occurred during active colitis. The mean time between the onset of colitis and the diagnosis of autoimmune haemolytic anaemia was 17 months. 3 of 5 patients with autoimmune haemolytic anaemia (60%) and 7 of 9 of all Coombs positive patients (77.7%) had total colitis. All patients with autoimmune haemolytic anaemia were treated initially with corticosteroids. 3 of 5 (60%) had a good haematological response. One patient responded to the addition of azathioprine and one underwent splenectomy and proctocolectomy. *Conclusions:* In this study the frequency of autoimmune haemolytic anaemia associated with ulcerative colitis was higher than in previous reports. The complication occurred early in the course of colitis and was related to the disease activity and extent. In contrast to other studies a male preponderance was found. A Coombs test and a detailed investigation for possible haemolysis are proposed for all patients with ulcerative colitis and anaemia. Although immunosuppressive therapy is successful in most cases, sometimes surgery is required. *Intestinal disorders: IBD diagnosis, monitoring Clinical practice: Epidemiology (non cancer) }* "Autoimmune Haemolytic Anaemia and Coombs Positivity without Haemolysis Associated with Ulcerative Colitis"

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"P P 17 0452" P 17 0452A **Five-Year Prospective Epidemiological Study of Ulcerative Colitis at Heraklion, Crete, Greece, 1990–1994**. Giannadcki,

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Gastroenterology Department, University Hospital, Heraklion, Crete

The *aim* of this descriptive epidemiological survey of ulcerative colitis (UC) in the Heraklion area (pop. 264,000 inh.) of the island of Crete was to obtain an accurate estimate of the incidence of UC in Crete and to compare the incidence rates with those of North and South Europe.

*Methods:* The medical, pediatric and surgical departments of the two hospitals of the Heraklion area, health centers as well as private doctors of the area agreed to refer patients with symptoms suggestive of UC. All pharmacists were asked to screen medication specific for UC. All patients were seen at our Department and underwent a complete work-up including stool examinations, radiology and colonoscopy with biopsies. Standard criteria were taken into account in reaching the final diagnosis. Annual and average UC incidences were calculated. For the aggregated data age standardized incidences were calculated by the direct method using as standard the European population. Ninety-five per cent confidence intervals (CI) were calculated using the exact binomial variance.

*Results:* The average incidence over the five year period was 8.9/100,000/year (CI 2–10.5), 11.6 for men and 6.3/100,000/y for women. There was an increasing trend of the incidence rates over the five years: 5.4–6.5–10.6–10.6–11.4/100,000 for the consecutive years 1990–1994. In regard to the incidences of UC by sex and residence, there was an incidence of 9.2/100,000 for the urban and 8.4/100,000 for the rural population. When incidences of UC by educational level were estimated, significant differences were found, with high incidences for high educational level (44.8) as opposed to middle (21.5) and low educational level (7.2/100,000). The average incidence of UC by age and sex revealed men to be more often affected than women, with two peaks of incidence at 35–44 years and 55–64 years respectively.

*Conclusions:* UC in the Heraklion area of Crete is more common in men than women, in patients with higher rather than middle and lower educational level. There is no significant difference in incidence of UC between rural and urban areas. The overall incidence of UC in Heraklion, Crete is as high as in Central and Northern European countries.

Intestinal disorders: IBD diagnosis, monitoring } "A Five-Year Prospective Epidemiological Study of Ulcerative Colitis at Heraklion, Crete, Greece, 1990-1994"

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"P P 17 0453" P 17 0453A **Randomised Trial Comparing Mesazlazine and Prednisolone Foam Enemas in Patients with Active Distal Ulcerative Colitis**

\*V. Mani, N.H.S. Wigan, N.H.S. Leigh

Trust Hospitals, Leigh Infirmary, Leigh, WN7 1HS, England *Background:* Mesalazine (5-ASA) foam enema has been shown to be superior to prednisolone foam enema in the treatment of relapse of distal ulcerative colitis (UC) at the end of 4 weeks. In this study we have compared the Clinical Research File (CRF) and diary data in the first two weeks of the same clinical trial. *Method:* In a multi-centre double-blind randomised study 295 eligible patients (range 18–88) received either 5-ASA 2 g (n = 147) or prednisolone foam enema 20 mg (n = 148) nocte for 4 weeks. Patients CRF (average no of stools per day, % of patients with blood in stools and mucus in stools) and diary cards (change in bowel frequency week 1–2, with number of days with blood, mucus and liquid stools) data were analysed. *Results:* Both groups were well matched with respect to age, sex, clinical history and base line sigmoidoscopic grades. In the first two weeks of the study, CRF data showed no difference between the treatment groups in the average number of stools per day. There was a significant difference in the percentage of patients with blood in the stools (14%) (CI: 3–24%) in favour of 5-ASA foam enemas (p = 0.014), but no significant difference noted with regard to mucus in stools. Diary data during the first two weeks indicated significantly fewer days with blood in stools (p = 0.007), as well as mucus in stools (p = 0.024) in the 5-ASA group. Prednisolone treated patients experienced significantly fewer days with liquid stools (p = 0.005) at two weeks. *Conclusion:* In this analysis, the time to onset of effect of 5-ASA foam enema has been shown to be clinically superior to prednisolone foam enema. This important aspect should be considered when treating acute relapses of distal ulcerative colitis. Intestinal disorders: IBD, therapy } "A Randomised Trial Comparing Mesazlazine and Prednisolone Foam Enemas in Patients with Active Distal Ulcerative Colitis"

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"P P 17 0454" P 17 0454 **Interrelations between Trace Elements, Immunologic Markers and Acute Phase Response in Well-Nourished Patients with Ulcerative Colitis (UC)** G.N. Dalekos<sup>1</sup>, J. Savaidis<sup>2</sup>, K.I. Seferiadis<sup>2</sup>, E.V. Tsianos<sup>1</sup>

<sup>1</sup> Division of Internal Medicine, School of Medicine, University of Ioannina, Greece

<sup>2</sup> Laboratory of Clinical Biochemistry, School of Medicine, University of Ioannina, Greece *Purpose:* This study was conducted in an attempt to assess the trace elements status and the possible interrelation(s) between them and various immunologic markers, acute phase reactants or standard haematological parameters in the circulation of well-nourished patients with UC. *Methods:* The serum levels of zinc, copper, soluble interleukin-2 receptors (sIL-2Rs), interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-2 (IL-2) tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), non-organ specific autoantibodies, CRP, C<sub>3c</sub> and C<sub>4</sub> components of the complement system, cerulo-plasmin and haematological parameters, were determined in 75 consecutive, selected well-nourished patients with UC (32 patients with active and 43 with inactive UC) and in 33 healthy individuals. *Results:* We found autoantibodies of at least one specificity (AUBS) in 77.3% of patients. The mean levels of sIL-2Rs were significantly higher in active disease than in inactive UC ( $p = 0.0001$ ) and in patients with ANA ( $p < 0.05$ ), ANCA ( $p = 0.01$ ) or AUBS ( $p < 0.05$ ). None of the patients had detectable IL-1 $\beta$ , IL-2, and TNF- $\alpha$  in their sera at least with the ELISAs used. The mean concentrations of zinc and copper were significantly higher (ANOVA,  $p < 0.005$  and  $p = 0.0001$ , respectively) either in active or in inactive UC compared with healthy controls ( $p < 0.05$ ). The copper was negatively correlated with haemoglobin ( $r = -0.22$ ,  $p < 0.05$ ) but positively with C<sub>3c</sub> ( $r = 0.41$ ,  $p < 0.0005$ ), C<sub>4</sub> ( $r = 0.38$ ,  $p < 0.001$ ) and ceruloplasmin ( $r = 0.44$ ,  $p < 0.0005$ ) whilst, zinc was correlated with ESR ( $r = 0.27$ ,  $p < 0.01$ ) C<sub>3c</sub> ( $r = 0.32$ ,  $p = 0.0005$ ) and ANA ( $p = 0.01$ ). Zinc and copper were also correlated with sIL-2Rs but without statistical significance ( $p < 0.10$ ). *Conclusions:* These findings indicate that in UC patients, zinc and copper are correlated either with haematological parameters of relapse of the disease or acute phase reactants and-although without statistical significance-with markers of immune cellular activation (sIL-2Rs). The high copper levels may be of relevance in perpetuating the inflammatory and immune processes in UC while an high zinc levels may indicate the increased zinc requirements to maintain the activity of the oxygen scavenger enzyme, superoxide dismutase. Intestinal disorders: IBD, basic }" "Interrelations between Trace Elements, Immunologic Markers and Acute Phase Response in Well-Nourished Patients with Ulcerative Colitis (UC)"

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"P P 17 0455" P 17 0455 **The p-ANCA Titers of Ulcerative Colitis Patients May Vary with Change of the Disease Activity**

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<sup>1</sup> Dept of Clinical Pathology, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea Studies have suggested that p-ANCA is an immunogenetic marker of ulcerative colitis (UC) and has no correlation with the disease activity. However, little information is available about the serial follow-up of p-ANCA titers in UC patients. *Aim:* We performed this study to test our hypothesis that p-ANCA titers may change with the disease activity. *Methods:* Of 71 Korean patients with UC (42 ANCA positive; 29 ANCA negative), 20 patients who were tested by indirect immunofluorescence for p-ANCA more than once (2–5 times) were analyzed for the change in p-ANCA titers. The disease activity was assessed according to L. Sutherland (Gastroenterol 1987; 92: 1894). The change in p-ANCA titers was defined as the change of the titer fourfold or more. *Results:* Titers of p-ANCA in 10 p-ANCA positive patients ranged from 1:80 to 1:2,560 (median 1:320) on initial check. On follow-up examination, 3 became p-ANCA negative and 4 showed a 4-fold decrease in titers after remission (n = 5) or improvement (n = 2). One patient who had demonstrated negative conversion after remission became positive after relapse of UC and showed a 4-fold decrease in the titer after improvement again. There was, however, no change in titers in 3 patients (two in remission, one with no change in activity). Of 10 patients who were initially p-ANCA negative, 9 remained p-ANCA negative after remission (n = 5), aggravation (n = 2) or no change (n = 2) in activity; one patient with mild disease on initial check became p-ANCA positive after remission. *Conclusion:* Our data suggest that, in some patients, although not in all, p-ANCA titers may have correlation with UC activity. We postulate that this apparent discrepancy may be partly due to heterogeneity of antigens involved in p-ANCA reaction. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "The p-ANCA Titers of Ulcerative Colitis Patients May Vary with Change of the Disease Activity"

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"P P 17 0456" P 17 0456 **Assessment of Ulcerative Colitis by Measurement of Superior Mesenteric Artery (SMA) Velocity with Doppler USN. Kalantzis<sup>1</sup>, A. Antoniou<sup>2</sup>, S. Tarazis<sup>1</sup>,**

\*C. Markoglou<sup>1</sup>, D. Mourikis<sup>2</sup>

<sup>1</sup> Department of Gastroenterology, NIMTS Hospital; Athens, Greece

<sup>2</sup> Department of Diagnostic Radiology, Areteion Hospital, Athens University, Greece *Purpose:* To test the hypothesis that increased velocity in the superior mesenteric artery (SMA) reflects disease activity and extension in patients with Ulcerative colitis. *Materials and methods:* Duplex Doppler sonographic measurement of SMA velocity were obtained in 28 patients (18 male – 10 female, A<sub>1</sub>: 13 patients with pancolitis, A<sub>2</sub>: 5 patients with subtotal colitis and B: 10 patients with left sided colitis) and 50 healthy volunteers (control group). Disease activity was determined with clinical and endoscopic findings (indicators). *Results:* A marked increase in SMA velocity (peak systolic and end-diastolic velocity) was noted in patients with pancolitis group A<sub>1</sub> ( $U_{\text{syst}} = 3.64 - 0.18$  m/sec and  $U_{\text{diast}} = 0.94 - 0.09$  m/sec) compared with healthy volunteers ( $U_{\text{syst}} = 1.49 - 0.07$  m/sec and  $U_{\text{diast}} = 0.38 - 0.04$  m/sec),  $p < 0.01$ . A lower increase in SMA velocity was noted in patients with subtotal colitis group A<sub>2</sub> ( $U_{\text{syst}} = 2.06 - 0.14$  m/sec and  $U_{\text{diast}} = 0.45 - 0.05$  m/sec) compared with healthy volunteers  $p < 0.01$ . In patients of group B with left sided colitis the changes in SMA velocity ( $U_{\text{syst}} = 1.45 - 0.08$  m/sec and  $U_{\text{diast}} = 0.36 - 0.03$  m/sec) compared with healthy volunteers were not statistically significant  $p < 0.05$ . *Conclusion:* Activity (extension) of Ulcerative colitis causes a substantial increase in SMA velocity. Measurement of SMA velocity may be an important non invasive, readily available method that can be used to monitor Ulcerative colitis extension-activity. Intestinal disorders: IBD diagnosis, monitoring }" "Assessment of Ulcerative Colitis by Measurement of Superior Mesenteric Artery (SMA) Velocity with Doppler US"

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"P P 17 0457" P 17 0457 **Serum IgG Against Specific Tropomyosin (TM) Isoforms in Ulcerative Colitis Patients and Unaffected Relatives** L. Biancone, R. Marasco, G. Monteleone, F. Pallone

Dpt. Med. Sper., Universit\ 'e0 di R. Calabria, Catanzaro, Italy *Background.* Genetic susceptibility has been shown in IBD. IgG antibodies against a putative autoantigen related to TMs have been reported in Ulcerative Colitis (UC). UC mucosal lymphocytes release IgG and IgG1 against TMs, supporting an autoantigenic role of TMs in UC. TMs are cytoskeletal proteins with organ specific isoforms. The TM isoforms related to the putative autoantigen in UC are unknown. *Aims.* 1. To investigate the human TM (hTM) isoforms recognized by serum IgG of UC patients. 2. To explore the immunorecognition of hTMs by serum IgG of healthy UC relatives. 3. To evaluate whether IgG immunoreactivity to hTMs is related to ANCA status. *Methods.* Source of serum samples: 33 UC patients, 21 Crohn's Disease (CD), 20 normal subjects (NS), 60 healthy UC relatives (39 1st degree and 21 nd) and 31 healthy CD relatives (20 1st degree and 11 2nd). IgG to hTMs were examined by ELISA using 4 recombinant hTM isoforms (hTM1, hTM2, hTM3, hTM5) as antigen. Sera were tested (1:100) using an A-P conjugated goat anti-human IgG. Data were expressed as Optical Density (OD) (m – SEM). p-ANCA were detected in sera (1:100) by ELISA followed by indirect immunofluorescence. 17/33 UC patients and 5/60 UC relatives were p-ANCA+ve. *Results.* Serum IgG reactivity to hTM1 and hTM5 was higher in UC patients than in CD and NS ( $p < 0.01$ ; T-test). IgG immunoreactivity to hTM1 was higher ( $p < 0.04$ ) in UC relatives than CD relatives and NS. Patients Relatives NS hTM-IgG UC (n = 33) CD (n = 21) UC (n = 60) CD (n = 31) (n = 20) hTM1 OD 0.113 – 0.017 0.050 – 0.014 0.068 – 0.012 0.030 – 0.007 0.018 – 0.009 hTM2 OD 0.105 – 0.018 0.084 – 0.019 0.061 – 0.014 0.046 – 0.010 0.073 – 0.011 hTM3 OD 0.056 – 0.011 0.018 – 0.007 0.025 – 0.009 0.005 – 0.003 0.018 – 0.010 hTM5 OD 0.117 – 0.015 0.044 – 0.014 0.014 – 0.003 0.014 – 0.006 0.011 – 0.016 Using the mean OD + 2SD from NS as a cut off, 52% of UC sera were positive for hTM1 and 64% for hTM5, while 13/60 (21%) UC relatives were positive for hTM1. Less than 5% of controls were positive for the 4 hTMs tested. In UC patients reactivity to hTM5 was higher in the ANCA+ve than in ANCA{ - }ve group (OD 0.144 – 0.020 vs 0.082 – 0.018  $p = 0.01$ ). *Conclusions.* Circulating IgG against hTM1 and hTM5 represent a feature of UC. Immunoreactivity against hTM1 differentiates UC relatives from controls. ANCA status may influence immunoreactivity to hTMs. Results indicate an autoimmune response and a genetic susceptibility to specific hTM isoforms or related peptides in UC. Intestinal disorders: IBD, etiology and genetics Immunology and microbiology: Host defense mechanisms Clinical practice: Epidemiology (non cancer) }" "Serum IgG Against Specific Tropomyosin (TM) Isoforms in Ulcerative Colitis Patients and Unaffected Relatives"

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"P P 17 0458" P 17 0458 **The Impact of Smoking Habit in Ulcerative Colitis Is Correlated with Sex Distribution**

\*G. Riegler, M. Tartaglione, R. Marmo, R. Carratu', ""Gruppo Italiano Studio Colon-Retto – GISC"", R. D'Inc'\e0, M.I. Russo, D. Valpiani, C. Papi, M. Astegiano, V. Annese, A. Andreoli, M. Ingrosso, M. Vecchi, M.C. DiPaolo, M.A. Pelli, M.R. Garcea, C. Mansi, G. Novelli, D. Cantarini, P. Usai, D. Assisi

Seconda Universit'\e0 Di Napoli, via v. Mosca 39, Napoli 80129, Italy Data concerning clinical picture of Idiopathic Ulcerative Colitis (IUC) in relation to the different age of patients are scarce and controversial. In fact it is difficult to recruit so many IUC patients in old age to let a valuable comparison with younger IUC patients. 1705 consecutive IUC patients (60.2% male, 39.8% female; mean age at diagnosis 38.5 – 16.04 years) were recruited in 17 clinics homogeneously distributed in our country. All patients were arranged in quartiles (0–25; 26–35; 36–50; = > 51 years of age) and the M/F ratios observed were respectively 1.13; 1.40; 1.79; 2.02 with a statistically significant difference ( $p < 0.001$ ). The sex distribution was investigated with regard to clinical parameters: smoking habit; symptoms at onset; disease extension and activity. Only smoking habit was found to be strongly correlated (Figure).

The M/F ratio was found to be correlated with a more frequent ex-smoker status observed in older men. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring Clinical practice: Epidemiology (non cancer) } " "The Impact of Smoking Habit in Ulcerative Colitis Is Correlated with Sex Distribution"

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"P P 17 0459" P 17 0459 **Appendicectomy, Smoking and Ulcerative Colitis: A UK Case-Controlled Study** S. Jain,

\*H.H. Tsai

Gastroenterology Department, Castle Hill Hospital, Castle Road, Cottingham, E. Yorkshire, U.K. HU16 5JQ There is an inverse relationship between appendicectomy and ulcerative colitis (UC) in a Belgian study. This effect is not seen in a American study and has not yet been confirmed in the U.K. There is also a possibility that this relationship may be linked with smoking. This case-controlled, prospective study examines the frequency of appendicectomy and smoking in a stable U.K. population. *Methods:* A total of 228 patients with a definitive diagnosis of inflammatory bowel disease were prospectively interviewed by a standardised questionnaire. There were 112 patients with a diagnosis of ulcerative colitis and 116 patients with Crohn's disease. 112 controls were recruited from accidents and emergency department and were matched for age and sex. *Results:* The appendicectomy rates amongst patients with UC was 2.7% (3/112) which was significantly lower compared to 16.1% (18/112) amongst controls ( $P < 0.005$ , Odds ratio: 6.96, 95% C.I. 37.7–1.93). 2 patients with UC had their appendicectomy performed after diagnosis. Appendicectomy rates amongst patients with Crohn's disease was significantly greater than controls: 34% (18/112) vs. 16.1% (39/116), ( $P < 0.01$ ; O.R. 2.65, 95% C.I. 5.31–1.34) but includes 9 patients who had appendicectomy as part of surgical intervention for Crohn's disease. The strong association of UC with non-smoking is confirmed (2% v 42%,  $P < 0.001$ , OR 35.6; 95% C.I. 308–8.68). However there appears to be no association between smoking and appendicectomy in all three groups. *Conclusion:* UC is associated with significantly lower appendicectomy rates than controls while appendicectomy rates in Crohn's disease is higher. This finding is independent of smoking. } "Appendicectomy, Smoking and Ulcerative Colitis: A UK Case-Controlled Study"

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## "P P 17 0460" P 17 0460 The Role of Reactive Oxygen Metabolites in Ulcerative Colitis

\*\dc. Dagli, M. Balk, D. Y\fccl, A. \dclker, H. \d6ver, \c7. Baysal, B. Sahin

Y\fksek Ihtisas Hospital, Ankara- Turkey Reactive oxygen metabolites (ROMs) contribute to tissue injury inflammatory bowel disease. The purpose of this study were (1) to determine the concentrations of malondialdehyde (MDA), superoxide dismutase (SOD) and myeloperoxidase (MPO) in intestinal mucosa of ulcerative colitis (UC) and to compare with the values in control mucosa, (2) to find out the relation between the disease activity and the concentrations of MDA, SOD and MPO. The study group consisted of 27 patients with UC (14 active, 13 quiescent) and 10 patients with anal disease as a control group. We measured the content of MDA, SOD and MPO in rectal biopsy. MDA was measured by thiobarbituric acid, SOD and MPO were measured with nitrobluetetrazolium and O-dianisidine as indicators. The Student t test was used to detect statistically significant differences between groups. Correlation data were analyzed using the Spearman random correlation method. The MDA, SOD and MPO tissue levels were found to be significantly different between the active UC, the patients with quiescent UC and the control subjects. A positive linear correlation is found between the tissue concentrations of MDA, SOD and the disease activity (r: 0.809, r: 0.74 respectively). The SOD concentrations were significantly and negatively correlated with the disease activity (r: { -}0.574). These findings might indicate a decreased endogenous intestinal protection against oxygen derived radicals in UC which contribute to the pathogenesis of the disease. Intestinal disorders: IBD, basic }

"The Role of Reactive Oxygen Metabolites in Ulcerative Colitis"

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"P P 17 0461" P 17 0461 **Immune Response Level and Genetic Markers in Ulcerative Colitis**

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Ukrainian Scientific Research Institute of Gastroenterology, Dnepropetrovsk, Ukraine  
Ulcerative colitis (UC) is a disorder of unknown aetiology and characterized by a variety of immunological abnormalities. It has become increasingly apparent that genetic factors play a major role in the development of various forms of IBD. HLA B5 and HLA B51 have been observed by ourselves to be genetic markers associated with UC in Ukrainian population. The aim of this study was to investigate a correlation between the frequency of HLA B5 and HLA B51, the level of immune response and severity of clinical manifestations of UC. *Materials and methods.* 107 patients with confirmed UC (60 males, 47 females, age range 18–65) were observed: mild – 4, moderate – 63, severe – 35. The identification of the MNC-genes was carried out in microlymphocytotoxic test according to Terasaky. In order to estimate the immune response level the amount of T- and B-cells in periphery blood was determined. *Results.* It has been founded that HLA B5 has positive association with severe UC, high level of B-cells in periphery blood and T-lymphopenia mainly decreased the number of T-helpers. An increased frequency of HLA B51 was observed in patients with mild and moderate UC and had a connection with normal or low level of B-cells and the normal number of T-cells and their sub-populations. *Conclusion.* The data obtained showed that the severity of disease and the level of immune response depends upon MNC-genes, that should provide new approaches to prognosis and therapy of UC. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Immune Response Level and Genetic Markers in Ulcerative Colitis"

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## "P P 17 0462" P 17 0462 Is the Tc-99m HMPAO Labelled Leukocyte Scintigraphy a Reliable Method for Assessment of Disease Activity and Localisation in Patients with Ulcerative Colitis?

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<sup>1</sup> Departments of Cerrahpasa Medical, Faculty of Istanbul University, Istanbul, Turkey  
The diagnosis of ulcerative colitis (UC) is based on endoscopy and histology. In the follow-up of UC patients, knowledge of current clinical activity and the extent of the involved bowel segments is necessary. The clinical activity can be determined on the basis of laboratory parameters or the UC activity index. The extent of inflammation can be investigated by means of colonoscopy and X-ray examination and labelled leukocyte scintigraphy (LS). Technetium-99m hexamethylpropylene amine oxime (99mTc-HMPAO) is a frequently used agent for in vitro leucocyte labelling. In this study, for the assesment of inflammatory activity and localisation, the grade of leukocyte accumulation was compared with the endoscopic, histologic findings and activity index. 17 patients (9 male and 8 female, mean age: 39) with known UC were enrolled the study. The inflammatory activity in 71 bowel segments of 17 patients was assessed by endoscopy, histology and 99mTc-HMPAO labelled LS using a numerical system. Sensitivity, specivity, diagnostic accuracy, positive and negative predictive values were 77%, 94%, 81%, 97% and 58% respectively. Scintigraphic activity score was significantly correlated with endoscopic, histologic and clinic activity scores ( $r = 0.3612$ ,  $p < 0.05$ ,  $r = 0.6505$ ,  $p < 0.05$  and  $r = 0.7407$ ,  $p < 0.05$  respectively). Our results suggested that 99mTc-HMPAO LS can be a reliable method for the assesment of severity and localisation of the inflammatory activity in UC. In new patients normal LS and rectosigmoidoscopy can be used to exclude UC and abnormal scans may enable further investigations to be efficiently targeted. Scintigraphy Scintigraphy + { - }  
Total Inflamed bowel segments 41 12 53 Normal bowel segments 1 17 18 Total 42 29 71  
Intestinal disorders: IBD diagnosis, monitoring } " Is the Tc-99m HMPAO Labelled Leukocyte Scintigraphy a Reliable Method for Assessment of Disease Activity and Localisation in Patients with Ulcerative Colitis?"

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"P P 18 0463" P 18 0463 **Distribution of Carbonic Anhydrase Isoenzymes I, II, IV, V, VI and MN/CA IX in the Human Intestine**

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<sup>4</sup> Institute of Virology, Slovak Academy of Sciences, Bratislava, Slovak Republic  
Carbonic anhydrases (CAs) are enzymes which regulate the acid-base and water balance in several gastrointestinal tract epithelia and digestive glands. This report presents immunohistochemical comparison of the distributions of CA isoenzymes in the human intestine. *Small intestine:* CA I was found to be present in the deep crypts of Lieberkühn of the jejunum and ileum. CA II appeared in the Brunner's glands of the duodenum and in the surface epithelium of duodenum and jejunum. Basolateral staining for MN/CA IX was found in the surface epithelial cells of the duodenum and jejunum, and in the deep crypts of the ileal mucosa. *Large intestine:* Intense cytoplasmic reactions for both CA I and II and strong mucosal brush border associated signal for CA IV were seen in the surface non-goblet epithelial cells throughout the large intestine. MN/CA IX gave a moderate reaction at the basolateral surfaces of the epithelium in the deep crypts of the caecum and ascending colon. The surface epithelial cells showed a positive staining for mitochondrial CA, CA V, in all segments of the gut. No signal for secretory CA VI was detected. The results indicate that CA isoenzymes are differentially expressed along the axis of the gastrointestinal canal. Several are expressed in small and large intestine where they likely form complementary systems that participate in electrolyte and water transport. Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport }  
"Distribution of Carbonic Anhydrase Isoenzymes I, II, IV, V, VI and MN/CA IX in the Human Intestine"

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"P P 18 0464" P 18 0464 **The Expression and Postnatal Development of Aquaporins in the Rat Small Intestine**

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Dept. of Woman and Child Health, Karolinska Institutet, Stockholm, Sweden *Background:* Intestinal water transport has for a long time been regarded as secondary to electrolyte or solute transport. Intestinal water transport in small children are more susceptible to osmotic changes and diarrhoeal diseases. Developmental changes in water transport has also been found in laboratory studies on rats. Aquaporins, a family of proteins responsible for the cellular transmembrane movement of water was discovered in 1993. So far 5 different aquaporins have been cloned. Different aquaporines are expressed in different organs and sites within the cell. The aim of this study was to explore the expression of the mRNA of aquaporins in the proximal small intestine of infant and adult rat. *Methods:* We used 10 day old and 40 day old rats which corresponds to infant and adult respectively. Total RNA was extracted from the proximal small intestine. The expression of aquaporin 1–5 was evaluated with semi quantitative PCR. { b}-actin was co-amplified as an internal control. *Results:* Our study showed that aquaporin 3 and 4 is present in the proximal small intestine of rats. Aquaporin 3 is weakly expressed in infant small intestine and increases dramatically in adult tissue. Aquaporin 1, 2, and 5 was not detected in the small intestine. *Conclusion:* Intestinal water absorption/secretion undergoes postnatal development and plays a great role during normal and pathological conditions. We have for the first time shown that aquaporin 3 and 4 are present in the small intestine and that aquaporin 3 undergoes postnatal development. The low expression of aquaporin 3 in the infant rat might explain some of the immaturity of the intestinal water transport. Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport } "The Expression and Postnatal Development of Aquaporins in the Rat Small Intestine"

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"P P 18 0465" P 18 0465 **Transport of Various Nutrients through the Small Intestine and the Ileocecal Region (ICR)** K. Lang,

\*J. Hammer, K. Kletter<sup>1</sup>, A. Gangl

General Hospital of Vienna, Abt. f. Gastroenterologie und Hepatologie, Austria

<sup>1</sup> Universitätsklinik f. Nuklearmedizin, Austria The terminal ileum —but not the small intestine — discriminates, at times, liquids from solids (Hammer et al, Gut, 1993). *Aims:* To scintigraphically determine small intestinal and ileocecal transit of solids and liquids after infusion of various nutrients and non-caloric solutions. *Methods:* 28 healthy volunteers (age: 24 – 3 years; 7 F, 21 M) fasted for 6 hours and then swallowed a tube that was positioned with its distal end at the Ligament of Treitz. 1 gram Amberlite resin pellets, labeled with 100 <sup>111</sup>InCl<sub>3</sub>, served as markers of the solid phase. They were injected and rinsed down the tube (infusion rate: 1 ml/min) by a fluid that was either 30 ml of Intralipid<sup>®</sup> 10% (1 kcal/ml), Albumin 10% (1 kcal/ml), NaCl 0.9% or an isoosmotic (Osm.) electrolyte solution (n = 7 each). Fluids were labeled with 2 mCi <sup>99m</sup>Tc-DTPA. { g }-camera images were obtained in 10 minute intervals until all radiolabels had entered the colon. A variable region of interest program quantified the arrival of radiolabels in the colon. *Results:* \* = significant vs. protein (p < 0.05, after Bonferroni correction) Start of % Counts in Duration of colonic filling the colon colonic filling # of boluses Infused (min) after 3 hours (min) fluid Tc = In Tc In Tc = In Tc In Lipid 50 – 8\* 99 – 3\* 90 – 6\* 131 – 7\* 3 – 1<sup>NS</sup> 2 – 1<sup>NS</sup> Protein 176 – 16 30 – 14 29 – 14 67 – 12 2 – 1 2 – 1 NaCl 123 – 2 58 – 11 71 – 9 97 – 7 3 – 1 3 – 1 Osm. 96 – 21\* 66 – 12 60 – 12 116 – 11 3 – 1 3 – 1 After infusion of lipids the small intestine started to empty earlier compared to all other solutions. Duration of colonic filling, i.e. the period when colonic filling started until the time when all counts entered the colon, was significantly delayed after lipid infusion. Movement of solids and liquids was simultaneous. *Conclusion:* Lipids transit the small intestine faster compared to proteins, but the ICR significantly slower. Solids and liquids are transported simultaneously through the small intestine and the ICR. Ileal contents mainly are transported in boluses into the cecum independent of the caloric content of the solutions. Motility, specific: Small bowel Nutrition: Nutrients and gut function } "Transport of Various Nutrients through the Small Intestine and the Ileocecal Region (ICR)"

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"P P 18 0466" P 18 0466 **Ethanol-Induced Alteration of Matrix Network in the Jejunal Mucosa of Chronic Alcohol Abusers** A. Casini<sup>1</sup>, A. Galli<sup>1</sup>, A. Calabr<sup>1</sup>, S. Di Lollo<sup>2</sup>, B. Orsini<sup>1</sup>, L. Arganini<sup>2</sup>, A.M. Jezequel<sup>3</sup>, C. Surrenti<sup>1</sup>

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<sup>2</sup> Institute of Pathology, University of Florence, Florence, Italy

<sup>3</sup> Institute of Experimental Pathology, University of Ancona, Ancona, Italy Excessive consumption of alcoholic beverages, may be associated with gastrointestinal symptoms such as dyspepsia and diarrhea. However, it remains controversial whether or not chronic alcohol ingestion damages the small intestinal mucosa. Aim of the study to investigate the effect of chronic alcohol abuse on the jejunal mucosa and, particularly, on its extracellular matrix (ECM) network. *Patients and Methods:* Jejunal biopsy specimens were obtained during upper gastrointestinal endoscopy from 50 chronic alcoholics without cirrhosis and 10 healthy subjects. Morphological studies were performed by routine histology, immunohistochemistry and electron microscopy. Morphometry of jejunal tissues was performed with a computerized image analyzer. *Results:* No significant jejunal epithelial changes were found in alcoholics despite an evident reduction in the enterocyte turnover. Myofibroblast-like cells were significantly increased in the villus stroma of alcoholics in comparison to controls. These cells stained positively for desmin, smooth muscle actin and for several ECM components. In alcohol abusers thickness of mucosal basement membrane was higher, and the staining for collagen I and III was enhanced both in the basement membrane and in the villus stroma. A higher expression of tenascin was also seen at the base of villi of alcoholics. *Conclusions:* These data indicate that chronic alcohol abuse may induce a fibrosis of jejunal villi which is associated with a transformation of villus iuxtaparenchymal cells into active subepithelial myofibroblast-like cells able to produce different ECM components. } "Ethanol-Induced Alteration of Matrix Network in the Jejunal Mucosa of Chronic Alcohol Abusers"

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## "P P 18 0467" P 18 0467 Intestinal Permeability Assessment — Evidence Against the Solvent Drag Hypothesis

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<sup>1</sup> Dept Gastroenterology & Nutrition, Central Middlesex Hospital, London NW10 7NS

<sup>2</sup> Dept. Biochemistry, Kings College Hospital, London SE5 9RS Intestinal permeability tests are widely used for diagnostic screening and therapeutic monitoring. However, the precise pathways used by the probes are unknown. One suggestion is that villous tip osmolarity is the main determinant of small probe permeation rates by regulating the degree of solvent drag [1]. It is reported that the addition of sodium (66 mmol/L) and glucose (100 mmol/L) to a 100 ml test solution containing lactulose and mannitol increased the permeation of mannitol by 1.7 fold, reducing the lactulose/mannitol excretion ratio 1.4 fold. 10 volunteers underwent a combined absorption-permeability test using lactulose (5 g), L-rhamnose (1 g), D-xylose (0.5 g) and 3-O-m-D-glucose (0.2 g) in 100 ml water as i) baseline, ii) with 66 mmol/L sodium and 100 mmol/L glucose and iii) 198 mmol/L sodium and 300 mmol/L glucose in an attempt to confirm the above results. The 5 hour urinary excretion (% dose) of the probes are below: Test substance Baseline sodium-glucose sodium-glucose 66, 100 mmol/L 198, 300 mmol/L Lactulose 0.29 – 0.04 0.38 – 0.05 0.33 – 0.03 L-rhamnose 11.65 – 1.09 10.77 – 0.91 10.22 – 0.60 \*D-xylose 33.59 – 1.56 31.42 – 2.91 29.56 – 1.61 \*\* 3-O-m-D-glucose 51.92 – 2.60 55.37 – 4.04 41.67 – 2.20 \* Lactulose/L-rhamnose 0.029 – 0.005 0.035 – 0.004 0.035 – 0.004 Differs significantly from baseline: \*p = 0.03, \*\* p < 0.01 No significant changes were found with the low dose sodium-glucose whilst active and carrier mediated transport and the non-mediated permeation of L-rhamnose were reduced significantly with the higher dose of sodium-glucose. The lactulose/L-rhamnose ratio was not significantly altered. *Conclusion:* These results are contrary to the hypothesis that solvent drag is an important regulator of small-probe permeation across the small intestine. The changes observed with the higher dose of sodium and glucose are in fact contrary to expectations.

Reference: Bijlsma P.B. et al., Gastroenterology 1995; 108: 687–696 Intestinal disorders, absorption: Epithelial transport } "Intestinal Permeability Assessment / Evidence Against the Solvent Drag Hypothesis"

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"P P 18 0468" P 18 0468 **Intestinal Permeability in Systemic Sclerosis** M. Secondulfo<sup>1</sup>, L. de Magistris<sup>1</sup>, A. De Luca, E. Tirri, C. Valentini,

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Intestinal permeability has been recently reported to be increased in chronic rheumatic diseases such as rheumatoid arthritis, ankylosing spondylitis, psoriasis arthritis. No such data are available in Systemic Sclerosis. Here we report the results of a preliminary study on intestinal permeability in Systemic Sclerosis (SSc). Eleven patients with SSc, all of whom satisfying the preliminary ARA criteria for the classification of the disease (F = 10, M = 1, mean age – SD = 44.91 – 11.90; with a disease duration ranging from 3 to 28, mean – SD = 17.20 – 10.14) were enrolled in the study. All the patients were carefully investigated in order to define the subset of the disease and the extent of skin and internal organ involvement. No patients had gastrointestinal symptoms. Small intestinal permeability was evaluated by Cellobiose/Mannitol (CE/MA) test. Cellobiose (5 g) and Mannitol (2 g) were given as an oral isosmolar load in the fasting state and urine collected for consecutive 5 h. The CE/MA ratio of % urinary excretion was considered as an index of intestinal permeability. In 32 normal subjects the CE/MA was < 0.038. In N = 11 sclerodermic patients the CE/MA ratio resulted 0.009 – 0.006 (mean – SD), with no statistical significant difference vs normal subjects. No correlation was detected among intestinal permeability values and epidemiological or clinical features. SSc has long been known to affect intestinal wall in a quite high percentage of cases. Our data point out a lack of intestinal permeability alteration in a preliminary series of asymptomatic SSc patients

Intestinal disorders, absorption: Malabsorption syndromes  
Intestinal disorders, absorption: Enterocyte biology }  
"Intestinal Permeability in Systemic Sclerosis"

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"P P 18 0469" P 18 0469 **In vivo Study of the Activity of L-Arginine and Nitric Oxide on Intestinal Secretion in Rat**

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<sup>4</sup> Centro Endocrinologia e Oncologia Sperimentale del C.N.R., Napoli

<sup>5</sup> Dept. of Pediatrics, Sect. of Gastroenterology, University of Chicago *Aim of the study:* Nitric oxide (NO) is involved in the regulation of several physiological and pathophysiological processes. NO is produced by NO-synthase during the conversion of L-arginine to L-citrulline. The latter functions as an oxygen donor and transforms NO into NO<sub>2</sub>. The endogenous synthesis of NO is specifically inhibited by the structural analogues of L-arginine and by carboxyphenyl-tetramethyl-imidazoline-oxyl-oxide (cPTIO). The role of the L-arginine-NO pathway in regulating the intestinal transport of water and electrolytes is still unclear and is the subject of the present study. *Methods:* Our approach was based on the *in vivo* perfusion of rat intestine. *Results:* The Table (column 1) shows the data obtained in the rat jejunum perfused with 10 mM L-arginine before and after the intraperitoneal injection of chlorpromazine (CPZ), an inhibitor of intestinal secretion. Increments indicate net water absorption from the intestinal lumen. L-arginine had a marked anti-absorptive effect. A dose-response curve indicated that the anti-absorptive effect was maximal at the concentration of 1 mMol/l. In order to assess the specificity of L-arginine, we measured the effect of another diamino acid, L-lysine, at the concentration of 10 mMol/l. The data in the Table (column 2) show that L-lysine does not modify the transport of water. In order to establish whether L-arginine exerted its effect after being converted to NO, cPTIO was added to the solution containing 1 mM L-arginine to be used for the perfusion experiment. The Table (column 3) shows that, in the presence of cPTIO, L-arginine had almost no effect. *Conclusion:* our data suggest that, in rat, NO is a mediator of the intestinal secretion of water and electrolytes. 1 2 3 H<sub>2</sub>O H<sub>2</sub>O H<sub>2</sub>O (\\b5/l/min/g) (\\b5/min/g) (\\b5l/min/g) Control 25.3 Control 10.3 Control 11.2 L-arg 11.2 L-lys 9.8 L-arg 4.99 CPZ+ 16.5 L-arg+ 9.63 L-arg cPTIO Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport }" "In vivo Study of the Activity of L-Arginine and Nitric Oxide on Intestinal Secretion in Rat"

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## "P P 18 0470" P 18 0470 The Effects of Cardiopulmonary Bypass on Intestinal Absorption

\*\dc Saritas, A. Saritas, O. Tarcan, N. Kantaroglu, T. \c7etintas, S.F. Katircioglu, O. Tasdemir, B. Sahin, K. Bayazit

Y\fksek Ihtisas Hospital, Departments of Gastroenterology, Cardiovascular Surgery and Biochemistry, Ankara, Turkey Following cardiac operations gastrointestinal complications are seen at a rate of %0.6–2 and their mortality is high (%15–65). Subclinical splanchnic damage is more common. In this prospective study, the effect of cardiopulmonary bypass (CPB) procedure on intestinal absorption is investigated on 44 patients. D-Xylose solution, that is containing 25 gr of D-Xylose in 100 ml of water, was given to the patients; and D-Xylose levels were measured in blood sample after 2 hours and in urine that was collected for 5 hours. This test was done 2 days before the operation, and on the first hour and third day postoperatively. Patients whose second hour blood D-Xylose was below 20 mg/dl and whose 5 hours' urine D-Xylose was below 5 gr were regarded as having defective intestinal absorption. Intestinal absorption was compared with clinical, laboratory and hemodynamic data. Intestinal absorption was defective in 30 patients (%68.18). Except one of the patients blood and urine D-Xylose levels were at normal levels on the third postoperative day. The patient with defective intestinal absorption on the third postoperative day was died due to multiple organ failure. Twenty-four of the 30 patients with defective intestinal absorption, had abdominal symptoms. The most commonly encountered symptoms were abdominal pain and nausea. There was no statistically significant correlation between absorption defect and age, sex, adjunctive treatment, body weight, cardiac output, hematocrit, intraoperative hypothermia, hypotension, central venous pressure, CPB time, cross clamp time and period of mechanical ventilation. The relation with cardiac index was marginally significant ( $p = 0.0633$ ); and the relation with coronary artery bypass grafting was statistically significant ( $p = 0.044$ ). There was no statistical relation between absorption defect and the period of intensive care unit or postoperative hospital stay. In conclusion, CPB procedure damages the intestinal absorption reversibly. This damage is more significant in patients who undergone coronary artery bypass grafting and whose cardiac index is low. This should be remembered when oral drug therapy or enteral feeding is to be started immediately after CPB. If absorption defect continues, it may cause endotoxemia and multiple organ failure leading to death; as was seen in one of our patients. Intestinal disorders, absorption: Malabsorption syndromes }" "The Effects of Cardiopulmonary Bypass on Intestinal Absorption"

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## "P P 18 0471" P 18 0471 Effect of (R){ $\alpha$ }-Methylhistamine on Duodenal Bicarbonate Secretion in the Rat

\*G. Coruzzi, G. Bertaccini

Institute of Pharmacology, University of Parma, Italy Previous studies from our laboratory showed that the histamine H<sub>3</sub> receptor agonist (R){  $\alpha$  }-methylhistamine (MHA) is able to protect the gastric mucosa against the damaging effects of different noxious stimuli (absolute ethanol, aspirin and stress). Electron microscopy studies revealed that both adherent and intracellular mucus are increased by MHA. In order to investigate other possible mechanisms, the effect of MHA on alkaline secretion was studied in the anaesthetized rat, in comparison with PGE<sub>2</sub>, cholinergic agents and intraluminal 10 mM HCl. Under urethane anaesthesia a duodenal loop was perfused with oxygenated saline at 37°C and the alkaline output was measured by titration at pH 6 with 10 mM HCl. MHA (3–30  $\mu$ mol/kg i.v.) induced a dose-dependent increase in bicarbonate secretion, with a maximum effect of 0.8  $\mu$ Eq HCO<sub>3</sub><sup>-</sup>/10 min. MHA at 100  $\mu$ mol/kg i.v. did not cause any effect. The novel H<sub>3</sub> receptor agonist impropip (3–100  $\mu$ mol/kg i.v.) induced negligible and variable effects, being the basal secretion slightly increased or decreased. The stimulatory effect of MHA 30  $\mu$ mol/kg i.v. was greatly enhanced (2.15  $\mu$ Eq HCO<sub>3</sub><sup>-</sup>/10 min) in the presence of the  $\alpha$ <sub>2</sub> adrenoceptor antagonist, yohimbine 100  $\mu$ g/kg/h; moreover this compound unmasked a stimulatory effect of MHA 100  $\mu$ mol/kg i.v., indicating that high doses of MHA can activate  $\alpha$ <sub>2</sub> adrenoceptors with consequent inhibition of bicarbonate secretion. These data indicate that MHA can influence bicarbonate secretion from the rat duodenum by opposite mechanisms: the involvement of histamine H<sub>3</sub> receptors in the stimulatory effect of MHA is still unclear; whereas the activation of inhibitory  $\alpha$ <sub>2</sub> adrenoceptors seems to be established. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Hormones and receptors: Receptor characterization } "Effect of (R)alpha-Methylhistamine on Duodenal Bicarbonate Secretion in the Rat"

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## "P P 18 0472" P 18 0472 Plasma Post-Absorptive Citrulline as a Biochemical Marker of Enterocyte Mass

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<sup>1</sup> Biochimie A, Hospital St-Antoine, Paris, France In animals models citrulline, an amino acid (AA) not incorporated into proteins, is specifically produced by enterocytes from glutamine (pyrroline 5 carboxylate synthase pathway); then citrulline is metabolized into arginine by the kidney (J Biol Chem 1994, 269, 32667). *Aim:* To test the hypothesis that plasma citrulline concentration give an index of enterocyte mass in non-clinically stressed short bowel (SB) patients on free oral diet, not on steroids and without visceral deficiency other than severe small bowel disease. *Methods:* Plasma venous AA concentrations were analyzed in post-absorptive state by ion exchange chromatography ( $\mu\text{mol/l}$ : mean – SD) in SB patients submitted to Parenteral Nutrition (PN) for more than 6 months with standard glutamine and citrulline-free AA solutions (n = 37), in SB patients without PN (n = 8), and in controls (n = 57); in addition 16 SB patients on PN had simultaneous plasma venous and arterial AA determination. Enterocyte mass was evaluated on a *in vivo* one dimension measurement of small bowel length (SBL) by opisiometer on X-ray films. *Results:* Plasma citrulline was 17 – 9\* in SB patients on PN, 33 – 15 in SB patients without PN, and 42 – 13 in controls. Plasma arginine concentration was decreased in SB patients (45 – 21\* vs 75 – 16 in controls) (\*p < 0.05 vs controls). Plasma citrulline concentration was not related to PN duration, to body mass index, to presence of colon, to AA solution and to site (venous vs arterial) of sampling but was related to albuminemia (p < 0.01) and to SBL (p < 0.0001). In multivariate analysis plasma citrulline remained only related to remnant SBL (p < 0.0001, r = 0.85) while presence of PN and albuminemia became non significant. *Conclusion:* Decrease of plasma citrulline in short bowel patients is compatible with the concept of a decrease in citrulline production due to the reduction of enterocyte mass. These data suggest that post-absorptive plasma citrulline is, independently of nutritional status, a biochemical marker of enterocyte mass. Nutrition: Metabolism Intestinal disorders, absorption: Malabsorption syndromes Clinical practice: Management strategy } "Plasma Post-Absorptive Citrulline as a Biochemical Marker of Enterocyte Mass"

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"P P 18 0473" P 18 0473 **Luminal Administration of Omeprazole Increases Human Proximal Duodenal Mucosal Bicarbonate Secretion**

\*J. Hillings<sup>1</sup>, A. Mertz-Nielsen, K. Bukhave, J. Rask-Madsen

Depts. of Gastroenterology and Clinical Physiology, Hvidovre Hospital, University of Copenhagen, Denmark

Dept. of Biochemistry and Nutrition, Technical University of Denmark, Denmark We have previously demonstrated that suprapharmacological doses of the proton pump inhibitor, omeprazole [1] (OME), used for acid suppression of the stomach, result in higher than normally observed rates of proximal duodenal mucosal bicarbonate secretion (PDMBS) in healthy volunteers. Apparently, the effect was independent of gastric acid secretion. To study whether OME itself, rather than a sulfenamide, may act on the duodenal mucosa we have assessed the effects of duodenal perfusion with half-maximum inhibitory concentrations or higher of OME for inhibition of *in vitro* stimulated human gastric glands [2]. *Methods:* A 3-cm segment of proximal duodenum was isolated by occluding balloons and continuously perfused (2 ml/min, 154 mM NaCl, 10 <sup>51</sup>CrEDTA), simultaneously with the stomach (5 ml/min, 154 mM NaCl, phenol red), in 12 healthy volunteers for a 1 h basal period followed by a 1 h test period. In the test period 3.45 mg/100 ml (n = 5) or 34.5 mg/100 ml (n = 7) OME was added to the perfusion solution. HCO<sub>3</sub> was determined in the duodenal effluents using a method corresponding to the back-titration method. Determination of phenol red, <sup>51</sup>CrEDTA and trypsin served as markers for recovery or contamination. *Results:* Duodenal perfusion with OME did not affect gastric pH or acid output. No significant change in PDMBS was observed after perfusion with OME 3.45 mg/100 while 34.5 mg/100 ml caused an increase in HCO<sub>3</sub> secretion from 130 – 14 <sup>5</sup>mol/h cm to 190 – 17 <sup>5</sup>mol/h cm (mean – SEM) (p = 0.008; t-test). *Conclusions:* These results demonstrate that intraduodenally administered OME, in doses insufficient to inhibit gastric acid secretion, causes a prompt increase in PDMBS. Thus, epithelial, glandular or heterotopic parietal cells lining the duodenal wall may be the site of proton pump inhibition.

Reference: Mertz-Nielsen A, Hillings<sup>1</sup> J, Bukhave K, Rask-Madsen J. Gut 1996; 38: 6–10

Elander B, Fellenius B, Leth R, Olbe L, Wallmark B. Scand J Gastroenterol 1986; 21: 268–72  
Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Luminal Administration of Omeprazole Increases Human Proximal Duodenal Mucosal Bicarbonate Secretion"

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## "P P 18 0474" P 18 0474 Mechanism of the Inhibitory Effect of Peptide YY on VIP-Stimulated Jejunal Fluid Secretion in Rats

\*A. Souli, O. Presset, A. Tsocas, J. Chariot, C. Roz

INSERM U410, Facult\ 'e9 de M\ 'e9decine X. Bichat, BP 416, 75870 Paris, France The hormonal peptide YY (PYY) potently inhibits net electrolyte and water secretion in the intestine in humans and in different animal species. In vitro data suggest a direct effect on enterocytes while some in vivo results suggest an indirect nervous mechanism. The aim of the present work was to study the mechanisms of the inhibitory effect of PYY on VIP-stimulated jejunal fluid secretion in rats. *Methods.* Net jejunal fluid secretion was studied in vivo in pentobarbital-anesthetized rats equipped with a closed jejunal loop. A proximal jejunal loop (20 cm long) was tied off and filled at time zero with 2 ml 0.9% saline. Jejunal secretion was stimulated by i.v. infusion of VIP (30 \b5g/kg.h for 30 min). After 30 min, the rats were sacrificed, the loop harvested, and the amount of absorbed or secreted fluid was calculated by weighing the full and empty loop. PYY (3–100 pmol/kg) was i.v. injected 15 min before time zero. Pharmacological antagonists were i.v. injected 5 min before PYY. In one group of animals, bilateral truncal cervical vagotomy was carried out 30 min before time zero. *Results.* 1. PYY inhibited VIP-stimulated jejunal net water flux in a dose-related manner (ID 50 # 6 pmol/kg). 2. The inhibitory effect of PYY (10 pmol/kg) was suppressed by tetrodotoxin, hexamethonium, and decreased (46%) by vagotomy. 3. The inhibitory effect of PYY was suppressed by BMY 14802, a specific antagonist of sigma receptors, and decreased (75%) by idazoxan, an antagonist of alpha-2 adrenoreceptors and imidazoline-1 receptors. 4. Devazepide, a CCK<sub>A</sub> antagonist, and L-NAME, a NO synthase inhibitor, did not modify the effect of PYY. *Conclusions.* 1. PYY prevents VIP stimulation of jejunal net water flux in rats. 2. This effect is mediated by a neural cholinergic nicotinic pathway, mediated in part by the vagus nerves. It involves sigma and/or alpha-2 receptors. 3. NO and CCK<sub>A</sub> receptors are not implicated in this effect. Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport } "Mechanism of the Inhibitory Effect of Peptide YY on VIP-Stimulated Jejunal Fluid Secretion in Rats"

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## "P P 18 0475" P 18 0475 Five-Hydroxytryptamine Receptor Antagonist Reduces Salmonella-Induced Net Fluid Accumulation in Porcine Small Intestine

\*M.B. Hansen, M.L. Grønndahl, G.M. Jensen, C. Nielsen, J.E. Olsen, E. Skadhauge

Departments of Anatomy & Physiology and Microbiology, The Royal Veterinary and Agricultural University, Copenhagen, Denmark *Background and purpose.* The pathophysiological mechanism(s) of Salmonella is not clear but seems to involve the release of a cholera toxin (CT)-like enterotoxin. Five-hydroxytryptamine (5-HT) is released locally in the intestine by CT and acts as a neurotransmitter and paracrine secretagogue in the small intestine in most species. Accordingly, 5-HT<sub>3</sub> receptor antagonists are potent inhibitors of CT-induced intestinal secretion. We *hypothesize*, that Salmonella induces intestinal secretion through a CT-like mechanism with a concomitant release of 5-HT. The purpose of the study was to evaluate the effect of a 5-HT<sub>3</sub> receptor antagonist on Salmonella typhimurium (St)-induced fluid accumulation. *Materials and methods.* 9 weeks old female Danish Landrace/Yorkshire pigs were used. Total anaesthesia was achieved by intravenous infusion of propofol (induction), continuous inhalation of isoflurane and cutaneous infiltration with bupivacaine. Supporting treatments included continuous intravenous infusion of Ringer-acetate liq. and artificial controlled respiration. Jejunal and ileal ligated loops were either unfilled (U), filled with 10 ml of Argenzio-4 test solution alone (T) or filled with test solution containing St phag. T123389-1 in 10<sup>10</sup> colony forming units. Loops were removed from the peritoneal cavity after 8 hrs and the net amount accumulated fluid was determined. Ondansetron (Glaxo-Wellcome, UK) is a 5-HT<sub>3</sub> antagonist and was injected subcutaneously (200 μg kg<sup>-1</sup>) before surgery and 6 hrs later. Results are expressed as means – SEM. N represents number of animals, and n the number of loops. Data were analyzed by Student's unpaired t-test. P < 0.05 as significant level (\*). *Results.* U and T loops accumulated no significant net amounts of fluid in any experiments (data not shown). Data for loops exposed to St accumulated the following amounts (mg fluid pr. mg dry loop weight): Controls (N = 5) Ondansetron-treated (N = 5) Jejunum 5.2 – 0.6 (n = 12) 3.1 – 0.4 (n = 30) \*Ileum 3.8 – 0.8 (n = 10) 2.2 – 0.3 (n = 29) \* *Conclusion.* These data *demonstrate* that ondansetron reduces the net fluid accumulating effect of ST by about one third in porcine small intestine. Furthermore, the results *suggest* the release of 5-HT and the activation of 5-HT<sub>3</sub> receptors in the secretory pathway of St, supporting the hypothesis of St inducing secretion partly via a CT-like mechanism. Intestinal disorders, absorption: Pathophysiology of diarrhea Hormones and receptors: Receptor characterization } " "Five-Hydroxytryptamine Receptor Antagonist Reduces Salmonella-Induced Net Fluid Accumulation in Porcine Small Intestine"

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## "P P 18 0476" P 18 0476 Comparison of the Antisecretory Effect of Endogenous Forms of Peptide YY on Fed and Fasted Rat Jejunum

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CNAM and INSERM U290, Hospital Saint-Lazare, 75010 Paris, France Its is intriguing that the antisecretory peptide YY is present in plasma in two forms PYY1-36 during fasting and PYY3-36 in fed state. In addition PYY3-36 has been found in human and rabbit blood within 30 min at the beginning of the meal, when the peak of water and electrolytes secretion occurs in the duodeno-jejunum. The aim of this study was therefore 1) to compare the antisecretory effect of PYY1-36 and PYY3-36 in fed and fasted rat jejunum 2) to assess the effect of PYY3-36 on secretion induced by different intestinal peptides. The variations in short-circuit current ( $I_{sc}$ ) due to the modification of ionic transport across jejunum were assessed *in vitro*, using Ussing chambers. In fasted rats, both PYY1-3- and PYY3-36 at  $2 \times 10^{-7}$  M in serosal medium induced a similar decrease in  $I_{sc}$  ( $-19 - 2.36$  versus  $-16.6 - 1.44$   $\mu A/cm^2$ ,  $p < 0.001$  for PYY3-36 and  $1.32$   $\mu Eq/hr.cm^2$ ,  $p < 0.001$  for PYY1-36). In addition, when a second stimulation with  $10^{-7}$  M PYY3-36 was performed 30 min after a previous challenging exposure at  $10^{-8}$  M, the decrease in  $I_{sc}$  was smaller than the one obtained after 60 min ( $-11.64 - 2.64$  versus  $-24 - 3$   $\mu A/cm^2$ ,  $p < 0.05$ ), suggesting a tachyphylaxis phenomenon. The increase in  $I_{sc}$  induced by  $2 \times 10^{-7}$  M gastrin I, motilin, pancreatic polypeptide, peptide Histidine Isoleucine, secretin, helodermin, substance P, atrial natriuretic factor (1-28), and vasointestinal peptide was abolished by  $2 \times 10^{-7}$  M PYY3-36 in fasted rat ( $p < 0.001$ ). In fed animals, PYY3-36 had no significant effect on  $I_{sc}$  ( $+1.65 - 2.36$   $\mu A/cm^2$ ), and the antisecretory effect of PYY1-36 was present but blunted ( $-10 - 1.01$   $\mu A/cm^2$ ). Net chloride secretion was also reduced by PYY1-36 to  $0.71$   $\mu Eq/hr.cm^2$   $p < 0.05$ , whereas PYY3-36 had no effect ( $-0.07$   $\mu Eq/hr.cm^2$ ,  $p > 0.05$ ). In fasted rats, this study confirms the antisecretory effect of PYY1-36, and shows that the endogenous form PYY3-36, displays a similar effect. In addition, PYY3-36, reversed secretion induced by various intestinal peptides. In fed rats, PYY3-36 the major form of postprandial circulating PYY has no antisecretory effect *in vitro*. This finding indicate that the 2 circulating forms of PYY does not display the same activity in fed animals. Although 3-36 PYY has an antisecretory effect against secretory peptides in fasted rats, the jejunal epithelium of fed rats does not respond to 3-36 PYY until 60 min after challenge. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Epithelial transport Hormones and receptors: Receptor characterization }"

"Comparison of the Antisecretory Effect of Endogenous Forms of Peptide YY on Fed and Fasted Rat Jejunum"

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"P P 18 0477" P 18 0477 **Pentoxifylline (PTX) Inhibits Cytokine Secretion by Peripheral Mononuclear Cells (PBMC) and Intestinal Biopsies in Inflammatory Bowel Diseases (IBD)**

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<sup>2</sup> Dept of Immunology, Immunopharmacology and Pathology, University of Strasbourg, France

<sup>4</sup> CNRS U491, University of Strasbourg, France Inflammatory cytokines are involved in the pathogenesis of IBD. In recent studies PTX has been shown to decrease tumor necrosis factor- $\alpha$  (TNF) secretion by normal PBMC *in vitro* and *in vivo*; on the other hand, anti-TNF antibodies were shown to be efficient in a pilot study of Crohn's disease therapy. Therefore we studied the effects of PTX upon TNF, interleukin (IL)-1 $\beta$  (IL1), IL6 and IL8 secretions of PBMC and intestinal biopsies in Crohn's disease (CD) and ulcerative colitis (UC) patients. *Methods*: PBMC of 11 CD and 7 UC patients were separated by mean of a Ficoll density gradient and cultured in standard medium over a 24 hour period ( $10^6$  cells/well, 95% air, 5% CO<sub>2</sub>, 37°C) with or without PTX (1, 10, 100  $\mu$ g/ml). Biopsies from inflamed (CD: 11, UC: 5) and morphologically (macroscopically and microscopically) normal CD intestinal mucosa (n = 6) underwent the same procedure. Supernatants were collected, filtered and frozen (-70°C) until cytokine assays (ELISA using 2 monoclonal antibodies, J.S. Kenney, Antibody Solutions, Half Moon Bay, CA, USA). *Results*: 1) PTX inhibited significantly and in a dose-dependent manner the TNF production by PBMC of IBD patients (79% of basal production at 1  $\mu$ g/ml of PTX, 66% at 10  $\mu$ g/ml and 46% at 100  $\mu$ g/ml). There was no difference between CD and UC. 2) IL8, 6, 1 and TNF concentrations in organ culture supernatants were increased for both involved and non-involved biopsies compared to normal subjects. 3) PTX (1, 10 and 100  $\mu$ g/ml) significantly decreased basal IL1 and TNF secretions (approximately 40%) by involved CD or UC, and unaffected CD mucosa. This effect was not different between CD and UC inflamed mucosa or between CD affected and unaffected mucosa. IL6 and 8 were less modified by PTX. *Conclusion*: PTX decreased TNF and IL1 secretions of inflamed intestinal mucosa organ cultures from CD and UC, whereas only TNF secretion by PBMC was affected. Interleukin-6 and IL8 secretions were less modified. In addition PTX decreased the raised TNF, and in a lower degree IL1, productions of biopsies from endoscopically and microscopically normal intestinal areas. These effects indicate a potential interest for PTX or related compounds in IBD therapy. Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Pentoxifylline (PTX) Inhibits Cytokine Secretion by Peripheral Mononuclear Cells (PBMC) and Intestinal Biopsies in Inflammatory Bowel Diseases (IBD)"

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## "P P 18 0478" P 18 0478 Apical Effect of Diosmectite on the Alteration in Intestinal Epithelial Barrier Induced by Basal TNF{ a}

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<sup>2</sup> IPSEN 24, rue Erlanger 75016 Paris, France In many digestive diseases, including infectious diarrhea, inflammatory bowel diseases and food allergy, the intestinal barrier is weakened by the release of proinflammatory cytokines due to the abnormal activation of the epithelial cells and underlying immune system. This study investigate the protective effect of apical mucosal diosmectite on the intestinal dysfunction induced by the proinflammatory cytokine TNF $\alpha$ . Filter-grown monolayers of the intestinal cell line HT29-19A, were incubated, for 48 h, in the presence of 10 ng/ml TNF $\alpha$  and 5 U/ml IFN $\gamma$ , in the basal medium. Afterward, diosmectite (1, 10 or 100 mg/ml) was placed in the apical medium during 1 hour. The intestinal function was then assessed in Ussing chambers by measuring the ionic conductance (G), and apico-basal fluxes of <sup>14</sup>C-mannitol fluxes (J<sub>man</sub>) and intact horseradish peroxidase (J<sup>HRP</sup>). In control intestinal monolayers, diosmectite did not modify significantly G, J<sub>man</sub> and J<sup>HRP</sup>. After incubation with TNF $\alpha$  and IFN $\gamma$ , the intestinal function was altered as attested by an increase in G (22.8  $\pm$  3.7 vs 9.6  $\pm$  0.5 mS/cm<sup>2</sup>), J<sub>man</sub> (33.8  $\pm$  7.5 vs 7.56  $\pm$  0.67  $\mu$ g/h.cm<sup>2</sup>) and J<sup>HRP</sup> (1.95  $\pm$  1.12 vs 0.14  $\pm$  0.04  $\mu$ g/h.cm<sup>2</sup>) compared to control values. G and J<sub>man</sub> were highly correlated suggesting that the increase in permeability was paracellular. Treatment with diosmectite (optimal concentration 10 mg/ml) restored all the parameters to values not statistically different from control values. In conclusion, these results confirm that basal TNF $\alpha$  disrupt the intestinal barrier at the tight junctional level, and further indicate that apical diosmectite fully counteract such deleterious effect. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Intestinal disorders, absorption: Pathophysiology of diarrhea } " Apical Effect of Diosmectite on the Alteration in Intestinal Epithelial Barrier Induced by Basal TNF $\alpha$ "

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"P P 18 0479" P 18 0479 **Topical Mucosal Production of Interleukin-1 Beta, Interleukin-6, Interleukin-8, Tumor Necrosis Factor Alfa and Interleukin-2-Soluble Receptor in Human Small and Large Bowel. A Pilot Study**

\*J. Bures, L. Pl'edskov'e1, S. Rejchrt, P. Zivn'fd, M. Sirok'fd, V. Palicka

Charles University Teaching Hospital, Hradec Kr'e1lov'e9, Czech Republic *Purpose of the study* was to evaluate different topical mucosal cytokine production of small and large bowel. *Methods.* Five patients [1 man, 4 women, aged 23–48] entered the study. Five biopsy specimens for *in vitro* culture and other five ones for histology were taken from each person during routine small bowel enteroscopy (from distal duodenum [D] and jejunum [J]) or routine colonoscopy (from rectum [R] and large bowel [LB]). Patient No 1 (functional dyspepsia) had normal both endoscopic and histological findings of jejunum. Patient No 2 (cow-milk allergy) had a severe chronic inflammation of jejunum. Patient No 3 (functional dyspepsia) had normal both endoscopic and histological appearance of large bowel. Patient No 4 had severe large bowel oxiuriasis. Patient No 5 had typical endoscopic and histological findings of severe ulcerative colitis. Biopsy specimens were cultivated in RPMI medium for 23 hours. Cytokines were measured in homogenate supernatants by means of ""sandwich"" EIA using Quantikine kits [R + D Systems] and kit of Immunotech: interleukin-1{ b } [IL-1{ b }], interleukin-6 [IL-6], interleukin-8 [IL-8], tumor necrosis factor- { a } [TNF- { a } ] and interleukin-2-soluble receptor [sIL-2R]. *Results* are given as median (in pg/ml, except sIL-2R in pM): Pat Biopsy IL-1{ b } IL-6 IL-8 TNF- { a } sIL-2R 1 D 5.37 0 0 2.61 28.301 J 2.74 3.69 0 19.00 32.502 D 3.08 12.10 263.0 – 36.402 J 23.60 > 300 > 2,000 – 80.303 R 0 0 0 8.57 85.303 LB 2.78 10.20 0 8.57 26.104 R 50.20 > 300 > 2,000 9.16 7.634 LB 32.50 > 300 1,730.0 7.03 1.765 R 7.39 > 300 > 2,000 3.29 05 LB 17.70 > 300 1,410.0 3.51 1.48 *Conclusions.* Cytokines are detectable in homogenate supernatants of small and large bowel specimens culture. They seem to reflect pathological mucosal changes in both small and large bowel. Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation Endoscopy, specific: Enteroscopy }" "Topical Mucosal Production of Interleukin-1 Beta, Interleukin-6, Interleukin-8, Tumor Necrosis Factor Alfa and Interleukin-2-Soluble Receptor in Human Small and Large Bowel. A Pilot Study"

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## "P P 18 0480" P 18 0480 **Neuronal Activity and CRF Receptor Gene Transcription in the Brain of Rats with TNBS-Induced Colitis**

\*B. Bonaz, J. Fournet, C. Feuerstein

Lab. Neurophysiology and Dept. of Gastroenterology, 38043 Grenoble cedex 09, France Colitis induced in rats by trinitrobenzene sulfonic acid (TNBS) is an immune challenge [1]. The immune-, endocrine- and central nervous systems communicate each other through cytokines, steroids and neuropeptides [2]. Brain CRF is one of these neuropeptides and acts through CRF receptors (CRF-R). *Purpose:* to study in the rat brain 1) neuronal pathways activated by TNBS-induced colitis using c-fos mRNA as a marker of neuronal activation, 2) the transcription of the genes encoding CRF-R1 [3] and CRF-R2alpha [4], 3) the localization of these transcripts in CRF perikarya in the paraventricular nucleus (PVN) of the hypothalamus, the main source for CRF in the brain. *Methods:* TNBS (30 mg in 50% ethanol, Sigma 5% weight/vol) or saline was administered in the colon of conscious fasted rats chronically fitted with a colonic catheter (10 cm proximal to the anus). Rats were fixed 1, 2, 3, 4, 6, 12 and 24 h later. Coronal frozen sections of the brain and spinal cord were cut and the rat c-fos, CRF-R1 and CRF-R2alpha mRNAs were assayed by *in situ* hybridization (ISH) using <sup>35</sup>S-labeled riboprobes [5]. Localization of these transcripts in CRF perikarya of the PVN was determined using a combination of immunocytochemistry and ISH [5]. *Results:* in TNBS-induced colitis 1) c-fos mRNA was expressed in the spinal cord, nucleus tractus solitarius, area postrema, lateral reticular nucleus, parabrachial nucleus, locus coeruleus, thalamus, arcuate nucleus, supraoptic nucleus, supraoptic and PVN, amygdala, subfornical organ, bed nucleus of the stria terminalis. This expression peaked at 1 h to 3 h, then progressively decreased to completely vanish after 12–24 h. 2) CRF-R1 mRNA appeared at 2 h in the parvo-PVN, was highly expressed at 3–6 h, decreased at 12 h and totally vanished at 24 h. 3) No change of the CRF-R2alpha mRNA was observed in the limbic structures, 4) In the PVN, numerous CRF perikarya expressed c-fos and CRF-R1 transcripts. *Conclusions:* TNBS-induced colitis is followed by a neuronal activation in brain nuclei involved in autonomic and stress responses. CRF pathways are selectively activated in the PVN mainly through CRF-R1 receptors.

Reference: *Gastroenterology* 87: 1344–1350, 1984.

*Progress Neurobiol.* 44: 397–432, 1994.

*Proc. Nat. Acad. Sci.* 90: 8967–8971, 1993.

*Endocrinology* 136: 4139–4142, 1995.

*J. Neurosci.* 15: 2680–2695, 1995. Hormones and receptors: Brain gut axis Hormones and receptors: Receptor characterization Immunology and microbiology: Inflammation } "Neuronal Activity and CRF Receptor Gene Transcription in the Brain of Rats with TNBS-Induced Colitis"

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"P P 18 0481" P 18 0481 **Differential Effects of Superoxide and Hydrogen Peroxide on Transepithelial Permeability and Heat Shock Expression in Cultured Intestinal Cells.**  
**Ries, C. Walter, B. Gebhardt, A. Schmitt, W.F. Caspary, J. Stein**

II. Department of Internal Medicine, Div. of Gastroenterology, J.W. Goethe-University, 60590 Frankfurt/Main, Germany *Background:* Reactive oxygen metabolites (ROM) are implicated in various pathologies in the GIT, such as inflammation or the ischemia-reperfusion syndrome. To improve our understanding of how oxidate stress affects intestinal cell function, we compared the effects of the hypoxanthine-xanthine oxidase system (X-XO) and that of H<sub>2</sub>O<sub>2</sub> on transepithelial permeability and heat shock protein expression in the cultured intestinal cell line CaCo-2. *Methods:* Cells were grown in permeable supports and mounted in Ussing chambers. Apically added FITC-Dextran 4400 D was used for measuring epithelial permeability. Data were expressed as FITC-dextran basolateral concentration as a percent of apical concentration after 240 min. Potential difference (PD) and short-circuit current (I<sub>sc</sub>) were monitored and transepithelial resistance (TER) was calculated by Ohm's law. Results are given as percent of the baseline resistance. To establish optimal HSP induction <sup>35</sup>S-methionine incorporation was assessed. Western analysis and 2-dimensional electrophoresis confirmed induction of HSP-70. LDH-release was measured photometrically. *Results:* Basolateral FITC-Dextran progressively accumulated even under control conditions (0.057 – 0.012), TER decreased slightly (88.2 – 4.1). The addition of 0.02 U or 0.2 U XO + 1 mM xanthine showed a dose dependent increase in transepithelial permeability (0.141 – 0.077%; p < 0.05/0.908 – 0.330%; p < 0.001), but only at higher concentrations a decrease of TER (89.4 – 5.3%; p > 0.05/68.2 – 2.8%, p < 0.001), compared with controls. In contrast addition of H<sub>2</sub>O<sub>2</sub> led to a significantly decrease of TER both at 0.05 mM (61.5 – 6.1; p < 0.01) and 0.1 mM (60.4 – 3.4; p < 0.01), while transepithelial permeability showed only a moderate increase (0.228 – 0.026; p < 0.05/0.374 – 0.094; p < 0.05). Compared to controls only exposure to XO (0.2 U/ml) showed a significantly (6-fold; p < 0.05) induction of HSP70 synthesis. In contrast LDH release was significantly (2.6-fold; p < 0.01) increased after H<sub>2</sub>O<sub>2</sub> (0.1 mM) exposure (0.2 U XO: 1.3-fold; p < 0.05). *Conclusion:* This study shows differential effects of superoxide and hydrogen peroxide on transepithelial permeability and heat shock protein expression in cultured intestinal cells implicating differential mechanism of ROM as mediators of epithelial dysfunction and injury. } "Differential Effects of Superoxide and Hydrogen Peroxide on Transepithelial Permeability and Heat Shock Expression in Cultured Intestinal Cells"

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"P P 18 0482" P 18 0482 **Induction of GST-PI by Short Chain Fatty Acids in the Intestinal Cell Line Caco-2O. Schröder, G. Oremek<sup>2</sup>, M. Lorenz<sup>1</sup>, W.F. Caspary,**

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Glutathione S-transferases (GSTs) are a multigene family of detoxification and metabolising enzymes, which have been linked with the susceptibility of tissues to environmental carcinogens. Beside their role as the main energy source in the colonic mucosa, short chain fatty acids (SCFAs) were found to act as potent anti-proliferative and differentiating agents in various cancer cell lines. The objective of this study was to evaluate the effects of SCFAs on the induction of GSTpi in the intestine as a possible new anticarcinogenic mechanism of SCFAs. Studies were performed in Caco-2 cells, a cell line resembling functionally-normal enterocytes. Cells, cultured in DMEM supplemented with 10% fetal calf serum, were studied from day 0 dpc (days post confluence) until 21 dpc and culture. SCFAs (acetate, propionate, butyrate) were added to give a final concentration of 5 mmol/L. At 0, 3, 6, 9, 15, and 21 dpc, protein, lactate dehydrogenase (LDH), alkaline phosphatase (aP) and GSTpi were measured. Butyrate supplementation significantly ( $p < 0.01$ ) increased GSTpi levels compared to controls in a concentration dependent manner. The effect was detectable within 3 dpc with a maximum at 14 dpc. In contrast to butyrate, the other SCFAs tested had no (acetate) or little effect (propionate). In *conclusion* our data suggests that the anticancer effect of butyrate in part may be based on the induction of GSTpi activity resulting in an enhanced detoxification capacity of the gut. } " "Induction of GST-PI by Short Chain Fatty Acids in the Intestinal Cell Line Caco-2"

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## "P P 18 0483" P 18 0483 **Conditionally Immortalized Rat Fetal Intestinal Epithelial Cell Line (2/4/A1): A Model for Studying Enterocyte Differentiation**

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Gastroenterology Unit, Guy's Hospital, UMDS of Guy's and St Thomas's Hospitals, London, U.K. *Background.* Intestinal epithelial cell culture models originate from either tumour cells or immature crypt cells. They maintain malignant and/or non-differentiated phenotype and do not express all features of the intestinal epithelial cell differentiation. 2/4/A1 cells, isolated from rat fetal intestinal epithelium and transfected with thermolabile SV40 large T antigen (pzipSV40tsa58 mutant), proliferate at 33°C, but eliminate the antigen, cease proliferating and undergo apoptotic cell death after being switched to 39°C. *Aim.* We evaluated proliferation and differentiation of 2/4/A1 cells, seeded at the permissive (33°C), intermediate (37°C) and non-permissive temperature (39°C), in order to establish a cell culture model which will follow the events from proliferation to terminal differentiation and apoptosis, similar to normal enterocytes. *Methods.* 2/4/A1 cells were maintained under serum-free conditions. Proliferation was assessed by thymidine incorporation assay, and differentiation was examined by brush border enzyme assays, transmission electron microscopy, and immunocytochemistry. Apoptosis was evaluated by staining with DAPI (diamino-phenylindole hydrochloride) and fluorescence microscopy. *Results.* 2/4/A1 cells grown at permissive temperature proliferated rapidly, forming multilayers consisting of immature enterocytes. The cells grown at 37°C and 39°C required extracellular matrix in order to attach and avoid rapid apoptotic death. Laminin-containing matrices enabled prolonged cell survival at these temperatures, and were significantly more efficient than collagens I and IV and fibronectin in either cell attachment and in delaying apoptosis at 39°C. At 37°C 2/4/A1 cells formed polarized monolayers with differentiated tight and adherence junctions; their tight junctions had functional integrity similar to that of the human small intestine. The activities of brush border enzymes increased significantly at 37 and 39°C in comparison to 33°C, indicating a considerable degree of the apical membrane differentiation. *Conclusion.* 2/4/A1 cell line might be a suitable model to study the factors involved in enterocyte differentiation Oncology, general: Proliferation, carcinogenesis Intestinal disorders, absorption: Enterocyte biology Oncology, specific: Small bowel } "Conditionally Immortalized Rat Fetal Intestinal Epithelial Cell Line (2/4/A1): A Model for Studying Enterocyte Differentiation"

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"P P 18 0484" P 18 0484 **Are Mutation of the Human Ileal Sodium-Dependent Bile Acid Transporteur (HISBT) Gene Implicated in the Genetic Susceptibility to Crohn's Disease (CD)?** D. Heresbach, M. Alizadeh, M. Pagenault, M. Gosselin, B. Genetet, G. Semana, J.F. Bretagne

Department of Gastroenterology and University Laboratory of Immunology, 35033 Rennes Recent studies have shown a single C to T transition resulting in a proline to serine substitution (P 290 S) at HISBT cDNA and genomic level in a CD patient. The inheritance of this mutation in the proband's family was confirmed by DNA sequencing; moreover, taurocholate uptake activity was abolished in HISBT (P 290 S)-transfected COS cells. An increased faecal excretion of taurine conjugates has been described in patients with inflammatory bowel disease in the active phase and in children during clinical remission. *The aim* of our study was to determine the frequency of this mutation (P 290 S) in a population of CD patients. *Patients and methods:* One hundred forty one CD patients and ethnically matched controls were included in this study: 8 patients with ulcerative colitis (UC) with age at onset below 16 years were also analyzed. DNA was isolated from peripheral blood leucocytes using salting out method. HISBT polymorphism was analyzed after DNA amplification by PCR using a sense primer 5{\a2}ACACGCAGCTATGTTCCACCATCG3' corresponding to HISBT nucleotides 915-939 and a antisense primers 5{\a2}TGAAATCGGATTGGCATGATTCCT3' corresponding to the flanking intron. After an initial denaturation step at 94\b0C for 5 min, PCR amplification was performed with 100 ng of genomic DNA for 30 cycles using an annealing temperature of 64\b0C. Brs-B1 digestion resulted in fragments that either remained intact (P at position 290 = allele 1) or were cut in two fragments (S at position 290 = allele 2). Fragments were analyzed by electrophoresis on 3% agarose gels containing 0.1% ethidium bromide. *Results:* Only one control, and 2 CD patients presented the HISBT mutation at position 290. All this 3 individuals were heterozygous for this gene. None of the UC patients or of CD patients with age at onset of symptoms below 16 years harbor the mutation. *Conclusions:* HISBT (P 290 S) was rare in controls and CD patients whatever age at onset of CD. These data argue against HISBT in pathogenesis of CD. Intestinal disorders: IBD, etiology and genetics }" "Are Mutation of the Human Ileal Sodium-Dependent Bile Acid Transporteur (HISBT) Gene Implicated in the Genetic Susceptibility to Crohn's Disease (CD)?"

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"P P 19 0485" P 19 0485 **The Amelioration of Acute Pancreatitis Using a TNF-Metalloproteinase Inhibitor**

\*A.N. Kingsnorth, P. Skaife, M. Wood<sup>1</sup>, N.S. Kulkarni<sup>2</sup>

Department of Surgery, University of Liverpool

<sup>2</sup> Department of Pathology, University of Liverpool

<sup>1</sup> British Biotechnology Laboratories Tumour necrosis factor (TNF) is a potent pro-inflammatory cytokine that has been shown to be an important mediator in the development of both local and systemic sequelae associated with severe acute pancreatitis. The effect of a TNF metalloproteinase inhibitor BB1101, known to be active at the post-translational step in TNF production, was studied in the microvascular ischaemic model of acute pancreatitis in male Wistar rats. Administration of BB1101 (3 mg/kg), given as a single intraperitoneal dose 30 minutes *after* induction of acute pancreatitis, significantly reduced ( $p = 0.01$ ) the rise of serum amylase (mean 2083; range 1646–2843) in treated animals *vs* controls (mean 2623; range 2071–3058), the pancreatic weight ( $p = < 0.005$ ), (mean 1.16 g; range 0.84–1.4 g) *vs* controls (mean 1.75 g; range 0.96–2.23 g), and the histology score was also significantly reduced ( $p = < 0.001$ ), (mean 8.25; range 5–11) *vs* control pancreata (mean 17; range 14–20). Pancreatic tissue levels of TNF are increased in experimental acute pancreatitis. Treatment with a TNF metalloproteinase inhibitor can ameliorate the disease progression and this may represent a new therapeutic strategy. Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "The Amelioration of Acute Pancreatitis Using a TNF-Metalloproteinase Inhibitor"

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"P P 19 0486" P 19 0486 **Pancreatic Ischemia and Tissue Concentrations of IMIPENEM in Acute Experimental Pancreatitis** K. Kotzampassi, E. Eleftheriadis, V. Siarkou<sup>1</sup>, A. Hrodotou, P. Skepastianos<sup>1</sup>, N. Harlaftis, N. Gougleri

Dept of Surgery, Faculty of Medicine, Univ. of Thessaloniki, Greece

<sup>1</sup> Dept of Microbiology, Faculty of Veter. Medicine, Univ. of Thessaloniki, Greece It is accepted that during the course of acute experimental pancreatitis pancreatic ischemia occurs; since Imipenem is considered as a well penetrating antibiotic into pancreatic tissue we decide to investigate its bioavailability in acute experimental pancreatitis in 72 Wistar rats subjected to sodium taurocholate pancreatitis or served as controls. Imipenem [Primaxin, Merck] was injected intravenously in a dose of 12.5 mg/100 g BW, while pancreatic microcirculation was monitored by laser Doppler flowmetry. At 30, 60 and 120 min, respectively, blood and pancreatic tissue were sampled for Imipenem concentration assessment by the thin layer diffusion on agar using the E. coli ATCC 25922 strain.

We conclude that in this model the pancreatitis induced reduction in pancreatic microcirculation lead to a diminution in pancreatic tissue concentrations; however Imipenem levels are higher than those of minimum inhibitory concentration for this strain of E. coli. } "Pancreatic Ischemia and Tissue Concentrations of IMIPENEM in Acute Experimental Pancreatitis"

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**"P P 19 0487" P 19 0487A Prospective Study of Hyperamylasemia and Post Pump Pankreatitis after Cardiopulmonary Bypass = Incidence, Significance and Risk Factors**

\*\dc Saritas, A. Saritas, O. Tarcan, N. Kantaroglu, A. Serin, O. Tasdemir, B. Sahin, K. Bayazit

Y\fksek Ihtisas Hospital, Departments of Gastroenterology, Cardiovascular Surgery and Biochemistry, Ankara, Turkey Severe acute pancreatitis is a rare but well defined complication of cardiac surgery performed under cardiopulmonary bypass (CPB). Hyperamylasemia is seen more frequently. In this prospective study, clinical importance and incidence of hyperamylasemia and post pump pancreatitis that develop after CPB and risk factors that have effects on these are investigated. Thirty-seven patients who had a cardiac operation under CPB between June 1995 and November 1995 are included in this prospective study. Serum amylase and lipase levels are measured 2 days before the operation and on the first hour and third day postoperatively. Patients with amylase levels above 220 U/L and lipase levels above 190 U/L are evaluated as post pump pancreatitis. Clinical, laboratory and hemodynamic parameters of these patients are compared with the drugs used, calcium chloride, blood transfusions and the amount of cardioplegia. Ten (%27.02) of 37 patients had high levels of amylase and lipase. All the patients had abdominal symptoms. One of the patients who had severe pancreatitis was dead on the 63. postoperative day due to multiple organ failure. There was no statistically significant correlation between post pump pancreatitis and age, sex, body weight, cardiac pathology, cardiac output, cardiac index, adjunctive treatment, accompanying diseases (diabetes mellitus, hypertension), intraoperative hypothermia, hypotension, central venous pressure, hematocrit and period of mechanical ventilation. CPB time and cross clamp time were significantly ( $p = 0.0283$ ,  $p = 0.05$ ) longer in the pancreatitis group. The amount of calcium chloride used intraoperatively and the amount of blood transfused were marginally significant ( $p = 0.0667$ ,  $p = 0.0908$ ). The correlation between the amount of cardioplegia and pancreatitis was highly significant ( $p = 0.007$ ). There was no correlation between the time of intensive care unit and pancreatitis; but the correlation with time of postoperative hospital stay was significant ( $p = 0.0274$ ). In conclusion, post pump pancreatitis is a common complication of CPB procedure, but severe pancreatitis is rare. It is a fatal condition when seen together with multiple organ failure. Long CPB and cross clamp times, excessive amounts of calcium chloride, cardioplegia and blood transfusions increase the risk of post pump pancreatitis. They increase the postoperative morbidity. Post pump pancreatitis that is frequently overlooked, remain undiagnosed and treated lately should be remembered in patients who have abdominal symptoms following cardiac operations; and the risk factors should be tried to be decreased. Intestinal disorders, absorption: Malabsorption syndromes }" "A Prospective Study of Hyperamylasemia and Post Pump Pankreatitis after Cardiopulmonary Bypass = Incidence, Significance and Risk Factors"

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"P P 19 0488" P 19 0488 **Necrotizing Pancreatitis with Sterile Percutaneous Aspiration: Clinical and Bacteriological Outcome**

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Centre Hospitalo-Universitaire Henri-Mondor, 94010 Cr'e9teil, France  
Diagnosis of necrosis infection is a crucial point in the management of necrotizing pancreatitis. Infection of necrosis requires surgical drainage but the treatment of sterile necrosis is still debated. In order to evaluate the significance of sterile necrosis on the outcome, we studied 17 patients with initially sterile percutaneous aspiration of pancreatic necrosis. Seventeen patients, hospitalized for necrotizing pancreatitis with signs of sepsis, had a first sterile CT- guided aspiration. Eight patients underwent a simultaneous percutaneous drainage of the punctured collection. A supportive therapy was carried on, unless severe biochemical deterioration or secondary infection of necrosis proven by iterative percutaneous aspiration indicated surgical necrosectomy and drainage. Among the 8 patients drained percutaneously, one died of septic shock, one was cured without sequelae and one had a pseudocyst treated by cystogastrostomy. Five patients were operated on and one died. Four of them had infected necrosis. Among the 9 patients who underwent only percutaneous aspiration, 7 were operated on, 2 had infected necrosis and 3 died. Secondary infection of necrosis was observed in 2 among 9 patients who had only fine needle aspiration of the collection (22%) and in 7 out of the 8 patients drained percutaneously (88%) ( $p = 0.03$ ). Hospital mortality rate reached 29% and was not affected by the bacteriological status of necrosis. Initial sterile aspiration of collections in severe acute pancreatitis did not warrant a favourable course and secondary infection of necrosis was observed in 65% of the patients. Percutaneous drainage of sterile collections favours secondary infection of necrosis and is not recommended. Pancreas: Pancreatitis, acute } "Necrotizing Pancreatitis with Sterile Percutaneous Aspiration: Clinical and Bacteriological Outcome"

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"P P 19 0489" P 19 0489 **Relationship between Neopterin Serum Levels and Severe Outcome of Acute Pancreatitis**

\*G. Uomo, S. Misso<sup>1</sup>, G. Manes, O. Spada<sup>2</sup>, B. Feola<sup>1</sup>, A. Minerva<sup>1</sup>, M. Laccetti, P.G. Rabitti

<sup>1</sup> Pancreas Unit, Immunohaematology, City Hosp., Caserta, Italy

<sup>2</sup> Pancreas Unit, Haematology, Cardarelli Hospital Napoli, Caserta, Italy *Aim:* of this study was to estimate neopterin (N), a useful *in vivo* marker of macrophages activation, in the prognostic assessment of acute pancreatitis (AP). Serum levels of N (nmol/ml), interleukin-6 (IL-6; pg/ml) and tumor necrosis factor (TNF; pg/ml) were measured in the 1st and 7th days of hospital admission in mild AP (n = 24) and severe AP (n = 17) – Atlanta classification-. Statistical analysis was performed by means of 2-way ANOVA, nonparametric tests and Spearman's correlation method. *Results:* N was significantly higher in severe AP (day 1: 42.9 – 30.; day 7: 111.3 – 46.7) than in mild AP (day 1: 28.6 – 10.2; day 7: 21.4 – 7.6); both groups showed higher values than controls (12.1 – 4.4) at admission, while at 7th day only values of patients with severe disease were significantly higher than controls. Considering intragroups data (severe and mild AP) N serum levels were significantly higher (p < 0.0001) in the 7th than in the 1st day in patients with severe forms only. Cutoff level of 40 nmol/ml reached a specificity and sensitivity of 92% in discriminating mild from severe AP at 7th day. No difference was observed as concerns TNF values. IL-6 at admission was significantly higher in severe vs mild AP and controls; in the severe AP, IL-6 serum levels at 1st day were significantly higher than values at 7th day. No correlation was found between N and IL-6 serum level. *Conclusions.* Initially enhanced N and IL-6 serum levels reflect the severity of the disease; N may be considered a reliable prognostic parameter also at a distance of AP onset, because it increases during the first week of AP in patients with severe forms only. Pancreas: Pancreatitis, acute } "Relationship between Neopterin Serum Levels and Severe Outcome of Acute Pancreatitis"

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"P P 19 0490" P 19 0490 **Role of Cell Calcium Overload in the Course of Conversion of Edematous to Necrotizing Pancreatitis: Effects of Verapamil on Cytosolic Free Calcium of Rat Pancreatic Acini**

\*J. Shen, Z.P. Wu, H. Xiao, Y.H. Song, M. Liu

Department of Surgery, Sichuan Continuing Education College of Medical Sciences, Chengdu 610041, P. R. China Since calcium channel blockades could improve the pancreatic circulation, limit the prostaglandin imbalance and influence the development of acute pancreatitis (AP), the influx of calcium ions may play an essential role in the pathophysiology of AP. Acute experimental pancreatitis was induced by biliopancreatic retrograde injection of 4.5% sodium taurocholate solution (0.1 ml/30 s/100 g) in 140 SD rats. In the treated group, a dose of 0.1 mg (0.25 ml/100 g) verapamil was given intraperitoneally at 5 min after induction of AP. Morphological alterations of the pancreas were monitored by histological and ultrastructural techniques, the intracellular free calcium concentration ( $(Ca^{2+})_i$ ) of pancreatic acinar cells was measured with Shimazu 5000-RF fluorescence spectrophotometer in the three groups. The results demonstrated that a characteristic feature of early phase of acute necrotic-haemorrhagic pancreatitis was at 2 and 3 hrs following induction of AP. After induced AP, the pancreatic acinar cell  $(Ca^{2+})_i$  was increased from sham-operated control (163.04 – 13.39 nM) to its highest (402.75 – 17.54 nM) at 2 hrs after induced AP in the AP group ( $P < 0.001$ ). In the treated group, the pancreatic acinar cell  $(Ca^{2+})_i$  was lower than that in AP group significantly ( $P < 0.001$ ). The correlation between the pancreatic acinar cell  $(Ca^{2+})_i$  and the severity of pancreatic damages was significant ( $r_s = 0.9227$ ,  $P < 0.001$ ) in the AP group. The verapamil treated rats exhibited significant increase in the survival rate and survival time. They also showed decrease in the severity of pancreatic haemorrhage and necrosis, and reduced the damages to the pancreatic cellular ultrastructures. These data suggest that in the early stage of AP, the cell calcium overload maybe a key role in the pathophysiology of bile-induced acute experimental pancreatitis in rats and prevent the cell calcium overload is a important role in therapeutic pathogenesis of calcium channel blockades treated AP. Pancreas: Acinar, duct cell function Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "Role of Cell Calcium Overload in the Course of Conversion of Edematous to Necrotizing Pancreatitis: Effects of Verapamil on Cytosolic Free Calcium of Rat Pancreatic Acini"

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## "P P 19 0491" P 19 0491 Early Indicators of the Need of Parenteral Nutrition in Acute Pancreatitis

\*P. Lage, J. Reis, M.E. Camilo, A. Figueiredo, A. Coutinho, P. Alexandrino, M. Carneiro Moura

Serviço de Medicina II, Hospital Santa Maria, Lisbon, Portugal *Background:* The institution of parenteral nutrition (PN) in acute pancreatitis (AP) is controversial. It is an useful adjuvant therapy when treating AP complications but there are no clinical/laboratory indices for early PN. In a previous retrospective study it was found that persistence of ileus at the 5th day, serum albumin < 2.9 g/dl, 20% reduction of Hb or hypocalcemia < 1.78 mmol/l at 72 hrs could be early indicators of the need of PN. *Aims:* To prospectively evaluate the previous indices as predictors for early institution of PN, according to a protocol. *Patients and methods:* Between 1991–6, were admitted, to our ICU, 179 patients with AP. PN was prescribed in 45 (25%) patients: 25 male and 20 female with an mean age of 54 (19–76) years. The pancreatitis aetiology was biliary in 20 (44%), alcohol in 18 (40%) and other in 7 (16%) patients. We have prospectively evaluated Ranson criteria, clinical and laboratory indices that were considered indicators for PN, morbidity and mortality. *Results:* The mean Ranson criteria was 4.6 – 2.1 (0–8), 42/45 (93%) patients developed complications, which were local in 7, systemic in 1 and both in the remaining 34 patients and the mean hospital stay was 24.7 – 16.8 (6–100) days. Early PN was started in 24 patients (group I), 4 with ileus and 20 with at least one of the previous laboratory parameters; all patients with albumin < 2.9 g/dl or a 20% reduction of Hb at 72 hrs developed local complications. In 14 patients (group II) PN was prescribed because local complications developed although none of the previous early indicators were present. The protocol was not followed in 7 patients (group III): in 4 of them early laboratory and/or clinical indicators were present but early PN was not prescribed, while in the remaining 3 patients there was no clear evidence for the need of PN. Mean time for PN onset was 4.5 – 1.4, 7.9 – 5.6, 9.4 – 4.5 days ( $p = 0.003$ ) and its mean duration was 14 – 12.9, 9.4 – 4.3, 7.4 – 4.7 days ( $p = 0.2$ ) in group I, II and III, respectively. Severe hypocalcemia was associated with mortality ( $p = 0.008$ ). *Conclusion:* The proposed laboratory indices are associated with a more severe clinical course and proved to be useful as early indicators for the need of PN. **Pancreas: Pancreatitis, acute Nutrition: Techniques of nutrition }** "Early Indicators of the Need of Parenteral Nutrition in Acute Pancreatitis"

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"P P 19 0492" P 19 0492 **Common Bile Duct Microlithiasis in Patients with Acute Idiopathic Pancreatitis (AIP)**

\*M. Kohut, A. Nowak, T.A. Marek, E. Nowakowska-Dulawa, R. Kaczor

Department of Gastroenterology, Silesian Medical Academy, Katowice, Poland *Aim:* After the exclusion of patients with acute pancreatitis (AP) of defined etiology (biliary lithiasis, alcohol abuse, etc.) some cases of acute pancreatitis of unknown origin (acute idiopathic pancreatitis – AIP) remain. The aim of the study was to investigate the presence of common bile duct (CBD) microlithiasis in patients with AIP. *Method:* Twenty-seven consecutive patients with AIP, treated from April 1994 through May 1996 were studied. Endoscopic retrograde cholangiopancreatography (ERCP) was performed as an urgent procedure (24 hours from admission) in every case of AIP. During ERCP bile from the CBD was collected via sterile catheter. Microscopic examination of bile was done immediately after the collection in the half of bile, the second half was examined after 24 hours of sterile incubation in the temperature of 37°C. The presence and amount of CBD microlithiasis (cholesterol monohydrate crystals (CMC) and calcium bilirubinate granules (CBG) were determined according to Juniper and Benson. *Results:* The table shows the presence of CBD microlithiasis: No of CMC CBG CMC + CBG Total with patients microlithiasis 27 3 12 8 23 (85%) *Conclusions:* 1. In patients with AIP microscopic examination of CBD bile taken during ERCP revealed microlithiasis in 85% of cases. 2. AIP, in most cases, is an acute pancreatitis of biliary origin. Pancreas: Pancreatitis, acute Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary } "Common Bile Duct Microlithiasis in Patients with Acute Idiopathic Pancreatitis (AIP)"

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## "P P 19 0493" P 19 0493A New Prognostic Scoring System for Patients with Acute Biliary Pancreatitis

\*T.A. Marek, A. Nowak, E. Nowakowska-Dulawa, R. Kaczor

Department of Gastroenterology, Silesian Medical Academy, Katowice, Poland

**Background:** The use of urgent endoscopic sphincterotomy (ES) for acute biliary pancreatitis (ABP) decreases the efficiency of presently used prognostic scoring systems (PSS). None of presently used systems includes the influence of ES. Construction of the new system, overcoming this problem, was the aim of the study.

**Material and methods:** The study comprised 150 consecutive patients with ABP treated by urgent ES from May 1993 through September 1995. The outcome was graded as mild (74%), complicated (19%) or fatal (7%). Clinical and laboratory factors significantly different in mild (uncomplicated) and severe (complicated and fatal) ABP, with specific cut-off points, were selected. The set of factors for the new system was chosen by the stepwise logistic regression. Sensitivity, specificity, accuracy, and Youden's index were used to compare the efficiency of the new and presently used PSS.

**Results:** Nine-factor system (called "Katowice") was found to have the best prognostic efficiency. The system includes: interval between onset of ABP and ES (> 48 h), C-reactive protein (> 240 mg/L), heart rate (> 115/min), WBC (> 11 G/L), glucose (> 130 mg/dL), creatinine (> 1.6 mg/dL), p<sub>a</sub>O<sub>2</sub> (< 70 mmHg), total protein (< 5.9 g/dL), and calcium (< 8.2 mg/dL). For all factors the worst result during first 48 hours in the hospital is evaluated; 4 or more positive factors predicts severe ABP. Table presents the comparison between "Katowice" and other PSS: Ranson Glasgow AP II CT Katowice

	Ranson	Glasgow	AP II	CT	Katowice
Sensitivity	46%	67%	69%	54%	92%
Specificity	92%	87%	79%	88%	93%
Accuracy	80%	82%	77%	79%	93%
Youden's index	0.38	0.54	0.49	0.42	0.85

**Conclusion:** New system "Katowice" appears to be more efficient in the prediction of severity in ABP, especially in ES-treated patients.

Pancreas: Pancreatitis, acute  
Endoscopy, specific: Biliary }

"A New Prognostic Scoring System for Patients with Acute Biliary Pancreatitis"

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"P P 19 0494" P 19 0494 **Oxygen Free Radicals and Complications of Acute Biliary Pancreatitis** A. Dziurkowska-Marek,

\*T.A. Marek, A. Nowak, T. Kacperek-Hartleb, E. Sierka, E. Nowakowska-Dulawa

Department of Gastroenterology, Silesian Medical Academy, Katowice, Poland *Background:* Oxygen-derived free radicals (OFR) are generated in the early phase of acute pancreatitis. The degree of oxidant-antioxidant balance changes reflects the outcome of the disease. The aim of the present study was the evaluation of relationship between type of complications and the intensity of OFR generation. *Material and methods:* The study comprised 74 consecutive patients with ABP, treated from October 1994 through September 1995. Plasma levels of malonyldialdehyde (MDA; 56 patients) and sulfhydryl groups (SH; 73 patients) were chosen as the indicators of OFR generation and antioxidant capacity of the organism, respectively. *Results:* Uneventful recovery (RC) was observed in 47 (63%) patients. Systemic complications (SC) alone developed in 14 patients (19%), whereas pancreatic complications (PC) were found in 13 (11 with systemic also) cases (18%). 3 patients with pancreatic complications (1 – sterile, 2 – infected necrosis) died (DE). Table presents the selected levels of plasma MDA and SH in above three groups of patients: RC SC PC DE *p, ANOVA*

	RC	SC	PC	DE	<i>p, ANOVA</i>
MDA no of pts.	36	10	7	3	
admission	9.5	10.8	8.8	12.4	0.0045
mean maximum	11.7	13.6	12.7	16.2	0.0009
[nmol/mL] increase (%)	24.6	26.3	47.4	32.2	0.0152
SH no of pts.	46	14	10	3	
admission	311.4	289.9	295.3	326.7	0.6426
mean minimum	230.3	206.0	194.2	166.3	0.0011
[nmol/mL] decrease (%)	24.4	27.4	33.0	50.4	0.0015

*Conclusion:* The generation of oxygen-derived free radicals seems to be more prominent when local (pancreatic) complications of ABP are present. Pancreas: Pancreatitis, acute Immunology and microbiology: Inflammation } "Oxygen Free Radicals and Complications of Acute Biliary Pancreatitis"

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**"P P 19 0495" P 19 0495A 21 Years Experience in Surgical Management of Acute Necrotizing Pancreatitis (ANP)**

\*Zhang Sheng-Dao, Zhang Chen-Lie, Tang Yao-Qing

Dept. of Surgery Rui-Jin Hospital, Affiliated to Shanghai 2nd Medical University, Shanghai, China From 1974 to 1995, 243 patients with ANP proved by operation or CT scanning were hospitalized. The severity of the disease had been evaluated by CT scoring system. The overall survival rate of this group was 70.4%. During 21 years basing on the understanding of the development of ANP by degrees, combining with our own experimental work, we changed the strategy in the surgical treatment of ANP twice. In the First stage (1974 – 1987), the strategy of treatment was resection of the necrosis as radical as possible, as early as possible, and the main type of operation was subtotal pancreatectomy. The survival rate of this period was 61.3% (49/80). In the second stage (1988 – 1991) inspired by our own experimental work, we recognized the importance of infection. And the strategy of the treatment had been changed into "Individualization" which means "In case of the pancreatic necrosis sterile, the conservative treatment is the first choice. In case of pancreatic necrosis infected, necrosectomy is performed early." In this period, the survival rate of conservative treatment was 85.7% (6/7); that of operative treatment was 67.1% (57/85) and overall survival rate of this period was 68.5% (63/92). In the third stage (1991 – 1994), we insisted: 1. late operation for the patient with necrosis infected; 2. comprehensive management for all patients with ANP. The survival rate of conservative treatment of this period was 100% (11/11); that of operative treatment was 80% (48/60), and overall survival rate of this stage was 83.1% (59/71). We conclude that comprehensive management combined with late operation for the patients with necrosis infected is a better strategy for the treatment of ANP. Pancreas: Pancreatitis, acute } "A 21 Years Experience in Surgical Management of Acute Necrotizing Pancreatitis (ANP)"

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## "P P 19 0496" P 19 0496 Gabexate Mesilate (FOY®) Inhibits Sphincter of ODDI Motility in Patients with Acute Recurrent Pancreatitis

\*V. Di Francesco, G. Angelini, P. Bovo, A. Castagnini, M. Filippini, B. Vaona, L. Frulloni, L. Rigo, M.P. Brunori, G. Borsini, G. Cavallini

Gastrointestinal Unit, University of Verona, Italy Gabexate Mesilate (GM), is an anti-protease drug which has been shown to be effective in the treatment of acute pancreatitis and recently also in the prevention of post-ERCP pancreatitis. GM action on sphincter of Oddi (SO) motility has not been investigated so far. Aim of our study was to verify SO motor response to an acute administration of GM in a group of patients with the same indication for SO manometry. Eight patients (5 M, 3 F, mean age 46 – 8 years), who had suffered from recurrent attacks of acute pancreatitis at least 3 months before the examination, entered the study. After an overnight fast they were sedated with diazepam 10 mg i.v. and then submitted to SO manometry. The procedure was performed endoscopically by using a perfusion system, connected to a computerized system (Polygram Synectis, Sweden) and a triple lumen modified catheter, with two recording and one aspirating channel (Wilson-Cook, USA). After a stable basal registration at least 1 min long was obtained, GM 100 mg i.v. was infused and the registration repeated. Intraduodenal pressure was taken as zero reference and then basal SO pressure, amplitude and frequency of phasic contractions (PC), area under the curve were calculated before and after GM administration. Wilcoxon Rank Test for paired data was used for statistical analysis. *Results:* two patients showed a picture of SO stenosis without any evident phasic activity. In these cases GM infusion did not affect manometric findings. In the other 5 patients with normal basal pressure, with a latency of about 1 min, GM administration caused a reduction of phasic sphincter activity, both in terms of PC amplitude and frequency (Table: value expressed as mean – SE). Before GM After GM P Basal pressure (mmHg) (n = 8) 39.5 – 2.8 36.5 – 10.5 0.061 PC amplitude (mmHg) (n = 6) 19.6 – 6.8 8.9 – 3.7 0.021 PC frequency (n/min) (n = 6) 5.5 – 1.1 3.75 – 1 0.021 Area (mmHg {b4} 1 min) (n = 8) 6205 – 2495 3173 – 621 0.014 In conclusion our preliminary data suggest that 1) GM induces SO motility inhibition and this action may be important in the treatment and prevention of pancreatitis; 2) GM affect manometric results, thus it must be avoided during SO manometry or, when GM prophylactic infusion is indicated, this must start after manometry. Pancreas: Pancreatitis, acute } "Gabexate Mesilate (FOY®) Inhibits Sphincter of ODDI Motility in Patients with Acute Recurrent Pancreatitis"

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## "P P 19 0498" P 19 0498 **Monitoring of Neutrophil Function and Inflammatory Mediators in Acute Pancreatitis**

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<sup>1</sup> Department of Experimental Surgery, University Medical School of Pécs, Hungary Although it is generally accepted, that inflammatory mediators and polymorphonuclear leukocytes (PMN) play important role in acute pancreatitis the inflammatory response reaction seems to be less investigated in the clinical practice. The current experiments were designed, to evaluate the stimulated state of neutrophils, to detect the changes of acute phase protein in patients suffering from acute pancreatitis. Peripheral venous blood samples were collected from 14 patients to measure the following markers: superoxide radical generation capacity of isolated neutrophils, enzyme level of myeloperoxidase (MPO), and PMN-elastase in the plasma, C-reactive protein (CRP) in the sera. The observation period started on the day of hospital admission and ended on the 20th day. All patients were treated conservatively because of their uncomplicated disease. Our results showed that superoxide radical production of isolated PMN was depleted already on the first day and the lowest value was registered on the 8-10th days (3.72 – 0.92 and 3.05 – 1.19 nmolO<sup>2</sup>/min/1.5 × 10<sup>6</sup> PMN respectively). The normal O<sup>2</sup> production of PMN was detected only at the end of observation period (13.14 – 1.98 nmolO<sup>2</sup>/min/1.5 × 10<sup>6</sup> PMN). In contrast MPO activity increased until the 6th day (1.23 – 0.28 to 2.50 – 0.61 OD/ml respectively) reaching the normal value after 2 weeks (0.84 – 0.19 OD/ml). There was an elevation of PMN-elastase at the time of hospital admission (65.8 – 10.8 ng/ml), comparing to the reference value (35.1 – 2.4 ng/ml), which persisted during the first week and was followed by a continuous fall towards the normal value on day 20. Measurement of CRP revealed that at the time of patients admission it was much higher than normal (83.4 – 32.2 mg/l) and remained on this level during the first 4 days. Mean values of CRP normalised on the 8–10th day (0–10 mg/l) and remained within this range during the further observation period. Our results suggest that functional state of neutrophils and C-reactive protein are in close correlation with the improvement of clinical outcome during the course of acute pancreatitis. The continuous monitoring of these parameters may give useful information to the clinical state and help to set up therapeutic strategies. Pancreas: Pancreatitis, acute Pancreas: Pancreatitis experimental Pancreas: Acinar, duct cell function } "Monitoring of Neutrophil Function and Inflammatory Mediators in Acute Pancreatitis"

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## "P P 19 0499" P 19 0499 The Relationship between Polyamines Metabolism and Phospholipase D Activity in Isolated Pancreatic Acini and during Regeneration after Acute Pancreatitis in Rats\*

\*G. Rydzewska, G. Jurkowska, A. Gabryelewicz

Gastroenterology Dept. Medical School, Bialystok, Poland Recently we have shown the involvement of phospholipase D activity and the importance of polyamines metabolism in pancreatic recovery after AP. The aim of the present study was to evaluate possible relationship between polyamines metabolism and PLD activity during caerulein (Cae) induced AP and *in vitro* in isolated pancreatic acini. *Methods:* The AP was induced by sc. injections of Cae in gelatin (12 \b5g/kg). Rats were then divided into six treatment groups: control + saline (C), control + ornithine decarboxylase inhibitor (ODC) { a }-difluoromethylornithine (DFMO) (C + DFMO), AP + saline (AP), AP + DFMO, AP + putrescine (AP + P), AP + DFMO + P, and treated for 2, 7 and 14 days. DFMO was given: 3 {\b4} 300 mg/kg b.w. i.p. during the first 3 days (1 day before and during 2 days of Cae injections) and during 2, 7 and 14 days of treatment, and additionally as 2% solution in drinking water during the first 3 days in C + DFMO, AP + DFMO and AP + DFMO + P groups. Putrescine was given 4 mg/kg b.w. i.p. tid. After the treatment, rats were sacrificed and pancreatic acini were prepared and loaded with <sup>3</sup>H myristic acid to measure <sup>3</sup>H phosphatidic acid (PA), a marker of PLD activity. *In vitro:* Pancreatic acini from healthy rats were prepared, loaded with <sup>3</sup>H myristic acid, preincubated 30 min. with 1 mM DFMO and stimulated with 500 pM Cae. After 30 min. of stimulation <sup>3</sup>H PA was separated and counted. *Results:* PLD activity was significantly elevated after 2 days and returned to control value after 7 and 14 days of AP. Treatment with DFMO significantly increased PLD activity in control animals and partially prevented the increase of PLD activity after 2 days of AP; DFMO did not influence PLD activity after 7 and 14 days of AP. Putrescine intake did not change PLD activity after 2 and 7 days, but increased this activity after 14 days of treatment. After 2 days in AP + DFMO + P group PLD activity was also comparable to AP; DFMO did not prevent the influence of putrescine. *In vitro* pretreatment with DFMO did not change Cae stimulated PLD activity in pancreatic acini. *In vivo* study suggests that inhibition of polyamines synthesis rather stimulates PLD activity in control and AP groups (except 2nd day of AP). However *in vitro* pretreatment of acini with DFMO did not change basal and Cae stimulated PLD activity. *Conclusions:* Inhibition of polyamines synthesis does not directly influence PLD activity in rat pancreatic acini (*in vitro* study), and modulation of this activity observed *in vivo* is dependent rather on indirect effects of polyamines metabolism on intracellular signaling pathways. It seems that polyamines metabolism and PLD activation are separated pathways leading to pancreas growth.\* partly supported by the grant KBN 4 S402 0306 Pancreas: Acinar, duct cell function Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "The Relationship between Polyamines Metabolism and Phospholipase D Activity in Isolated Pancreatic Acini and during Regeneration after Acute Pancreatitis in Rats\*"

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## "P P 19 0500" P 19 0500 The Role of Transforming Growth Factor $\beta$ s in Human Acute Pancreatitis: Repair Mechanism?

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Departments of Medicine and Biological Chemistry, University of California Irvine, USA Transforming growth factor (TGF)- $\beta$ 1, - $\beta$ 2, and - $\beta$ 3 are multifunctional polypeptides that have been implicated in the regulation of cell growth and the formation of extracellular matrix and fibrosis. Upregulation of TGF- $\beta$  transcription has been reported in several in vivo models of tissue injury and repair. In the present study we examined the expression of TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3 in relation to changes in collagen expression during the course of pancreatic remodeling process following acute pancreatitis (AP) in humans and in an experimental model of AP. *Design:* Pancreatic tissue samples were obtained from 13 patients (median ranson score: 6 (range 1–9)) with a median age of 65 years (range: 37–77 years) with necrotizing AP undergoing necrosectomy. Operation was performed on day 5.5 (range 4–17) after the onset of AP. Tissues obtained from 12 previously healthy organ donors (median age: 43 years) served as controls. In male rats (body weight 240–260 g) AP was induced by cerulein infusion (10  $\mu$ g/kg body weight/h) for 4 hours. 4, 8, 24 hours, 2, 3, 4, 5, 6, and 7 days following AP induction the rats were sacrificed and the pancreas was removed. *Methods:* The expression of TGF- $\beta$ 1, - $\beta$ 2, - $\beta$ 3, amylase and collagen was analyzed by Northern blot analysis. In addition, immunohistochemical analysis using TGF- $\beta$  isoform-specific polyclonal antibodies was performed. *Results:* By Northern blot analysis there was a marked increase in TGF- $\beta$ 1, and TGF- $\beta$ 3 and a slight increase in TGF- $\beta$ 2 mRNA expression in the human AP samples. In contrast, amylase mRNA expression was markedly decreased and collagen mRNA was increased in human AP. Immunohistochemistry demonstrated intense TGF- $\beta$ 1–3 immunoreactivity in the remaining acinar and ductal cells in human AP. Induction of AP in rats led to a biphasic peak pattern of TGF- $\beta$ 1–3 mRNA expression with a marked increase between day 1 to 3 and again at day 5 to 7. Immunostaining revealed moderate to strong TGF- $\beta$ 1–3 immunoreactivity in the pancreatic acinar cells after induction of AP whereas only weak TGF- $\beta$  immunoreactivity was present in a few cells of the normal pancreas. *Conclusion:* Overexpression of TGF- $\beta$ s might play an important role in pancreatic repair and remodeling after AP. The enhanced levels of TGF- $\beta$ s might contribute to the changes in the extracellular matrix and to the repair process which occurs after pancreatic damage. Support: SNF grant 32-39529. Hormones and receptors: Growth factors Pancreas: Pancreatitis, acute Hormones and receptors: Molecular biology } "The Role of Transforming Growth Factor  $\beta$ s in Human Acute Pancreatitis: Repair Mechanism?"

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"P P 19 0501" P 19 0501 **Effects of CCK-A Receptor Antagonist (Devazepide) and Nitric Oxide Synthase Inhibitor (L-Name) on Acute Pancreatitis in Rats**

\*H. Yamada, D. Chen, K. Kimura, R. Hakanson

Department of Pharmacology, University of Lund, Lund, Sweden *Background/aim:* Although the pathogenesis of acute pancreatitis is poorly understood, CCK is thought to play a role. The purpose of the study was to examine possible protective effects of a CCK-A receptor antagonist (devazepide) and a nitric oxide synthase inhibitor (L-NAME) on two types of acute pancreatitis. *Methods:* Male Sprague-Dawley rats weighing 200–300 g were used. Acute pancreatitis was induced as follow: (1) Caerulein (CR)-induced pancreatitis; CR (5.0 μg/kg/h) was infused intravenously for 4 hrs. (2) Taurocholate (TC)-induced pancreatitis; 200 μl of 4.0% sodium taurocholate was injected retrogradely into the pancreatic duct. Devazepide (60 μg/kg) and L-NAME (N<sup>G</sup>-nitro-L-arginine methyl ester, 60 mg/kg) were given by intravenous bolus injection 30 min before the administration of CR and TC. Controls received 0.9% NaCl. Body weight, pancreatic wet weight, serum amylase levels and plasma CCK concentration were measured. *Results:* (1) Serum amylase levels, plasma CCK concentration and pancreatic wet weight were increased after CR administration. The increase in serum amylase levels and pancreatic wet weight was prevented by devazepide or L-NAME. (2) Serum amylase levels, plasma CCK concentration and pancreatic wet weight were increased after TC administration. Devazepide or L-NAME was without effect. *Conclusions:* Devazepide and L-NAME prevented caerulein-induced pancreatitis, but failed to inhibit taurocholate-induced pancreatitis. **Pancreas: Pancreatitis experimental }** "Effects of CCK-A Receptor Antagonist (Devazepide) and Nitric Oxide Synthase Inhibitor (L-Name) on Acute Pancreatitis in Rats"

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"P P 19 0502" P 19 0502 **Effect of Early Jejunal Feeding on Septic Complications in Acute Pancreatitis: A Prospective, Randomized Study**

\*A. Ol\'e1h, G. Pardavi, Gy. Varga, T. Bel\'e1gyi

Petz Alad\'e1r County Hospital, Dept. of Surgery, Gyo\'r, Hungary *Purpose of study:* The necrotized tissue of pancreas is colonized by bacteria mainly from the colon which may lead to abscess or infected necrosis. Our purpose was to prove, that early jejunal feeding — preventing the atrophisation of mucosa and disruption of mucosal mechanical barrier, preventing the increased permeability and bacterial translocation, decreasing the paralytic condition and distension of colonic wall and preserving the normal colonic bacterial flora — can reduce the rate of septic complications. *Patients and method:* The study included 64 patients admitted to our department in 1995 with acute, non-biliary pancreatitis, randomizing into two groups. In group "A" (n = 30) jejunal feeding was started in the first 24 hours (Survimed OPD). In group "B" (n = 34) conventional parenteral nutrition was applied. Between the two groups neither in the male:female ratio (23:7 and 30:4), nor in the average age (47.2 and 43.8 years) nor in the etiology (21 and 25 alcoholic; 9 and 9 idiopathic) were significant difference found. *Results:* Necrosis developed altogether in 20 patients (31.3%). In group "A" two infected necrosis, one abscess and five sterile necrosis were detected. In group "B" five infected necrosis, five abscess and two sterile necrosis were found. Septic complication due to bacterial contamination developed so in 3 cases in group "A" (10%) and in 10 cases in group "B" (29.4%). Statistical difference is marginally significant (p = 0.09; Fisher-test). In group "A" five patients, in group "B" ten patients underwent operating procedure. The difference in the mortality rate was not significant between the two groups (2 and 4 patients; p = 0.42). *Conclusion:* Our results suggest that early jejunal feeding in the treatment of acute pancreatitis can reduce the rate of bacterial contamination of necrotized pancreatic tissue, mainly in the later phase of disease, after the first week. Pancreas: Pancreatitis, acute } "Effect of Early Jejunal Feeding on Septic Complications in Acute Pancreatitis: A Prospective, Randomized Study"

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"P P 19 0503" P 19 0503 **Experimental Study on the Usefulness of Hemodiafiltration in Decreasing Contrast Medium of the Therapy of Severe Acute Pancreatitis**

\*M. Sogabe, T. Okahisa, S. Hayashi, S. Taoka, H. Matunaga, Y. Ohkita, A. Tsutsui, T. Fukuda, N. Muguruma, M. Yasuda, T. Yokoi, S. Okamura, H. Shibata, S. Ito

Second Department of Internal Medicine, School of Medicine, The University of Tokushima, Tokushima, Japan *Purpose:* Contrast-enhanced computed tomography (CECT) is used to detect poorly perfused areas in severe acute necrotizing pancreatitis. However, intravenous contrast media increase acute renal failure. We studied the efficacy of Hemodiafiltration (HDF) in decreasing contrast medium in the blood in *in vitro* bovine blood models. *Methods:* HDF was performed for 6 hrs (blood flow; 100 ml/min, dialysate flow; 10 ml/min, filtrate flow; 10 ml/min) using a polysulfone filter (PS filter CF, surface area; 0.7 m<sup>2</sup>, Kuraray Co. Ltd., Japan). The extracorporeal circuit was anticoagulated with nafamostat mesilate (Torii Co. Ltd., Japan) at 30 mg/hr. After the start of HDF, 200 ml of contrast medium (Iomeprol 300, 300 mgI/ml, MW 777, Eizai Co. Ltd., Japan) was added to the 5 L of blood in the tank. Iomeprol was measured in blood and ultrafiltrate with HPLC. Clearance (CL), half-life time (t<sub>1/2</sub>) and elimination rate (ER) were calculated. *Results:* The clearance was 18.1 ml/min. The half-life time was 1.8 hrs. After 6 hrs, 89.3% of IPM was eliminated in ultrafiltrate by HDF (ER 1 hr = 24.4%, ER 2 hrs = 46.1%, ER 4 hrs = 75.4%, ER 6 hrs = 89.3%). *Conclusion:* Iomeprol was easily filtrated by HDF. If HDF is applied to severe acute pancreatitis at the time of CECT, the risk of renal failure will be decreased. Pancreas: Pancreatitis, acute } "Experimental Study on the Usefulness of Hemodiafiltration in Decreasing Contrast Medium of the Therapy of Severe Acute Pancreatitis"

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"P P 19 0504" P 19 0504 **Treatment of Severe Acute Pancreatitis Using Continuous Venovenous Hemodiafiltration**

\*T. Okahisa, M. Sogabe, S. Hayashi, S. Taoka, H. Matunaga, Y. Ohkita, A. Tsutsui, T. Fukuda, N. Muguruma, M. Yasuda, T. Yokoi, S. Okamura, H. Shibata, S. Ito

Second Department of Internal Medicine, School of Medicine, The University of Tokushima, Tokushima, Japan *Purpose:* Although the effectiveness of continuous hemodiafiltration (CHDF) in treating severe acute pancreatitis has been reported, its efficacy has not yet been adequately studied. We evaluated whether CHDF leads to extraction of chemical mediators, which are related to the increase of multiple organ failure, from circulation of patients with severe acute pancreatitis and explored the optimum method of using CHDF to treat severe acute pancreatitis. *Methods:* We used CHDF in 4 cases of severe acute pancreatitis. CHDF was performed for a mean of 13.5 days (range, 1–43 days) using a polysulfone filter (PS filter CF, surface area; 0.7 m<sup>2</sup>, Kuraray Co. Ltd., Japan). The flow rate of CHDF was as follows; blood flow = 100 ml/min, dialysate flow = 10 ml/min, filtrate flow = 10 ml/min. The extracorporeal circuit was anticoagulated with nafamostat mesilate (Torii Co. Ltd., Japan) at 30 mg/hr. Cytokines (TNF {  $\alpha$  }, IL-6 and IL-8), endotoxins and pancreatic enzymes (Trypsin, Phospholipase A2, Trypsin like activity) were measured in blood and ultrafiltrate. Their clearance (CL) and elimination rate (ER) were calculated. *Results:* CHDF resulted in elimination of cytokines (ER (IL-8) = 5.8%/hr, ER (IL-6) = 1.7%/hr) and endotoxins (ER (endotoxin) = 1.2%/hr) into the filtrate and adsorption of these factors onto the filter. In addition, pancreatic enzymes suppressed by nafamostat mesilate (an anti-coagulant used during CHDF) (ER (TLA) = 1.3%/hr). *Conclusion:* CHDF leads to extraction of chemical mediators, which are related to the increase of multiple organ failure. At present, the principal role of CHDF is thought to be to control water and electrolytes in cases of severe acute pancreatitis complicated by renal failure. But if CHDF is used in the early stages of severe acute pancreatitis, the prognosis of this disease may be improved. Pancreas: Pancreatitis, acute }" "Treatment of Severe Acute Pancreatitis Using Continuous Venovenous Hemodiafiltration"

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"P P 19 0505" P 19 0505 **Local Therapy with Octreotide (Sandostatin) in Acute Necrotic Pancreatitis and Pancreatic Pseudocysts**

\*N. Grigorov, A. Mendisova

Clinical Centre of Gastroenterology, University Hospital "Queen Joanna", Sofia, Bulgaria *Aim.* Control and results of the local therapy in acute necrotic pancreatitis and pancreatic pseudocysts. *Clinical material and method:* 12 patients with acute necrotic pancreatitis (7 – in acute and 5 – in subacute stage) and 9 patients with formed pancreatic pseudocysts have been treated locally with Sandostatin applied 0.2 mg once or several times. This treatment has been performed on a background of the perceived by us as a routine percutaneous drainage and lavage under US-control and Sandostatin (0.1–0.3 mg daily s.c.). *Results:* The combined parenteral and local treatment coupled with percutaneous drainage reduces the healing period significantly, compared with that one from our previous studies (16/21 – 76.4%). This effect is also confirmed by the fact, that in 7 patients, who did not have a significant improvement (US and CT control) from the perceived until now basic therapy, the additional local application (via the catheter) of Sandostatin sharply improved the clinical state and shortened the healing period. *Discussion:* The pathogenic mechanism is probably connected with a direct influence on difficulty closing fistulas, which complicate this mechanism and make ineffective the basic procedures. With the exception of one patient (transitory flush and slight dyspepsia), the other did not show side effects. *Conclusion:* The local application of Sandostatin can be added to the therapeutic approach in acute necrotic pancreatitis and pancreatic pseudocysts, especially in protracted cases. *Clinical practice: Management strategy* Pancreas: Pancreatitis, acute Radiology and ultrasound: Therapy } "Local Therapy with Octreotide (Sandostatin) in Acute Necrotic Pancreatitis and Pancreatic Pseudocysts"

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## "P P 19 0506" P 19 0506 **Pancreatic Elastase I in Serum: Low Sensitivity for Detection of Acute Pancreatitis**

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Medizinische Klinik II, Universit'e4t Leipzig, Germany

Inst. f. Anaesthesie Mannheim, Universit'e4t Heidelberg, Germany For diagnosis of acute pancreatitis measurement of serum elastase is thought to offer the highest sensitivity. Due to its long half life in serum it is also assumed, that pancreatitis can still be detected by elastase measurement several days after onset of the disease. This was controlled in a series of 253 patients admitted to hospital due to acute abdominal pain. *Methods:* Samples were taken at admission, after 3–4 and 6–7 days. Concentrations of amylase, lipase (kinetic assay), elastase (Elisa), and C-reactive protein were measured. Further samples from 14 patients with proven acute pancreatitis were taken daily and the parameters noted above were analysed. *Results:* The main final diagnosis were acute cholecystitis (42 patients), ulcer (33), and acute pancreatitis (30). Serum elastase was elevated above control value (3.5 ng/mL) in only 23 of the patients 33 patients with acute pancreatitis (Sensitivity 73%) and in 7 of the remaining 220 patients without evidence for pancreatitis (specificity 97%). The sensitivity of lipase (97%) and amylase (82%) were higher whereas the specificity of both enzymes was 81 and 84%. In most patients with elevated elastase, the enzyme concentration was already normal after 4 days. Consequently, the sensitivity of elastase after 3 days was lower (20%) than for lipase (80%) or amylase (50%). Furthermore, serum samples from 14 separate patients with acute pancreatitis were taken daily and elastase, lipase, and amylase were measured. Amylase or lipase was elevated in all patients, whereas elastase was negativ in one. Highest values were measured at admission. Half life of amylase, lipase or elastase in serum was below 2 days. Sensitivity of elastase was 70% after two and only 25% after 3 days. *Conclusion:* Contrary to published data we found that for primary diagnosis of acute pancreatitis serum elastase is not superior to lipase and may also not be helpful in the later stage of the disease. Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "Pancreatic Elastase I in Serum: Low Sensitivity for Detection of Acute Pancreatitis"

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## "P P 19 0507" P 19 0507 Serum Pancreatic Elastase-1 in Acute Pancreatitis

\*C. Millson, K. Charles, P. Poon, J. MacFie, C.J. Mitchell

Combined Gastroenterology Service, Scarborough Hospital, United Kingdom  
The pathophysiology of acute pancreatitis (A. P) is complex, involving ischaemic injury, neutrophil infiltration and enzyme activation. Pancreatic Elastase 1 (PE-1) has been shown to play a key role in the consequent destructive inflammatory process and might therefore provide a useful marker to predict severity. We have used an ELISA method [Schebo Tech, Germany] to evaluate serum PE-1 in 25 patients with acute pancreatitis. Twenty-five patients (11 M, 14 F aged 29–93) with AP were studied. The diagnosis of AP was based on clinical criteria, a 3.5-fold rise in serum amylase and either CT or ultrasound scans. The aetiology of the AP was gallstones in 13, alcohol 2, idiopathic 6, and miscellaneous 4, and was graded as mild in 20 and severe in 5. AP was graded using the Glasgow criteria. Serial measurements of CRP, amylase and PE-1 were evaluated. There was no significant difference between PE-1 levels in mild (median 34, range 2–40) and severe (median 35, range 0–176) pancreatitis. The same was true for CRP and amylase. The serial levels of PE-1 were not significantly different in patients developing complications, in patients with mild and severe pancreatitis and in those patients who died. The correlation coefficient of PE-1 levels with amylase was 0.74 ( $p < 0.001$ ). In this study, serum PE-1 correlated closely with serum amylase activity, but did not provide further prognostic information with respect to mortality or morbidity. Pancreas: Pancreatitis, acute } "Serum Pancreatic Elastase-1 in Acute Pancreatitis"

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"P P 19 0508" P 19 0508 **Serum Pancreatic Elastase-1 as a Diagnostic Test for Acute Pancreatitis: A Prospective Evaluation**

\*C. Millson, K. Charles, P. Poon, J. MacFie, C.J. Mitchell

Combined Gastroenterology Service, Scarborough Hospital, United Kingdom The proteolytic enzyme Pancreatic elastase 1 (PE-1) is an important marker of pancreatic pathology, however it has yet to be evaluated prospectively as a diagnostic test. This study examined the diagnostic value of serum PE-1 in all patients in whom acute pancreatitis was suspected. Over a 3 month period, all requests for amylase tests received in the laboratory were also tested for PE-1 using an ELISA test (ScheboTech, Germany). Patients with pancreatitis were identified by standard diagnostic criteria. Requests for amylase were made on 566 patients, (mean age 56.4 years, range 4–98). A diagnosis of pancreatitis was made in 25 (4%) patients. Other diagnoses included non-specific abdominal pain 220 (39%), surgical intra-abdominal emergencies 63 (11%), biliary tract disease 39 (7%), carcinoma of pancreas 11 (2%) and chronic pancreatitis 7 (1%). The sensitivity and specificity of PE-1 were 72% and 91% respectively. Diagnostic efficiency was 90%. This compares with sensitivity of 84% and specificity of 99% for serum amylase (using a cut-off of 3.5 {\'b4} normal). Measurements of serum PE1 as a diagnostic test for acute pancreatitis in patients presenting with abdominal pain confers no benefit above the use of the cheaper and widely available measurement of serum amylase. Pancreas: Pancreatitis, acute }" "Serum Pancreatic Elastase-1 as a Diagnostic Test for Acute Pancreatitis: A Prospective Evaluation"

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## "P P 19 0509" P 19 0509 Role of Non Esterified Fatty Acids in Necrotizing Pancreatitis: An Experimental Study

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INSERM U410 Facult<sup>1</sup>e9 X., Bichat, Paris, France Non-esterified free fatty acids (NEFA) released by pancreatic lipase are supposed to favor tissue necrosis by their detergent properties. The aims of this work were to determine if NEFA are released in blood stream and peritoneal cavity in a rat model of taurocholate-induced pancreatitis, and to precise their action on the necrotic process, using a specific covalent inhibitor of pancreatic lipase, injected intra-peritoneally (i.p.). Three groups of male anaesthetized Sprague-Dawley rats were studied. The first group (control, n = 5) was submitted to a sham laparotomy. In the second group (T, n = 10), a retrograde infusion of 0.3 ml/100 g of 5% taurocholate induced a necrotizing pancreatitis, followed by 4 i.p. injections of saline at 6 hrs intervals. The third group (T + THL, n = 10) received both the retrograde taurocholate and 4 i.p. injections of 1 mg of the lipase inhibitor tetrahydropipstatin (THL). The animals were sacrificed after 24 hours by aortic puncture, preceded by a last saline i.p. injection. Ascitis was harvested, macroscopic lesions were scored, and the pancreas was removed for histological examination. The taurocholate retrograde infusion induced pancreatic necrosis, extra-pancreatic fat necrosis, ascitis and pancreatic edema, absent in the control group. The raise of plasma and ascitis lipase levels was significantly less pronounced in the T + THL group than in the T group. Plasma NEFA levels were comparable in the 3 groups, whereas the raise of NEFA levels in the ascitis, observed in the T and T + THL groups compared to control, was significantly less pronounced in the T + THL group than in the T group (0.31 – 0.02 mmol/l vs 0.75 – 0.1 mmol/l p < 0.01). Fat necrosis was also significantly less extended in the T + THL group than in the T group. No measurable release of NEFA occurred in circulation in this experimental necrotizing pancreatitis. But a NEFA release by pancreatic lipase occurred in the abdominal cavity and could play a role, locally promoting fat tissue necrosis.

Pancreas: Pancreatitis experimental } "Role of Non Esterified Fatty Acids in Necrotizing Pancreatitis: An Experimental Study"

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"P P 19 0510" P 19 0510 **Early Microvascular Damage in Caerulein Induced Acute-Pancreatitis in the Rat**

\*C.A. Hernandez, C. Emparan, Z.G. Zhou, R. Jover-Clos, L. Bisaro, E. Hliba, S.D. Fahimi, N. Senninger

University of Cordoba, Universitätsklinikum Heidelberg *Introduction:* edematous acute pancreatitis induced by caerulein is a well known model used in experimental pancreatitis. In order to see the events produced in early steps of acute pancreatitis a model of subcutaneous injection of caerulein has been used. *Material and Methods:* 200 g. Wistar male rats were fasted overnight and were treated with: A) a volume of saline similar to that used in treatment groups (n = 6). B) subcutaneously injected caerulein (5, 5, and 7.5 microg/kg weight) at the beginning of the experiment, hour 1 and hour 2 (n = 12). Four hours after the beginning of the experiment blood samples were collected, and tissue samples of the pancreas were taken for optic and electronic microscopy studies. In group B two different techniques were used for obtaining tissue samples 6 animals were fixed in glutaraldehyde, while the other six were perfused intraaortically with Ringer's lactate prior to introduce the glutaraldehyde and fixed the pancreatic tissue. *Results:* macroscopic findings of acute pancreatitis were found in caerulein treated group. Blood amylases were higher (2) in caerulein treated groups in a similar way to the presented in the first 20–30 minutes of i.v. caerulein induced acute pancreatitis. Under optic microscopy vacuoles were shown in pre-sphincteric interlobular arterioles, this damage was correlated with a great amount of vacuoles and early mitochondrial damage in endothelial and smooth muscle cells of pancreatic arterioles, and macrovasculature. *Conclusions:* subcutaneous induced acute pancreatitis correlates with early steps of other experimental designs such as i.v perfusion. In the early steps of acute pancreatitis vascular damage in endothelial and smooth muscle cells can be demonstrated, and are probably related with N.O. activity. Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "Early Microvascular Damage in Caerulein Induced Acute-Pancreatitis in the Rat"

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## "P P 19 0511" P 19 0511 **Changes of Hormones in Pancreatico-Duodenal Vein in Acute Experimental Pancreatitis**

\*A. Gidayatov, V. Gidayatova

Azerbaijan Medical University Baku, Azerbaijan In the present study we investigated the levels of insulin (I), Glucagon (G), Somatostatin (SS) in pancreatico-duodenal vein (PDV) in acute experimental pancreatitis (AEP). The experiments were carried out on 10 dogs. The biliary pancreatitis was induced in 5 dogs. The other 5 dogs made up a control group. The blood for the studies was taken from PDV prior to the inducing of AEP and on the 3-rd day (at the height of pancreatitis development) relaparotomy was carried out and the blood was taken prior to the administration of Pancreozymin (PZ) (2 u/kg), at 20-th and 40-th min. after the PZ administration. *Methods.* The levels of hormones were determined by RIA. *Summary of the results.* The I level in PDV prior to the inducing of AEP was  $99.4 \pm 4.7$  u/ml; on the 3-rd day after the inducing of AEP the I level was reduced two-fold: to  $40.5 \pm 6.2$  u/ml ( $p < 0.05$ ). The G concentration in PDV was  $129.6 \pm 12.8$  ng/ml; on the 3-rd day the hormone level was markedly increased up to  $253.5 \pm 16.8$  ng/ml ( $p < 0.05$ ). The SS level was also considerably increased in AEP (from  $60.9 \pm 7.6$  pg/ml to  $116.5 \pm 9.4$  pg/ml;  $p < 0.05$ ). The PZ administration in dogs with AEP caused the rise of the I level by 31%, as compared with the initial one; in control animals the I level was increased by 105% following the PZ administration. The G content in AEP in response to PZ was increased by 12%; while in control group the content of G was increased by 77%. The SS level in PDV the animals with AEP after the PZ administration, was increased by 30%. This index in the control group was 70%. *Conclusion.* The results of the present investigations showed that in AEP: 1) hypoinsulinemia, hyperglucagonemia and hypersomatostatinemia are observed in PDV; 2) the response reaction of hormones to the stimulus is markedly decreased. Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute Hormones and receptors: Brain gut axis } "Changes of Hormones in Pancreatico-Duodenal Vein in Acute Experimental Pancreatitis"

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**"P P 19 0512" P 19 0512 C-Reactive Protein in Comparison with Haptoglobin and Amylase as Indicators of Necrosis in the Early Phase of Experimental Acute Pancreatitis**

\*Z.P. Wu, J. Shen, H. Xiao, Y.H. Song, M. Lui

Department of Surgery and Pancreatology Laboratory, Sichuan Continuing Education College of Medical Sciences, Chengdu 610041, P. R. China To clarify the relationship between changes in serum C-reactive protein (CRP) and pathological changes in pancreatic parenchyma, this study was performed by using dog model with acute pancreatitis (AP). The models were induced by intrapancreatoductal injection of fresh trypsin and trypsin bile mixture respectively for acute edematous and necrotizing pancreatitis (AOP and ANP) in 24 dogs. CRP, haptoglobin (HPT) and amylase levels in the serum were determined for 2 and 4 hrs after the development of AP. At 2 hrs after the development of AP, amylase level rose directly in both pancreatitis groups ( $P < 0.01$ ), CRP and HPT levels in ANP group rose markedly ( $P < 0.001$ ), but only CRP level was significant difference between either of the pancreatitis groups ( $P < 0.001$ ). At 4 hrs after the development of AP, amylase and CRP levels were increased in two pancreatitis group, only HPT rose in dogs of ANP group ( $p < 0.01$ ). On the other hand, CRP level in ANP group was higher than that in AOP group ( $p < 0.001$ ). In the three parameters, only the correlation between the serum CRP level and the severity of pancreatic damages was significant ( $r_s = 0.7964$ ,  $P < 0.001$  and  $r_s = 0.8246$ ,  $P < 0.001$ ) respectively at 2 and 4 hrs after induced AP in ANP group. Dogs with lethal outcome (83.3% mortality) had markedly elevated initial serum CRP level (from  $34.64 - 2.66$  to  $148.77 - 7.25$  mg/dl) at 2 hrs after AP ( $P < 0.001$ ) in ANP group. These results suggest that serum CRP levels is reliable parameter with a high detection rate for pancreatic necrosis and available for the prognostic evaluation of AP in the early phase of acute necrotizing pancreatitis. Pancreas: Acinar, duct cell function Pancreas: Pancreatitis experimental Pancreas: Pancreatitis, acute } "C-Reactive Protein in Comparison with Haptoglobin and Amylase as Indicators of Necrosis in the Early Phase of Experimental Acute Pancreatitis"

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## "P P 19 0513" P 19 0513 Retrospective Analysis of Etiology of Acute Pancreatitis

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*Purpose of study:* It is well-known that alcoholic etiology of acute pancreatitis is outstanding high in Hungary. In most of European countries the rate of this etiologic factor is much lower. The aim of our retrospective study was to analyse the etiology of our patients and the relationships between etiology and morbidity, mortality rates.

*Patients and method:* Between 1990 and 1994 altogether 374 patients were admitted in our surgical department with acute pancreatitis. This enormous great number doesn't include a lot of mild cases which were hospitalized in departments of internal medicine. Diagnosis was based on clinical signs, elevation of serum enzymes and imaging studies (US, CT, ERCP). Necrosis was detected by contrast enhanced CT scan or by surgery.

*Results:* In the whole group 220 pts had alcoholic, 115 pts had biliary and 39 pts had other (postoperative, traumatic or hyperlipidaemic) etiology. More than 60% of alcoholic pts consumed > 60 gr/day/> 5 years. Necrosis developed in 127 pts. The rate of alcoholic etiology was 80.3% in this group (102 pts) and only 7.9% of the biliary lithiasis (10 pts). Fifteen pts had other etiology (11.8%). In the oedematous group (247 pts) the rate of alcoholic and biliary etiology was about same (47.7% and 42.5%). Overall mortality was 5.8% (22 pts) and 15% (19 pts) of the necrotizing group. According to etiology we lost 14 pts from the alcoholic (6.4%), 3 pts from the biliary (2.6%) and 5 pts from the other — mostly hyperlipidaemic — group (33.3%).

*Conclusion:* Our data support that in Hungary about 80% of the cases of necrotizing pancreatitis have alcoholic etiology with significantly worse prognosis.

Pancreas: Pancreatitis, acute } "Retrospective Analysis of Etiology of Acute Pancreatitis"

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## "P P 19 0514" P 19 0514 Serum Interleukin 10 in Human Acute Pancreatitis

\*P. Billi, R. Miniero, R. Pezzilli

Emergency Department and Central Laboratory, St. Orsola Hospital, Bologna, Italy Interleukin 10 (IL-10) recently emerged as an anti-inflammatory cytokine which inhibits the secretion of proinflammatory cytokines by monocytes and/or macrophages and the release of free oxygen radicals. It has been reported that treatment with IL-10 decreases the severity of experimental pancreatitis, mainly by inhibiting cellular necrosis. We did the present study because there are no data about serum levels of IL-10 in human acute pancreatitis. Forty-five patients with acute pancreatitis (25 M, 20 F, mean age 60 years, range 20–82) were studied; the diagnosis was based on characteristic abdominal pain associated with a two-fold increase of serum lipase, and it was confirmed by imaging techniques. Acute pancreatitis was of biliary origin in 30 patients, due to alcohol abuse in 10, due to pancreas divisum in 1, and of unknown origin in the remaining 4. According to the Balthazar criteria, 19 patients had scores less or equal to 2 points and 26, had scores greater than 2 points. Twelve healthy subjects were also studied as controls. Serum IL-10 was determined in all subjects on admission, and in acute pancreatitis patients also daily for the subsequent 4 days using a commercial kit (Predicta Human Interleukin-10 kit, Genzyme Co., USA). Healthy subjects had no detectable serum levels of IL-10. In acute pancreatitis patients, serum IL-10 levels peaked on the first day of the disease (mean – SE: 193 – 171 pg/ml) and subsequently, decreased significantly (mean – SE: 137 – 96 pg/ml on the 2nd day of illness, 117 – 18 pg/ml on the 3rd day, 2.4 – 1.4 pg/ml on the 4th day and 2.5 – 1.0 pg/ml on the 5th day;  $P < 0.01$  vs. the first day of the disease). On the first day of the acute pancreatitis, patients with the Balthazar scores less or equal to 2 points had serum levels of IL-10 (mean – SE: 424 – 389 pg/ml) significantly higher than those with scores greater than 2 points (mean – SE: 15 – 6 pg/ml) ( $P < 0.05$ ). In the subsequent 4 days serum IL-10 levels decreased in both groups of patients in a similar fashion. The results of our study demonstrated that in patients with acute pancreatitis there is a secretion of IL-10 on the first day of the illness which is more marked in patients with mild acute pancreatitis than in those with the severe form of the disease. In the subsequent days there is a significant decrease of IL-10 secretion in both groups of patients. In patients with acute pancreatitis, especially those having the severe form of the illness, the administration of IL-10 should be considered in order to explore its potential therapeutic effect.

Pancreas: Pancreatitis, acute } "Serum Interleukin 10 in Human Acute Pancreatitis"

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"P P 19 0515" P 19 0515 **Does Inhibition of Polyamines Synthesis Affect the Pancreas Regeneration after Acute Pancreatitis. Ultrastructural and Biochemical Study**

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<sup>1</sup> Pathomorphology Dept., Medical School, Bialystok, Poland The factors involved in pancreas regeneration after acute pancreatitis (AP) are poorly clarified. The importance of polyamines in tissue growth and regeneration was shown. *The aim* of the present study was to evaluate the effect of polyamines synthesis inhibition on pancreas regeneration after AP. *Methods:* AP was induced in male Wistar rats by s.c. injections of caerulein (12 mg/kg) for 2 days t.i.d. with control (C) receiving saline. After AP induction rats were treated with inhibitor of polyamines synthesis a-difluoromethylornithine (DFMO) or saline for 2, 7 or 14 days. DFMO was given 3 {\\b4} 300 mg/kg bw i.p. during three treatment periods and additionally for the first 3 days (1 day before and during 2 days of caerulein injections as: i.p injections and 2% solution in drinking water). Pancreatic weight (PW), total protein, enzymes, DNA, RNA contents were evaluated and ultrastructural examination of tissue specimens was performed. *Results:* Two days after AP induction the interstitial edema, inflammatory infiltration and destruction of some acinar cells were observed. The mitosis of acinar cells were seen in both AP groups. After 14 days nearly complete recovery of pancreas ultrastructure in AP untreated rats was observed. DFMO treatment of AP animals (especially after 7 and 14 days) was connected with more pronounced injury of acinar cells. They showed the signs of RER lesion accompanied with large, dilated cisterns of Golgi apparatus. The amount of zymogen granules and condensing vacuoles were lowered after 7 and 14 days of treatment with DFMO when compared to untreated AP-rats and C. The evident polymorphism of mitochondria was also seen in AP rats treated with DFMO. Concurrently to morphological changes the biochemical parameters showed, that pancreas injury occurred 2 days after AP induction. The spontaneous recovery was observed after 14 days in both AP groups, however, in DFMO treated rats PW and RNA content still remained significantly lower than in C. *Conclusion:* These results suggest that the inhibition of polyamines synthesis delay the spontaneous regeneration after acute pancreatitis. Supported from the grant KBN 4 S402 03 06 Pancreas: Pancreatitis experimental }" "Does Inhibition of Polyamines Synthesis Affect the Pancreas Regeneration after Acute Pancreatitis. Ultrastructural and Biochemical Study"

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"P P 19 0516" P 19 0516 **The Role of Oxidative Stress in Acute Pancreatitis**

\*A. Gabryelewicz, U. Wereszczynska-Siemiatkowska, M. Jedynak

Department of Gastroenterology, Medical School, Bialystok, Poland The oxidants/antioxidants imbalance as an important pathway in experimental acute pancreatitis (AP) has been found. The *aim* of this study was to evaluate the impairment of oxidants/antioxidants balance in the serum and urine of patients with AP. *Methods.* The studies were performed in 44 patients with mild (n = 16), moderate (n = 11), and severe (n = 17) AP. The serum and urine malondialdehyde (MDA) concentration as an index of oxidant-mediated lipid peroxidation, and sulfhydryl groups (SH) – major nonenzymatic antioxidant were measured at admission and at 2, 5, 10-th day of disease. The statistical analysis was performed using Wilcoxon and Mann-Whitney U tests. *Results.* Serum phospholipase A<sub>2</sub> (PLA<sub>2</sub>) at admission was increased by 31%, 40%, 54% in mild, moderate and severe AP respectively (p < 0.01). Serum MDA concentration in severe AP was elevated by 44% (p < 0.01) at admission and 50% (p < 0.01) after 10 days in comparison to mild AP and by 27% (p < 0.01) and 34% (p < 0.05) in comparison to moderate AP, respectively. The highest urine MDA concentrations in severe AP in 2 day (by 38% p < 0.01), 5 day (by 45% p < 0.05) in comparison to admission values were observed. In this time in mild and moderate AP urine MDA concentration was significantly lower in comparison to severe AP. Serum SH concentration in severe AP was lowered after 2, 5, 10 days by 18% (p < 0.01), 22% (p < 0.001), 23% (p < 0.001) respectively, while in moderate AP after 10 days by 31% (p < 0.01) in comparison to admission; in mild AP slight differences were found. In acute pancreatitis the increase of serum and urine MDA concentration was associated with decrease of serum and urine SH groups concentration. The disturbance of oxidants/antioxidants balance coexists with the increase of serum phospholipase A<sub>2</sub> activity. *Conclusion.* An association of oxidants/antioxidants imbalance with severity of acute pancreatitis suggest an important role of oxidative stress in pathogenesis of acute pancreatitis. Partly supported by grant nr 513777. Pancreas: Pancreatitis, acute } "The Role of Oxidative Stress in Acute Pancreatitis"

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## "P P 19 0517" P 19 0517 Factors Influencing Outcome in Pancreatic Necrosis

\*P.C. Leeder, I.G. Martin, M.J. McMahon

Department of Surgery, The General Infirmary at Leeds, UK 144 patients with acute pancreatitis were treated consecutively over a seven year period by one consultant (MJM). 70 were admitted from our local population and 74 were transferred from other hospitals. The median age was 54 years (17–91) and 90 patients were male (1.7:1.0). The aetiology was thought to be ethanol in 44 patients, gallstones in 51, idiopathic in 33 and due to other causes in 16 patients. Dynamic CT imaging was performed in 99 patients. Pancreatic necrosis was diagnosed in 54 patients on CT. In 24 of these patients (44%), infection was demonstrated within the necrosis either by fine needle aspiration or subsequently at operation. 1 patient was found to have infected pancreatic necrosis which was not diagnosed at CT. The majority of organisms were of gut origin, with a number of staphylococci and yeasts grown. Of the 54 patients, 26 were managed conservatively and 28 had operation. Of these, 22 patients required pancreatic debridement. Surgery was carried out a median of 22 days after presentation. Overall 26 of the 144 (18%) patients died from their pancreatitis. The best predictor of overall mortality was the APACHE II score on admission ( $p < 0.001$ ). 14 (56%) patients with infected pancreatic necrosis died compared with only 6 (20%) of those with demonstrated sterile pancreatic necrosis. 70% of patients undergoing pancreatic debridement died, a mean of 68 days from onset of their attack. The tertiary referral group had a significantly higher mortality following pancreatic debridement, compared to those presenting locally ( $p < 0.03$ ). This we feel is due to both a delay in referral and transfer of patients to a specialist centre, exacerbated by a lack of intensive care beds. Patients with pancreatic necrosis should therefore be referred earlier to a specialist unit where optimum diagnostic and therapeutic services are available to deal with this difficult condition. Clinical practice: Management strategy Pancreas: Pancreatitis, acute } "Factors Influencing Outcome in Pancreatic Necrosis"

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## "P P 19 0518" P 19 0518 **Morbidity and Mortality in Acute Pancreatitis: An Update**

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Surveys on morbidity and mortality of acute pancreatitis date back a few decades. Newer studies concentrate mainly on the treatment of severe acute pancreatitis, i.e. only on a special aspect of the disease. Our retrospective study aimed to obtain more up-to-date data based on a substantial number of patients diagnosed and treated for acute pancreatitis during the last 15 years. *Patients and Methods.* The course of the disease was studied in 602 patients who were admitted between 1/1/1980 and 30/9/1993 to the University Hospital of G\fttingen (n = 417) and between 16/11/1986 and 30/6/1994 to the Municipal Hospital of L\fcneburg (n = 185). *Results.* Etiologies were biliary tract disease in 227 (37.7%), alcohol abuse in 177 (29.4%), unknown in 133 (22.1%), and other in 65 (10.8%) patients. Mean hospital stay was 27.9 – 24 days (x – SD), median 23 days. Within the first 48 hours, respiratory insufficiency was observed in 63.2% patients (of 204 patients undergoing arterial blood gas analysis) as well as renal insufficiency in 32.6% of all 602 patients. Artificial ventilation was indicated in 12.5% and dialysis in 7% patients. Pancreatic pseudocysts developed in 14.3% patients and surgical treatment was necessary in 11.1%. Mortality rate was 6.1% and did not differ between the university and the non-university hospital. However, mortality rate significantly correlated with respiratory and renal insufficiency, artificial ventilation and dialysis procedures (p < 0.001). Mortality rate was significantly higher in patients secondarily admitted as compared to patients primarily admitted to hospital (12.1 vs. 4.6%; p < 0.005). *Conclusion.* Mortality rate was distinctly lower than those reported in the last 3 decades of 10% to 25%. The higher mortality rate of secondarily admitted patients indicates the need for early transfer of patients with severe acute pancreatitis to specialized hospitals. Clinical practice: Epidemiology (non cancer)Pancreas: Pancreatitis, acute } "Morbidity and Mortality in Acute Pancreatitis: An Update"

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## "P P 19 0519" P 19 0519 Predictors of the Etiology of Acute Pancreatitis

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The purpose of the study was to identify which laboratory parameter or combination of parameters predicts alcoholic or non alcoholic acute pancreatitis. A hundred and sixty-seven patients were divided into groups A (alcoholic pancreatitis) and NA (non alcoholic pancreatitis). Group NA consisted of groups B (biliary pancreatitis) and NANB (non alcoholic, non biliary pancreatitis). The values of serum amylase, lipase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin, lipase/amylase (L/A) ratio, erythrocyte means corpuscular volume (MCV) and urine amylases were analysed. Univariate analysis (Wilcoxon rank sum test) showed significant differences in serum amylase, ALT, AST, ALP, L/A ratio, MCV and urine amylase between the groups A and NA. Multivariate analysis (logistic regression) showed that three variables were simultaneously significant predictors of alcoholic or non alcoholic pancreatitis: L/A ratio ( $p < 0.001$ ), MCV ( $p = 0.023$ ) and ALP ( $p = 0.071$ ). Resulting mathematical model for these three parameters has higher sensitivity (87.5%), specificity (97.8%) and diagnostic efficiency (95.8%) than any individual parameter analysed by univariate analysis. We conclude that L/A ratio, MCV and ALP are the most significant variables for the prediction of alcoholic versus non alcoholic pancreatitis. Pancreas: Pancreatitis, acute } "Predictors of the Etiology of Acute Pancreatitis"

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"P P 19 0520" P 19 0520 **The Effect of SMS 201–995 on Rats Pretreated with L-Asparaginase** Ahmet G\ 'f6rg\ 'fcl,

\*Kayhan Bur\ 'e7ak, Kayhan Basak, Menten B\ 'fclent

G\ 'dcTF, Ankara, T\ 'fcrkiye The aim of the study was to investigate the effect of SMS 201–995 on L-asparaginase induced hyperamylasemia and/or pancreatitis in rats. *Materials and methods:* 60 Wistar albino rats were into 5 groups. In the first group 100 \ 'b5g SMS 201–995 (ip) was administered 6 times with 2 hours intervals. The second group received a single dose of 5000 IU L-asparaginase (ip). In the third group, first 0.5 cc caerulein (ip) 2 times with 2 hours intervals and then 5000 IU L-asparaginase were given (ip). In the fourth group; we added 100 \ 'b5g SMS 201–995 (ip) 6 times with 2 hours intervals to the third group's treatments. The last group received 5000 IU L-asparaginase (ip) and 100 \ 'b5g SMS 201–995 (ip) 6 times with 2 hours intervals. Twelve hours after the first treatment doses, rats were killed with the withdrawal of 5 cc blood and the pancreatic tissue was removed. We compared both EC 3.2.1 amylase and EC 3.1.1.3 lipase levels. The pancreatic tissue samples were evaluated by two blinded pathologist. *Results:* We scored the severity of pancreatitis in all groups. According to the scoring system, group 1 lacked any evidence of pancreatitis. Groups 2 and 4 had mild or moderate pancreatitis; group 3 had severe pancreatitis; and group 5 had mild pancreatitis. EC 3.1.1.3 lipase activities were all with in normal ranges in all groups, but EC 3.2.1 amylase activities were significantly increased in all groups except for group 1. *Conclusion:* SMS 201–995 did not inhibit hyperamylasemia in rats induced by L-asparaginase. On the other hand, the microscopical findings of pancreatic injury induced by caerulein, L-asparaginase, or both of them were prevented by SMS 201–995, within the time limits of this study. Pancreas: Pancreatitis experimental }" "The Effect of SMS 201-995 on Rats Pretreated with L-Asparaginase"

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"P P 19 0521" P 19 0521 **Acute Pancreatitis in Cholesterolosis: Preliminary Results of a Prospective Study**

\*M. Ventrucci, D. Festi, G.M. Ubalducci, A. Sangermano, A. Colecchia, E. De Vergori, P. Fusaroli, M. Orsini, P. Simoni, E. Roda

Dept of Gastroenterology, University of Bologna, Italy

Dept of Physiopathology, University of Chieti, Italy  
The etiological role of cholesterolosis in acute pancreatitis remains unclear. The presence of supersaturated bile with formation and migration of cholesterol crystals, impaction of detached cholesterol polyps at the sphincter of Oddi and biliary dysmotility have been suggested as putative factors. The aim of this study was to look for evidence of pancreatic damage in cholesterolosis and investigate its pathophysiology.  
*Methods:* 72 pts with ultrasonographic evidence of cholesterolosis were studied for follow-up periods ranging from 1 to 4 years. The presence of this condition was confirmed at repeat ultrasonography (within 12 months) performed by another examiner. Serum pancreatic isoamylase and lipase were determined in each patient. Biliary lipid analysis and crystal detection by microscopy were performed in the duodenal bile of 22 pts. Gallbladder motility was evaluated by ultrasound after a standard liquid meal in 40 pts. *Results:* During the follow-up period acute edematous pancreatitis occurred in 2 pts (3%) and mild abdominal pain not typical of acute pancreatitis was reported in 23 (32%). Abnormal pancreatic findings by ultrasound were observed only in one patient who had acute pancreatitis prior and during the study. Significant elevation (> 2 times the upper normal limit) of serum pancreatic amylase and lipase was detected in only one patient with nonpancreatic abdominal pain. Supersaturated bile was found in 14/22 pts (64%), two of them with acute pancreatitis. Cholesterol and/or calcium bilirubinate crystals were seen in 12/22 (54%), two of whom with acute pancreatitis. Gallbladder motility, evaluated by both fasting and residual volumes and emptying, was normal in all pts. *Conclusion:* These preliminary results confirm the existence of a relationship between cholesterolosis and acute pancreatitis. The presence of supersaturated bile and of cholesterol or calcium bilirubinate crystals may be a factor in the pathophysiology of acute pancreatitis in this condition. Pancreas: Pancreas, cystic fibrosis  
Liver and bile ducts, 2: Gallstones, formation, treatment } "Acute Pancreatitis in Cholesterolosis: Preliminary Results of a Prospective Study"

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"P P 19 0522" P 19 0522 **Pancreatitis in Acute Gastroenteritis** M. Fuchs,

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<sup>1</sup> II. Med. Klinik, University of Leipzig, Germany

<sup>2</sup> Dep. of Anesthesiology, University of Mannheim, Germany A raised serum lipase activity has been demonstrated in 22% of patients with acute gastroenteritis who had neither clinical nor sonographic signs of pancreatitis (GE 1995: 108 A 384). The underlying mechanism is still unknown. An increase in the intestinal permeability (IP) and not an inflammation of the pancreas has been proposed to be responsible for the hyperlipasemia in salmonella enteritis (Schw Med Wochenschr 1993; 123: 1482–86). As a highly specific marker of acute pancreatitis the pancreatitis associated protein (PAP) has recently been described (J Clin Invest 1992: 90, 2284–91). The aim was to investigate the relationships between a raised serum lipase and the IP and the serum PAP concentrations. *Methods:* 33 consecutive patients (20 women, 20–85 years) hospitalized for acute gastroenteritis participated in the study. IP was assessed by cellobiose (C) mannitol (M) ratio measured in urin collected during 5 hours, serum PAP concentration was determined by a competitive ELISA with a monoclonal antibody, and serum lipase activity was measured by a clinical routine method. *Results:* (Mean – SEM) Lipase (< 190 U/l) Lipase (> 190 U/l) Normal PAP (< 100 ng/ml) 20 1 Elevated PAP (491 – 53 ng/ml) 2 10 Normal IP (C/M 0.004 { - } 0.03) 11 4 Elevated IP (C/M > 0.03) 9 9 Using chi-square test with Yate's correction, there was a significant relationship between the elevation of lipase activity and PAP concentration (p < 0.0005), but not between lipase and IP. *Conclusion:* The association between the increased lipase activity and PAP concentration suggests a pancreatic damage in some patients with acute gastroenteritis. Lipase elevation in acute gastroenteritis is not due to an increased IP. Pancreas: Pancreatitis, acute Immunology and microbiology: GI infections in adults } "Pancreatitis in Acute Gastroenteritis"

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"P P 19 0523" P 19 0523 **Protection of Pancreatic Exocrine Secretion in the Course of Acute Experimental Pancreatitis in Rats**

\*J. Jaworek, J. Bilski, A. Dembinski, Z. Warzecha, S.J. Konturek

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The effects of calcitonin gene-related peptide (CGRP) and stimulation of pancreatic sensory nerves (SN) on secretory activity of isolated pancreatic acini in the course of caerulein-induced pancreatitis (CIP) were investigated in intact and capsaicin-denervated rats. CIP was produced by infusion of caerulein (10 µg/kg-h<sup>4</sup> 5 h) to the conscious rats. To stimulate duodenal sensory nerves 0.5 mg/kg of capsaicin (CP) was given intraduodenally (i.d.). To inactivate sensory nerves 100 mg/kg of CP was given s.c. over 3 days. CGRP (2 µg/kg s.c.) was injected before and during infusion of caerulein and in control tests. CIP significantly diminished the volume of isolated pancreatic acini (by 75%), and maximal secretion of amylase from these acini produced by caerulein or urecholine (by 45% and 40%, respectively) whereas basal enzyme release and pancreatic weight increased (both by 30%). Deactivation of sensory nerves by CP aggravated the changes produced by CIP. These harmful effects of ablation of sensory nerves on CIP were completely reversed by administration of CGRP into the CP-denervated rats. In intact rats treatment with CGRP, or stimulation of sensory nerves by CP, significantly attenuated all changes produced by CIP. Deactivation of sensory nerves and (or) administration of CGRP did not affect significantly all parameters tested. *Conclusion:* Administration of CGRP, or stimulation of pancreatic sensory nerves, attenuated the damage of pancreatic acini produced by CIP. Pancreas: Acinar, duct cell function Pancreas: Secretion, regulation Pancreas: Pancreatitis experimental } "Protection of Pancreatic Exocrine Secretion in the Course of Acute Experimental Pancreatitis in Rats"

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"P P 20 0524" P 20 0524 **Clinical Impact of Additional Information from Octreoscan Scintigraphy (SRS) on the Management of Patients with Zollinger-Ellison Syndrome (ZES)**

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<sup>1</sup> Dpt of Nuclear Medicine, CHU Bichat-Claude Bernard, 75877 Paris Cedex 18, France SRS detects gastrinomas not visualized by any other techniques. *Aim:* To evaluate the information provided by SRS that could have an impact on the management of patients with the ZES, in function of the 3 main clinical situations (sporadic, multiple endocrine neoplasia type 1-MEN1, liver metastases-LM) and our current therapeutic strategy. *Methods:* 85 consecutive ZES patients without known extra-abdominal metastases were divided into the 3 following groups independently of SRS results: 1- sporadic ZES without LM (n = 48), 2- MEN1 + ZES without LM (n = 18) and 3- LM (n = 19). Results of conventional imaging techniques (endoscopic US in 85% of sporadic ZES pts and bone scintigraphy in all LM pts) were compared to those of SRS. *Definition of SRS Additional Information having an Impact on Management (AIIM)* within each of the 3 groups: 1- AIIM in *sporadic group*: all additional information provided by SRS (considering the systematic surgical attitude); 2- AIIM in *MEN1 + ZES group* (no systematic surgery): additional information suggesting LM or another unknown endocrinopathy, especially thymic and bronchial carcinoids; 3- AIIM in *LM group*: additional information suggesting extra-abdominal metastases, and when LM were resectable, presence of other LM precluding resection. Results of follow-up of pts with AIIM was given. *Results:* 1- *SRS global positive rate:* 33 pts (69%) with sporadic ZES, 12 pts (67%) with MEN1 and 17 pts (89%) with LM. 2- *AIIM:* A- Sporadic ZES: 22 AIIM in 20 pts (42%): hot spots in duodenopancreatic area (11), liver (2), mediastinum (1), pituitary area (1) and adrenals (1), hot spot at a site of a doubtful pancreatic lesion (2), higher number of hot spots in the duodenopancreatic area than the number of visualized tumors (4), B- MEN1: 6 AIIM in 4 pts (22%): liver (1), mediastinum (3), lungs (2) and C- LM: 3 AIIM in 3 pts (16%): bones (2), contralateral liver (1). 3- *Follow-up of AIIM* was available in 13/20 sporadic ZES pts (15 AIIM), 3/4 MEN1 pts (4 AIIM) and 3/3 LM pts (3 AIIM). Confirmation of AIIM during follow-up: 10 (67%) in sporadic ZES, 4 (100%) in MEN1 pts and 3 (100%) in LM pts. *Conclusion:* These results suggest that SRS should be performed mainly before surgery in sporadic ZES and before liver surgery. In the other situations, SRS should not be systematic. Hormones and receptors: Clinical disorders Oncology, specific: Endocrine }" "Clinical Impact of Additional Information from Octreoscan Scintigraphy (SRS) on the Management of Patients with Zollinger-Ellison Syndrome (ZES)"

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"P P 20 0525" P 20 0525 **Hepatic Arterial Chemoembolization with Streptozotocin in Patients with Liver Metastases of Endocrine Digestive Tumors**

\*S. Dominguez<sup>1</sup>, A. Denys<sup>2</sup>, V. Vilgrain<sup>2</sup>, Y. Menu<sup>2</sup>, P. Bernades<sup>1</sup>, P. Ruzsniwski<sup>1</sup>

<sup>1</sup> Federation of Hepato-Gastroenterology, 92118 Clichy Cedex, France

<sup>2</sup> Radiology, Hospital Beaujon, 92118 Clichy Cedex, France Hepatic arterial chemoembolization (CE) with doxorubicin is an effective palliative treatment for progressive liver metastases of endocrine digestive tumors. Systemic chemotherapy with streptozotocin (STZ) is the drug of choice for the treatment of these tumors; STZ has not been used for the CE so far. *Patients and methods:* 8 consecutive patients (pts), mean 58 years old, were included prospectively between July 1993 and February 1995. All had progressive liver metastases (histological confirmation: 6/8): 6 carcinoid tumors, 1 pancreatic gastrinoma, 1 non-secreting endocrine pancreatic tumor. The metastases were synchronous to the primary tumor in 6 pts, metachronous in 2, diffuse in 5 pts. Systemic chemotherapy had been ineffective in 3 pts. STZ was administered under general anaesthesia at a dose of 1.5 g/sqm in emulsion with iodized oil (LUF) before embolization with gelatine sponge. 2 to 6 sessions (median: 3) were performed in 6 pts (1 session in 2 pts). The modifications in size of liver metastases were evaluated by tomodensitometry or MRI according to WHO criteria. The median follow-up was 16 months (3–27). *Results:* An objective response (> 50% decrease in tumor size) was observed in 4 pts (50%) during 10, 12, 20 and 24 months, respectively. A tumoral stabilization was observed in 1 pt during 10 months. Progression was noted in 3 (37.5%) pts. One patient died in relation with tumoral progression after 9 months. Minor side effects of CE were nausea, fever and abdominal pain. An acute and reversible tubular necrosis attributed to CE was observed in 1 pt with previous nephrectomy. Bleeding peptic ulcer was recorded in one patient. *Conclusion:* STZ could be more effective than doxorubicin in palliative treatment of liver metastases of endocrine digestive tumors. The high specificity of STZ for endocrine tumors could account for these better results. Comparative studies with doxorubicin are necessary. Hormones and receptors: Clinical disorders Oncology, general: Therapy Oncology, specific: Pancreas } "Hepatic Arterial Chemoembolization with Streptozotocin in Patients with Liver Metastases of Endocrine Digestive Tumors"

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"P P 20 0526" P 20 0526 **Effect of Alpha-Interferon in Combination with Octreotide on Metastasized Gastroentero-Pancreatic Endocrine Tumours**

\*M. Frank, U. Kajdan, K. Ehlenz, R. Arnold

Department of Gastroenterology, Philipp University, Marburg, Germany *Objective:* The first prospective German Sandostatin multicentre phase II trial demonstrated a longlasting antiproliferative effect of octreotide in 37% of patients with progressive metastatic endocrine gastroenteropancreatic (GEP) tumours (Arnold et al, Gut 1996). From case reports and a few prospective studies it has been suggested that the combination of octreotide and alpha-interferon (IFN) exhibits synergistic antiproliferative properties in patients unresponsive to octreotide alone. *Patients:* 20 patients (10 carcinoid syndromes, 6 non-functioning tumours, 3 gastrinoma, 1 vipoma) with tumour progression during octreotide treatment were enrolled in this open prospective trial. The patients received 200 µg octreotide thrice daily plus 5 million IU IFN thrice weekly. *Results:* Effect of therapy Regression Standstill Progression Patients 1 (5%) 11 (55%) 8 (40%) Duration of response 36 months 20 months Inhibition of 5-HIAA 8 (73%) 3 (28%) An inhibition of tumour growth (regression, standstill) was observed in 60% of patients with progressive GEP tumours. A hormonal response was observed in 73% of patients with carcinoid syndrome. No correlation between tumour size response and patient's characteristics could be detected. In 11 patients (55%), side effects (fever, weight loss, diarrhoea) developed, however benign and transitory. Five patients died of their metastatic disease. *Summary:* In conclusion, the combination of alpha-interferon and octreotide can be recommended as an antiproliferative strategy in patients with tumour progression during octreotide monotherapy. Oncology, specific: Endocrine Oncology, general: Therapy } "Effect of Alpha-Interferon in Combination with Octreotide on Metastasized Gastroentero-Pancreatic Endocrine Tumours"

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"P P 20 0527" P 20 0527 **Clinical Role of Somatostatin Receptor Scintigraphy in Patients with Neuroendocrine Gastro-Entero-Pancreatic Tumors**

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Department of Internal Medicine and Gastroenterology, Nuclear Medicine Dpt., S. Orsola Malpighi University of Bologna

Nuclear Medicine Div. National Institute of Tumors, Milano-Italy Somatostatin receptor scintigraphy (SRS) is a validated method for non-invasive imaging of primary and metastatic gastroenteropancreatic neuroendocrine tumors. The aim of this study was to evaluate the role of SRS in the clinical management of patients with these lesions. Eighty patients with known or suspected GEP tumors were studied with SRS: planar and SPECT images were taken at 4 and 24 hours after injection of 200–250 MBq of <sup>111</sup>In-Pentatreotide. In addition to SRS, all patients were studied with at least one other imaging method: computed tomography (CT) in 65 patients, ultrasonography (US) in 63, and other procedures in 50. Results are detailed in the table: SRS CT US Primary tumors 21/26 (81%) 13/21 (62%) 11/19 (58%) Metastases 33/38 (87%) 25/37 (68%) 22/31 (71%) Of the 80 patients studied, a total of 66 were eventually diagnosed with GEP tumors, all of which were confirmed by histology and distinguished as follows: 38 carcinoids, 9 gastrinomas, 2 insulinomas, 1 glucagonoma, 1 PPoma, 1 somatostatinoma, 14 non-functioning pancreatic tumors. In 17/66, SRS was the only imaging procedure able to correctly identify lesions; in the remaining 14, no evidence of tumor was found by SRS or the other studies performed. Regarding the role in clinical management, SRS supported the findings of other diagnostic modalities in all cases, and in 16 of the 66 GEP-positive patients the therapeutic approach was modified. *Conclusions:* our results confirm that SRS is a highly valid means of detecting GEP tumors and, consequently, has an important role in their management; it should be considered an essential procedure for all patients in whom these tumors are suspected. Oncology, specific: Endocrine Oncology, specific: Pancreas Radiology and ultrasound: Diagnosis } "Clinical Role of Somatostatin Receptor Scintigraphy in Patients with Neuroendocrine Gastro-Entero-Pancreatic Tumors"

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"P P 20 0528" P 20 0528 **Combining Imaging and Surgical Procedures in Detecting Gastrinoma Tumors Does Not Improve the Clinical Outcome of Related Syndromes**. Angeletti, O. Schillaci<sup>2</sup>, M. Marignani, N. Basso<sup>1</sup>, E. Poletti, G. Gualdi, G. Antonelli, F. Scopinaro<sup>2</sup>, A. Materia<sup>1</sup>, C. Bordi<sup>3</sup>, B. Annibale,

\*G. Delle Fave

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<sup>2</sup> Dept. Radiology, Univ. La Sapienza Rome, Italy

<sup>3</sup> Dept. of Pathology, Univ. La Sapienza Parma, Italy *Background:* Prognosis and management of patients with gastrinoma tumors depends by the tumors mass, extension and localizations. We and others authors have demonstrated the potential value of preoperative staging of tumors by combining <sup>111</sup>In Octreotide-""Octreoscan"" Scintigraphy and Magnetic Resonance (MR). The lack of data on the ""clinical outcome"" after such procedures plus surgical therapy led us to aim a study to investigate such aspects. *Methods:* 15 pts (8 M, 7 F mean age 49.1 yrs; range 11–74), 13 ZES, 2 MEN-I, (10 with multiple and 5 with single Presumable Tumor Lesion: PTL) underwent imaging studies: Octreoscan-scintigraphy (Images-plus SPET: Single Photon Emission Tomography-taken at 4 and 24 hours after radionuclide injection) and MR (Gyroscan T5, 5 mm thickness contiguous scans, 256 256 matrix, T1 and T2 weighted spin echo and stir sequence), and were electively sent to surgery and operated on by the same surgeon in blind. The imaging studies were repeated 1 year after surgery. The follow-up of pts was prolonged at least at 24 mos. *Results:* Combined pre-surgical diagnostic procedures (Octreoscan plus MR) identified 48 PTL. At surgery 72.9% (35/48) were removed. 30 of them were histologically confirmed be tumors (62%; 30/48). At the post-surgery (1 year) imaging combined procedures 19 PTL were still detected. Two pts were cured (symptoms and PTL free 13.3%). The need of Omeprazole-therapy were reduced by 30%. The gastrin values were also decreased by 80% (pre vs post surgery values:  $p < 0.001$ ). *Conclusions:* Even if the preoperative combined imaging (Octreoscan plus MR) increase the ability to detect more PTL and the debulking of tumor mass decreases significantly the values of circulating serum gastrin and improves the clinical symptoms but the rate of cured pts remains poor. Hormones and receptors: Clinical disorders Oncology, specific: Endocrine Oncology, specific: Pancreas } ""Combining Imaging and Surgical Procedures in Detecting Gastrinoma Tumors Does Not Improve the Clinical Outcome of Related Syndromes""

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"P P 20 0529" P 20 0529 **P53 in Endocrine Tumors of Pancreas**

\*L.E. Gurevitch, I.A. Kazantseva, A.P. Kalinin

Moscow Regional Research Clinical Institute (MONIKI), Moscow, Russia Accurate diagnosis, treatment and prognosis of endocrine tumors of pancreas (ETP) are extremely difficult due to their morphological heterogeneity and variability in peptides are secreted by the tumor's cells. There is no universal approach for the evaluation of malignant potential in ETP that can be important for the choice of postoperative treatment regime and prognosis. The aim of our study was to determine the criteria for the evaluation of malignant potential in ETP using proliferating cell nuclear antigen (PCNA) and p53 protein. The expression of PCNA (clone P-10) and p53 (clone BP53-12) was revealed by immunohistochemistry, using microwave pretreatment in 10 surgical formalin fixed specimens of ETP. The hormonal profile of each tumor was determined by PAP technique with monoclonal antibodies against insulin, proinsulin, glucagon, gastrin, somatostatine, VIP, serotonin, calcitonin, chromogranine A. According PCNA and p53 expression 3 groups of tumors were revealed: Group I – with low proliferative rate (PCNA < 10% of tumor cells), p53 low/negative staining (3); Group II – with moderate proliferative rate (PCNA in 10–30% tumor cells), p53 positive (5); Group III – with high proliferative rate (PCNA > 30% tumor cells), p53 negative (2). Group III tumors were associated with poor prognosis and have clear morphological features of high malignancy: tumors' cell atypia, vessel invasion, and in one case liver metastasis. Group I tumors were associated with multihormonal profile and better prognosis. The data were found show that highly malignant ETP can be the result of mutation totally deleting p53 gene and so, they were usually associated with high proliferative and invasion rates. In contrast, moderately malignant ETP can be the result of mutation that partially deletes p53 gene (wild type expressed), and associated with moderate proliferative rate. *In conclusion:* Coexistence of high PCNA labeling and p53 negative staining found in ETP can be the markers of highly malignant potential of the tumor. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Pancreas } "P53 in Endocrine Tumors of Pancreas"

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**OT4 0530 Does Tumor Necrosis Factor (TNF) Microsatellite Define a Crohn's Disease-Associated Haplotype on Chromosome 6 in a French Population? D. Heresbach, A. Bourienne, M. Alizadeh, A. Dabadie, N. Leberre-Heresbach, B. Genetet, M. Gosselin, G. S'e9mana, J.F. Bretagne**

Depts of Gastroenterology and University Laboratory of Immunology, 35033 Rennes Some HLA class II association with Crohn's disease (CD) or ulcerative colitis (UC) may be due to their critical role in antigen presentation or act as markers for other closely linked genes on chromosome 6. Among the non HLA candidate genes the TNF locus is located in the MHC region centromeric to class I and telomeric to class II alleles. Furthermore, genetic polymorphisms at the TNF locus correlate with differences in TNF production as exhibited in CD or UC. Recently, five (a, b, c, d, e) microsatellites (MS) have been identified within the human TNF locus with 13, 7, 2, 5 and 4 alleles respectively. *The aim* of the study was to compare TNF MS allele frequencies at 5 loci in french populations of CD and UC patients with an ethnically matched control population. *Patients & Methods:* 60 UC and 100 CD patients are included in this study and compared to 65 ethnically matched controls (C) (distribution of age and sex was comparable between patients and controls). Genomic DNA (isolated from peripheral blood leucocytes) was amplified using a two-step PCR; 2 \b5l of the first PCR reaction were amplified separately with specific primers pairs for each MS locus. Comparison of allele frequencies were tested by  $\chi^2$  test and corrected ( $p_c$ ) according to multiple comparison. *Results:* Allele frequencies at the 5 TNF microsatellite loci are not significantly different between CD or UC patients and C. Haplotypes, defined as 5 loci allelic combinations previously identified were also analysed: there is no significant difference between patients and controls, especially for  $a_2 b_1 c_2 d_4 e_1$  haplotypes (24% in CD, 23% in UC and 20% in C). Despite a non significant increase of this latter in CD patients receiving azathioprine (32% vs 16%,  $p < 0.05$ ) compared to patients who responded to first line treatment (ie, steroid or 5-ASA therapy) no haplotype association could be described according to clinical criteria. *Conclusions:* Our data did not support any association between TNF MS haplotypes and CD, particularly considering  $a_2 b_1 c_2 d_4 e_1$  which have been previously reported associated with CD. Intestinal disorders: IBD, etiology and genetics }" "Does Tumor Necrosis Factor (TNF) Microsatellite Define a Crohn's Disease-Associated Haplotype on Chromosome 6 in a French Population?"

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## OT4 0531 Inhibition of Lamina Propria Cell Derived TNF- $\alpha$ Synthesis by IL-10 in Inflammatory Bowel Disease

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**Aim:** Because of its anti-inflammatory properties, IL-10 is currently studied in the treatment of IBD. This trial was performed to investigate the inhibitory effect of IL-10 on mucosal TNF- $\alpha$  synthesis in vitro. **Methods:** Lamina propria mononuclear cells were isolated from colonoscopic biopsies which were taken from both inflamed (i) and non-inflamed (ni) mucosa of patients with CD, UC or controls. Cells were cultured without (w/o) or with PHA (1% v/v) and with the addition of IL-10, IL-4 or IL-13, all at 10 ng/ml. After a 24 h incubation, supernatants were harvested and assayed for TNF- $\alpha$  by a specific ELISA (values given in ng/ml or % of PHA stimulation). **Results:** Unstimulated TNF- $\alpha$  production did not differ between groups. After PHA stimulation, TNF- $\alpha$  levels increased significantly. Compared to controls, CD-i and UC-i but also CD-ni showed a lower TNF- $\alpha$  synthesis. The addition of IL-10 inhibited TNF- $\alpha$  production by { @ } 30% in all groups. IL-4 decreased TNF- $\alpha$  levels in UC-ni only (10%). IL-13 showed a similar inhibition in CD-i, CD-ni and UC-ni. CD-i CD-ni UC-i UC-ni Control w/o (ng/ml) 0.05 – 0.03 0.2 – 0.2 0.2 – 0.06 0.08 – 0.03 0.1 – 0.03 +PHA (ng/ml) 2.2 – 0.5<sup>\*\*</sup> 4.5 – 0.9<sup>\*</sup> 2.3 – 0.3<sup>\*\*</sup> 7.1 – 1.7 10.5 – 1.4<sup>\*\*\*</sup> +IL-10 (%) 74 – 3<sup>##</sup> 68 – 5<sup>##</sup> 68 – 4<sup>##</sup> 60 – 4<sup>#</sup> 70 – 12<sup>\*\*\*\*</sup> +IL-4 (%) 95 – 2 102 – 5 99 – 3 90 – 5<sup>#</sup> 96 – 6<sup>\*\*\*</sup> +IL-13 (%) 94 – 3<sup>#</sup> 89 – 4<sup>#</sup> 103 – 5 88 – 2<sup>##</sup> 92 – 5<sup>\*\*</sup> p < 0.001, \*p < 0.01, compared to control (by Wilcoxon Test). <sup>##</sup>p < 0.01, <sup>#</sup>p < 0.05, compared to PHA alone (by paired T-Test) **Conclusion:** PHA induced TNF- $\alpha$  production is markedly decreased in inflamed mucosa. The decrease in TNF- $\alpha$  production of macroscopic non-inflamed CD mucosa might reflect sampling of CD microlesions. IL-10 has the best inhibitory effect on TNF- $\alpha$  synthesis which is preserved in inflamed mucosa. IL-10 is therefore a reasonable candidate for the treatment of IBD. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Inhibition of Lamina Propria Cell Derived TNF- $\alpha$  Synthesis by IL-10 in Inflammatory Bowel Disease"

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## OT4 0532 Interleukin-1 $\beta$ Converting Enzyme (ICE) is Expressed by Macrophages in the Lamina Propria of Active Inflammatory Bowel Disease (IBD) Mucosa

\*M.E. McAlindon, C.J. Hawkey, Y.R. Mahida

Division of Gastroenterology University Hospital, Nottingham, U.K. Interleukin-1 $\beta$  (IL-1 $\beta$ ) is a pro-inflammatory cytokine which is produced as an inactive pro-IL-1 $\beta$  and processed by ICE to mature, active IL-1 $\beta$ . We have recently shown that lamina propria cells isolated from active IBD mucosa produce mature IL-1 $\beta$  and the active form of ICE (as assessed by Western blot analysis). Normal colonic lamina propria cells produced only pro-IL-1 $\beta$  and the inactive form of ICE (Gastroenterology 1996; 110: A961). In this study, we have identified cells in the lamina propria that express ICE. Lamina propria cells were isolated from normal (3) and active IBD (7) mucosal samples. ICE expression and macrophages were studied in cytospin preparations and cryostat sections by immunohistochemistry using anti-ICE and anti-CD68 antibodies. Isolated IBD lamina propria cells were also incubated with opsonized zymosan for 1 h and cytospin preparations labelled with anti-ICE antibody. Using the anti-ICE antibody, scattered, weakly positive lamina propria cells with the morphology of macrophages were seen in tissue sections of normal intestinal mucosa. In IBD tissue, strong ICE-expressing cells, with the morphology of macrophages, were seen in the lamina propria and submucosa. Studies on isolated cells confirmed that the ICE-expressing cells were macrophages as demonstrated by the presence of numerous ICE-positive mononuclear cells that had phagocytosed opsonized zymosan. Median 63.5% (range 20–100%) of macrophages (CD68+ve) isolated from IBD mucosa expressed ICE. Of the other cell types, there was weak staining of lymphocytes and eosinophils in some cytospin preparations. *Conclusion.* In active IBD mucosa, cells strongly positive for ICE are present in the lamina propria and submucosa. As previously shown for IL-1 $\beta$ , ICE is expressed predominantly by macrophages.\* Supported by the British Digestive Foundation. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Interleukin-1 $\beta$  Converting Enzyme (ICE) is Expressed by Macrophages in the Lamina Propria of Active Inflammatory Bowel Disease (IBD) Mucosa"

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## OT4 0533 Effect of Immunoregulatory Cytokines on Activated Monocytes from Patients with IBD

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**Introduction:** Activated monocytes with increased production of proinflammatory cytokines seem to play a major role in IBD. The aim of our study was to determine the in vitro capacity of immunoregulatory cytokines (IL-4, IL-10 and IL-13) to down-regulate activated monocytes under various culture conditions and to examine the effect of a combined administration of these cytokines.

**Methods:** Peripheral monocytes from patients with active IBD (CD, n = 27; UC, n = 27) were isolated over Ficoll and hypotonic Percoll gradient centrifugation and stimulated with Pokeweed mitogen (PWM, 10<sup>5</sup> g/ml). IL-4, IL-10, IL-13 and a combination of IL-4/IL-10 and IL-10/IL-13 were added at different concentrations (1–1000 U/ml) and different times. Secretion of IL-1 $\beta$ , TNF- $\alpha$  and IL-6 was assessed using sandwich ELISA-systems. 7-day cultured monocytes (stimulation with GM-CSF) were used as a model for matured macrophages.

**Results:** The antiinflammatory cytokines IL-13, IL-4 and IL-10 were all capable to inhibit the monocyte secretion of the proinflammatory cytokine IL-1 $\beta$  in a dose dependent manner in controls. With regard to IL-13 and IL-4, there was a diminished suppression of TNF- $\alpha$  and IL-6 production from patients with active IBD compared with controls and patients with inactive IBD. The inhibitory effect of IL-13 on TNF- $\alpha$  and IL-6 production in 7-day cultured, differentiated macrophages was also reduced in patients with IBD as well as in controls. In monocytes from disease controls we also observed a diminished inhibition of TNF- $\alpha$  and IL-6 by IL-13. IL-10 plus IL-4 and IL-10 plus IL-13, respectively, inhibited the proinflammatory cytokine response of monocytes as well as matured macrophages much more than either IL-4, IL-10 or IL-13 alone in controls as well as in IBD-patients. Even at suboptimal concentrations for each cytokine alone, a combination of cytokines showed synergistic inhibitory effects.

**Conclusion:** First, the hyporesponsiveness of activated and differentiated monocytes to IL-13 and IL-4 which is observed in patients with active IBD does not seem to be a disease specific phenomenon. Second, a combination of antiinflammatory cytokines is much more effective in down-regulating the response of activated and differentiated monocytes than using the cytokines alone and may have a potential therapeutic benefit for patients with IBD.

Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Intestinal disorders: IBD, therapy } "Effect of Immunoregulatory Cytokines on Activated Monocytes from Patients with IBD"

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## OT10 0534A Prospective Randomised Trial of Cimetidine Therapy in Gastric Cancer: An Interim Report

\*M.T. Hallissey, J.A. Dunn, P.G. Baker, J.G. Davis, L.J. Billingham, J.W.L. Fielding, M.J. Langman, British Stomach Cancer Group

CRC Trials Unit, University of Birmingham, Birmingham, UK Cimetidine has been reported to improve the survival of patients with gastric cancer at all stages of disease. The aim of the fourth British Stomach Cancer Group trial was to assess the survival benefit of adjuvant cimetidine in gastric cancer. The study is a randomised double-blind trial comparing cimetidine at 2 dose levels, 800 or 400 mg twice daily with matching placebos. Eligible patients had biopsy proven gastric adenocarcinoma, with any stage of disease, were considered fit to enter the trial (life expectancy > 3 months) and were able to give informed consent. The study recruited 442 patients between February 1990 and March 1995 from 59 consultants in 39 hospitals throughout the UK. Analysis has been undertaken on an intention-to-treat basis. There is now 12 months follow up on all patients with a median follow up of 41 months. The treatment allocation was balanced for sex, age, and stage. The median age of the patients in the study population is 68 years, (range 23–88 years). The male to female ratio was 1:2.5. The majority of patients had stage III (31%) or stage IV (46%) disease, with 63 (15%) stage II and 36 patients (8%) stage I. The trial results demonstrate no survival benefit for cimetidine when comparing the survival for all patients receiving cimetidine against placebo ( $\chi^2 = 1.77$ ,  $p = 0.18$ ). When adjustment is made for dose (400 vs 800 mg), stage (I/II, III, IV), age (< 68, 68+) and sex, there is no survival benefit for the use of cimetidine. The median survival is 11 months for the cimetidine group compared to 12 months for the placebo group. The median survival within the cimetidine group is 11 months (95% CI 6–16 months) for 800 mg BD and 12 months (95% CI 8–14) for 400 mg BD. The results of this trial do not support the use of cimetidine as an adjuvant therapy in gastric cancer. The need to continue trials of therapy in gastric cancer remains. Oncology, specific: Stomach Oncology, general: Therapy Clinical practice: Management strategy } "A Prospective Randomised Trial of Cimetidine Therapy in Gastric Cancer: An Interim Report"

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## OT10 0535 Use of Laparoscopic Ultrasonography (LUS) in the T-Stage Evaluation of Gastric Cancer. Preliminary Results

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The most accurate method in the assessment of T-stage in gastric cancer is Endoscopic Ultrasonography (EUS). But evaluation is often compromised due to stenotic tumors. A new method for gastric cancer staging, LUS, have been introduced, but how accurate is this new method?  
15 consecutive patients with gastric cancer. (4 female 11 male, mean age 61 (37–76)) 11 Patients were histopathological evaluated. Four patients were not resected because of distal metastases. All patients underwent CT/eksternal ultrasonography, EUS and blinded; Laparoscopy with LUS.  
**Results:** n (%) CT/UL EUS LAP LUS  
Correct 0 (0%) 9 (82%) 3 (27%) 9 (82%)  
Understaging 6 (55%) 1 (9%) 0 (0%) 0 (0%)  
Overstaging 0 (0%) 0 (0%) 0 (0%) 1 (9%)  
Insufficient 5 (45%) 1 (9%) 8 (72%) 1 (9%)  
There were no T1 tumors, 1 T2, 7 T3, and 3 T4 cancers. EUS understaged 1 patient with a stenotic non-traversabel tumor. LUS overstaged 1 patient with an absces located in cardiac region as having a T4 tumor.  
**Conclusion:** These preliminary results indicate that Laparoscopic Ultrasonography is a highly accurate method in T staging of gastric cancer. Larger blinded and prospective studies are needed.  
Laparoscopic surgery: DiagnosisOncology, specific: StomachEchoendosonography: Echoendoscopy } "Use of Laparoscopic Ultrasonography (LUS) in the T-Stage Evaluation of Gastric Cancer. Preliminary Results"

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## OT10 0536 Does the Addition of Cisplatin to High Doses of 5-Fluorouracile and Epirubicin in Advanced Gastric Cancer Results in Better Response to Therapy

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The aim of the study was to determine activity of high doses of 5-fluorouracile and epirubicin (FE) vs. the same combination + cisplatin (FEP) in advanced gastric cancer. From September 1991 to March 1996, 104 patients with advanced gastric cancer entered phase III clinical trial. Out of 104 patients 95 (65 males and 30 females) were evaluable (2 cycles of chemotherapy). The range of patients age was 27–71 years (M = 55), and ECOG performance status was 3. The predominant metastatic sites were lymph nodes and liver. The treatment involved in FE arm 1000 mg/m<sup>2</sup> in 6-hour infusion of 5-fluorouracile on days 1, 2, 3, 4, 5 and 120 mg/m<sup>2</sup> of epirubicin i.v. on day 1; in FEP arm the same combination of cytostatics + cisplatin 30 mg/m<sup>2</sup> on days 2, 4 was administered. The cycles were repeated after 4 weeks. In FE arm 48 patients were evaluable with 1 complete and 14 partial remissions (31.25%), and in FEP arm out of 47 evaluable patients 2 complete and 17 partial remissions (40.42%) were observed. Median survival in FE group was 6.6 mos, and in FEP group 8.8 mos. The survival difference is statistically significant if Logrank test Statistica 4.0 Statsoft, 1993 is used (p = 0.02573), and is not statistically significant if Logrank test M. Peto, 1977 is used (hiq = 2.92). The most frequent toxic side effect was alopecia. Febrile neutropenia (grade IV) was observed in 3 patients in arm FE and in 5 patients in arm FEP. The treatment related death was not registered. The final results will provide a definite answer with regard to the value of cisplatin in combination with high doses of 5-fluorouracile and epirubicin in advanced gastric cancer. Oncology, general: Therapy Oncology, specific: Stomach } "Does the Addition of Cisplatin to High Doses of 5-Fluorouracile and Epirubicin in Advanced Gastric Cancer Results in Better Response to Therapy"

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## OT11 0537 *H. Pylori Vac A Gene Differences and Cag A Gene Existence in Patients with Duodenal Ulcer and Gastritis*

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The purpose of this study was to compare the genetic divergence of *vacA* genes and the presence of *cagA* gene in *H. pylori*-infected patients. The study was carried out on 34 patients with duodenal ulcer (DU) and 33 patients with *H. pylori* associated chronic gastritis (GA). Patients were diagnosed histologically, by CLOtest and PCR amplified fragment of *urease A* gene in gastric mucosa lysates. Two other biopsy specimens were taken from the corpus and antrum. Lysates of these tissue samples were used for PCR amplifications of *vacA* gene fragments (with the primers described by Atherton et al., JBC 1995; 270: 17771) and *cagA* gene fragment. In DU patients *cagA* gene was found in 51% of biopsy specimens, and in GA patients in 31% of the samples. There were no differences in the frequency of *cagA* existence determined in biopsy specimens, taken from the antrum and corpus, in both studied groups. Amplification of the *vacA* middle region sequences revealed very similar DNA patterns among the studied patients. The predominant sequence type present was m2 (found in about 50% of the all samples), whereas m1 type was found in about 25% of biopsy lysates. In a few samples, both m1 and m2 fragments could be amplified, and in about 20% specimens neither m1 nor m2 was detected. The s2 signal sequence was found more frequently in GA than in DU patients (50% and 31%, respectively), whereas s1a and s1b sequences were shown more often in DU than GA patients (85% and 62% for s1a, and 15% and 2% for s1b, respectively). *VacA* amplification patterns for two different biopsy specimens from the same patient were identical in 64% GA and 47% DU patients. The results of this study suggest: 1) there is no single *vacA* gene type predominant in DU patients, 2) in most of our patients more than one *H. pylori* strain exists. Supported by grant 4 S402 034 07 from the National Research Committee Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Hormones and receptors: Molecular biology } "H. Pylori Vac A Gene Differences and Cag A Gene Existence in Patients with Duodenal Ulcer and Gastritis"

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**OT11 0538 Helicobacter Pylori (Hp) Genotyping: Association between Cytotoxic Strains and Peptic Ulcer**  
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It has been suggested that the cytotoxic strains of Hp play a major role in the pathophysiology of various gastroduodenal diseases, among which gastric and duodenal ulcer. Aims of the present study were: 1. to evaluate the genetic pattern of Hp infecting the gastric mucosa by the identification of urease gene A (UreA), cytotoxin associated gene A (CagA) and vacuolating cytotoxin gene (VacA); 2. to assess if there were any association between any genetic pattern of Hp and gastroduodenal diseases or the presence of intestinal metaplasia. A total of 129 patients were studied; 59 were affected by antral gastritis (AG), 10 by active (APU) or healed (HPU) (n = 27) peptic ulcer, 4 by chronic atrophic gastritis (CAG), 22 by duodenitis (DUO) and 7 by oesophagitis (OES). Gastric juice and gastric mucosal samples, obtained during endoscopy, were used for DNA extraction and further polymerase chain reaction (PCR) to identify the following genes: a) UreA with the primers: 5{\a2}GACATCACTATCAACGAAGG3{\a2} and 5{\a2}TGAAAACACGCTCTTTAG3{\a2}; b) CagA with the primers: 5{\a2}GATAACAGGCAAGCTTTTGAGG3{\a2} and 5{\a2}CTGCAAAGATTGTTTGGCAGA3{\a2}; c) the polymorphism of the mid region and of the signal peptide of VacA using the primers described by Atherton et al. [1], which identify cytotoxic (S1M1 or S1M2) and non cytotoxic (S2M2) genotypes. Hp infection, assessed by UreA, was found in 48% AG, 90% APU, 70% HPU, 100% CAG, 64% DUO and 57% OES. Three genotypes of VacA were found: S1M1, S1M2 and S2M2; the association S2M1 was never found. CagA was associated with S1M1 in 84%, with S1M2 in 72% and with S2M2 in 9% of the cases. CagA was significantly associated with both APU and HPU ( $X^2 = 4.9$ ,  $p < 0.05$  and  $X^2 = 5.7$ ,  $p < 0.05$ ). S1M1 VacA genotype was significantly associated with APU ( $X^2 = 7.5$ ,  $p < 0.05$ ) but not with HPU ( $X^2 = 4.3$ ,  $p$ : ns). No association was found between Hp genotype and the presence of intestinal metaplasia in the gastric mucosa. In conclusion: 1. Hp infection was confirmed to be extremely frequent in patients with active or healed peptic ulcer; 2. the cytotoxic genotype of Hp was frequently, although not exclusively associated with CagA; 3. both VacA cytotoxic genotype and CagA were significantly associated with the presence of peptic ulcer disease, suggesting a key role of the vacuolating cytotoxin in the pathogenesis of this disease; 4. the vacuolating cytotoxin is probably not involved in the pathogenesis of gastric intestinal metaplasia.

Reference: Atherton JC, et al., J Biol Chem 1995, 270: 17771–7. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Helicobacter Pylori (Hp) Genotyping: Association between Cytotoxic Strains and Peptic Ulcer"

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## OT11 0539 Effect of Macrolides on Gastric Acid Secretion under Basal and Stimulated Conditions

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In a previous study, we have shown that iv erythromycin (ERY) decreased gastric acid secretion during continuous enteral nutrition. This effect could be the consequence of the gastric emptying increase or a direct effect of ERY on gastric secretion. Clarithromycin (CLARI), in association with gastric acid secretion inhibitors, is an effective treatment for Helicobacter Pylori eradication. The *aim of the study* was to evaluate the effect of ERY and CLARI on gastric acid secretion under basal conditions and stimulated by pentagastrin. *Methods*: 8 healthy male subjects were studied. Each subject received in randomized order either iv ERY (150 mg/h for the 3 hours of the test period), oral ERY (500 mg), oral CLARI (500 mg) 1 hour before the test period or placebo. Gastric emptying and acid secretion were evaluated 1 h before and 2 h during pentagastrin perfusion (0.8 ug/kg/h). The method used has been described by Muller-Lissner (Dig Dis Sci 1986, 31: 807–10). Luminal somatostatin was measured during iv ERY and placebo. *Results* mean – SEM; \* p < 0.05 compared to placebo.

	iv ERY	Oral ERY	CLARI	Placebo
<i>Secretion (mM/h)</i>				
Basal	1.8 – 0.3*	2.6 – 0.6	3.0 – 1.2	3.7 – 0.9
Pentagastrin 1 h	16.5 – 3.7*	27.6 – 3.1	25.6 – 3.3	30.8 – 1.7
Pentagastrin 2 h	14.5 – 3.6*	31.1 – 5.0	28.3 – 3.3	34.6 – 2.2
<i>Emptying rate (%/min)</i>				
Basal	14.4 – 0.9*	11.7 – 0.8	12.2 – 0.5	10.8 – 1.3
Pentagastrin 1 h	9.5 – 1.2*	4.8 – 1.0	5.0 – 1.2	4.4 – 1.0
Pentagastrin 2 h	9.2 – 1.3*	4.3 – 1.2	5.5 – 1.1	4.0 – 1.4

Luminal somatostatin was not statistically different. *Conclusions*: iv ERY decreases gastric acid secretions and increases gastric emptying under basal conditions as well as during pentagastrin perfusion. It would need further investigations to determine its mechanism of action. In our experimental conditions, oral ERY and CLARI did not modify gastric response.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic

Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation

Motility, specific: Stomach } "Effect of Macrolides on Gastric Acid Secretion under Basal and Stimulated Conditions"

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## OT11 0540Molecular Typing of Helicobacter Pylori Strains Isolated amongst Infected Family Members

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*The aim* of this study was to investigate the spread of the Helicobacter Pylori (HP) infection amongst the members of the families of infected individuals, using a direct DNA amplification technique and restriction pattern analysis (REA-PCR). *Patients-Methods:* Eleven symptomatic index patients (7 children aged 6–14 years, 4 adults) seropositive for HP antibodies, and their 18 seropositive for HP antibodies family members were found to be HP positive by histology and culture. Biopsy specimens were taken from the duodenum, antrum and fundus of the above patients to assess the possibility of multiple HP strains infection. Amplification by PCR of UreA and UreB genes of HP, followed by restriction pattern analysis was used for the comparison of HP strains isolated in the index patients and their family members. *Results:* The results of our study were the following: 1) In 3 out of 6 families the children and their parents were infected by similar HP strains. 2) In 4 out of 8 couples, identical HP strains were harboured by each spouse. 3) In 5 out of 11 families (45%) at least two identical HP strains were found in each family. 4) In only one patient were two different HP strains isolated in the antrum and fundus. *In conclusion* vertical and/or horizontal transmission of HP within families is possible, although a common source of infection cannot be precluded. However, in 55% of the families, different sources of HP infection of the family members can be suspected. Infected individuals by multiple HP strains can be found but it is a rather rare phenomenon. Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: EGD disorders in children } "Molecular Typing of Helicobacter Pylori Strains Isolated amongst Infected Family Members"

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## OT11 0541 Comparison of Two Alternative Strategies for the Management of Duodenal Ulcer: An Economic Model

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<sup>5</sup> Reims, France This study aimed to compare two strategies for the management of duodenal ulcer 5 years after diagnosis with or without *Helicobacter pylori* eradication. **Methods:** A cost-effectiveness (C/E) and cost-benefit (C/B) analysis were performed using simulated Markovian modelling on 100,000 individuals. Relevant clinical data introduced to the model were obtained from published data or from a consensus of experts. The C/E analysis evaluated the cost of one additional unit of efficacy, either the number of patients healed after the initial 4 week treatment without recurrence at time t, or the mean number of months before the first recurrence. The C/B analysis (from a collectivity point of view) evaluated the costs avoided per French Franc (FF) invested. The costs taken into account were the costs of treatment (H<sub>2</sub> antagonists for the no eradication strategy, omeprazole plus two antibiotics, followed in case of failure by H<sub>2</sub> antagonists in eradication strategy), the cost of medical visits and the costs of gastroscopy. A sensitivity analysis was carried out to evaluate the effect of variations in clinical probabilities and costs, eg gastroscopy. The results presented are those where the strategy without eradication has a maximal efficacy (max) (recurrence without maintenance treatment: 50% within 2 years; with maintenance treatment: 17% within 2 years) and the treatment with eradication a minimal efficacy (min) (eradication: 55%) and maximal efficacy (max) (eradication: 95%). **Results:** 5-year figures: H1 \*\* H2 \* Cost-effectiveness Erad (max eff)/AH2 (max eff) 1048 FF 1375 FF ratio \* Erad (min eff)/AH2 (max eff) 3006 FF 3944 FF Cost-benefit Erad (max eff)/AH2 (max eff) { - } 5.28 FF { - } 5.16 FF ratio \*\*\* Erad (min eff)/AH2 (max eff) { - } 0.51 FF { - } 0.32 FF \* patient without recurrence; \*\* Depending on the mean cost of gastroscopy; \*\*\* Cost reduction per 1 FF invested. **Conclusion:** The results support the eradication strategy option with maximal success of eradication as confirmed currently by triple drug regimens. This strategy gives a 5-year benefit of more than 5 FF for each franc invested (1\$ = 4.90 FF). Clinical practice: Management strategy Oesophageal gastric duodenal disorders: Helicobacter Pylori } " Comparison of Two Alternative Strategies for the Management of Duodenal Ulcer: An Economic Model "

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## OT12 0543 The Costs of Crohn's Disease in Sweden

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<sup>5</sup> Astra Draco, Lund, Sweden *Background:* Crohn's disease (CD) is a chronic disease which mainly manifests in the early adulthood. It is characterized of either recurrent clinical flare-ups or chronic continuous disease. Patients therefore need regular medical attendance including visits, hospitalisation, endoscopies, pharmacological and/or surgical treatment. Swedish health care is predominantly public. With respect to the chronicity and early onset of the disease, the costs for medical service for these patients are not negligible. *Aim:* To evaluate the costs during the first 5-year period of CD with respect to extent of disease at diagnosis and type of medical measures. *Material & Methods:* From four different centres in Sweden, patients aged > 18 years who got the diagnosis of CD between 1983 and 1988 were included into the study. All CD related measures were registered and fixed the price of. The costs were related to different periods of disease, inpatient care, outpatient care, drugs and extent of disease at diagnosis. *Results:* 189 patients were included in the study. The mean costs per patient for the first 5-year period was 135540 SEK. (1 SEK = 0.15 US dollar) with the highest costs for the first year after diagnosis (52371 SEK.). Of the total costs, inpatient care accounted for 78.5%, outpatient care for 12.9%, costs related to time for diagnosis including the 6 preceding months for 3.7% and drugs for 4.8%. The mean costs for patients requiring surgery was twice as high as for the unoperated patients. Discontinuous ileocolonic disease accounted for the highest costs regarding extent of disease. *Conclusion:* The major costs of Crohn's disease are during the first year of diagnosis and mainly due to surgery and associated morbidity inpatient care. Pharmacological treatment and outpatient attendance account for minor costs and consequently frequent medical visits and treatment seem legitimated to avoid surgery as long as not deemed necessary. Intestinal disorders: IBD, basicClinical practice: Management strategy }" "The Costs of Crohn's Disease in Sweden"

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OT12 0544 **Optimisation of Diagnostic and Therapeutic Strategies before Laparoscopic Cholecystectomy (LC): A Decision Analysis Study** P. Burtin, S. Carpentier, J.P. Arnaud, G. Houbiers, C. Casa, B. Person, J. Boyer

University hospital, Gastroenterology unit, 49033 Angers, France Endoscopic ultrasonography (EUS), and retrograde cholangiography (ERCP) have made complex the management of patients before LC. *Aim:* To select the best cost-effectiveness strategy before and after LC, taking into account the expected performances of endoscopists and surgeons. *Methods:* The expected results of EUS, diagnostic and therapeutic ERCP, and laparoscopic extraction of biliary stones (LCBDE) in the management of bile duct lithiasis were estimated according to the results of published data. Following primary LC, 3 different decision trees were built, using ERCP, LCBDE or open surgery to treat residual biliary stones. After selection of the more optimal surgical strategy, 3 other decision trees were also built, using respectively EUS only, ERCP only, and both EUS and ERCP before LC. Costs per patient were calculated for each strategy according to private practice (cost 1) or public practice (cost 2) in French Francs (1 ECU = 6.34 FF). The results of the 4 more relevant strategies are given below. *Results:* LC, then LCBDE, ERCP, then EUS, ERCP ERCP then ERCP LC and LC Low risk of biliary lithiasis (2.5%) Death rate (%) 0.32 0.40 0.53 0.33 Hospital stay (days) 2.4 2.5 3.3 3.3 Cost 1 (FF) 9,300 9,600 13,800 13,300 Cost 2 (FF) 8,400 8,800 11,100 11,500 Medium risk of biliary lithiasis (40%) Death rate (%) 0.63 0.86 0.72 0.60 Hospital stay (days) 6.5 4.5 4.3 4.6 Cost 1 (FF) 15,100 12,200 16,000 17,000 Cost 2 (FF) 21,000 15,600 14,300 15,500 In patients with high probability of stones (80%), the best strategy was primary ERCP, followed by LC or LCBDE according to the results of ERCP (death rate: 0.93%, hospital stay: 5.4 days). *Conclusions:* In asymptomatic patients, LC followed by eventual ERCP is the best cost-effective method to manage gallbladder lithiasis. In patients with a medium risk of biliary stone, it is preferable to perform EUS and ERCP before LC. Liver and bile ducts, 2: Gallstones, formation, treatment Laparoscopic surgery: Therapy Endoscopy, general: Instrumentation, diagnosis } "Optimisation of Diagnostic and Therapeutic Strategies before Laparoscopic Cholecystectomy (LC): A Decision Analysis Study"

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## OT12 0545 Comparison of the Cost-Effectiveness of Different Approved Dual Therapy Regimens for *H. Pylori* Eradication

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<sup>3</sup> PA Consulting Group, London, UK *Purpose:* Dual therapies comprising an antisecretory agent plus an antibiotic are increasingly being used by primary care physicians to eradicate *H. pylori*. A decision tree model was built to compare the cost-effectiveness of different approved eradication regimens. *Methods:* The target patient population for the model are those patients who present to a primary care physician with symptoms and a previous history of duodenal ulcer (DU). The decision tree model caters for four different management strategies, which depend on whether DU diagnosis is determined by endoscopy or presumed based on symptoms/DU history and whether *H. pylori* status is determined. The model examines outcomes over a two year period. Each regimen involves co-prescription of an antisecretory drug and one antibiotic for 2 weeks to eradicate *H. pylori*, followed by a further 2 weeks of antisecretory treatment to ensure DU healing. The following regimens were compared: Regimen Eradication phase Healing phase RBC + C Ranitidine Bismuth Citrate (400 mg bd) RBC (400 mg bd) + Clarithromycin (1–1.5 g daily) O + C Omeprazole (20 mg bd) + O (20 mg daily) Clarithromycin (1–1.5 g daily) O + A O (20 mg bd) + Amoxicillin (2 g daily) O (20 mg daily) *Results:* The results using UK cost data, for the case in which the presence of DU is confirmed and *H. pylori* status is tested, are: Regimen \*Improvement in % \*\*% Decrease in costs comparison relapse rate per treatment success RBC + C vs. O + C 10 20 RBC + C vs. O + A 20 30 \*RBC + C has better health outcome, with lower costs in preventing DU relapse. *In conclusion:* RBC + C is more cost-effective than O + C or O + A in the treatment of DU. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Comparison of the Cost-Effectiveness of Different Approved Dual Therapy Regimens for H. Pylori Eradication"

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## OT12 0546 Choledochocholedochostomy with or without Drainage in Liver Transplantation

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Biliary complications following liver transplantation (LT) represents a high-frequency cause of morbidity. Choledochocholedochostomy (CC) with bile duct drainage through a T-tube represents the standard technique, but T-tube related complications are common after LT. The need for bile drainage remains questionable. In a retrospective study, we analysed the biliary complications following choledochocholedochostomy with or without T-tube in a series of 135 patients. *Patients and methods.* From October 1990 to October 1995, 214 LT were performed in 210 patients. Of them, 69 patients with hepaticojejunostomy and 10 with CC surviving less than 3 months were excluded from the study. Finally, 135 LT in 135 patients with a mean follow-up of 27.7 months were studied. There were 100 males and 35 females with a mean age of 44 years (range: 3 to 62). Main indications for LT were viral (42%) and alcoholic cirrhosis (38%). Patients were divided in 2 groups according to the use (group I, n = 50) or not (group II, n = 85) of a biliary drainage. In group I, post-operative cholangiography through the T-tube was performed between day 10 and day 16 post-LT, then the drain was closed until a new control 3 to 4 months later before removal. The two groups were comparable for age, sex, liver diseases, donor age, cold ischemic time and intra-operative blood products transfusions but different for operative procedure duration (GI: 382 mn vs GII: 312 mn; p = 0.001). Statistical analysis was made by ANOVA and chi-Square tests, differences were considered statistically different at p < 0.05. *Results.* After a mean follow-up of 38 months for GI and 21 months for GII, 44 (88%) and 83 (97.6%) patients were alive with their first graft. Seventeen (34%) and 6 (7%) patients experienced biliary complications in groups I and II respectively (p < 0.05), requiring operative management in 5 (10%) and 3 (3.5%) of them and endoscopic manoeuvres in 5 and 2 cases respectively. None of the deaths were related to biliary complications. In group I, 15 early complications were T-tube related (T-tube dislodgement leading to bile leak in 4 cases, bile leak at the T-tube site occurring after removal and responsible for peritonitis in 6 cases, haemobilia in 2 cases and symptomatic cholangitis in 3 last cases). During the late follow-up (at 4 and 7 months) 2 anastomotic stenoses were diagnosed. In group II, early biliary leaks happened in 2 cases at the end of the first week post-LT requiring urgent operative anastomotic biliary conversion to a successful hepaticojejunostomy. Later, 2 months post-LT another patient experienced an anastomotic leak because of duodenum perforation and was treated using biliary stents. Late anastomotic stenoses (at 2, 4 and 8 months) occurred in 3 patients. *Conclusions.* This study demonstrates the potential deleterious effects of the use of the T-tube which is responsible for the main biliary complications after LT. Our results underline the validity of choledochocholedochostomy without drainage which can be a safe and efficient technical option in liver transplantation. Liver and bile ducts, 1: Liver transplantation }"  
"Choledochocholedochostomy with or without Drainage in Liver Transplantation"

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**OT18 0547 Weekly High Dose of 5-Fluoruracil (5FU) 24 Hour Infusion + Oral L-Leucovorin (L-LV) in Advanced Colo-Rectal Cancer: A Phase II Study** M.C. Barzacchi, O. Sanguineti, M.T. Nobile,

\*P. Cognein, S. Bertoglio, P.M. Meszaros, P.L. Percivale, A. Lavarello, R. Rosso

National Institute for Cancer Research, Genoa, Italy We aimed at improving the clinical efficacy of the combination of 5-FU + L-LV for advanced colorectal cancer. We designed a phase II study based on a weekly outpatient regimen of oral L-LV and continuous 24 hr 5-FU infusion as follows: L-LV 100 mg/sqm by 4 hr i.v. infusion followed by 5-FU 2600 mg/sqm over 24 hr infusion combined with a fixed dose of oral L-LV (50 mg) every 4 hrs for 5 times. 57 pts (44 M, 13 F, mean age 63 yrs; mean performance status 1) were enrolled. All pts required subcutaneous port insertion and portable external infusion pump to allow outpatient regimen. All pts were evaluable. 37 pts did not receive any previous CT: 15 pts responded (7 CR and 8 PR, overall response rate: 40.5%). 20 pts received previous CT: no CR, 6 PR, overall response rate: 30%. The overall objective response was 35.5%, median duration of remission was 22 weeks. Major side effects were Hand-Foot Syndrome grade I–II 44.7%; Nausea-Vomiting grade I–II 42.5%; Fatigue grade I–II 34%; diarrhoea grade I–II 31.9% – grade III 17%; oral mucositis grade I–II 21.3%; Leukopenia grade I–II 8.5%. Concluding remarks: 1) high rate of objective responses, overall in those pts who did not respond to a previous chemotherapy; 2) acceptable toxicity rate; 3) feasibility in outpatient regimen. Oncology, specific: Colon, rectum } "Weekly High Dose of 5-Fluoruracil (5FU) 24 Hour Infusion + Oral L-Leucovorin (L-LV) in Advanced Colo-Rectal Cancer: A Phase II Study"

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**OT18 0548 Liposomal Versus Free Fluorouracil in the Treatment of Human Colon Carcinoma Cells: An In Vitro Ultrastructural and Cytotoxicity Study** J.N. Giannios,

\*J.A. Karagiannis

Gastroenterology Unit, St. Savvas Anticancer Hospital, Athens, Greece

Colorectal adenocarcinoma is an aggressive malignant tumour with high metastatic potential and poor response to conventional chemotherapy. The latter is mainly due to high expression of MDR-1 gene encoding a 170 kDa plasma membrane P-glycoprotein, rendering malignant cells resistant to chemotherapeutic agents. On the other hand, quantitative studies have shown that colon malignant cells exert a high expression of low-density lipoprotein (LDL) receptors for the highly needed uptake of cholesterol compared to normal colon cells. Solid liposomal bilayers were prepared followed by 5-FU molecule entrapment in dehydration-rehydration vesicles so that 5-FU constituted part of their bilayers. The amount of 5-FU entrapped was approximately 86 µg/liposome. Malignant colon adenocarcinoma cells were prepared after collagenase digestion of tissue specimen obtained after surgical excision from colon cancer patient. Malignant cells ( $2.06 \times 10^6$ /ml) were incubated (95% air, 5% CO<sub>2</sub>, 37°C) with a) control liposomes, b) liposomal 5-FU bilayers and c) free 5-FU (10 mg/ml) for 10, 30 and 60 min. After incubation both cytotoxicity assays (trypan blue exclusion test, LDH activity, protein synthesis and colonies-forming capability) and electron microscopy (both transmission and scanning EM). Liposomal 5-FU treated malignant cells showed lower viability by trypan blue exclusion test (80% v. 95% at 10 min, 45% v. 90% 30 min, 5% v. 86% 60 min), higher LDH activity (25% v. 8% 10 min, 55% v. 10% 30 min, 96% v. 12% 60 min), decreased protein synthesis (79% v. 96% 10 min, 35% v. 95% 30 min, 8% v. 90% 60 min) and impaired colonies-forming capability (60% v. 93%, 20% v. 92% 30 min 6% v. 90% 60 min) compared to free 5-FU treated cells (% values refer to incubation with control liposomes). EM studies showed fusion of 5-FU loaded liposomes with cell surface and high granular cytoplasm breakdown of plasma and nuclear membranes while control liposomes didn't cause any damage to the tumour cells. Free 5-FU treated cells showed minimal structural changes. The above results suggest that liposomal 5-FU is capable of entering human colon adenocarcinoma cells resistant to conventional chemotherapeutic agents by circumventing the P-glycoprotein. Oncology, general: Therapy Oncology, specific: Colon, rectum }

"Liposomal Versus Free Fluorouracil in the Treatment of Human Colon Carcinoma Cells: An In Vitro Ultrastructural and Cytotoxicity Study"

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OT18 0549 **Prognostic Value of LDL Receptor Expression in Colorectal Carcinoma** M.G. Caruso, M. Notarnicola, A.R. Osella<sup>1</sup>, S. Leo<sup>2</sup>, I. Giorgio<sup>3</sup>,

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Cancer cells require more cholesterol than normal ones. A higher HMG-CoA reductase activity or a higher cholesterol uptake by the Low Density Lipoprotein Receptor (LDLR), whose expression have been also found in normal and neoplastic gastrointestinal mucosa [1,2], seem to satisfy this requirement. Since in breast cancer tissue the LDLR content has a prognostic significance [3], our *aim* was to verify whether the content of LDLR in neoplastic tissue could be of any prognostic value in patients with colorectal carcinoma (CRC). *Materials and Methods:* The LDLR content was detected in 93 patients (29 of whom had died) with CRC by ELISA method (using an anti-human LDLR mouse monoclonal antibody IgG-C8 – Oncogene Science, Uniondale, N.Y.). No patient was lost to follow-up (35 – 19 months, M – SD). Kaplan-Meier estimates and Cox proportional hazard model were performed to evaluate the survival time and the relative risk (RR) of prognostic factors. *Results:* Thirty-three of 93 cases (35%) were ELISA positive for LDLR, while 60 of 93 (65%) were LDLR negative. The survival of patients without LDLR expression in the neoplastic tissue was shorter than that of patients with LDLR one (log rank test,  $P < 0.01$ ). By performing Cox model, only LDLR status (RR 0.40) and Dukes' stage (RR 5.02, 10.16) resulted statistically significant on the CRC-related death survival, after controlling for age, sex, tumour site and histological differentiation. *Conclusions:* These findings suggest an association between the LDLR absence in neoplastic mucosa and a shorter survival of CRC patients. This is probably due to an abnormally high endogenous HMG-CoA reductase activity with high levels of isoprenoid compounds. These substances could potentially confere a growth advantage to colorectal neoplastic cells.

Reference: Int J Cancer 61: 461–464, 1995.

Ital J Gastroenterol 25: 361–367, 1993.

BMJ 292: 580–582, 1986. Hormones and receptors: Receptor characterization  
Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum } "Prognostic Value of LDL Receptor Expression in Colorectal Carcinoma"

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## OT21 0550 Auxiliary Liver Transplantation for Fulminant Liver Failure: Limits of an Attractive Concept

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<sup>1</sup> Department Hepatology, Hospital Beaujon, University Paris VII, Clichy, France Auxiliary liver transplantation (ALT) theoretically bridges the period of acute liver failure until the native liver (NL) recovers and immunosuppression can be discontinued. However, this attractive concept is burdened by technical problems and by the selection of candidates. We report our experience of ALT with special references to early and long term graft function in a prospective study including all patients who underwent emergency liver transplantation for acute liver failure from April 1993 to October 1995. *Patients:* Thirty patients aged from 16 to 62 years with acute liver failure were candidates for emergency liver transplantation according to Clichy criteria. Causal disease was drug toxicity (n = 10) including paracetamol in 3; hepatitis B (n = 6); hepatitis A (n = 2) and other (n = 12). We decided to perform OLT in 18 because of age > 60 years (n = 3), pre-existing chronic liver disease (n = 4), haemodynamic instability (n = 4), poor liver graft (n = 2) and poor neurological status with immediate risk of cerebral herniation (n = 5). Seven patients died postoperatively including 5 after ALT; in the latter group mortality was due to vascular thrombosis (n = 3) graft compression (n = 1) and sepsis (n = 1). With a follow up ranging from 3 to 31 months among the 7 surviving patients, graft was removed in 2 respectively after 1 and 7 months, immunosuppression was stopped in 2 respectively after 9 and 27 months. Liver biopsy demonstrated the presence of mild fibrosis in 3 respectively after 6 and 9 months. *Conclusion:* After auxiliary liver transplantation for fulminant hepatitis, there is no predictive value of the extent nor the delay of sufficient regeneration of the native liver. The higher operative risk associated with ALT suggests that this procedure should: (a) not be indicated earlier than standard OLT; (b) be restricted to patients < 50 years without haemodynamic instability and (c) be performed using good quality ABO compatible graft. Liver and bile ducts, 1: Liver transplantation } "Auxiliary Liver Transplantation for Fulminant Liver Failure: Limits of an Attractive Concept"

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## OT21 0551 Cytokine Responses after Surgery in Obstructive Jaundice Indicate Endotoxin Tolerance

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Department of Surgery, Free University Hospital, Amsterdam, The Netherlands In obstructive jaundice postoperative complications are related to gut derived endotoxemia and possibly mediated by cytokines like TNF and IL-6. This study investigated the course of IL-6 and TNF following surgery in bile duct ligated rats (BDL) treated with and without the enteral endotoxin binder cholestyramine. Endotoxin in rat plasma was determined by blocking cytokine production in human whole blood cell cultures stimulated by rat plasma using antibodies directed against the endotoxin (CD14) receptor. Rat and human TNF and IL-6 were measured using bioassays and specific ELISA's. Results showed that in saline treated BDL rats (BDL SAL) surgery elicited a significant IL-6 response (max 900 U/L). In these rats there was no increase in plasma TNF after surgery and values remained at their low preoperative levels ( $\approx$  20 U/mL). In cholestyramine treated BDL animals no TNF and IL-6 levels were measured prior to surgery but in contrast to BDL SAL rats both TNF (max  $\approx$  300 U/mL) and IL-6 (max  $\approx$  1500 U/mL) were significantly raised after surgery. BDL SAL plasma samples from all time points elicited significant TNF and IL-6 responses in human blood cell cultures (TNF max at  $t = 2$  h  $\approx$  630 pg/ml). These responses could be inhibited by CD14 blockade ( $p < 0.001$ ) indicating endotoxemia before and after surgery. In cholestyramine treated BDL rats only the plasma samples taken at  $t = 2$  h after surgery elicited human blood cell TNF (max 290 pg/mL) and IL-6 responses that were significantly lower compared to BDL SAL responses. This response was also inhibited by CD14 blockade ( $p < 0.01$ ) indicating low grade postoperative endotoxemia. The absent postoperative plasma TNF response in the BDL SAL group, in the continuous presence of endotoxin, indicates endotoxin tolerance for TNF production in postoperative BDL rats. Gut endotoxin neutralization prevented immune cells of BDL rats to develop endotoxin tolerance as was evidenced by the high plasma TNF levels in response to postoperative endotoxemia. Immunology and microbiology: Inflammation Liver and bile ducts, 2: Bile formation, cholestasis Immunology and microbiology: Host defense mechanisms } "Cytokine Responses after Surgery in Obstructive Jaundice Indicate Endotoxin Tolerance"

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## OT21 0552 <sup>13</sup>C-Galactose Breath Test: An Early Indicator of Liver Fibrosis in Hepatitis C Virus Infection

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Simple, non invasive tests are still needed to measure liver function mass. In cirrhotic patients, we have previously shown that the <sup>13</sup>C-galactose breath test (GBT) is well correlated to the severity of liver disease (Gastroenterology 1995; 108: A1124). *The goal* of this study was to measure liver function mass by GBT in patients with HCV chronic hepatitis and no cirrhosis, and to correlate the results of the GBT with the severity of fibrosis on liver biopsy specimens. *Methods.* GBT was performed in 6 healthy volunteers [mean age: 44 (range: 32–63), 4 men and 2 women] and 16 liver biopsy-proven chronic virus C hepatitis patients [mean age: 48, range: 25–64), 12 men and 4 women]. GBT was done after an overnight fast: galactose was given iv in less than 10 minutes (0.5 g/kg of body weight of unlabeled galactose + 5 mg/kg of body weight of <sup>13</sup>C-galactose). Breath samples were obtained before galactose administration (basal) and every 10 minutes thereafter until 210 minutes. <sup>13</sup>C/<sup>12</sup>C isotopic ratio was determined in each breath sample by GC-IRMS, and the amount of galactose oxidized to CO<sub>2</sub> per unit of time (μmol/min) was calculated. On liver biopsy specimens, the degree of inflammation, necrosis, and steatosis was assessed as mild, moderate or severe, while the intensity of fibrosis was measured according to the Knodell fibrosis score (1 or 3). Statistical analyses were performed by regression analysis and one-way ANOVA. *Results.* GBT was significantly lower in HCV patients compared to controls (85 – 5 vs 141 – 10 μmol/min, p < 0.0001). In HCV patients, the results of GBT were independent from the levels of serum ALT and AST, the severity of hepatic steatosis, necrosis and inflammation. They were significantly lower in the group with a Knodell fibrosis score of 3 (11 patients) than in the group with a Knodell fibrosis score of 1 (5 patients): 77 – 5 vs 102 – 9 μmol/min, p < 0.05. *In conclusion,* GBT is altered early in the course of HCV chronic hepatitis, and is significantly correlated to the degree of liver fibrosis. This test could thus be useful in monitoring the efficacy of anti-viral therapy in HCV chronic hepatitis.

Liver and bile ducts, 1: Hepatitis viral, diagnosis  
Clinical practice: Management strategy }

"<sup>13</sup>C-Galactose Breath Test: An Early Indicator of Liver Fibrosis in Hepatitis C Virus Infection"

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## OT22 0553 **The Split Liver in Liver Transplantation: A Recent Experience**

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The good results of liver transplantation (LT) have allowed its larger use. However this increased use of LT has uncovered a relative organ shortage. The split liver is one of the means to increase the number of available grafts. We report here our recent experience with this technique. From January to December 1995, a systematic proposal to perform a split was made to the French organ sharing network as often as possible. Ninety LT were performed using 61 whole grafts, 27 split liver grafts, 2 reduced size grafts. Twenty livers were splitted at our center generating 40 split liver grafts: 23 transplanted at our center in 23 patients and 17 shipped to other centers. We received 4 split liver grafts from 4 livers splitted in other centers. Our 27 patients were transplanted for cirrhosis in 19 cases, amyloid polyneuropathy in 6 cases and fulminant hepatitis in 2 cases. Operative mortality (< day 60 post-LT) occurred in one case of fulminant hepatitis and long term mortality (> day 60 post LT) occurred in 1 case of cirrhosis. One patient was retransplanted at day 6 for primary non function due to a too small graft (the lowest liver to recipient weight ratio = 0.87). Patient and graft actuarial survival are respectively 91.4 – 5.8% and 87.5 – 6.8%. Twelve technical complications occurred in 10 patients: 3 arterial complications (2 thrombosis and 1 dissection) of which 2 were successfully treated by urgent desobstruction; biliary fistula: 4 cases, biliary stenosis: 2 cases; hemoperitoneum: 2 cases, segment 4 necrosis: 1 case. Eight of these complications needed surgery to be controlled.

*Conclusion:* 111 LT were performed with 87 livers realising an economy of 24/111 grafts (22%). During the same period, 16 proposals of split were refused in France. The graft economy would have been of 28%. When used for elective transplantation, the split LT gives good results comparable to those of whole LT. Our results promote the use of split LT every time it is possible. }

"The Split Liver in Liver Transplantation: A Recent Experience"

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## OT22 0554 **Quadruple Versus Triple Initial Immunosuppression in Liver Transplantation**

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Rejection following liver transplantation (LT) represents one of the main causes of morbidity, graft loss and patient death. Conventional triple immunosuppressive regimen using Cyclosporine (Cya), steroids and Azathioprine (AZA) is still responsible for high rate of rejection in the early post-operative period after LT, underlying the need for improved therapies. In a retrospective study, we compared the effects of standard triple immunosuppressive therapy versus an initial quadruple therapy using anti-thymocytes globulines in a series of 113 LT.

*Patients and methods.* From September 1991 to March 1995, 155 LT were performed in 151 patients. Of them, 42 liver transplant cases were excluded from the study (29 children, 10 adults surviving less than 3 months and 3 adults who had prophylactic OKT3 immunosuppressive regimen). Finally, 113 LT in 113 adults patients were studied. There were 75 males and 38 females with a mean age of 44 – 9 years (range: 18 to 63). Main indications for LT were viral (49%) and alcoholic cirrhosis (32%). All LT were donor/recipient ABO group identical. Patients were divided in 3 groups according to the type of immunosuppressive regimen; group I (n = 37): standard triple therapy using Cyclosporine, steroids and Azathioprine, group II (n = 35): when introduction of Cya or AZA had to be delayed because of renal dysfunction or thrombopenia, a rabbit anti-thymocyte globulin (Thymoglobulines, Pasteur Mérieux) was administered intravenously at the dose of 2.5 mg/kg/day 1 to 5 days after LT for 10 to 14 days until the triple regimen could be applied, group III (n = 41): a quadruple immunosuppressive therapy was done with intraoperative induction of Thymoglobulines which was given furthermore for 9 days. The three groups were comparable for age, sex and liver diseases. Statistical analysis was made by ANOVA and chi-Square tests, differences were considered statistically different at  $p < 0.05$ .

*Results.* A rejection episode occurred in 73%, 46% and 32% of patients in groups I, II and III respectively ( $p < 0.05$  G II and G III versus G I). OKT3 therapy was needed in 32%, 18% and 7% of patients in groups I, II and III respectively ( $p < 0.05$ ). The number of rejection episodes was significantly lower in G II and III than in G I, none of patients from G II and III experienced more than 3 and 2 episodes respectively. The date of rejection occurrence was different between the 3 groups, 75 to 85% of the first episode of graft rejection happened in the first two weeks in G I, in the first two months in G II and during months 2 and 3 in G III. Only 1 case of chronic rejection happened in G I and none in the other groups. Grafts and patients one year survival were 84%, 94% and 97% in groups I, II and III respectively ( $p < 0.05$  G II and III versus G I).

*Conclusions.* This quadruple regimen using initial anti-thymocytes globulines added to the three standard immunosuppressive drugs especially when given early intraoperatively allowed a decreased rate and severity of rejection episodes, an improved graft and patient survival without increased morbidity rate.

Liver and bile ducts, 1: Liver transplantation } "Quadruple Versus Triple Initial Immunosuppression in Liver Transplantation"

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## OT22 0555 Vitamin D Receptor Gene Polymorphism and Bone Loss after Liver Transplantation

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<sup>1</sup> NIDDK, Bethesda, USA Bone loss is a frequent complication of orthotopic liver transplantation (OLT). A relationship between common allelic variants in the gene encoding the vitamin D receptor (VDR) and bone mineral density (BMD) has been demonstrated. *Aim and Methods:* To investigate the influence of VDR gene polymorphism on bone loss after OLT, 55 cirrhotic male patients who underwent OLT were studied. VDR polymorphism were assigned blind with respect to the BMD data following restriction enzyme (Bsm1) digestion of PCR amplified DNA extracted from formalin fixed tissue. To measure BMD, dual energy X-ray absorptiometry at lumbar spine was performed before OLT, and repeated at 3 mo (n = 36), 6 mo (n = 33) and 12 mo (n = 22) and 24 month (n = 12) after OLT. Values of BMD are reported as Z score (standard deviations from the age and sex adjusted mean). Changes of BMD after OLT are expressed as percentage of the initial value. *Results:* Genotype bb was detected in 22 patients (40%), Bb in 27 (47%) and BB in 7 (13%). Before OLT, there were not differences between Z score of bb patients compared to the other genotypes (bb: { - }0.508 vs Bb + BB: { - }0.690, NS). Changes of BMD after OLT and p values between bb and Bb/BB groups are shown in the table below

Time (mo)	bb (%)	Bb/BB (%)	p value
3 mo	-1.2% (16)	+0.4% (16)	p < 0.05
6 mo	+0.4% (16)	+4.1% (8)	p = 0.11
12 mo	+4.1% (8)	+11% (5)	p = 0.25
24 mo	+11% (5)	+4.3% (20)	p = 0.05 (# = significant intragroup changes from baseline BMD)

Both groups were similar in all other parameters studied. *Conclusions:* In male patients, VDR gene polymorphism influences BMD changes after OLT. Genotype bb protects against the rapid bone loss seen in the early months after OLT. Liver and bile ducts, 1: Liver transplantation } " "Vitamin D Receptor Gene Polymorphism and Bone Loss after Liver Transplantation"

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## OT22 0556 Liver Transplantation for Familial Amyloidotic Polineuropathy. Evolution of Peripheral Neuropathy

\*L. Tomé, O. Mota, A. Mestre, J. Ferrás, R. Perdigoto, L. Furtado

Transplantation Unit, University Hospital, Coimbra, Portugal Peripheral neuropathy in familial amyloidotic polineuropathy (FAP) depends on the deposition of an abnormal transthyretin in the nervous system. Most of the abnormal protein is synthesized in the liver. Hepatic replacement should halt the progression of the disease and eventually correct established neurologic alterations. Our program transplanted 35 patients (35.8 sd 7.6 years old) suffering from FAP. The symptoms were known for 5.2 sd 3 years (from 1 to 12). The neurologic deficiency (Macedo, E. et al, 1988) reached 36.2 sd 10.6%. The time elapsed from the beginning of symptoms and the neurologic score correlated significantly ( $F: 13.87; r = 0.55; p = 0.0008$ ). The neurologic score evaluated before transplantation (148 sd 99 days before) and the score observed at least 180 days after the operation (621 sd 321 days after) could be compared in 15 such patients. They were not significantly different ( $p = 0.68$ ). We conclude that liver transplantation stops the evolution of familial amyloidotic polineuropathy but does not promote a resolution of established lesions at least in the short term. Liver and bile ducts, 1: Liver transplantation } "Liver Transplantation for Familial Amyloidotic Polineuropathy. Evolution of Peripheral Neuropathy"

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**OT23 0557 Treatment of Malignant Liver Tumours by Cryotherapy R. Adam, E. Akpinar, M. Johann, F. Kunstlinger, H. Bismuth**

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The use of cryotherapy for the treatment of liver tumours has been established as a therapeutic option when resection is not possible. The aim of this study was to determine the real place of this treatment in the therapeutic strategy of liver tumours.

**Methods:** From Oct 1993 to July 1994, 41 patients (pts) have been treated by cryotherapy at our institution, either as a single treatment (Group 1–11 pts), as combined with partial resection (Group 2–19 pts) or as complementary to a complete resection with no sufficient margin of normal liver around the tumour (Group 3–11 pts). There were 7 hepatocellular carcinoma all with underlying cirrhosis, 25 metastases of colorectal cancer and 9 metastases of other malignant tumours. Mean number of tumours was 3.9 (Range 1–8) in Group 1, 3.8 (2–9) in group 2 and 5.9 (1–9) in Group 3. Mean maximum tumour size was 56 mm (20–130), 40 mm (10–100), and 48 mm (16–80) respectively for the same groups. We used the LCS 2000 device (Cryogenic Technology Ltd, Belper, UK) designed specifically for hepatic cryotherapy to deliver liquid nitrogen to the tip of a triple lumen probe applied under ultrasound guidance to the lesion to be frozen.

**Results:** There were 2 peroperative complications related to the procedure: one rupture of the tumour during the freezing process and one perforation of the liver capsule. Both complications were easily controlled by suture. Operative mortality within 2 months was 2.4% (1/41), unrelated to cryotherapy (cardiac infarct at day 3). Serum transaminases increased post operatively in relation to the duration of cryotherapy and the number of treated lesions. They normalized within 5 days. In Group 1 (Cryo alone), a reduction of tumour size was observed in 4 pts (36%), with disappearance of a treated lesion in one case. Tumour markers were decreased in 3/4 pts with preoperative increased levels. Four pts with huge multinodular lesions died of progression of the disease from 2 to 6 months after cryotherapy. Seven pts are alive of whom 2 were subsequently submitted to hepatic resection. In Group 2 (Cryo + Resection), a reduction in cryotreated tumour size was observed in 6 pts (32%). Decreased tumor markers were demonstrated in 4 cases (21%). One patient died at 9 months, of local and extrahepatic recurrence. The remaining 18 pts are alive of whom 5 with local recurrence and 4 with recurrence outside the cryotreated site. In Group 3 ("Adjuvant" cryotherapy), one patient died 2.5 months after the procedure of sepsis unrelated to cryotherapy. All the other pts are alive without local recurrence. Overall, the main determinants of recurrence following cryotherapy were maximum tumour size > 5 cm and number of lesions > 3. Of 6 pts with both risk factors, 5 have currently recurred and 2 died of progressive disease.

**Conclusion:** Cryotherapy is a simple and safe procedure that may be useful in the treatment of unresectable malignant liver tumours and as an adjuvant to liver resection. Objective criteria of anti tumoral effects are demonstrated but need confirmation with a longer follow-up. Selection of pts should exclude all those with large multinodular tumors. }

"Treatment of Malignant Liver Tumours by Cryotherapy"

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## OT23 0558 Percutaneous Ethanol Injection under General Anesthesia of Hepatocellular Carcinoma on Cirrhosis: Three Years Survivals in 107 Patients

\*A. Giorgio, L. Tarantino, N. Mariniello, G. de Stefano, A. Perrotta, V. Aloisio, F. Esposito

V Divisione, D. Cotugno Hospital, Naples, Italy Percutaneous ethanol Injection (PEI) under general anesthesia (u.g.a.) is a new therapy for treatment of large and/or multiple Hepatocellular Carcinoma (HCC) by the injection of large amount of ethanol in the tumor. We report our results with 3 years survival rates in patients with HCC on cirrhosis treated with PEI u.g.a. *Patients and methods:* between october 1992 and december 1995, 112 cirrhotic patients (79 male; age: 45–80; mean: 64 years) with 215 HCC nodules (diam. = 0.6–14 cm; mean: 4.1 cm; median: 3.5 cm) underwent PEI u.g.a. 53 patients had one nodule (diam. = 3–14 cm; mean = 4.2 cm; median = 3.5 cm), 59 had 2 or more (2–5) nodules (diam. = 0.6–13 cm; mean = 3.9; median = 3.5 cm). Total ethanol injected per treatment ranged between 16–205 cc. Survival rates and statistical analysis were calculated according to Kaplan-Meier method and Wilcoxon test respectively. *Results:* 5 patients died within 7 hours–10 days after the treatment for rupture of aoesophageal varices in 3 cases, rupture of subcapsular HCC in 1 case and liver failure in 1 case. In the remaining 107 patients, dynamic CT, performed 72 hours–one month after the treatment, showed complete necrosis in 76 (71%) cases and incomplete necrosis (although always > 50%) in 31. Survival rates at 1, 2, 3 years in all 107 patients were 88%, 76% and 76% respectively. Survival rates in Child class A patients were 100%, 92%, 92% and in class B patients were 84%, 72% e 72% at 1, 2, 3 years respectively; in class C were 100% e 50% at 1 and 2 years respectively (p = n.s.). Survival Rates in patients with one nodule were 80%, e 68% at 1 and 2 years, while in the patients with two nodules or more were 95%, 82% e 82% at 1, 2 and 3 years respectively (p = n.s.). Survival rates in patients with nodules < 5 cm were 88%, 73%, 73% while in patients with nodules > 5 cm were 89%, 77% e 77% at 1, 2 and 3 years respectively (p = n.s.). During the follow-up (5–46 months) 48 (45%) patients showed intrahepatic recurrences; 41 out of them were retreated with new sessions of PEI-u.g.a. or conventional PEI. *Conclusions:* PEI-u.g.a. is more aggressive than traditional PEI and can cause also the death of the patient. Moreover, it is an effective, fast and inexpensive therapy in patients with large and/or multiple HCC on cirrhosis. Although the treatment was performed on unselected patients, survival rates of PEI-u.g.a. seems similar to those obtainable by conventional PEI and even better than surgery. Radiology and ultrasound: Therapy Oncology, specific: Liver, biliary }" "Percutaneous Ethanol Injection under General Anesthesia of Hepatocellular Carcinoma on Cirrhosis: Three Years Survivals in 107 Patients"

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## OT23 0559 Percutaneous Radiofrequency Interstitial Thermal Ablation of Hepatocellular Carcinoma

\*L. Buscarini, S. Rossi, M. Di Stasi, E. Buscarini

Gastroenterology Department, Hospital of Piacenza, Italy *Purpose:* To evaluate the long-term results of interstitial thermal ablation (RITA) of hepatocellular carcinoma (HCC). *Methods:* 27 men and 17 women (all cirrhotic but one), mean age 66.7 years (52–82), with 46 HCC nodules < 3.0 cm in diameter underwent monopolar and/or bipolar RITA procedure (using 15–18 G caliber electrode needles or modified electrode needles with retractable lateral exit jackhooks on the tip; exposed tip of 1.0–2.0 cm; temperature of 90°C; 3–20 minutes/thermal lesion). The needles were placed into the tumor under US-guidance. *Results:* Tumor destruction was achieved in a mean of 3.1 RITA sessions, demonstrated by US-guided biopsies, dynamic CT and angiography. During a mean follow-up of 24.6 months (range 3–73), 2/44 patients showed local recurrences and 14/44 new lesions. Nine patients with a first and four patients with a second recurrence underwent new effective RITA treatment. 11/44 patients died: five from cancer and six from other causes. Histology on five treated HCCs showed total necrosis in four and subtotal in one. 5-year survival rate was 0.40. No complications were observed. *Conclusions:* RITA is a useful percutaneous treatment for HCC. Oncology, general: Therapy Oncology, specific: Liver, biliary } "Percutaneous Radiofrequency Interstitial Thermal Ablation of Hepatocellular Carcinoma"

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**OT23 0560 Hepatocellular Carcinoma (HCC) and Liver Transplantation: Evaluation of Diagnostic Accuracy of Lipiodol-CTA. Veltri, M. Grosso, D. Regge, M.C. Martina, M. Cogoni, P. Busolli**

Istituto di Radiologia, Università di Torino, Italy *Purpose* To assess the diagnostic accuracy of lipiodol-CT in the diagnosis of HCC based on the histopathological study of explanted livers. *Materials and Methods* The results of lipiodol-CT in 66 cirrhotic patients were retrospectively examined and compared to histopathological findings, which demonstrated 41 lesions (diameter range: 0.8 to 4.0 cm, mean: 2.1 cm) in 33 patients. *Results* Lipiodol-CT correctly diagnosed 32/41 nodules (78%) in 27/33 patients (81.8%). The specificity was 66.6%; the diagnostic accuracy was 74.2% with 16 false positive nodules in 12 patients. The positive predictive value for the presence of a lesion was 66.6%; the negative predictive value was 78.6%. *Conclusions* Based on our experience, the results obtained indicate a poor diagnostic accuracy of lipiodol-CT. In particular, only the patient-based sensitivity (> 80%) appears acceptable, while the number of lesions detected, the specificity and the diagnostic accuracy were inferior in comparison to traditional integrated imaging methods (sonography, CT, and angiography). The results, in accordance with some recently reported data, suggest not to include lipiodol-CT in the diagnostic-staging work-up of HCC while awaiting liver transplantation. Liver and bile ducts, 1: Liver transplantation Oncology, specific: Liver, biliary Radiology and ultrasound: Diagnosis } "Hepatocellular Carcinoma (HCC) and Liver Transplantation: Evaluation of Diagnostic Accuracy of Lipiodol-CT"

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## OT24 0561 Overexpression of p53 Protein Correlates with Enhanced Aggressiveness of Pancreatic Cancer

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<sup>1</sup> Istituto di Anatomia Patologica, Universit  di Pisa, Italy The aim of this study was to ascertain the frequency and the prognostic significance of p53 overexpression in pancreatic cancer. Paraffin embedded specimens from 70 pt.s operated on for ductal adenocarcinoma of the pancreas were analysed. Using the monoclonal Ab D07, the nuclear overexpression of the mutated p53 protein was immunohistochemically determined in both the primary tumor and its lymph node metastases (LNM). T and N status, tumor stage, histological grade (HG) and proliferation index (PI) were also recorded. Minimum follow-up was 12 months and complete data were available in all cases. Survival curves were constructed by Kaplan-Meier method. Fifty-seven percent of our cancers showed p53 overexpression of either focal or diffuse patterns. No relationship was discovered between p53 overexpression and T status, HG or PI respectively. Thirty-two cases (46%) had histologically documented LNM. 28 out of 38 N0 tumors (74%) were p53 negative while 20 out of 32 N1 cancers (63%) were p53 positive ( $p = 0.005$ ). LNM were significantly related to reduced survival times ( $p = 0.02$ ). Moreover, comparing pt.s with p53 negative LNM with those of the same stage bearing p 53 positive metastases a wide difference became clearly evident ( $p = 0.003$ ) (figure 1).

Nuclear overexpression of p53 in pancreatic cancer seems to correlate with increased lymphatic spread and poor prognosis. In particular, the occurrence of lymph node metastases overexpressing the mutated p53 protein, seems to imply a dreadful prognosis. The possibility of improving these results by treating these cases with new adjuvant therapies, such as the newly proposed treatment with antisense oligonucleotides directed against p53 oncogene, adds further interest to this observation. Oncology, specific: Pancreas } "Overexpression of p53 Protein Correlates with Enhanced Aggressiveness of Pancreatic Cancer"

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## OT24 0564 Enhanced Expression of Plasminogen Activators in Pancreatic Cancer is Associated with Poor Prognosis

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Departments of Visceral and Transplantation Surgery and Pathology, University of Bern, Switzerland

Departments of Medicine and Biological Chemistry, University of California Irvine, Irvine USA uPA (urokinase plasminogen activator) is a serine proteinase which plays an important role in cancer invasion and metastasis. It binds to a specific cell surface receptor which is called uPA receptor (uPAR). uPA activates plasminogen to form plasmin, which, like uPA, participates in tissue degradation and proteolysis. Binding of uPA to its receptor accelerates uPA's own activation from pro-uPA, enhancing the activity of the uPA/uPAR cascade. *Patients:* Pancreatic cancer samples were obtained from 30 patients (12 women, 18 men) with a median age of 66.5 years (range: 32–79 years) undergoing pancreatic resection. Pancreatic tissue samples obtained from 30 previously healthy organ donors (14 women, 16 men, median age: 41 years) served as controls. *Methods:* Tissues destined for RNA extraction were frozen in liquid nitrogen immediately upon surgical removal. In addition, freshly removed tissue samples were fixed in Bouin solution and paraffin embedded for histological analysis. Expression of the uPA and uPAR was analysed by Northern blot analysis using specific cDNA probes. In addition, immunohistochemical analysis using specific monoclonal antibodies was performed. The Northern blot data were correlated with the survival periods of the patients. *Results:* Immunohistochemical analysis demonstrated moderate to strong immunostaining of both factors in most pancreatic cancers. Cancer lesions with signs of invasion exhibited the strongest immunohistochemical signals for both factors. In addition, in desmoplastic areas adjacent to the cancer cells, moderate uPA and uPAR immunoreactivity was detectable. Northern blot analysis revealed a 6-fold and a 4-fold increase in uPA and uPAR mRNA levels in pancreatic cancer, respectively, in comparison with normal controls ( $p < 0.01$ ). Correlation of the Northern blot data with the clinical parameters of the patients indicated that patients with concomitant overexpression of uPA and uPAR had a shorter postoperative survival (median: 9 months; mean – SD: 10.2 – 3.6 months) than patients in whom only one or none of these factors were overexpressed (median: 18 months; mean – SD: 20.3 – 8.7 months) ( $P < 0.002$ ). *Conclusion:* Our data suggest that uPA and uPAR may serve as prognostic markers in human pancreatic cancer and that the marked overexpression of both factors may create an environment that enables pancreatic cancer cells to invade surrounding tissues. Support: SNF 32-39529. Oncology, specific: Pancreas Oncology, general: Proliferation, carcinogenesis Oncology, general: Molecular biology, genetics } "Enhanced Expression of Plasminogen Activators in Pancreatic Cancer is Associated with Poor Prognosis"

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## OT25 0565 Immediate and Long-Term Results of Pancreatic Ductal Drainage in Severe Painful Chronic Pancreatitis

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Department of Gastroenterology, Erasme Hospital, Brussels, Belgium  
The aim of the present study is to evaluate the symptomatic improvement of 119 chronic pancreatitis patients (93 men, 26 women, median age 45 y, median disease duration 3 y) submitted to different endoscopic drainage procedures and extracorporeal shock wave lithotripsy (ESWL). The inclusion criteria of the patients were: 1) history of recent severe acute pancreatic pain, 2) no previous pancreatic surgery; 3) demonstration of main pancreatic duct (MPD) obstruction (stenosis or stones) with upstream ductal dilatation on endoscopic pancreatography or CT scan. Deep MPD cannulation was possible in 96% of the patients. Fifty-three patients (group 1) underwent pancreatic sphincterotomy alone or in combination with ESWL. Sixty-one patients with MPD distal stricture (group 2) also required pancreatic stents. Complications occurred in 4% of the patients and none needed surgical intervention. No mortality was observed. Sixty-nine patients had a minimal 2 y follow-up (FU) (median: 64 m, range: 24–100 m). Eighty-six percent of them experienced a dramatic improvement (58%) or complete relief (28%) of pain. Worsening of endocrine and exocrine functions was observed in only 13 and 5 patients respectively over the FU period. Ten patients (14%) did not improve and eight of them were surgically treated. The following observations were seen with the same frequency in groups 1 and 2: successful ductal stone clearance and MPD drainage, immediate and long-term pain relief, median number of recurrent pain attacks and surgical requirement. However, complete pain relief tended to be more frequent in group 1 (37% vs 21%,  $p = 0.14$ ). It is concluded that endoscopic MPD drainage is an effective treatment of painful chronic pancreatitis. It causes immediate and long-term pain relief in 91% and 86% of the cases, respectively, and preserves endocrine and exocrine functions in most cases. Endoscopy, specific: PancreaticPancreas: Pancreatitis, chronicEndoscopy, general: Instrumentation, therapy } "Immediate and Long-Term Results of Pancreatic Ductal Drainage in Severe Painful Chronic Pancreatitis"

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## OT25 0566 Fecal Elastase-1: Not Helpful in Diagnosing Chronic Pancreatitis with Slight to Moderate Exocrine Pancreatic Insufficiency

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<sup>1</sup> University of Rostock, Germany Preliminary studies on the value of fecal elastase-1 to estimate exocrine pancreatic insufficiency (EPI) were controversial but mostly favorable (Gastroenterology 106: A290, A300, A325, 1994; Gastroenterology 108: A341, 1995). For a definitive evaluation, elastase-1 estimations were compared with fecal chymotrypsin results in patients categorized according to grades of exocrine pancreatic function using the gold standard tests, the secretin-pancreozymin test (SPT) and fecal fat analysis, and to grades of morphological changes, the presence and absence of calcifications and duct changes. *Patients and Methods.* An SPT and fecal fat analysis as well as fecal chymotrypsin and fecal elastase-1 estimations were performed in 64 patients in whom EPI was suspected. Grading categories for EPI were *slight* (enzyme secretion reduced, bicarbonate concentration and fecal fat excretion normal), *moderate* (SPT abnormal, fecal fat excretion normal), and *severe* (SPT abnormal plus steatorrhea). Patients were further staged for calcifications and duct changes according to the Cambridge classification. *Results.* Exocrine pancreatic function was normal in 34 (53%) patients (group 1) and abnormal in 30 (47%) patients (group 2). In group 1, fecal chymotrypsin was normal in 27 (79%) and elastase-1 in 32 (94%) patients. In group 2, both tests were abnormal in 17 (57%) and 16 (53%), respectively. When group 2 was split into slight (n = 10), moderate (n = 9), and severe EPI (n = 11), chymotrypsin was abnormal in 30%, 44% and 91%, respectively, and elastase-1 in 40%, 33% and 82%, respectively. Pancreatic calcifications were present in 12 (40%) of all patients and duct changes in 62% of 13 investigated patients. The percentage of abnormal chymotrypsin and elastase-1 estimations was the same in patients with and without calcifications/duct changes. *Conclusion.* Fecal elastase-1 estimation is not superior to traditional fecal enzyme estimation and helpful only in detecting severe, but not slight to moderate EPI which is the more frequent and difficult clinical problem and does not correlate significantly with severe morphological changes of chronic pancreatitis. Clinical practice: Management strategy Intestinal disorders, absorption: Pathophysiology of diarrhea Pancreas: Pancreatitis, chronic } "Fecal Elastase-1: Not Helpful in Diagnosing Chronic Pancreatitis with Slight to Moderate Exocrine Pancreatic Insufficiency"

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## OT25 0567 Results after 5 and 10 Years Following Surgery for Chronic Pancreatitis: Long Term Survival Is Unrelated to Surgical Technique

\*G. Spiliopoulos, B. Chareton, C. Stasik, M.A.C. Machado, J.P. Campion, B. Meunier, B. Launois

Department of Digestive Surgery and Transplant Unit, CHR Pontchaillou, Rue Henri Le Guilloux, 35033 Rennes, France In papers published by Leger [1] and Moreaux [2] in 1974 and 1984 it was suggested that pancreaticoduodenectomy should be banned from the surgical arsenal of chronic pancreatitis because of the disappointing long-term results. The aim of the present study was to review long-term outcome of patients having undergone surgery in our Department. *Patients and methods:* between 1972 and 1994, 381 patients underwent surgery for chronic pancreatitis at a referral centre. There were 322 males and 59 females with a mean age of 45 – 12.3 years. Alcohol abuse was the prevailing etiological factor (89.7%). Surgical procedures included 153 resections (87 Whipple procedures, 62 distal pancreatectomies, 4 total pancreatectomies), 113 bypasses (40 pancreatic + biliary and/or digestive bypasses, 73 biliary and/or digestive bypasses) 89 cystoenteric anastomoses, 4 splenectomies and 22 exploratory laparotomies. *Results:* Operative mortality was 7.8% for resections, 5% for pancreatic bypasses, cystoenteric anastomoses and exploratory laparotomies. Morbidity was 17% for resections and cystoenteric anastomoses and 7.5% for pancreatic bypasses, 5 and 10 years survival was 92% and 76% for resections, 79.7% and 53.8% for cystoenteric anastomoses, 85% and 66% for pancreatic bypasses. (n = N.S.). Diabetes mellitus developed in 39% of patients who underwent resections and 37.5% of patients having bypasses. Persistent pain was present in 24% of patients following resection and bypass. *Conclusion:* the long-term outcome of patients with chronic pancreatitis is unrelated to the type of surgery.

Reference: Leger L. Ann. Surg. 1974; 180: 185–191.

Moreaux J. World J. Surg. 1984; 8: 346–350 Clinical practice: Management strategy Pancreas: Pancreatitis, chronic Oncology, general: Therapy } "Results after 5 and 10 Years Following Surgery for Chronic Pancreatitis: Long Term Survival Is Unrelated to Surgical Technique"

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## OT25 0568 Effects of Ethanol (EtOH) on Neutrophils in the Pancreas

\*P.U. Reber, A.G. Patel, M.K. Schilling, W. Uhl, H.U. Baer, H.A. Reber, M.W. Buchler

Depts of Surgery, Inselspital Bern, Switzerland, UCLA Los Angeles, CA Although EtOH is a common cause of pancreatitis, the mechanisms by which it damages the pancreas remain poorly understood. Studies in other systems suggest that neutrophils may cause tissue injury in a variety of conditions. Here we studied the effects of EtOH on neutrophil activation and extravasation in an in vivo perfused cat pancreas. *Methods:* The pancreata of adult cats (2.5–3 kg) were isolated and perfused at a constant flow rate with various concentrations (0.2–2 mg/dl) of EtOH in an oxygenated physiological perfusate. The control group received perfusate without EtOH. Neutrophil activation and extravasation were assessed by measuring pancreatic tissue myeloperoxidase activity (MPO) by the oxidation of tetramethylbenzidine with hydrogen peroxide. *Results:* Perf. time Control (6) EtOH (0.25 mg/dl) (6) EtOH (2 mg/dl) (6) 0.1.1 – 0.3 U 1.3 – 0.4 U 1.4 – 0.3 U 60 min 1.6 – 0.2 U 1.7 – 0.9 U 9.1 – 0.7 U <sup>186</sup>120 min 1.9 – 0.2 U 3.2 – 0.8 U\* 11.8 – 1.4 U <sup>186</sup>\*p < 0.05 vs control, <sup>186</sup>p < 0.05 vs EtOH (0.25 mg/dl) and control. *Conclusions:* EtOH perfusion of the pancreas at concentrations of 0.25 mg/dl or more, caused a time dependent neutrophil activation, which was directly related to [EtOH]. EtOH (0.2 mg/dl) had no effect (data not shown). This suggests a new mechanism by which EtOH, in physiologically relevant concentrations, and independent of its effects on pancreatic blood flow, may cause pancreatic injury. Pancreas: Pancreatitis, chronic } "Effects of Ethanol (EtOH) on Neutrophils in the Pancreas"

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**OT26 0570 Severe Acute Pancreatitis: Initial and Evolutive Bioclinical Prognostic Evaluation on 234 Patients. A Multicenter, Prospective Study of the French Associations for Surgical Research**

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Centre Hospitalo-Universitaire Henri-Mondor, 94010 Cr\`eteil, France During the past 25 years many studies were carried out to appreciate the best methods to differentiate between mild and severe pancreatitis. Nonetheless, within the group of patients with severe acute pancreatitis some will have a relatively uneventful course and others will have local and general complications. In order to identify the patients at risk of developing complications, the French Associations for Surgical Research began a multicenter prospective study including 234 patients with a first episode of severe AP. The purpose of this study was firstly to compare the predictive value of bioclinical data and specific and non specific bioclinical scoring systems at admission and to define, during the course of pancreatitis, the parameters indicating the occurrence of local infection (pancreatic abscess or infected necrosis) and death. Nineteen bioclinical parameters were recorded on admission, on day 3 and then every 4 days as well as preexisting diabetes mellitus, respiratory, cardio-vascular and hepatic disorders. Specific and non specific scoring systems (Ranson, Imrie, Simplified Acute Physiologic Score, Organ System Failure) were also assessed. To summarize prognostic information multivariate analysis used the Cox's model. Bioclinical data collected at admission and indicating local infection occurrence were: age > 55 years, systolic pressure < 120 mmHg, hematocrit < 30%. Bioclinical data collected at admission and predictive of survival were: age > 55 years and serum urea > 9 mmol/l. Ranson score and SAPS were predictive of survival while SAPS and OSF were predictive of local infection. Multivariate analysis of bioclinical data collected during the course of pancreatitis showed that pulse rate > 100/mn, systolic pressure < 120 mmHg, hyperthermia were significantly associated with survival. Increased pulse rate, hyperthermia and septicemia were significantly associated with local infection occurrence. This study confirms the predictive value of Ranson scoring system and SAPS. Some easily collected prognostic parameters, at admission and during the course of the disease were also identified. Pancreas: Pancreatitis, acute }" "Severe Acute Pancreatitis: Initial and Evolutive Bioclinical Prognostic Evaluation on 234 Patients. A Multicenter, Prospective Study of the French Associations for Surgical Research"

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## OT26 0571 Pancreatic Tissue Penetration of Amikacin, Amoxicillin/Clavulanic Acid, Piperacillin and Ofloxacin in Acute Experimental Pancreatitis

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**Background & Aims:** Pancreatic infection is an often lethal complication of acute necrotic pancreatitis. The tissue/serum (T/S) ratio is an important criterion in deciding on antibiotic treatment but an influence of pancreatic inflammation on the tissue concentration and on the T/S ratio of antibiotics has not yet been evaluated. *The aim* of our study was to evaluate pancreatic tissue penetration and T/S ratios of amikacin, amoxicillin/clavulanic acid (augmentin), piperacillin and ofloxacin in normal (NR) and acute pancreatitis (AP) rats. *Methods:* Bolus of antibiotics was administered via the external jugular vein. In NR, the antibiotic concentrations were evaluated in blood and pancreatic tissue 90 min after antibiotics administration. In AP, severe necrotic acute pancreatitis was induced by infusion of 2 ml of 5% sodium taurocholate into the pancreaticobiliary duct, and 3 hours thereafter the antibiotics were administered. *Results:* Amikacin Augmentin Piperacillin Ofloxacin NR AP NR AP NR AP n = 11 n = 11 n = 11 n = 11 n = 11 n = 11 n = 11 n = 11 Serum concentration 1.9 2.2 14.7 23 29.5 20.4 1.1 1.1 5.0 4.0 0.7 4.3 25.1 15.2 4.4 7.2 1.1 1.0 Tissue concentration 0.3 0.2 4.8 6.5 7.6 6.3 0.8 0.5 0.1 0.3 2.3 4.2 2.3 3.0 0.4 0.7 Tissue/serum ratio 0.16 0.07 0.24 0.23 0.27 0.26 0.59 0.52 0.04 0.06 0.15 0.11 0.12 0.13 0.56 0.21 (NR-normal rats, AP-acute pancreatitis rats, data are medians [IQ distance]) All antibiotic concentrations in serum were higher than in tissue ( $p < 0.05$ ). In AP, tissue concentrations were not different as compared to NR for each antibiotic. In both, NR and AP, the highest T/S ratio was observed during ofloxacin as compared to the other antibiotics ( $p < 0.003$ ). T/S ratios for piperacillin and augmentin were similar and higher as compared to amikacin ( $p = 0.016$ ). Pancreatic tissue concentrations as well as T/S ratios were similar in NR and AP except for amikacin where the T/S ratio was lower in AP than in NR ( $p = 0.02$ ). *Conclusion:* Ofloxacin showed the best pancreatic tissue penetration of the four antibiotics tested. The penetration of ofloxacin, augmentin and piperacillin was not influenced by pancreatic inflammation, while the penetration of amikacin was diminished by inflammation. Pancreas: Pancreatitis experimental } "Pancreatic Tissue Penetration of Amikacin, Amoxicillin/Clavulanic Acid, Piperacillin and Ofloxacin in Acute Experimental Pancreatitis"

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## OT28 0572 The Mouse Model of Infection with Cytotoxin Expressing Strain of *Helicobacter Pylori* (Hp) in Studying the Pathogenesis of Chronic Gastric Ulcer

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Dept Med I, Univ Erlangen-Nuremberg, Erlangen, Germany *Purpose:* Hp infection in humans is known to be responsible for gastritis and peptic ulcers but studies on the pathogenesis of Hp infection and peptic ulceration is limited by the absence of adequate animal model. *Methods:* We studied the effects of inoculation of conventional BULB/c mice with bacteria expressing both cytotoxin-associated gene A (CagA) and vacuolating cytotoxin (VacA) (SPM 326 type I) and non-cytotoxic Hp strain (SPM 314 type II), obtained from fresh clinical isolates, on the course of healing of chronic ulcers induced in the stomachs by serosal application of acetic acid. Inoculation of type I or II strain ( $2 \times 10^9$  CFU) or vehicle saline was made at day 2, 4 and 6 upon ulcer production and the mice were killed at day 7 and 14. The ulcer area was measured by planimetry, the mucosal blood flow was determined by laser Doppler and mucosal biopsy samples were taken for histology and Hp culture. *Summary of results:* General condition of all animals subjected to Hp was fine and their weight increased normally. Hp infection was positive at 1 and 2 wk both by histology and cultural status. Neutrophil infiltration mainly at the submucosa was apparent in type I strain infected mice indicating the occurrence of gastritis. After 1 and 2 wk upon ulcer formation in vehicle-treated mice, the ulcer area was reduced by – 46% and 93%, respectively, and similar rate of healing was observed in type II Hp strain infected mice. In contrast, in type I strain infected mice no tendency of ulcer healing was observed after 1 and 2 wk. Blood flow was significantly lower in the ulcer area in type I strain than in type II strain infected or vehicle treated mice. *Conclusions:* Conventional mice can be successfully colonized by Hp strain expressing CagA and VacA and this infection delays healing of chronic gastric ulcers, at least in part, due to reduction in gastric blood flow. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "The Mouse Model of Infection with Cytotoxin Expressing Strain of *Helicobacter Pylori* (Hp) in Studying the Pathogenesis of Chronic Gastric Ulcer"

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**OT28 0573 Helicobacter Inhibits Directly Acid Secretion by H<sub>3</sub> Receptor Mediator Pathway**  
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INSERM U10, Hospital Bichat & Institut Pasteur, Paris-France Helicobacter modifies gastric acid secretion interfering with gastrin, somatostatin and histamine. It increases N-methylhistamine a known H<sub>3</sub> selective receptor agonist. Previous study from us and others have shown that activation of H<sub>3</sub> receptor reduces stimulated gastric acid secretion. The aim of the present study was to investigate H<sub>3</sub> receptor pathway *in vivo* in cat before and after eradication. *Materials*. Six adult cats (Iffa Credo) provided with a fistula in the stomach were examined for the presence of Helicobacter using biopsies submitted to CLO test, histology, culture and/or PCR analysis. Meal-, histamine (20–160 µg/kg/hr)- and gastrin (G5 1–32 or G17 0.5 µg/kg/hr)-stimulated H<sup>+</sup> outputs were analysed after 18 hr fasting before and 5 weeks after Helicobacter eradication (15 days PPI + 2 antibiotics therapy). The effect of thioperamide, N-methylhistamine (H<sub>3</sub> receptor antagonist) on the G17-stimulated acid secretion and serum gastrin (RIA) level (4 × 15 min) in response to meal were analysed before and after eradication. *Results*: Before eradication histology did not show mucosal inflammation. Before eradication CLO test was positive and *H. felis* (n = 4) and *Heilmanni* (n = 2) were characterized; after eradication no bacterium was found and CLO tests were negative. Meal-stimulated gastrin level remained unchanged by eradication therapy. Acid secretion increased (40%) significantly (p < 0.01) after eradication in a dose-dependent manner in response to pentagastrin or histamine and to G17 (i.e. 1580 + 300 µEq/15 min vs 940 + 190 µEq/15 min). The level of gastric acid output under "thioperamide + G17" before eradication was similar to that observed under "G17 alone" after eradication. *Conclusion*. These results demonstrate that Helicobacter but no inflammatory cells inhibits acid secretion in cat. Since thioperamide reversed this inhibition, we suggest that *Helicobacter* inhibits acid secretion *via* an H<sub>3</sub> receptor mechanism. } "Helicobacter Inhibits Directly Acid Secretion by H<sub>3</sub> Receptor Mediator Pathway"

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OT28 0574 **Role of Selectins in the Formation of Leukocyte-Platelet Aggregates Elicited by *H. Pylori* Infection**

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Extracts of *Helicobacter pylori* have been shown to induce leukocyte adhesion in mesenteric venules, but the effect of this chronic infection in the gastric microvessels is still unknown. The objective of the present study was to characterize the effects of *H. pylori* infection on leukocyte-endothelial cell interactions in the gastric microcirculation, and to assess the role of selectins in such interactions. Mice were orally inoculated with fresh clinical cagA+ vacA+ *H. pylori* isolates 3 times at 2-day intervals. Infection was assessed by culture and/or urease test of gastric specimens obtained at the end of the experiments. Controls included mice inoculated with *E. coli* or saline. Leucocyte-endothelial cell interactions were characterized in the stomach using intravital microscopy after fluorescent labeling of leukocytes and platelets with acridine orange. In non infected animals the number of rolling leukocytes in the gastric venules was low (2 – 0.8 cells/min). Infection with *H. pylori* induced a marked increase in rolling both at one (11.2 – 3.6) and two weeks (8 – 0.2) after inoculation. In addition, in these animals leukocyte-platelet aggregates were observed both at one (19.6 – 3.0) and two weeks (10.8 – 5.8 aggregates/min) after inoculation. By contrast, aggregates were never observed in non-infected controls. In animals inoculated with *E. coli*, the number of rolling leukocytes in gastric venules (2 – 0.7) was the same as in controls, and platelet-leukocyte aggregates were rarely observed (1.2 – 0.7 aggregates/min). To assess the role of selectins in the formation of aggregates, anti L-, P-, and E-selectin mAbs were iv given after basal observation. Whereas anti E- selectin didn't exert any effect in the number of aggregates, they markedly decreased following anti L- (from 21 – 3 to 4 – 2 aggregates/min) or anti P-selectin (from 19 – 4 to 1.5 – 0.5 aggregates/min) mAbs administration. The results of the present study indicate that infection with *H. pylori* induces leukocyte rolling and elicits the formation of L- and P-selectin dependent leukocyte-platelet aggregates in the gastric microvasculature. These microvascular alterations may contribute to the pathogenesis of mucosal damage in *H. pylori* infection.  
Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Inflammation } "Role of Selectins in the Formation of Leukocyte-Platelet Aggregates Elicited by *H. Pylori* Infection"

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**OT28 0575 Helicobacter Heilmanil Type 1 (Hh1) Infection Induces Increased Gastric Emptying of Liquids in Rats I. Duval-Araújo,**

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The association between *H. pylori* and gastric motility abnormalities is not well evaluated and is still controversial due in part by the lack of an appropriate animal model. It was recently demonstrated that (Hh1), a spiral bacterium that infects the stomach of both humans and pig, easily colonizes and induces an inflammatory response in the gastric mucosa of rodents. For these reasons, we aimed to study the relationship between gastric motility in rats experimentally infected by Hh1 correlating the results with serum gastrin and gastric somatostatin concentration, since these hormones seem to be involved in the gastrointestinal motility. Twenty Wistar female rats were divided in two experimental groups: A, 10 non-infected animals (control group) and B, 10 animals inoculated *per os* with 0.2 ml of gastric mucus of a Hh1 positive swine. After 56 days of inoculation, the animals were anesthetized with ketamine chloride (50 mg/Kg body weight) and gastric emptying was studied by scintigraphy after oesophageal administration of 0.2 ml <sup>99m</sup>Tc-fitate diluted (1:1) in 2.5% peptone solution. After the scintigraphic study, the animals were sacrificed, blood samples were collected for serum gastrin contents measurement and fragments of the gastric antrum were obtained for somatostatin contents evaluation and Hh1 diagnosis. The results were analysed by the Kruskal-Wallis test and the level of significance was set at  $p < 0.05$ . All animals of the group B were Hh1-positive by carbolfuchsin stained smears and urease test and all group A animals were Hh1-negative. There was an increase in the gastric remnant in group A when compared to the group B (72.7 – 17.7% vs. 47.7 – 13.9%,  $p = 0.01$ ). Serum gastrin levels of group B were higher than in the group A (median 64.3 pg/ml; range 26.7 to 197.5 vs. 30.3 pg/ml; range 20.9 to 84.1,  $p = 0.03$ ) and gastric somatostatin levels were lower in the group B when compared to group A (0.9 ng/mg; range 0.7 to 3.2; and 2.9 ng/mg; range 1.2 to 5.2,  $p = 0.01$ ). In conclusion, gastric motility is altered in rats infected by Hh1. This abnormality could be related to the concurrent abnormalities of gastrin and somatostatin secretion.

Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Motility, general: Functional GI disorders Motility, specific: Stomach } "Helicobacter Heilmanil Type 1 (Hh1) Infection Induces Increased Gastric Emptying of Liquids in Rats"

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## OT29 0576 Referral for Anorectal Function: The Dutch Experience

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*The purpose of the study* was to evaluate the impact of Anorectal Function Evaluation (AFE) on patients and referring specialists. *Methods.* In one year 135 patients (fecal incontinence 31%, constipation 17%, fistula 16%, pain 14%, other 22%) were referred for AFE. AFE consisted of proctoscopy, anal manometry, rectal compliance, anal mucosal sensitivity and anal endosonography. From 128 patients an address was available; 100 returned the questionnaire (78%). The response of the referring specialists was 91%. *Results.* Forty-one patients (30%) were referred from other hospitals. In 70% there was total agreement about the referring and final diagnosis. (R 0.76 ( $p < 0.0001$ )). Patients questionnaire: The visual analogue scales (VAS, 0–10) for the experience of referral for AFE were for embarrassment 4.4 (SD 3), pain 3.6 (SD 3.6) and traveling time 2.4 (SD 3.2). The sex of the investigator did not matter in 87% of the patients. Of the women, 13% preferred a female investigator. Fifty-nine patients answered that they had received (another) treatment: surgery (32), medication (16), diet (5), physiotherapy (1), combination of the above (7) or otherwise (4). Of the 41 patients who did not receive (another) treatment, 29 were reassured and 12 said to have had no benefit from the visit. The medical situation before AFE and at follow-up (VAS 0–10) improved overall from before 4.4 (SD 3.8) to after 6.3 (SD 3.6) ( $p < 0.0001$ ), caused by the treated group (58) with an improvement from 4.1 (SD 3.9) to 6.9 (SD 3.4) ( $p < 0.0001$ ). Specialists questionnaire: The advice was followed by the referring specialist in 84% of the patients. Physiotherapy was followed in only 67%, while surgery, depending of the type, was followed up to 100%. The quality of the advice was considered good in 84%. The possibility for referral for AFE was considered useful in 93% patients. In 71 patients information of both specialist and patient was obtained. Three patients had therapies that were not advised, 19 patients did not follow up their (mainly diet) advice. In the 135 patients, AFE changed the management in 34 (25%) patients. In the other 101 patients, mainly endosonography was of value, by determining size of sphincter defects or fistula tracts. *Conclusion:* AFE is well tolerated and changed management in 25% of patients. Treatment advised after AFE improved the clinical condition significantly. Specialists considered referral useful in 93%. Dietary advices and physiotherapy were less frequently followed by both patient and specialist. Anal endosonography seems the most valuable test. Clinical practice: Epidemiology (non cancer) Intestinal disorders: Anorectal disorders Echoendosonography: Therapy } "Referral for Anorectal Function: The Dutch Experience"

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## OT29 0577 Validation of a Questionnaire for Functional Dyspepsia (FD) in a Multicenter Setting

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1st Medical Clinic, S. Orsola Hospital via Massarenti 9, 40138 Bologna, Italy *Purpose:* Whether symptom questionnaires can be applied in multicenter studies on FD has not been validated. We tested intra- and inter-centers reproducibility, responsiveness to changes (i.e. to treatment), and validity (i.e. capability of distinguishing FD from health) of a symptom questionnaire, in 7 gastroenterological Italian centers. *Methods:* Based on the clinical judgment of experienced gastroenterologists and the negative findings at upper GI endoscopy (and of other appropriate tests when deemed), 43 pts (M/F: 19/24; age 34.6 – 9.8 yrs, m – SD) were diagnosed as having FD. Each patient was administered a visual analogue scale of general well being (VAS: 0–100) and a symptom questionnaire, both being relative to the 2 wks preceding the interview, on different occasions: 0L) at entry (by a local interviewer: L); 1L) 1 wk later (by L); 1R) immediately after 1a (by a reference interviewer: R, VAS was not administered in this occasion), 6) at the end of a 5 wk treatment period (by L): lansoprazole 30 mg bid + clarithromycin 250 mg bid + amoxicillin 1 g bid for 1 wk, followed by cisapride 10 mg tid for 4 wks, in HP+ve pts; cisapride 10 mg tid for 5 wks, in HP{ -}ve pts. Multiple point adjectival scales were used to grade 0–4 severity (S) and frequency (F) of 9 symptoms (epigastric pain/burning/bloating, cardiac pain/burning, postprandial fullness, early satiety, nausea, vomiting). VAS and questionnaire were also administered to 50 healthy controls (HC, M/F: 21/29), 36.4 – 12.4 yrs), at time 0 (by L). 0L-HC 0L-FD 1L-FD 1R-FD 6L-FD VAS 83.7 – 11.1 41.7 – 17.0<sup>{a}</sup> 52.3 – 22.8<sup>{?}</sup> – 67.4 – 23.7<sup>{d}</sup> S 0.06 – 0.30 0.77 – 1.15<sup>{a}</sup> 0.62 – 1.06<sup>{b}</sup> 0.67 – 1.15 0.18 – 0.57<sup>{e}</sup> F 0.04 – 0.20 0.85 – 1.32<sup>{a}</sup> 0.71 – 1.23<sup>{g}</sup> 0.76 – 1.36 0.24 – 0.74<sup>{e}</sup> m – SD; <sup>{a}</sup>p < 0.001 vs 0-HC (Mann-Whitney U-test); <sup>{b}</sup>p < 0.01 vs 0-FD; <sup>{g}</sup>p < 0.05 vs 0-FD; <sup>{d}</sup>p < 0.01 vs 1a-FD; <sup>{e}</sup>p < 0.001 vs 1a-FD (Wilcoxon matched pairs test); <sup>{?}</sup>p = 0.086 vs 0-FD. A good agreement was found as to symptom S and F between 1L-FD and 1R-FD (S: K = 0.70; F: K = 0.62), while a fair agreement was found between 0L-FD and 1L-FD (S: K = 0.48; F: K = 0.43). *Conclusion:* The questionnaire we tested presents high responsiveness and validity and is reproducible in a multicenter setting. The weaker intra-center reproducibility is likely due to the design of this protocol which did not correct for the spontaneous -fluctuations of the syndrome. *Clinical practice:* Management strategy Motility, specific: Stomach Oesophageal gastric duodenal disorders: Helicobacter Pylori } " Validation of a Questionnaire for Functional Dyspepsia (FD) in a Multicenter Setting"

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## OT29 0578 Academic Gastroenterology in Western Europe in the Past 5 Years: Publications in Specialty Journals

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GI Unit, Department of Internal Medicine, University of Udine, Udine, Italy *Aims:* To evaluate publications in gastroenterology, hepatology and digestive endoscopy in Belgium (B), Denmark (DK), France (F), Germany (D), Great Britain (GB), Holland (NE), Italy (I), Spain (ES), Sweden (S), Switzerland (CH). *Methods:* The nine top-rated specialty journals i.e. Am. J. Gastroenterol, Dig. Dis. Sci, Endoscopy, Gastroenterology, Gastrointest. Endoscopy, Gut, Hepatology, J. Hepatology and Scand. J. Gastroenterol, years 1991–95, were screened by Silver Platter<sup>®</sup> for full articles and reviews/editorials bearing the name of the above countries as the site of the first institution. Papers were rated according to the the Impact Factor (IF) – Institute of Scientific Information<sup>®</sup> – 1994. Linear regression was used to analyze the past 5 years behaviour of each country IF. This survey does not take into account non-specialty journals and small changes in journals IF in the last few years. A more comprehensive search is under way. *Results:* As randomly tested, the computer search had an error of – 5%. Total number of papers, total IF and average IF per single paper (in parenthesis) were: GB: 1473–5020 (3.4), F: 668–2787 (4.2), D: 751–2726 (3.6), I: 770–2695 (3.5), ES: 418–1740 (4.2), NE: 409–1389 (3.4), B: 176–1072 (6.1), S: 386–1072 (2.8), DK: 253–679 (2.7), CH: 165–677 (4.1). Fifty-two percent of the IF for GB was from Gut, while thirty percent of IF for S came from the Scand. J. Gastroenterology. For comparison, equivalent figures for the United States (U.S.) were 3806–15072 (4.0) and for Japan (J) 1337–4689 (3.5). Sixty-one percent of total IF for the U.S. came from Gastroenterology and Hepatology. Total IF in the past five years (percent per year) increased substantially for ES (+17.9) and CH (+14.9) and less for I, D and F (+7.3, +4.1 and +6.9 respectively) with no change for the others and a small decrease for DK (–3.3). For the U.S., IF decreased by 4.4% while for J it increased by 17%. *Conclusions:* GB totalled the highest total IF and the highest number of papers published in gastroenterology specialty journals in the past five years. Without the publications in Gut and given the small error of this search, figures are virtually identical for F, D, GB and I. As defined in this study, scientific production in gastroenterology appears on the rise in western Europe and Japan and slightly declining in the U.S. Clinical practice: Epidemiology (non cancer) } "Academic Gastroenterology in Western Europe in the Past 5 Years: Publications in Specialty Journals"

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## OT31 0580 Stimulation of Antral Motility by the New Motilide ABT-229

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<sup>2</sup> U-Gen Research, Utrecht, The Netherlands ABT-229 is a recently developed erythromycin derivative with motilin agonist activity, but devoid of antibiotic activity. We studied the effects of ABT-229 on postprandial antroduodenal motility. The effects of an oral dose of 4 mg, 16 mg ABT-229 and placebo were studied in 9 healthy male volunteers, using a double-blind randomized 3-period cross-over design. A water-perfused catheter, with 4 antral sideholes (A1–A4; spaced 1 cm) and 4 duodenal sideholes (D1–D4; spaced 10 cm) was introduced transnasally. Transmucosal potential difference was measured between the distal antral (A4) and proximal duodenal (D1) sidehole (spaced 5 cm) to monitor the position of the catheter. The drug (Abbott Laboratories, IL, USA) was given in enteric coated granules during phase II. 45 min later a solid meal (bread and egg, 150 ml water; 250 kcal) was taken, after which postprandial activity was recorded for 4 h. Thereafter, a second, identical meal was consumed and recordings continued for another 4 h. The number of pressure waves (P) and their mean amplitude were calculated. During the first 2 postprandial hours after the first meal the propagation of PWs over antrum and duodenum was studied. After the 1st meal ABT-229 dose-dependently increased both the number of antral PWs (mean – SEM; placebo; 4 mg; 16 mg; 162 – 16; 212 – 20; 279 – 23;  $p < 0.01$ ) and their mean amplitude (7.3 – 0.7; 10.0 – 0.9; 13.3 – 0.7;  $p < 0.01$ ). ABT-229 selectively increased PWs propagated over the antrum (A1–A4; 5.4 – 1.8; 18.7 – 3.1; 34.5 – 4.6;  $p < 0.01$ ) and PWs propagated over the antrum onto the duodenum (A1–D1; 18.0 – 5.6; 32.3 – 3.7; 39.2 – 4.4;  $p < 0.01$ ). No effect was seen after the 2nd meal. No changes were found in the number and amplitude of duodenal PWs after both meals. Phase III-like activity increased after 16 mg ABT-229 (2.3 – 0.6; 2.6 – 0.4; 4.2 – 0.4;  $p < 0.01$ ) and originated more often in the antrum (43%; 70%; 92%;  $p < 0.01$ ). *Conclusion:* The new motilin agonist ABT-229 increases the strength and length of the antral pump by increasing the number, amplitude and the propagation of antral PWs and induces antral phase III-like activity. ABT-229 bears the potential of becoming a new prokinetic drug for gastric motility disorders. Motility, specific: Stomach Motility, general: Receptors and signals } "Stimulation of Antral Motility by the New Motilide ABT-229"

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**OT31 0581 Second Report of a Multicenter Study on Electrical Stimulation for the Treatment of Gastroparesis The GEMS Study Group**

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Bakken Research Center B.V., Maastricht, The Netherlands *Introduction:* Patients with severe gastroparesis (GP) are often refractory to medical therapy. Although gastric electrical stimulation (GES) has been advocated as therapy for GP, results of previous trials have been inconclusive. This is a preliminary report of a prospective multicenter study of GES for GP. *Methods:* 21 patients (16 M and 5 F) mean age 36 (18–49) with drug refractory GP (5 IDDM, 16 Idiopathic) were enrolled using entry criteria of delayed gastric emptying (GE), Vomiting (V) and Nausea (N). The study consisted of two phases – I percutaneous temporary stimulation (TS) and II permanent stimulation using an implantable pulse generator. Stimulation parameters were 12 bpm (0.2 Hz), 5 mA and pulse width 330 μs. GE, as well as frequency of N and V were measured at baseline, end of TS, and 3 months post permanent implantation. *Results:* Of the 21 pts 18 were selected for PS. The weekly frequency of V and N, median (range), after solid food were significantly reduced (\* p < 0.05 sign test) with pacing at end TS and 3 M post implant. Baseline # pts End TS # pts 3 months # pts Vomiting 21 (0–210) 19 0 (0–2)\* 17 0 (0–7) 9 Nausea 21 (7–168) 18 2 (0–21)\* 17 3 (0–14)\* 9 GE data were considered improved (↑) or deteriorated (↓) if changed ≥ 30% from baseline. Lower differences were considered as no change (=). End TS # pts 3 Months # pts GET T50 solid 2 ↑ 3 ↓ 13 18 0 ↓ 0 ↓ 6 = 6 GET T50 liquid 8 ↑ 0 ↓ 7 15 5 ↓ 0 ↓ 1 = 6 *Conclusions:* Gastric pacing with a fully implantable system is feasible and has an important antiemetic effect. GET T50 liquid improves in more than half of the patients while the result is inconclusive for GET T50 solid. Motility, specific: Stomach/Intestinal disorders: IBD, therapy } "Second Report of a Multicenter Study on Electrical Stimulation for the Treatment of Gastroparesis"

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## OT32 0582 Lack of Compensatory Hyperphagia in HIV-Infected Patients with Malabsorption

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Dept of Gastroenterology and Infectious Diseases, Hospital Rothschild, Paris, France Patients with malabsorption due to the short bowel syndrome (SBS) have adaptive hyperphagia that tends to compensate their absorptive handicap. Thus, many of them maintain a normal nutritional status in spite of marked malabsorption. Whether compensatory hyperphagia occurs in malabsorption due to other causes remains unknown. *Methods.* Daily food intake and simultaneous measurement of fecal weight, fat and nitrogen were performed in postsurgical patients (10 with ileal pouch anal anastomosis, IPA; 75 with SBS), patients with small bowel diseases (SBD; 26 celiac disease, 4 unexplained enteropathy, 12 others) and HIV-infected patients with chronic, intractable diarrhea [cryptosporidia (n = 22), microsporidia (n = 18), no detectable enteropathogen (n = 26)] or without diarrhea (n = 13). Patients were stratified according to the level of fat malabsorption (fecal fat/fat intake). *Results.* (mean) IPA (n = 10) SBD (n = 9) HIV (n = 13) P\*Fat malabsorption 0–5% Energy intake (kcal/IBW/d) 30.5 34.8 23.5 0.004 Fat malabsorption 18–31% SBS (n = 22) SBD (n = 16) HIV (n = 34) Energy intake (kcal/IBW/d) 29.2 30.9 23.7 0.0004 Fat malabsorption > 31% SBS (n = 53) SBD (n = 13) HIV (n = 32) Energy intake (kcal/IBW/d) 35.6 27.6 21.5 < 10<sup>-6</sup> } IBW: ideal body weight. \* differences between groups assessed using Kruskal-Wallis test. In postsurgical patients (but not in others), energy intake increased at the higher levels of malabsorption (p = 0.046). *Conclusion.* HIV-infected patients have a reduced energy intake at all levels of malabsorption comparatively with SBS and SBD patients. There is no compensatory hyperphagia such as in SBS patients. These results suggest that reduced energy intake has a prominent role in body weight loss of HIV-infected patients with malabsorption. Nutrition: Nutrients and gut function Immunology and microbiology: GI infections in adults Intestinal disorders, absorption: Malabsorption syndromes } "Lack of Compensatory Hyperphagia in HIV-Infected Patients with Malabsorption"

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**OT32 0583 Plasma Amino Acid Metabolism in Asymptomatic HIV Infected Patients J. Ockenga, U.J.F. Tiedge, U. Sittmann, M.J. Bahr, A. Metzger, K.H.W. Bloker, M.P. Manns**

Gastroenterology and Hepatology and Clinical Immunology, Medical School Hannover, FRG Malnutrition and wasting are known features of human immunodeficiency virus (HIV) infection and are associated with a predominant loss of body protein. Malnutrition can develop from undernutrition or from disease-induced alteration in metabolism. We could show, that a positive protein balance is possible in symptomatic, malnourished HIV infected patients by a protein intake > 1.2 g/kg/day using parenteral nutrition [Metabolism 44; 9: 1159–65]. But there is only limited information about nutritional status, protein intake and amino acid (AA) metabolism in asymptomatic HIV infected patients. Therefore we studied in 15 asymptomatic HIV infected patients (CDC < III, temperature < 38°C, C-reactive protein < 6 mg/l) and in 30 age and sex matched patients AA concentrations by liquid chromatography. In 10 of these HIV patients we investigated body composition (bioelectric impedance analysis, anthropometry), albumin, malabsorption (D-xylose test and serum vitamin B12 serum concentration), resting energy expenditure (indirect calorimeter), food intake (7-day record), soluble TNF receptor p55 + 75, and CD4 count. 8/21 AA levels are significantly decreased to the control group: LEU (108.3 vs. 145.6,  $p < 0.001$ ), ILE (58.3 vs. 73.3,  $p < 0.01$ ); VAL (202.2 vs. 241.3,  $p < 0.01$ ); PHE (54.5 vs. 70.3,  $p = 0.01$ ); LYS (182.3 vs. 214.8,  $p < 0.05$ ); MET (19.8 vs. 27.5,  $p = 0.001$ ), CYS (21.7 vs 50.7,  $p < 0.001$ ) and TAU (62.8 vs 78.5,  $p < 0.05$ ). REE is 1775 – 174 and the mean difference to predicted REE (Harris Benedict) is 9.24 – 5.9%. Energy intake is 2670 – 381 kcal/d [= 1.52 (range 1.15–1.90)  $\times$  REE]. Protein intake is 91.46 – 13.4 g/d (= 1.35 – 0.31 g/kg/d). REE/kg body cell mass is 57.24 – 3.38 kcal/kg/d and is negatively associated with Plasma concentrations of PHE ( $R = -0.91$ ,  $p < 0.01$ ), VAL ( $R = -0.87$ ,  $p < 0.01$ ), LEU ( $R = -0.82$ ,  $p < 0.01$ ), and GLU ( $R = -0.82$ ,  $p < 0.05$ ). Changes in AA concentrations are independent from total calorie intake, protein intake, body composition, CD4 count, and soluble TNF receptors. The significant decrease of the essential amino acids LEU, ILE, VAL, PHE, LYS, and MET are not related to a lower protein intake. Our data suggest that these changes reflect the altered metabolism with a probably higher protein turnover in asymptomatic HIV infected patients. In addition the decrease of natural antioxidants like CYS and TAU may be due to chronic oxidative stress in these patients. Nutrition: Metabolism Immunology and microbiology: GI infections in adults } "Plasma Amino Acid Metabolism in Asymptomatic HIV Infected Patients"

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## OT32 0584 Does Anal Mucosal Immunity Prevents Anal Dysplasia? Results of a Prospective Study

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*Introduction:* The incidence of anal dysplasia is increased in patients suffering from AIDS. The aim was to investigate prospectively the incidence of anal dysplasia and cancer and to assess immunologic characterization of anal mucosa in patients examined in coloproctology department in 1995. *Patients and methods:* All consecutive AIDS patients suffering from anal ulcerations and/or condyloma (n = 79; 70 men; mean age 36 yrs), 45 HIV negative patients (32 men; mean age 45 yrs with hemorrhoids (n = 30) or fissuration (n = 15)) and 25 HIV negative homosexual men (mean age 31 yrs, with intra anal condyloma) were included. Anal biopsies were obtained for immunohistochemistry using CD1a, CD3 and CD4 antibodies, and HPV, EBV and HSV detection by in situ hybridization. Blinded histology examination was performed to detect dysplasia and/or cancer. When HPV failed to be detected by ISH, PCR was performed on stains. Percentage of Langerhans' cells and lymphocytes was calculated for each patient (45 controls, 25 VIH negative patients with condyloma and 27 patients with AIDS). The t test and correlation tests were used for statistical analysis. *Results:* 65% of patients with AIDS had CD4 lymphocytes < 50/ml in serum. Two moderate dysplasia and two anal carcinomas were observed in this subgroup of AIDS patients vs no dysplasia nor carcinoma in all other groups. Percentage of Langerhans' cells and mucosal lymphocytes (5 – 1 and 27 – 7, respectively) were significantly inferior in anal mucosa of AIDS patients compared to controls (17 – 2 and 64 – 27) or negative HIV patients with condyloma (20 – 8 and 53 – 10 respectively). HPV typing and PCR to detect oncogenic HPV in anal mucosa are in progress. *Conclusion:* Incidence of anal dysplasia or carcinoma is higher in AIDS patients compared to negative VIH patients. This may be related to the alteration of anal mucosal immunity. Intestinal disorders: Anorectal disorders  
Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum }  
"Does Anal Mucosal Immunity Prevents Anal Dysplasia? Results of a Prospective Study"

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**OT36 0585 Regulation of Mucin Secretion in Human Gallbladder Epithelial Cells: Predominant Role of Calcium and Protein Kinase C. Dray-Charier, A. Paul, M. Bouin, M. Mergey, D. Veissière, P. Ballardur, J. Capeau,**

\*C. Housset

INSERM U. 402, Facult\ 'e9 de. M\ 'e9decine St Antoine, Paris, France *Background/Aims:* Mucins are major compounds of bile. They are secreted in the biliary tract, predominantly although not exclusively in the gallbladder. Their main attributed function is to ensure the cytoprotection of the biliary epithelial cells which are exposed to highly concentrated bile acids. Under pathological circumstances, biliary mucins contribute to the formation of gallstones and supposedly to that of bile plugs in diseases such as cystic fibrosis. Despite the important biological role of biliary mucins, the mechanisms regulating their secretion in humans are unknown. To address this question, we used human gallbladder epithelial cells in primary culture. *Methods:* [ $^{14}\text{C}$ ]-glucosamine-labeled glycoproteins secreted *in vitro* were analysed, and quantified after exposing cells to activators and inhibitors of the main transduction pathways, and to potential biologically active secretagogues. *Results:* Secreted glycoproteins exhibited the characteristics of biliary mucins. Activators of cyclic AMP-dependent pathway as well as secretin and VIP did not significantly modify mucin secretion. By contrast, ionomycin and PMA increased mucin secretion by 292 – 48% and 134 – 19% over basal level, respectively. The effects of these two agents were additive and were respectively mediated, by a calcium-dependent pathway implicating  $\text{Ca}^{2+}$ /calmodulin-dependent protein kinase II ( $\text{Ca}^{2+}$ /CaM-kinase II), and by the action of protein kinase C (PKC), as ascertained by the use of inhibitors. In addition, mucin secretion was stimulated by extracellular ATP via  $\text{P}_{2\text{U}}$  receptors and PKC, and by taurochenodeoxycholic acid via intracellular calcium increase and  $\text{Ca}^{2+}$ /CaM-kinase II. *Conclusions:* Mucin secretion in human gallbladder is regulated predominantly by calcium-dependent pathways implicating  $\text{Ca}^{2+}$ /CaM-kinase II and PKC. Constituents of bile such as extracellular ATP and bile acids may play a major role in the regulation of biliary mucin secretion, by activating these different signalling pathways. Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Regulation of Mucin Secretion in Human Gallbladder Epithelial Cells: Predominant Role of Calcium and Protein Kinase C"

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## OT36 0586 Cisapride Reverses the Effects of Octreotide (OT) on Intestinal Transit and the Proportion of Deoxycholic Acid (% DCA) in Bile and Serum

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<sup>3</sup> Dept of Endocrinology, The Radcliffe Infirmary, Oxford, UK *Background:* We showed recently that, in addition to its effect on gallbladder (GB) emptying, OT prolongs intestinal transit and increases the % DCA and the cholesterol saturation of GB bile — factors important in the pathogenesis of OT-induced GB stones (GBS). It seemed important, therefore, to see whether the prokinetic drug, cisapride, might overcome these effects. *Methods:* Therefore, in 8 acromegalic patients (age range 22–69; 4 women) receiving long-term OT (LTOT; 100–200 µg tds), we used a randomised, double-blind, placebo-controlled, cross-over design to study the effect of cisapride (10 mg qds for 2 weeks) on; (i) mouth-to-caecum transit time (MCTT), measured by the breath hydrogen technique, (ii) large bowel transit time (LBTT), measured using marker shapes, and (iii) the % DCA in fasting serum (since there is an exchange, and ultimately an equilibrium, between bile acids in serum and bile). We then compared these results with those obtained in 8 acromegalics (age range 30–69; 3 women) untreated with OT. *Results:* Mean values – SEM Acromegalic patients no OT LTOT + placebo LTOT + cisapride MCTT (min) 171 – 14.7\*\* 268 – 18.3 183 – 17.1\*\* LBTT (h) 39 – 4.9\* 54 – 4.3 30 – 4.4\*\* %DCA 15 – 1.8\* 24 – 2.9 13 – 4.5\*\* p < 0.05, \*\* p < 0.005 compared to LTOT + placebo. There was a linear relationship between LBTT and % DCA for all 3 groups (n = 24, r = 0.76, p < 0.005). *Summary/Interpretation:* These results clearly show that cisapride reverses the effects of OT on both small and large bowel transit and prevents the rise in the % DCA in serum, and by implication, in bile. If changes in intestinal transit are rate-limiting in the pathogenesis of OT-induced GBS, cisapride should prevent their formation. Liver and bile ducts, 2: Gallstones, formation, treatment Liver and bile ducts, 2: Bile acids synthesis Motility, specific: Colon, anorectum } "Cisapride Reverses the Effects of Octreotide (OT) on Intestinal Transit and the Proportion of Deoxycholic Acid (% DCA) in Bile and Serum"

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## OT36 0587 **Biliary Lipid Determinants of Bile Lithogenicity and Cholesterol Gallstone Formation**

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Increased cholesterol saturation index (CSI) of gallbladder bile is a prerequisite for cholesterol gallstone (CGS) formation. It is calculated from the relative molar concentrations of cholesterol (C), phospholipid (P) and bile acid (BA), thus it does not give information on the absolute modification of biliary lipids in gallbladder bile. It is still debated whether enrichment of bile with deoxycholic acid (DCA) is associated with CGS formation. Our aim was to assess the independent biliary lipid determinants of lithogenic bile and CGS formation in a consecutive series of 79 subjects, 22 of whom had CGS. We used an already validated method of nasoduodenal bile sampling and cholescintigraphy in order to measure biliary lipid masses within the gallbladder. Bile acid composition was measured by high performance liquid chromatography. Subjects were initially stratified according to CSI  $\leq 1$  (N = 35; 21 M) and CSI > 1 (N = 44; 22 M). Between the two groups respectively, there was no difference in age, mass of P and BA, whereas C mass was 169 – 32 vs 397 – 49  $\mu\text{mol}$  ( $p < 0.001$ ) and % DCA was 13 – 2 vs. 22 – 2 ( $p < 0.001$ ). CSI was significantly associated with C mass. % DCA was significantly associated with CSI, age, C mass and P mass. By fitting a multiple linear regression model, % DCA ( $p < 0.01$ ) and P mass ( $p < 0.001$ ), but not age, gender and BA mass, were independent determinants of an increased C mass in gallbladder bile. In order to assess the determinants of CGS formation, we then stratified the 44 subjects with CSI > 1 according to the absence (GS<sup>-</sup>; N = 22; 11 M) or presence (GS<sup>+</sup>; N = 22; 11 M) of gallstone disease. CSI was similar in the two groups. The GS<sup>+</sup> group was older (54 vs 39 years,  $p < 0.001$ ) and had increased % DCA in bile (26 – 2 vs. 18 – 3;  $p < 0.05$ ). No significant difference was observed for the biliary lipid masses between the two groups, although GS<sup>+</sup> had a trend towards lower BA mass (2.4 – 0.3 vs. 3.2 – 0.4 mmol) and increased P mass (1.1 – 0.2 vs. 0.7 – 0.1 mmol). To test the hypothesis that CGS formation occurs in supersaturated bile with time and is favoured by a reduction in biliary BA, we fitted a logistic regression model using the absence or presence of CGS as dependent variable and age, mass of biliary lipids and % DCA as independent variables. Decreased BA mass was the only significantly independent determinant of CGS ( $p < 0.05$ ). We conclude that lithogenic bile is due to an increased mass of C in gallbladder bile, which in turn is associated with biliary enrichment with DCA. Formation of CGS seems to depend on a superimposed reduction of BA mass occurring with time in patients with bile supersaturated with cholesterol. An increase in percent biliary DCA seems to occur with time, and in subjects with supersaturated bile a further increase in % DCA may play a role in the process of CGS formation.

Liver and bile ducts, 2: Gallstones, formation, treatment } "Biliary Lipid Determinants of Bile Lithogenicity and Cholesterol Gallstone Formation"

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## OT38 0588 Effect of Insulin on Pancreatico-Biliary Secretion During Hyper- and Normoglycemia

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Acute hyperglycemia (HG) is known to inhibit gastrointestinal motility and secretion. In non-diabetic subjects acute HG stimulates endogenous insulin release. It is not known, however, whether hyperinsulinemia contributes to the inhibitory effect of HG on gastrointestinal function. Therefore we have investigated the effect of hyperinsulinemia (aimed at 200 mU/l) both during normoglycemic clamping (blood glucose 5 mmol/l, plasma insulin 200 mU/l; hyperinsulinemic normoglycemic clamp; HI) and during hyperglycemic clamping (blood glucose 15 mmol/l, plasma insulin 200 mU/l; hyperglycemic hyperinsulinemic clamp; HG) on pancreatico-biliary secretion in healthy subjects and compared with the results obtained during normoglycemia (NG). Nine healthy subjects (age 22–52 yr) were studied on 3 separate occasions during HI, HG and NG. Pancreatico-biliary secretion was measured under basal conditions (60 min) and during cholecystokinin infusion (CCK 0.25 IDU.kg<sup>-1</sup>.h<sup>-1</sup>) for 60 min. Plasma CCK and pancreatic polypeptide (PP) levels were determined.

**Results:** (p \* < 0.05) NG HG HI Basal trypsin (U/h) 24 – 5 7 – 2\* 8 – 3\* bilirubin (µmol/h) 13 – 4 5 – 2\* 3 – 1\* CCK trypsin (U/h) 39 – 10 20 – 7\* 55 – 14 bilirubin (µmol/h) 64 – 22 29 – 14\* 40 – 7 Plasma CCK levels was not sign. different between the 3 experiments. Plasma PP secretion during HG (0.2 – 0.06 nM.120 min) and HI (0.8 – 0.2 nM.120 min) were sign. (p < 0.05) reduced compared to NG (1.5 – 0.2 nM.120 min).

**Conclusions:** HG inhibits basal and CCK stimulated pancreatico-biliary secretion. HI inhibits basal but does not affect CCK stimulated pancreatico-biliary secretion. Hyperinsulinemia contributes to the inhibitory effect of hyperglycemia on basal pancreatico-biliary secretion. The impaired PP secretion points to vagal cholinergic inhibition both during HG and HI. Pancreas: Secretion, regulation Nutrition: Metabolism Nutrition: Nutrients and gut function } "Effect of Insulin on Pancreatico-Biliary Secretion During Hyper- and Normoglycemia"

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## OT38 0589 **In vivo and in vitro Antagonist Properties of a New Peptide Bombesin Derivative**

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<sup>1</sup> LAPP, ESA CNRS 5075, 34060 Montpellier Cedex, France Bombesin (BN) elicit a broad spectrum of biological activities including stimulation of exocrine pancreatic secretion and mitogenic effect on human small cell lung carcinoma. These results increased the interest for obtention of potent and specific BN receptor antagonists. Various BN related peptides with C-terminal modifications display antagonist properties on rat pancreatic acini in vitro. Among these, JMV 736 (D-Phe-Gln-Trp-Ala-Val-Gly-His-NH-CH[CH<sub>2</sub>-CH(CH<sub>3</sub>)<sub>2</sub>]-\*CHOH-CH<sub>2</sub>-CH-(CH<sub>3</sub>)<sub>2</sub>; \* 50% S, 50% R) has been used. Its agonist and antagonist properties were studied in vitro on amylase secretion by isolated rat pancreatic acini and in vivo on external pancreatic secretion in anaesthetized rats. Its ability to inhibit BN-induced proliferation was also measured on Swiss 3T3 cells in vitro. BN (pGlu-Gln-Arg-Leu-Gly-Asn-Gln-Trp-Ala-Val-Gly-His-Leu-Met-NH<sub>2</sub>) stimulated amylase secretion in vitro with an EC 50 of 0.07 – 0.03 nM and total protein output in vivo with an ED 50 of 0.36 – 0.07 nmol/kg.h. JMV 736 had a high affinity for BN acinar receptors with a K<sub>i</sub> of 0.67 – 0.08 nM. JMV 736 did not stimulate amylase secretion from isolated acini but inhibited stimulation induced by 1 nM BN with an IC 50 of 1.6 – 0.3 nM. In vivo, JMV 736 did not stimulate pancreatic secretion but inhibited the stimulation induced by 10 nmol/kg.h BN with an ID 50 of 10.5 – 2.15 nmol/kg.h on total protein output. BN dose dependently stimulated Swiss 3T3 cell proliferation. JMV 736 had a high affinity for BN Swiss 3T3 cell receptors with a K<sub>i</sub> of 0.56 – 0.11 nM. JMV 736 did not stimulate 3T3 cell proliferation even at high doses (up to 10 <sup>5</sup>M) but inhibited proliferation induced by 100 nM BN with an IC 50 of 88 – 11 nM. These results indicate that the reported modification of the C-terminal end of the BN molecule produced a potent antagonist which displayed ID 50 in vivo and IC 50 in vitro in the same dose range as the maximally effective dose of BN on pancreatic secretion. This antagonist was also very effective to inhibit Swiss 3T3 cell proliferation induced by BN. The high potency of this antagonist associated with its good in vivo tolerance suggest that it may become an useful tool to analyze the role of BN in physiological and pathological processes. Pancreas: Secretion, regulation Hormones and receptors: Receptor characterization Hormones and receptors: Growth factors } "In vivo and in vitro Antagonist Properties of a New Peptide Bombesin Derivative"

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## OT38 0590 Comparative Clinical Evaluation of <sup>13</sup>C-Starch Breath Test as a Novel Indirect Pancreatic Function Test

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The clinical relevance of the <sup>13</sup>C-starch breath test was evaluated in comparison to the secretin-caerulein test (SCT), fecal elastase and fecal chymotrypsin in 30 patients with mild (n = 15) or severe (n = 15) exocrine pancreatic insufficiency, 23 patients with gastrointestinal diseases of non-pancreatic origin and 31 healthy controls. As "gold standard" the SCT was performed in all patients to define or exclude exocrine pancreatic insufficiency. 50 g of normal starch of maize were orally administered and breath samples were taken before and in 30 min intervals for 6 hours after oral ingestion and the increase of the relation of <sup>13</sup>C/<sup>12</sup>C-isotopes was analysed by mass spectrometry. Furthermore, various correlation studies were performed with the different parameters of the SCT. <sup>13</sup>C-starch breath test Fecal elastase Fecal chymotrypsin Max. value AUC 180 min 240 min. (< 200 U/g) (< 3 U/g) Sensitivity Mild 53% 53% 60% 47% 87% 47% Severe 87% 87% 87% 87% 100% 73% Total 73% 73% 77% 70% 93% 60% Specificity 74% 72% 74% 69% 93% 93% Significant correlations (p < 0.001) were found between duodenal lipase activity (SCT) and the maximal value (r = 0.626) as well as AUC (r = 0.668) of the <sup>13</sup>C-starch breath test. Conclusions: Using naturally occurring starch of maize, the <sup>13</sup>C-starch breath test reveals in comparison to chymotrypsin higher and to fecal elastase lower sensitivity. As known from the other indirect pancreatic function tests (exception: fecal elastase 87%), insufficient low sensitivity was found for patients with mild exocrine pancreatic insufficiency during the <sup>13</sup>C-starch breath test. With regard to the evaluation in comparison to the SCT as "gold standard" fecal elastase determination is superior compared to <sup>13</sup>C-starch breath test and fecal chymotrypsin and remains to be the most reliable and practical indirect pancreatic function test available today. Pancreas: Pancreatitis, chronic Pancreas: Pancreas, cystic fibrosis Clinical practice: Management strategy } "Comparative Clinical Evaluation of <sup>13</sup>C-Starch Breath Test as a Novel Indirect Pancreatic Function Test"

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## OT38 0591 RNA Expression of Immunoregulatory Cytokines and Polymeric Immunoglobulin Receptor in Pancreatic Duct Cell Lines

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<sup>1</sup> Dept. of Microbiology, Univ. of Alabama, Birmingham, AL, USA *Introduction:* Chronic pancreatitis is histologically characterized by infiltration with inflammatory cells as well as an extended fibrosis. It was suggested that cytokines are involved in this inflammatory process, Therefore, we investigated the cytokine RNA expression by pancreatic duct cell lines. In addition, we monitored the RNA expression of polymeric immunoglobulin receptor (pIgR) indicating epithelial cell activation. *Methods:* RNA expression of cytokines and pIgR were demonstrated in 6 pancreatic epithelial duct cell lines (AsPC-1, BxPC-3, Capan 1, Capan 2, PANC-1, and PaCa 44) and SV 40 immortalized human pancreatic duct cells. RNA was extracted from cultured cells and RNA expression was analyzed using RT-PCR with specific primers for pIgR, IL-1, IL-2, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, TGF{ b }1, TNF{ a }, IFN{ g }, and GM-CSF. *Results:* All cell lines and immortalized pancreatic duct cells expressed message for TGF{ b }1, IL-7, and IL-8. pIgR expression was found in all cell lines except PANC-1. In PANC-1 and AsPC-1, the IL-6 and the GM-CSF RNA could not be detected.. Capan 2 cells were negative for IL-1 and IL-6 RNA. All other cell lines and immortalized cells expressed in addition to TGF{ b }1, IL-7, and IL-8 also GM-CSF, IL-1, and IL-6. No RNA expression was found for IL-2, IL-4, IL-10, IL-12, IL-13, IFN{ g }, and TNF{ a }. *Conclusion:* Pancreatic duct epithelial cells are able to produce TGF{ b }1, IL-1, IL-6, IL-7, IL-8, and GM-CSF which can affect lymphocytes and macrophages as well as fibroblasts in pancreatic tissue. Based upon this ability, epithelial cells could play an important role influencing the cytokine network in inflamed pancreatic tissue. pIgR is also expressed to allow transport of polymeric IgA and IgM across the epithelial cell layer. Supported by BMBF, FKZ 01/ZZ/9102 and NIH, DK 28537. Pancreas: Acinar, duct cell function Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation } "RNA Expression of Immunoregulatory Cytokines and Polymeric Immunoglobulin Receptor in Pancreatic Duct Cell Lines"

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"P P 21 0592" P 21 0592 **Apoptosis in Barrett's Oesophagus**

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<sup>2</sup> Department of Internal Medicine III, University of Leipzig, Germany

<sup>3</sup> Institute of Pathology, University of Leipzig, Germany *Background:* Barrett's epithelium is known as the most important risk factor for adenocarcinoma of the oesophagus. In the metaplasia, dysplasia, adenocarcinoma sequence of Barrett's oesophagus the expression of mutated p53 protein or proliferations indices as proliferating cell nuclear antigen is well-known, whereas the role of apoptotic cell death in this sequence is uncertain. Therefore, we determined the frequency of apoptosis in different stages of Barrett's oesophagus. *Methods:* We investigated paraffin embedded tissue sections from patients with Barrett's oesophagus (gastric metaplasia n = 8, intestinal metaplasia n = 4, dysplasia n = 3, adenocarcinoma n = 3, and controls with normal fundic epithelium n = 3) by in situ DNA-labelling technique (Apoptag, Oncor, USA). The apoptotic labelling index (LI) was calculated after counting 2000 nuclei. *Results:* The LI was 1.6% (range: 0.8–2.8%) for gastric metaplasia, 1.6% (0.7–2.8%) for intestinal metaplasia, 0.9% (0.5–1.4%) for dysplasia, 0.8% (0.6–1.0%) for adenocarcinoma and 6.8% (2.8–13.1%) for normal fundic epithelium, respectively. *Conclusions:* Our results suggest that the rate of apoptosis in Barrett's oesophagus with gastric and intestinal metaplasia may be different from epithelium with dysplasias and adenocarcinoma. Our preliminary data have to be confirmed by larger series of patients. Thus, studies on apoptosis may improve our understanding of the metaplasia, dysplasia, adenocarcinoma sequence in Barrett's oesophagus. Oncology, specific: Oesophagus Oncology, general: Proliferation, carcinogenesis }" "Apoptosis in Barrett's Oesophagus"

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"P P 21 0593" P 21 0593 **Evaluation of CD44 Protein Expression in the Progression of Barrett's Mucosa to Invasive Cancer** C. Lagorce, S. Dubois, C. Degott, D. H<sup>9</sup>nin,

\*J.F. Fl<sup>e</sup>9jou

Service d'Anatomie et de Cytologie Pathologiques, Hospital Beaujon, Clichy,

France *Background, aims and methods:* Barrett's adenocarcinoma develops by a multistep process in which the specialized metaplastic columnar epithelium progresses to dysplasia and eventually to adenocarcinoma. CD44 is a surface adhesion molecule that can be expressed in the form of various splice variants in human tumours, including colorectal carcinoma. It has been suggested that CD44 molecules have a role in tumor progression and metastasis. This study investigated the expression of CD44H (hematopoietic form), V4 and V6 by immunohistochemistry on tissue samples of Barrett's mucosa (34), and Barrett's adenocarcinoma (35) obtained from surgical resection specimens from 35 patients. *Results:* CD44H and V6 expression was found in 56% and 48% of Barrett's specialized mucosa negative for dysplasia. CD44H expression was found in 68% of low grade dysplasia, 80% of high grade dysplasia and 84% of Barrett's adenocarcinoma. CD44V6 expression was found in 57% of low grade dysplasia, 68% of high grade dysplasia and 78% of Barrett's adenocarcinoma. CD44H and V6 variant were expressed at the deeper part of the crypts in Barrett's metaplasia negative for dysplasia and at the upper part of the crypts in high grade dysplasia. CD44V4 was not expressed in Barrett's esophagus. *Conclusion:* These data indicate that both CD44H and CD44V6 protein are frequently expressed in Barrett's esophagus. The increasing rate of expression that we observed from mucosa negative for dysplasia to adenocarcinoma suggests that CD44H and V6 may be involved in the carcinogenesis of Barrett's esophagus. Whether or not patients with CD44 protein expression are at increased risk for progression to adenocarcinoma should be determined by prospective endoscopic biopsy analysis. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Oesophagus } "Evaluation of CD44 Protein Expression in the Progression of Barrett's Mucosa to Invasive Cancer"

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"P P 21 0594" P 21 0594 **Spatiotemporal Reflux Characteristics in Gastro-Oesophageal Reflux Disease (GORD), with and without Barrett's Metaplasia**

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<sup>1</sup> St. Antonius Hospital, Nieuwegein, The Netherlands

<sup>2</sup> University Hospital, Utrecht, The Netherlands Previous studies have shown that in GORD distal oesophageal acid exposure increases with increasing mucosal injury. To investigate the characteristics of reflux at more proximal oesophageal levels in GORD patients with various stages of the disease, we studied 16 patients (age: 53.1 – 12.2 yr; mean – SD) with endoscopy-negative GORD, 14 patients (46.8 – 16 yr) with oesophagitis grade I and II and 15 patients (64.4 – 10.4 yr) with Barrett's oesophagus (> 3 cm). Multichannel ambulatory 24-hr pH measurements were performed using a pH-catheter (Sentron) with 5 ISFET sensors at intervals of 3 cm, (distal sensor at 3 cm above the LOS) and a portable data logger (MMS). Acid inhibiting agents were discontinued at least 5 days before measurements. At 3 cm above the LOS 24-hr acid exposure was significantly higher ( $p < 0.01$ ) in patients with oesophagitis (pH < 4: 8.6 – 5.9%; mean – SD) than in endoscopy-negative reflux patients (5.4 – 6.9%). In patients with Barrett's oesophagus distal oesophageal acid exposure was much higher (36.0 – 19.0%;  $p < 0.001$ ). These differences were largely determined by differences in nocturnal reflux. Significant differences in oesophageal acid exposure were also found at 6 and 9 cm above the LOS. However, at the more proximal levels the differences between patient groups faded out; at 15 cm above the LOS 24-hr acid exposure was similar in the 3 patient groups (resp. 2.9 – 9.8%, 4.2 – 4.0% and 3.2 – 2.1%). Other reflux variables (number of reflux periods, episodes > 5 min and duration of the longest episode) showed similar differences in spatiotemporal characteristics between the groups. *Conclusions:* In GORD increasing mucosal damage is associated with increasing acid exposure at distal oesophageal levels, however at more proximal levels acid exposures are similar in all grades of the disease. Oesophageal gastric duodenal disorders: EG Reflux }" "Spatiotemporal Reflux Characteristics in Gastro-Oesophageal Reflux Disease (GORD), with and without Barrett's Metaplasia"

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"P P 21 0596" P 21 0596 **Intestinal Metaplasia of the Cardia Epithelium in Light Esophagitis: Histochemical and Ultra Structural Study**

\*M.M. Tolentino, J.G. Faifer, E.A. Trentini, A.C.M. Stipp

Unigastro Rua Antonio Garcia N<sup>o</sup> 2–21, Bauru, Brasil Thirty consecutive subjects with gastro-oesophageal reflux disease (GORD) were studied without hiatus hernia or classical Barrett esophagus, who had showed light esophagitis at endoscopic examination (Savary-Miller grade 1). The presence of one or two digitiform prolongations of the columnar epithelium above the Z line was not an exclusion criterium. A group of 9 asymptomatic volunteers was used as control group. Four Z line biopsies were taken (level 1), followed by other four biopsies 5 mm below Z line (level 2 – cardia). The biopsies were dyed with hematoxylin-eosin, PAS + Alcien-Blue and Alcien-Blue pH 2.5. Extra fragments at level 2 were taken from the 12 first cases for transmission electron microscopic study. The findings were analysed as a group and individually taking into consideration: the biopsy level and the type of epithelium in which changes were detected (lining or glandular). In 22 cases (73.3%) at least 1 of the fragments showed any metaplastic changes cells such as globets cells or lining cells with thin acid mucins deposits. Dyeing with PAS- Alcien-Blue improved much the viewing of light metaplasia foci ( $p < 0.01$ ). Among 10 out of 22 positives (45.5%) changes appeared in only 1 of the fragments. Metaplastic changes at level 1 were found in 17 subjects (56.6%) and level 2 in 14 subjects (46.6%) without statistical difference. In 5 cases (16.7%) the changes occurred only at level 2. The comparison of positivity between the two levels demonstrated some statistical difference ( $p < 0.05$ ) when the exclusive changes of the glandular epithelium were considered (mainly level 1) and the lining epithelium (mainly at level 2). The remaining comparisons were not significant. The electron microscopy showed the presence of epithelium cells with suggestive ultrastructural changes of metaplastic transformation in 7 out of 12 subjects (58.3%). Such a finding is a meaningful coincidence with a positivity to PAS + Alcien-Blue ( $p < 0.05$ ). It has been concluded that the cardia epithelium (lining as well as glandular) demonstrate meaningful changes at GORD. Multiple biopsies conducted at different levels of Z line and the analysis of the biopsies through PAS + Alcien-Blue coloring are fundamental for the diagnosis of early metaplasia. The incidence of metaplastic changes is high (histochemical and ultrastructural) in the cases of light esophagitis. Oesophageal gastric duodenal disorders: EG Reflux Endoscopy, specific: Oesophagus } "Intestinal Metaplasia of the Cardia Epithelium in Light Esophagitis: Histochemical and Ultra Structural Study"

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## "P P 21 0598" P 21 0598 DNA Ploidy and p53 Overexpression as Markers of Malignant Potential in Barrett's Oesophagus

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Abnormal nuclear DNA-content and TP53 gene mutations are early events during neoplastic progression of Barrett's oesophagus. The aim of this study was to investigate the value of DNA-ploidy and p53 immunostaining in an endoscopic surveillance protocol of patients with Barrett's oesophagus. *Patients – Methods:* 45 patients with Barrett's oesophagus participated in the study. Endoscopic follow-up was obtained for all patients. Multiple biopsy samples were taken using a rigorous protocol. Dysplasia was graded according to Riddell criteria. Flow cytometric DNA content analysis was performed according to the method described by Vindelov. Immunohistochemistry was performed with DO7 monoclonal antibody. *Results:* The mean follow-up was 27 months. Initial diagnosis n p53 (+) DNA-aneuploidy No dysplasia or indefinite for 38 1 3 dysplasia (ND/I) Low grade dysplasia (LGD) 6 3 2 High grade dysplasia (HGD) 1 1 1 Total 45 5\* 6\*\*4 patients had simultaneously p53 overexpression and aneuploidy. Of the 38 patients who were graded initially ND/I, 1 patient progressed to LGD; he had p53 overexpression and increased G2M fraction. A cancer developed in 1 of the 6 patients with LGD: the patient had p53 overexpression and DNA-aneuploidy; among the 5 other patients, LGD was not confirmed during subsequent follow-up. The patient with HGD progressed to a carcinoma. Among the patients who were p53 ( - ) and had a normal DNA content, no progression was noted. Both adenocarcinomas were diagnosed at an early stage. *Conclusion:* These results confirm the difficulty of histologic assessment of dysplasia in Barrett's oesophagus. Although the follow-up is still too short, they suggest that combination of p53 immunostaining and flow cytometric evaluation might be useful in managing the cancer risk in patients with Barrett's oesophagus. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux } "DNA Ploidy and p53 Overexpression as Markers of Malignant Potential in Barrett's Oesophagus"

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"P P 22 0599" P 22 0599 **Outcome Research in GORD: Retrospective Analysis of Prescription Data (Mediplus' UK) on Cisapride (CIS), Ranitidine (RAN) and Omeprazole (OME)** A. Eggleston<sup>1</sup>, A. Wigerinck<sup>1</sup>, A. Haycox<sup>2</sup>

<sup>1</sup> Janssen Research Foundation, B-2340 Beerse, UK

<sup>2</sup> Dpt Pharmacol Ther, University of Liverpool, UK Clinical trials often represent a highly selective patient sample. Little is known about the use of and response to antireflux agents in a real life situation. The database MediPlus was used to collect information on drug use in patients (pts) with a first diagnosis of GORD treated with CIS, RAN or OME, as an hypothesis generating exercise, addressing initial success and relapse rates in pts. *Methods.* Pts with a first diagnosis of GORD occurring after 1.1.1993 and treated initially (antacids excluded) with either CIS, RAN or OME were identified. A random sample from each treatment group was selected for screening. "Success" was arbitrarily defined as reflux medication prescribed for a period of {^3} 3 months (mo). Treatment was considered a "failure" in case of switch of prescriptions to another antireflux agent in the first 3 mo or if subsequent reflux prescriptions were given for > 3 mo. Among successfully treated pts, the relapse rates in the subsequent 6 mo period were evaluated. Pts with a recurrent diagnosis of GORD, H<sub>2</sub>-refractory GORD, or an index indicative of referral prior to the first Rx were excluded. *Results.* 279 of 790 pts were eligible. "Success" rates for the different drugs tested were 70% in the CIS group, 79% in the RAN group, 75% in the OME group. In each group, – half of the pts received medication for {^3} 1 mo. Among the failures, switch of medication occurred after the first prescription in almost all pts of the CIS group, but was temporally dispersed in the other groups. The failures continuing the initial medication > 3 mo accounted for 12% of the CIS and RAN pts vs 21% in the OME group. Relapse rates at 6 months were 23% for CIS, 52% for RAN, 37% for OME. At the end of the observation period, 21% of the CIS group, 31% of the RAN group and 39% of OME group took regular or continued medication (respectively 7%, 5% and 34% took OME). *Conclusion.* There is little evidence to support a hypothesis of differences in response rates in pts presenting with a first episode of GORD in primary care. However, a hypothesis of lower relapse rates with CIS is supportable, to be confirmed in a randomised study. Treatment and outcomes in primary care, therefore, appear to differ from that previously generated in clinical trials from specialist centres. Oesophageal gastric duodenal disorders: EG Reflux Motility, general: Functional GI disorders Clinical practice: Management strategy }"  
"Outcome Research in GORD: Retrospective Analysis of Prescription Data (Mediplus® UK) on Cisapride (CIS), Ranitidine (RAN) and Omeprazole (OME)"

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"P P 22 0600" P 22 0600 **Cost of Gord-Medication in Clinical Practice in Patients with a First Diagnosis of Gord Based on Prescription-Data Analysis (Mediplus UK) A. Eggleston<sup>1</sup>, A. Wigerinck<sup>1</sup>, A. Haycox<sup>2</sup>**

<sup>1</sup> Janssen Research Foundation, B-2340 Beerse, Belgium

<sup>2</sup> Dpt Pharmacol Ther, University of Liverpool, UK Cost calculations of anti-reflux medication so far have been based on outcome measures obtained in controlled clinical trials. Such calculations do not take into account real drug use and interventions in real life, nor may they apply to primary care. *Objective:* To describe from a primary care perspective, based on a retrospective prescription database analysis, the cost of outpatient treatment associated with GORD during the first 6 treatment months, in patients, initiated on treatment with either cisapride (CIS), ranitidine (RAN) and omeprazole (OM) for their first diagnosis of uncomplicated GORD. *Method:* Calculation of all anti-reflux medication (antacids inclusive) and interventions linked to the index diagnosis of GORD among patients (pts) with a first episode of GORD. Pts with initial referral (< 13%) were excluded. *Results:* The costs over 6 months per CIS, RAN and OME patient were respectively £137, £178 and £189. The number of one-month-equivalent treatments of the comparator drugs were respectively 1.85, 2.56 and 2.96, leading to costs of £349, £367 and £3105 per patient respectively. Antacid and alginate/antacid use was higher in CIS and RAN group (1 Rx of 500 ml or 56–60 tabs per patient versus 0.4 for OME), but their contribution to the total cost per patient was low (< 2%). The number of consultations varied between 2.4 and 2.9 per patient (CIS: 2.4 (£360.3), OME: 2.6 (£365.5) and RAN: 2.9 (£373.0)). The total number of referrals, endoscopies, Barium or X-rays, outpatient visits were the highest in the RAN group (0.034 versus < 0.02 in the CIS and OME group), their cost being respectively £323.8, £39.6 and £311.1 per patient. Their contribution to costs in the RAN group was offset by the lower cost of medication, when compared to the OME group. *Conclusion:* The data from this retrospective analysis indicate that the "step up" approach starting with CIS, combined with antacid/alginate use, is the least costly approach of the 3 comparators in primary care patients with uncomplicated GORD. The calculations do not support a lower cost of the "step-down" approach using OME initially in these patients. Oesophageal gastric duodenal disorders: EG Reflux Motility, general: Functional GI disorders Clinical practice: Management strategy } "Cost of Gord-Medication in Clinical Practice in Patients with a First Diagnosis of Gord Based on Prescription-Data Analysis (Mediplus UK)"

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"P P 22 0601" P 22 0601 **Gastroesophageal Reflux Disease in Children. Usefulness of Scintigraphic Studies** A.I. Santos,

\*A.I. Lopes, T. Martins, C. Rodrigues, P. Magalhães Ramalho, F. Godinho

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Unidade de Gastrenterologia do Serviço de Pediatria, HSM, Lisboa, Portugal Nowadays, it is known that gastroesophageal reflux (GER) may be part of a complex disease, where other disturbances of the digestive tube may exist. Our purpose was not only to compare pHmetry with the scintigraphic detection of RGE, but also to study if there was any gastric emptying abnormality that correlated with the presence of gastroesophageal reflux. We have performed 21 studies in 18 children, all of them with symptoms that required pHmetry. Four of these children had negative pHmetry and no other known disease, 2 had only gastroesophageal reflux and 12 were neurologically impaired children. The pHmetry was performed with a DIGITRAPPER MKIII and, for purposes of comparison with the scintigraphic studies the following parameters were considered: Reflux Index (refl/hour) and Esophageal Clearance (min/refl). The scintigraphic study was performed with a milky meal, adapted to the age and habits of the child, with a lipid content > 20% and labelled with Tc-99m-stannous colloid. Immediately after the ingestion, a dynamic study was started with 180 frames of 20 seg each, in a 64 {\'b4} 64 matrix. Planar images of 60 seg each were also acquired at 90 min, 2, 3 and 4 hours. The following parameters were calculated: Gastroesophageal Reflux Index (%) and Gastric Retentions of the meal at 15, 30, 45, 60 and 90 min and 2, 3 and 4 hours (%). To statistically compare the values obtained we used linear regression. We found a positive strong correlation between scintigraphic gastroesophageal reflux index and esophageal clearance ( $r = 0.91$ ;  $p < 0.001$ ). This same scintigraphic parameter and gastric retention at 4 hours also correlated ( $r = 0.64$ ;  $p < 0.05$ ), as well as the latter and esophageal clearance ( $r = 0.61$ ;  $p < 0.05$ ). Although the true pathological meaning of these correlations is still to be elucidated, it does seem that the gammagraphic detection of GER is associated with esophageal disturbances and eventually with slow gastric emptying. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus }" "Gastroesophageal Reflux Disease in Children. Usefulness of Scintigraphic Studies"

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## "P P 22 0602" P 22 0602 One-Year Prophylactic Efficacy and Safety of Pantoprazole in Healed Reflux Oesophagitis

\*J. M\ 'f6ssner<sup>1</sup>, H. Koop<sup>2</sup>, H. Porst<sup>3</sup>, H. W\ 'fcbbolding<sup>4</sup>, A. Schneider<sup>5</sup>, C. Maier<sup>5</sup>

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<sup>2</sup> Krankenhaus Buch, Berlin, Germany

<sup>3</sup> Krankenhaus Friedrichstadt, Dresden, Germany

<sup>4</sup> Weizenkamp 1, Damme, Germany

<sup>5</sup> Byk Gulden, Konstanz, Germany *Aim:* The safety and prophylactic efficacy of pantoprazole (40 mg per day) was assessed in an open, 1-year, multicenter trial in Germany, in 222 patients whose Stage II or III reflux oesophagitis had been healed after 4 or 8 weeks of treatment with pantoprazole or omeprazole. *Methods:* Patients with symptoms of reflux oesophagitis for at least 3 consecutive days underwent endoscopy, and those with endoscopically confirmed disease were classified as having relapsed. Efficacy was assessed by Kaplan Meier survival analysis for all patients who provided data by returning to the first 3-months follow-up visit. *Results:* In the per-protocol group, including only endoscopically confirmed relapses as treatment failures (n = 10), estimated cumulative rates of confirmed relapse were 2% at 6 months and 6% at 12 months. Median serum gastrin levels rose from 52 ng.l<sup>-1</sup> } at the start of the acute trial to 108 ng.l<sup>-1</sup> } at 6 months, but showed no further increase in the next 6 months. There were no other changes in laboratory variables. Adverse events occurred in only 24% of patients, which is similar to the rate with placebo [1]. 15 patients withdrew with adverse events. Serious adverse events were reported for 12 patients, including 6 who withdrew (with lumbago, skin carcinoma, gastrointestinal carcinoma, brain tumour, pulmonary embolus, and an orthopaedic operation). These adverse events were not considered to be related to study treatment. *Conclusion:* Pantoprazole is highly effective with a good safety profile in the long-term prophylaxis of reflux oesophagitis.

Reference: Bate CM et al. Gut 1995; 36: 492–498 Oesophageal gastric duodenal disorders: EG RefluxEndoscopy, specific: Oesophagus } "One-Year Prophylactic Efficacy and Safety of Pantoprazole in Healed Reflux Oesophagitis"

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"P P 22 0603" P 22 0603 **Prophylactic Efficacy and Safety of 40 Mg Pantoprazole Against Relapse in Patients with Healed Reflux Oesophagitis — A One Year Study**

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Department of Medicine and Gastroenterology, University of Konstanz, Germany *Aim:* The prophylactic efficacy and safety of pantoprazole (PAN; 40 mg/day) was assessed in an open, 1-year, multicentre, follow-up trial in South Africa. *Methods:* 157 outpatients (pts), 64 female/93 male, median age: 46 years, with healed stage II or III reflux oesophagitis (Savary-Miller classification) were included in the study after an initial healing phase of 4 or 8 weeks with either 40 mg or 80 mg PAN in 8 study centres. Pts were seen after 3, 6, 9 and 12 months or whenever symptoms occurred on more than 3 consecutive days. An endoscopy was done in these cases and routinely at the beginning of the trial and after 12 months. Endoscopically confirmed relapses were evaluated as treatment failures. During the study period 30 pts were lost to follow-up due to e.g. protocol violation. *Results:* The 12-months' remission rate was 87.4% (111/127 pts; 95% confidence interval 80–93%). The pts experienced 11 possible drug related adverse events (AEs) as judged by the investigators. These AEs were: increase in liver enzymes (n = 2) or alkaline phosphatase (n = 2), diarrhoea, nausea, dry mouth, headache, weight gain, rash, eructation of air (n = 1 each). Four pts were withdrawn due to unrelated AEs. One pt who had increased his alcohol consumption concomitantly, was withdrawn due to possible drug related moderate increase in liver enzymes. *Conclusion:* This study proved that PAN is a safe and efficacious treatment for the long-term prophylaxis (one year) of reflux oesophagitis. Oesophageal gastric duodenal disorders: EG Reflux } "Prophylactic Efficacy and Safety of 40 Mg Pantoprazole Against Relapse in Patients with Healed Reflux Oesophagitis / A One Year Study"

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**"P P 22 0604" P 22 0604 Comparison of Cisapride Plus H-2 Antagonist Vs. H-2 Antagonist Monotherapy in the Prevention of Reflux Esophagitis Relapses S. Gullini, S. Anna, CIS-ITA-24 Study Group**

Gastroenterol. Div. Arcispedale, Ferrara, Italy This study (controlled, double-blind, randomised and in parallel groups) was carried out in 34 Italian centers in order to evaluate the efficacy and tolerability of the association cisapride 20 mg/die plus H-2 antagonist (cimetidine 400 mg/die; ranitidine 150 mg/die; famotidine 20 mg/die) vs. H-2 antagonist monotherapy (cimetidine 400 mg/die; ranitidine 150 mg/die; famotidine 20 mg/die) in the prevention of reflux esophagitis relapses. 198 patients previously suffering of esophagitis, after treatment with a drug therapy, were enrolled in the study (24-weeks long) and treated, by oral route, with the association cisapride/H-2 antagonist or H-2 antagonist in monotherapy for relapse prevention. All patients, at the enrolling visit, did not show any endoscopic sign of pathology. Severity of symptoms [reflux symptoms (frequency, time, intensity and duration) (reflux score) and associated symptoms (epigastric pain/burning, dysphagia, pain on swallowing, early satiety, bloating, epigastric distention, anorexia, nausea, vomiting, nocturnal coughing and shortness of breath)] were arbitrarily scored, on a 4-point scale, at each control examination. In addition, patients, at each visit completed two visual analogue scales related to general conditions and severity of the reflux occurred in the previous 7 days. Instrumental evaluation was performed through esophago-gastroduodenoscopy at baseline and at the end of the study (or before, in case of symptomatic relapses): results were expressed by a 5-point analogue severity scale. Finally 174 patients (87 treated with the association cisapride/H-2 antagonist and 87 with H-2 antagonist in monotherapy) were included in statistical analysis (both parametric and non-parametric). Results demonstrated the efficacy and tolerability of cisapride/H-2 antagonist combined treatment. All patients in this group reported a clear and progressive improvement ( $p < 0.001$  vs  $p < 0.05$  at week 24) in reflux score compared to the baseline score. On the contrary, the treatment with H-2 antagonist in monotherapy did not produce any significant improvement of reflux score. A significant and progressive reduction of associated symptoms and severity of reflux and improvement of general conditions compared to those at baseline was also observed in all patients treated with cisapride/H-2 antagonist and, only in a lesser extent, in patients treated with the monotherapy of H-2 antagonist. Even though no statistically differences between the two treatments were observed, the overall efficacy assessed by both physicians and patients ranged from excellent and good in 78.5% (association) and 66.6% (H-2 monotherapy) of the patients. Eight patients (8.7%) in the association group and 12 patients (12.8%) in the H-2 group showed endoscopic relapses. Five patients (3 in association group and 2 in H-2 group) reported adverse effects. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Comparison of Cisapride Plus H-2 Antagonist Vs. H-2 Antagonist Monotherapy in the Prevention of Reflux Esophagitis Relapses"

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**"P P 22 0605" P 22 0605 Comparison of Two-Dose-Regimens of Cisapride in the Prevention of Reflux Esophagitis Relapses A. Del Genio, CIS-ITA-20 Study Group**

<sup>1</sup> Gastroenterol. Surg., II Univ. of Naples, Naples, Italy This study (controlled, randomised and in parallel groups) was carried out in 36 Italian center in order to evaluate the efficacy and tolerability of two dosing regimens of cisapride (20 mg u.i.d. vs. 10 mg b.i.d.) in the prevention of reflux esophagitis relapses. 203 patients suffering of esophagitis, after treatment with a drug therapy, were enrolled in the study (24-weeks long) and treated, by oral route, with cisapride 10 mg b.i.d. (n = 96) or 20 mg u.i.d. (n = 107) for relapse prevention. All patients, at the enrolling visit, did not show any endoscopic sign of pathology. Severity of symptoms [reflux symptoms (frequency, time, intensity and duration) (reflux score) and associated symptoms (epigastric pain/burning, dysphagia, pain on swallowing, early satiety, bloating, epigastric distention, anorexia, nausea, vomiting, nocturnal coughing and shortness of breath)] were arbitrarily scored, on a 4-point scale, at each control examination. In addition, at each visit, patients completed two visual analogue scales related to general conditions and severity of the reflux occurred in the previous 7 days. Instrumental evaluation was performed through esophago-gastroduodenoscopy at baseline and at the end of the study (or before, in case of symptomatic relapses): results were expressed by a 5-point analogue severity scale. Finally 177 patients (85 treated with 10 mg b.i.d. cisapride and 92 with cisapride 20 mg u.i.d.) were included in statistical analysis (both parametric and non-parametric). Results demonstrated the efficacy and tolerability of both cisapride treatments. All patients reported a clear and progressive improvement ( $p < 0.001$  at week 24) in reflux score compared to the score reported at the enrolling examination. No significant differences were observed between cisapride 10 mg b.i.d. and 20 mg u.i.d. A significant and progressive reduction of associated symptoms and severity of reflux and improvement of general conditions compared to those reported in enrolling examinations were also observed in patients treated with both cisapride dosing regimens. The overall efficacy assessed by both physicians and patients was comparable and ranged from excellent and good in 91% (10 mg b.i.d.) and 80.5% (20 mg u.i.d.) of the patients. Furthermore, only 5 patients (5.2%) in the 10 mg b.i.d. group and 7 patients (6.5%) in the 20 mg u.i.d. group showed endoscopic relapse. Five patients (4 in the 20 mg u.i.d. group and 1 in the 10 mg b.i.d group) reported adverse effects. The endoscopic relapse percentages obtained with cisapride in our study seem to be lower than those usually reported after pharmacological treatments for reflux esophagitis relapse prevention. Further studies to confirm our results should be performed. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Comparison of Two-Dose-Regimens of Cisapride in the Prevention of Reflux Esophagitis Relapses"

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"P P 22 0606" P 22 0606 **Efficacy of Omeprazole 20 mg or 10 mg in the Long-Term Management of Symptomatic Reflux Complicated by Confluent or Circumferential Erosive Esophagitis**

\*J. Laurent, P. Cassan, J.F. Rey, T. Helbert, A. Caekaert, P. Barth

Cregg, Angh. Essey les Nancy, Vichy, Saint Laurent du Var, Marseille, Astra France This study aimed to evaluate a treatment regimen using several doses of omeprazole in the management of symptomatic reflux complicated or not by esophagitis. The results observed in patients with simple reflux or low grade esophagitis have already been presented (Laurent, Gastroenterology 1995, A145). We report here the symptomatic and endoscopic results observed in patients with esophagitis grade 2 followed for 1 year. *Methods:* Patients with confluent erosive esophagitis (Savary-Miller grade 2–3) were treated by omeprazole 20 mg (O20) or 40 mg (O40) (in case of a severe concomitant disease) for 4 months (period 1, P1). At the end of this period, patients healed (absence of erosion) and relieved were treated for 8 months (period 2, P2) by omeprazole 10 mg (O10) or 20 mg, depending on the dose administered during the fourth month (M4). Endoscopy was repeated after 12 months (M12). Symptoms of reflux were assessed by the heartburn severity score (HSS) on a scale of 1 to 4 (1 = absent, 4 = severe) and the Spechler activity index (Spechler, N Engl J Med 1992). At M4 and M12, success was defined as the absence of erosion at endoscopy and a HSS  $\leq 2$ . Early study withdrawals other than lost to follow-up (P1: n = 10; P2: n = 12) were considered as failures. *Results:* 196 patients (58 – 14 years; M/F 143/53; grade 2/3: 125/71) were included in the study. 160 patients took part in P2. P1 (n: 196, O40: 21%, O20: 79%) P2 (n: 160, O20: 12%, O10: 88%) M0 M4 M4 M12 Endo success – 83% – 71% Sympt. success – 94% – 87% Complete success – 82% – 70% Spechler 112 – 20 78 + 8 78 – 7 79 – 9 Complete success was identical for grades 2 and 3. *Conclusion:* After healing of severe esophagitis by omeprazole, reduction of the dose after 4 months of induction treatment maintained endoscopic and symptomatic remission in 2/3 of patients. Oesophageal gastric duodenal disorders: EG Reflux } "Efficacy of Omeprazole 20 mg or 10 mg in the Long-Term Management of Symptomatic Reflux Complicated by Confluent or Circumferential Erosive Esophagitis"

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## "P P 22 0607" P 22 0607 Treatment of Patients with Esophagitis and Laryngitis

\*M. Tuncer, A. Dobrucali, I. Yurdakul, S. Tuncer, F. Hamsioglu, A. \c7elik, K. Bal, H. Uzunismail, E. Oktay

Gastroenterology Department of Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey *Aim:* Despite the varied classic symptomatic presentation of gastroesophageal reflux disease (GERD), some patients have atypical presentation. Sometimes, chronic persisting cough or hoarseness may be caused by GERD. Esophagitis is increasingly suggested as a cause of chronic laryngitis and there is some evidence that GERD is more common in patients with laryngitis. The purpose of the study was to evaluate if patients with esophagitis and laryngitis benefit from ranitidine medication. *Patients and Methods:* 68 patients with endoscopically proven GERD were asked for laryngeal symptoms (sore throat, cough, hoarseness) and underwent laryngoscopy. In case of association between reflux esophagitis and laryngitis, patients received 4 weeks of ranitidin 600 mg per day. The questionnaire and endoscopy were repeated at 2 and 4 week. *Results:* Eighteen patients (26%) had both esophagitis (grade II and III. Savary-Miller classification) and symptomatic laryngitis. After ten days administration of ranitidine, esophageal and laryngeal symptoms had improved in all patients. No patient suffered from drug induced side effects. Endoscopically, the healing rate of esophagitis and laryngitis was 72% resp. 33%. At four weeks control, all patients were free of complaints and no sign of esophageal and laryngeal inflammation could be found. *In Conclusion;* Patients who have esophageal and laryngeal symptoms should have adequate anti-reflux therapy. The findings and symptoms of associated esophagitis and laryngitis improve with the treatment of ranitidine suggesting that esophageal reflux is the underlying etiology. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } " "Treatment of Patients with Esophagitis and Laryngitis"

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## "P P 22 0608" P 22 0608 Cisaprid and its Effect at Severe Forms of Reflux Esophagitis

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I. Clinic of Internal Medicine, Faculty Hospital Kosice, Slovakia

Cisaprid as an effective prokinetic agent is a drug of choice in the treatment of moderate and medium severe forms of reflux esophagitis (r.e.). It increases the resting pressure of the lower esophageal sphincter (LES), reduces the frequency and duration of its transitory relaxations and increases the amplitude of peristaltic contractions. The aim of our study was to find out whether this effect is also similar in severe forms of r.e. (stage III by the Savary-Miller classification) accompanied by severe lower sphincter incompetence. 74 patients with the endoscopy findings of r.e. were examined. On the basis of the achieved values of LES the patients were divided into three groups: *Group A*: 22 patients, LES < 5 mm Hg; *Group B*: 24 patients, LES 5–12 mm Hg; *Group C*: 28 patients, LES > 12 mm Hg. Ambulatory manometry was performed under basal conditions and 1 hour after the administration of 10 mg of cisaprid orally. After the triple registration of LES values (rapid pull through method), the amplitude of three peristaltic contractions before and after the drug administration was measured. A significant increase of LES after the administration of cisaprid was found only in the patients of Group B and C ( $p < 0.02$ ). In Group A with a predominantly severe degree of esophagitis there was an insignificant increase in the LES (3.9 – 0.8 mm Hg to 7.1 – 2.9 mm Hg,  $p < 0.05$ ). There was a significant increase in the amplitudes of peristaltic contractions also in this group (72.5 – 14 mm Hg to 91.3 – 12 mm Hg,  $p < 0.02$ ).

**Conclusions:** 1) In r.e. with a severe incompetence of the lower sphincter with LES < 5 mm Hg the basal pressure is not affected more significantly by cisaprid. However, in some patients (15% from our sample) there was a significant increase. 2) In severe forms of r.e. the effect of cisaprid on the amplitudes of peristaltic contractions is retained. 3) Cisaprid can be used as a pharmacological test of severe sphincter incompetency. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus }

"Cisaprid and its Effect at Severe Forms of Reflux Esophagitis"

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"P P 22 0609" P 22 0609 **A Multicenter Randomized Clinical Trial of Sodium Alginate Versus Cisapride in Patients with Non-Severe Oesophagitis** T. Poynard, C. Richard-Berthe<sup>2</sup>, A.L. Knellwolf<sup>2</sup>, H. Agostini<sup>3</sup>, Multicenter Group

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<sup>3</sup> Quanta-Médical, Rueil Malmaison, France *The aim* of this trial was to compare the efficacy of a non-expensive treatment, sodium alginate (GAV), to cisapride (CIS) in the treatment of reflux symptoms in patients with non-severe oesophagitis. *Patients and methods:* Patients with severe oesophagitis or with motor-like dyspepsia were not included. 353 patients, mean age 40 years, 51% males, 33% smokers, 43% drinkers were randomized, 180 treated by GAV (4 sachets/day) and 173 by CIS (5 mg q.i.d) for 1 month. They were followed every 2 weeks. The main end point was the intensity of reflux estimated by an analogic visual scale (AVS) at 4 weeks (range 0–100). Secondary endpoints were the score at 2 weeks, the number of patients considered as failure, the impact of reflux on activity and sleep, the number of pain episodes, the adverse events, and the direct costs. Univariate and multivariate analyses have been performed without knowledge of treatments received according to the intention to treat method. *Results:* At randomization there was no difference between groups according to epidemiological factors or symptoms (AVS: 74 – 18, m – sem, in GAV vs 73 – 20 in CIS). There was a difference in favor of GAV vs CIS, for AVS at 2 weeks (29 – 35 vs 35 – 25,  $p = 0.01$ ) and at 4 weeks (12 – 17 vs 20 – 23,  $p = 0.001$ ), for the number of episodes at 4 weeks (2 – 2 vs 3 – 4,  $p = 0.001$ ), the pain associated to activity impairment (3% vs 10%,  $p = 0.009$ ), pain associated to sleep impairment (3% vs 14%,  $p = 0.004$ ) and patients considered as failure (11% vs 24%,  $p < 0.001$ ). Adverse events occurred in 13 patients treated by GAV vs 23 treated by CIS ( $p = 0.06$ ). Compliance was similar in both groups (97% vs 96%). Mean cost was lower for GAV (130 FF) than for CIS (175 FF,  $p < 0.001$ ). Sensitivity analyses conducted according to per-protocole gave same results. *Conclusion:* Sodium alginate has a greater efficacy and a lower cost than cisapride for the treatment of symptoms in patients suffering from non-severe oesophagitis. } "A Multicenter Randomized Clinical Trial of Sodium Alginate Versus Cisapride in Patients with Non-Severe Oesophagitis"

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"P P 22 0610" P 22 0610 **Omeprazole Is More Effective than Cimetidine in the Prevention of Recurrence of GORD-Associated Heartburn and the Occurrence of Underlying Oesophagitis**

\*C.M. Bate, J.R.B. Green, A.T.R. Axon, G. Tildesley, F.E. Murray, S.M. Owen, C.E. Emmas, M.D. Taylor

Gastroenterology units in Wigan, Stoke-on-Trent, Leeds, Hartlepool, Dundee and Astra Pharmaceuticals Ltd., Kings Langley, U.K. There is a paucity of data on the use of omeprazole 10 mg o.d. and cimetidine in the prevention of recurrence of symptoms in GORD patients, a group which includes the large number of patients with symptoms but no oesophagitis. This study compared omeprazole 10 mg o.d. with cimetidine 800 mg nocte in the prevention of recurrence of GORD-associated heartburn. Patients who had symptomatic non-ulcerative oesophagitis (81%) or symptoms without oesophagitis (19%), achieved symptomatic remission (no more than mild heartburn on 1 out of 7 days) following 4 weeks of omeprazole 20 mg o.d. (66%; 74/112) or cimetidine 400 mg q.d.s. (31%; 34/109) ( $p < 0.0001$ ) and, if required, a further 4 weeks of omeprazole 20 mg o.d. (67%; 54/81). Patients in symptomatic remission (100 male, 56 female) aged 48 – 14 years (mean – SD) were then randomised to receive, double-blind, either omeprazole 10 mg o.d. ( $n = 77$ ) or cimetidine 800 mg nocte ( $n = 79$ ) for 24 weeks. A greater proportion of patients receiving omeprazole, compared with those receiving cimetidine, were in symptomatic remission after 12 (69% vs 27%) and 24 weeks (60% vs 24%) (each  $p < 0.0001$ ). The median time to symptomatic relapse was longer for patients receiving omeprazole (169 vs 15 days) ( $p = 0.0001$ ). Analysis of prognostic factors identified treatment with omeprazole ( $p = 0.0001$ ), increased age ( $p = 0.001$ ) and shorter duration of the patient's most recent episode of heartburn prior to entry ( $p < 0.01$ ) as increasing the probability of maintaining symptomatic remission. Of patients leaving the study in symptomatic remission, a greater proportion receiving omeprazole, compared with cimetidine, were free of oesophagitis at endoscopy (84% vs 53%;  $p < 0.05$ ). A greater proportion of patients receiving omeprazole were satisfied with their medication after 12 (69% vs 45%) and 24 weeks (68% vs 45%) (each  $p = 0.005$ ). Doctor satisfaction with the treatment was also greater for omeprazole after 12 (74% vs 55%;  $p < 0.05$ ) and 24 weeks (76% vs 58%) (each  $p < 0.05$ ). In conclusion, omeprazole 10 mg o.d. is more effective than cimetidine 800 mg nocte in the prevention of recurrence of GORD-associated heartburn. Patients in symptomatic remission are more likely to be free of oesophagitis following treatment with omeprazole 10 mg o.d. than cimetidine 800 mg nocte. Oesophageal gastric duodenal disorders: EG Reflux } "Omeprazole Is More Effective than Cimetidine in the Prevention of Recurrence of GORD-Associated Heartburn and the Occurrence of Underlying Oesophagitis"

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"P P 22 0611" P 22 0611 **Comparison of Two Dosing Regimens of Cisapride (CIS) in the Treatment of Reflux Oesophagitis**

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Hospital de Brabois, Vandoeuvre les Nancy, France

Aalsters Sted. Ziekenhuis, Aalst, Belgium

Hospital de la Seguridad Social, Valencia, Spain

Arciospedale S. Maria Nuova, Reggio Emilia, Italy *Objective:* The aim of this international multicentre, double-blind trial was to document the therapeutic equivalence of two dosing regimens of CIS on endoscopic healing and symptom improvement in patients with proven reflux oesophagitis grade I or II (Savary-Miller). *Methods:* 407 patients (256 M/151 F) between 18 and 75 years of age were randomly allocated to treatment with either CIS 10 mg qid or CIS 20 mg bid for 8 to 12 weeks depending on whether complete healing was found at endoscopy. The primary parameters of efficacy were cure of oesophagitis and improvement of the reflux symptom score (frequency, time, intensity, duration of heartburn and regurgitation). Secondary efficacy parameters included Visual Analogue Scales for reflux symptoms, general well-being and severity of oesophagitis as well as global evaluation by the investigator and severity of associated symptoms. *Results:* 326 patients were included in an on-protocol analysis. The healing rates at endpoint were 85% and 87% in the CIS 10 mg qid and 20 mg bid group respectively. The mean total reflux symptom score decreased from baseline to endpoint from 8.0 to 1.2 (CIS 10 mg qid) and 7.9 to 1.5 (CIS 20 mg bid). Both treatment groups showed also a reduction of associated symptoms and an improvement in the patient's feeling of general well-being. Both treatment regimens were well tolerated. The most frequently reported adverse event (diarrhoea) can be explained by the pharmacological action of CIS. *Conclusions:* The results of the study demonstrated that CIS 10 mg qid and 20 mg bid were highly statistically equivalent in efficacy and safety in the treatment of reflux oesophagitis. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus }  
"Comparison of Two Dosing Regimens of Cisapride (CIS) in the Treatment of Reflux Oesophagitis"

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"P P 22 0612" P 22 0612 **Pantoprazole is Superior to Famotidine in the Treatment of Reflux Esophagitis — A Multicenter Study**

\*H.G. Dammann, E.G. Hahn, G. Adler, M. Schlander

Hamburg, Erlangen, Ulm and Konstanz, Germany *Objective:* Pantoprazole is a new, precise proton pump inhibitor. It was the aim of the present study to compare the efficacy and tolerability of pantoprazole and famotidine in outpatients with acute gastro-esophageal reflux disease (grade II and III according to Savary/Miller). *Methods and patients:* Open, 2:1 randomized, controlled, multicenter trial. 129 Investigators enrolled 734 outpatients to receive pantoprazole (P; n = 495) 40 mg o.a.d. (morning) or famotidine (F; n = 239) 40 mg o.a.d. (evening) for 4 weeks, or 8 weeks if healing was incomplete by 4 weeks. Demographic data and severity of disease at baseline were comparable in both study groups. *Results:* Endoscopically proven healing rates (primary study endpoint, *intent-to-treat* analysis [per protocol]): 4 weeks 8 weeks Pantoprazole 69% [80%] 83% [93%] Famotidine 48% [57%] 62% 72%] p < 0.001 [p < 0.001] p < 0.001 [p < 0.001] Patients with pain prior to treatment achieved complete relief of principal symptoms (i.e. heartburn, acid regurgitation, pain on swallowing) after 4 weeks in 78% with P compared to 53% with F (p < 0.001). Pantoprazole and famotidine were equally well tolerated. *Conclusions:* Pantoprazole (40 mg o.a.d.) was significantly superior to famotidine (40 mg o.a.d.) in terms of healing rates and symptom relief in patients with reflux esophagitis, grade II and III. Both treatments were well tolerated. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation }"  
"Pantoprazole is Superior to Famotidine in the Treatment of Reflux Esophagitis / A Multicenter Study"

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"P P 22 0613" P 22 0613 **Pantoprazole Once Daily Versus Twice Daily: A PH-Metry Study** H. Fuder<sup>1</sup>, A. Ehrlich<sup>1</sup>, G. Wieckhorst<sup>1</sup>, P.W. L'fcker<sup>1</sup>,

\*C.R. Cain<sup>2</sup>

<sup>1</sup> Institut f\for klinische Pharmakologie, Gr\fcnstadt, Germany

<sup>2</sup> Byk Gulden, Konstanz, Germany *Purpose:* to compare the acid suppressant effects of pantoprazole (P) 40 mg o.d. with P 40 mg b.d. in volunteer subjects who were *H. pylori* (Hp) positive. *Methods:* 12 males were recruited into the study, their Hp status was determined prior to study begin by serology (IgG). The study was monocentre, randomized, double-blind, cross-over in design. Gastric pH was measured 2 days prior to, and on days 1 and 7 of therapy. *Results:* the age-range of the volunteers was 21–43 years. The effects of the two doses of P were: 24-hour median gastric pH Baseline Day 1 Day 7 P 40 mg o.d. 1.6 2.1 5.0 P 40 mg b.d. 1.5 3.1<sup>\*\*</sup> 5.2<sup>\*\*</sup> Significance between treatments: <sup>\*\*</sup>  $p < 0.01$  [Koch] *Conclusions:* a) pantoprazole 40 mg b.d. raises the intragastric pH more quickly than pantoprazole 40 mg o.d., primarily due to an effect on night-time pH b) the twice daily dosage may be of advantage in the more rapid relief of symptoms when pantoprazole is used alone or in combination with antibiotics in Hp positive peptic ulcer patients c) at steady state pH differences between the two regimens are unlikely to be clinically relevant. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Pantoprazole Once Daily Versus Twice Daily: A PH-Metry Study"

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"P P 23 0614" P 23 0614 **Is Laparoscopic Floppy Nissen Fundoplication (Lap FNF) as Trouble Free as the Publications Would Suggest?** Thomas C.B. Dehn

Royal Berkshire Hospital, London Road, Reading, Berkshire UK *Aim* Assess post-op course and complications following lap FNF. *Method* Prospective, independent data collection. Patients assessed pre-operatively, 6 weeks, 6 months and 1 yr post-operatively. pH pre and 6 months post-op. *Patients* n = 70 (M:F 50:20) age 38 (10–70) yr. *Surgery* Short floppy wrap constructed over 56 Malonie bougie with division of short gastric vessels. *Results* 1/1/93–12/5/96: 8 (11.4%) conversions (lack access 3, port site bleeding 3, short gastric 1, liver 1). No conversions in last 30 cases. Post-op Visick grading: 6 weeks I = 28, II = 26, III = 7, IV = 1 (I + II = 85%), six months I = 22, II = 16, III = 5 (I + II 88%), 1 year I=23, II = 10, III = 3, IV = 2 (I + II = 86%). Of 8 initial Visick III/IV patients, 5 were for dysphagia, 2 for failure to control reflux: 3 persisted in III/IV scores for 1 year post-op. Dysphagia for solids > 2 weeks occurred in 11/62 (17.7%): 10 patients required between 1 and 3 dilatations post-operatively with relief of dysphagia in 8. Further surgery in 6: 2 for relief of dysphagia, 3 for later wrap herniation and 1 for adenocarcinoma in situ. Of 62 successful lap FNF 59 regard their operation as successful. Post-op + pH tests were recorded in 4 (2 asymptomatic). *Conclusion* Although successful in relieving GORD symptoms dysphagia may be underestimated following lap FNF. The procedure is not as trouble-free as some data might suggest. Laparoscopic surgery: Therapy Oesophageal gastric duodenal disorders: EG Reflux } "Is Laparoscopic Floppy Nissen Fundoplication (Lap FNF) as Trouble Free as the Publications Would Suggest?"

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"P P 23 0615" P 23 0615 **Does 5 Port Laparoscopy Aid the Pre-Resection Assessment of Patients with Oesophageal Cancer?** Thomas C.B. Dehn

Royal Berkshire Hospital, London Road, Reading, Berkshire, UK *Surgery* 5 ports: day case laparoscopy. Assessment of liver, peritoneum, omentum & nodes. Samples obtained where possible. *Patients* 40; M:F 35:5; age 63 (21–73). Sites: OGJ 12, lower third 21, middle third 7. Adenocarcinoma 37; Squamous carcinoma 3. *Results* Hepatic nodules 6, malignant histology 5; ascites 4, malignant cytology 3; peritoneal nodules 2, malignant 1. Nodes seen in 32 (3 unsuccessful, 5 hepatic metastases). Enlarged ? malignant 16; biopsied 7, malignant 5. Of the 7 biopsied, 5 underwent resection, 4 dead within 12/12 of metastatic disease. Enlarged ? malignant, not biopsied: 7 resected, 5 had positive nodes on resection specimen. 16 with normal appearing nodes, not biopsied: 5 of the 15 resected had positive nodes on resection specimen. One died 18/12 post-operatively. *Conclusion* Prior laparoscopy prevented needless laparotomy in 6, facilitated laparotomy in 2 (benign ascites and peritoneal nodule). Nodal assessment and sample is difficult but those with laparoscopically malignant nodes have high mortality. Laparoscopy does aid assessment. Oncology, specific: Oesophagus Laparoscopic surgery: Diagnosis } "Does 5 Port Laparoscopy Aid the Pre-Resection Assessment of Patients with Oesophageal Cancer?"

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## "P P 23 0616" P 23 0616 **Selective Antireflux Surgery in the Repair of Paraesophageal Hiatus Hernia**

\*A. Francis, C. Duignan, J.G. Temple, M.T. Hallissey

Dept of Surgery, Queen Elizabeth Hospital, Birmingham, UK The management of paraesophageal, type II, hiatus hernia is surgical and has centred on the anatomical repair of the hernia and associated gastric volvulus. Review of the results of this procedure in 23 patients showed that 17% had significant gastro-oesophageal reflux post-operatively. All had experienced gastro-oesophageal reflux symptoms prior to surgery. A policy of the selective addition of an antireflux procedure was adopted and the impact of this approach on post operative symptoms has been assessed. All patients undergoing repair of a paraesophageal hiatus hernia under the care of 2 consultants at a single institution over a 15 year period have been studied. During the first 10 years, surgery consisted of an anatomical repair of the hiatal defect with a fundopexy. For the remaining 5 years of the study, in addition to the anatomical repair, a Nissen's fundoplication was performed in patients with pre-operative symptoms of gastro-oesophageal reflux. A total of 51 patients have undergone surgery. In three patients, the paraesophageal hiatus hernia developed following antireflux surgery and these patients will not be considered further. During the initial 10 years, twenty-three patients had an anatomical repair alone. Of the 25 patients operated on in the last 5 years, 15 underwent anatomical repair alone and in 10 anatomical repair was combined with a Nissen's fundoplication. In the initial period, 4 of the 23 patients had symptomatic gastro-oesophageal reflux requiring medical management. No patient in the second period has developed symptomatic reflux and there have been no symptoms attributable to the fundoplication. Gastro-oesophageal reflux symptoms following anatomic repair of paraesophageal hiatus hernia can be troublesome. The incidence can be reduced by the use of pre-operative symptoms to select a group for antireflux surgery. This approach is not associated with additional morbidity or post-operative symptoms. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux } "Selective Antireflux Surgery in the Repair of Paraesophageal Hiatus Hernia"

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"P P 23 0617" P 23 0617 **Laparoscopic Nissen Fundoplication (LAP FNF) for Patients with  
"Symptom-Index" Only (Sensitive, Irritable Oesophagus) Gord Thomas C.B. Dehn**

Royal Berkshire Hospital, London Road, Reading, Berkshire, UK A group of patients exists with GORD symptoms, unresponsive to medical therapy, without endoscopic oesophagitis and with normal acid exposure times (AET) on pH. The only abnormality is a positive symptom index (SI), sometimes called sensitive or irritable oesophagus. *Aim* Assess effectiveness of lap. FNF in this group. *Patients* n = 10 (M:F 4:6), aged 32 (14–53) yr. *Method* 24 hr pH test, medication and independent symptom score before and 6 months post lap FNF. *Results* No conversions. All failed medical therapy. AET pre-op was 2.1 (0.9–4.3)% and post-op 0.3 (0–1.7)% Reflux symptoms/24 hr pre-op were 20 (15–103) vs 0 (0–34) post-op. SI 74 (50–100)% pre-op VS 0 (0–50) post-op. Pre-op 8 were taking omeprazole 40 mg, 1 lansoprazole 30 mg and 1 ranitidine 600 mg/day without effective symptom relief. Post-op: no patient needed anti reflux medication. Of 9 patients assessable 1 yr post-op 4 are Visick I, 5 Visick II and 1 Visick IV (severe dysphagia – revisional surgery). *Conclusion* Lap FNF is an effective procedure in patients with "symptom index" only GORD. Laparoscopic surgery: Therapy Oesophageal gastric duodenal disorders: EG Reflux } "Laparoscopic Nissen Fundoplication (LAP FNF) for Patients with "Symptom-Index" Only (Sensitive, Irritable Oesophagus) Gord"

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"P P 23 0618" P 23 0618 **The Effect of Anti-Reflux Surgery on Esophageal Motility in Patients with Reduced Clearance**

\*H. Van der Walt, J.B. Van den Bogaerde

Department of Surgery, & Gastroenterology, University of Pretoria, South Africa *Purpose:* The purpose of this study was to determine whether anti-reflux surgery improved motility in patients with reduced pre operative clearance. *Methods:* A prospective study was undertaken in patients suffering from gastro-esophageal reflux disease, refractory to medical therapy, who received either a floppy Nissen fundoplication or a modified Toupet operation. Patients who consented to pre- and post-operative manometry were entered into the trial. Those with reduced esophageal clearance, defined as a distal pressure of less than 40 mm Hg. or propagation of less than 60%, were selected pre-operatively. Post-operative manometry was then performed. The results of the pre- and post-operative manometric studies were then compared. Statistical analysis was performed using Microsoft Excel'. Data were compared using the two tailed T test. Significance was defined as a p value of less than 0.01. The null hypothesis read as follows: ""Anti-reflux surgery does not improve esophageal motility in patients with reduced clearance."" *Summary of Results:* Fifty nine patients were assessed. All had reduced clearance pre-operatively. Post-operative clearance improved in 29 out of 59 patients. The mean distal pressure pre-operatively was 30.4 mm Hg. (Standard deviation 21.6) Post-operative manometry (performed on average 44 days after surgery) produced a mean value of 44 mm Hg. (Standard deviation 7.57). This represents a significant difference ( $p < 0.01$ ). On the basis of these data the authors reject the null hypothesis. *Conclusion:* These data suggest that anti-reflux surgery may improve clearance in a cohort of patients with reduced pre-operative clearance. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux Laparoscopic surgery: Therapy } "The Effect of Anti-Reflux Surgery on Esophageal Motility in Patients with Reduced Clearance"

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"P P 23 0619" P 23 0619 **Postoperative Dysphagia after Laparoscopic Nissen Repair: An Univariate and Multivariate Analysis in 198 Patients**

\*A. Fingerhut, E. Blezel, J.C. Etienne, B. Millat, B. Vinson-Bonnet, J.M. Hay, A.R.C.

8, Avenue des Peupliers, 92270, Bois Colombes, France *Purpose:* to determine which, if any, operative steps in laparoscopic Nissen repair could be held responsible for postoperative dysphagia. *Methods:* Between July 1994 and March 1996, 198 patients (115 males and 83 females) underwent a laparoscopic Nissen or Nissen-Rosetti repair for gastroesophageal reflux disease (GERD). *Results:* Mean age of patients was 44.8 years old (21–82), the mean duration of operation was 230 minutes (70–480). The mean duration of hospital stay was 4.8 (2–25) days. 60 patients (30%) had dysphagia during the first postoperative month. Only two lasted more than one month and underwent pneumatic dilatation. One was in fact associated with peptic ulcer disease. Through univariate and multivariate analysis we showed that neither calibration (40 French) before suture, ligation of the short vessels, nor closure of the crus (steps performed or not) were contributing factors to dysphagia. *Conclusion:* Laparoscopic Nissen repair associated with crura closure corrects GERD effectively without persistent dysphagia and should be proposed as a gold standard of treatment for this disease. Oesophageal gastric duodenal disorders: EG Reflux Laparoscopic surgery: Therapy } "Postoperative Dysphagia after Laparoscopic Nissen Repair: An Univariate and Multivariate Analysis in 198 Patients"

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"P P 23 0620" P 23 0620 **Laparoscopic Mesh Repair for Rolling Hiatus Hernia** Thomas C.B. Dehn

Royal Berkshire Hospital, London Road, Reading, Berkshire, UK Rolling hiatus hernia is a rare, but potentially dangerous condition affecting the elderly. *Aim* Assess feasibility of laparoscopic mesh repair. *Method* Prospective study. *Patients* 12 (M 2:F 10), age 68 (53–85) yr ASA grade I-2, II-8, III-2. Symptoms present for 27 (1–144) m and were obstructive in 9. Two patients had UGIH. *Repair* Laparoscopic stapled mesh crural repair in 12, with 180° anterior hemi fundoplication in 8 and epigastric port gastropexy 8. Conversion 1 due to adhesions. Post-op stay was 2 (1–7) nights. Major complications – 1 (cardiac arrhythmia). Follow-up 16 (1–34) m: no recurrences. Post-op Visick I-9, II-3. *Conclusion* Laparoscopic stapled mesh repair is feasible, safe and effective in elderly patients with rolling hiatus hernia. Laparoscopic surgery: Therapy }  
"Laparoscopic Mesh Repair for Rolling Hiatus Hernia"

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## "P P 23 0621" P 23 0621 Laparoscopic Modified Toupet Operation for the Treatment of Gastro Esophageal Reflux Disease

\*H. Van der Walt, J.B. Van den Bogaerde

Department of Surgery, & Gastroenterology, University of Pretoria, South Africa *Purpose:* The purpose of this study is to present the authors' experience with the laparoscopic Modified Toupet procedure. *Methods:* Patients presenting with gastro-esophageal reflux disease (GERD) refractory to medical therapy, underwent laparoscopic modified Toupet anti-reflux surgery. Pre-operative work up included: clinical examination, symptom scoring, endoscopy, esophageal manometry and 24 hour Ph study. Post-operative work up included: symptom scoring, endoscopy, and manometry where possible. A defective lower esophageal sphincter (LES) was defined as a mean pressure of less than 6 mm Hg., intra-abdominal length of less than 1 cm, or a total length of less than 2 cm. Reduced esophageal clearance was defined as a distal pressure of less than 40 mm Hg. or propagation of less than 60%. *Results:* The laparoscopic Modified Toupet procedure was performed on 343 patients. Mean age was 41 years (range 12 to 78). Mean hernia size was 3 cm. Pre-operative LES pressure was 4.29 mm Hg. Of the 343 patients, 296 had defective LES. Reduced clearance was found in 103 patients. Theater time was 52 minutes. There was minimal morbidity and no mortality. Symptom scoring improved post operatively in all patients. Post-operative manometry was performed on 215 patients. Mean post-operative LES pressure was 12.1 mm Hg. Mean abdominal LES length was 2.7 cm. Four patients had defective LES post-operatively. Gasbloat or dysphagia occurred in less than 5% and resolved in all but one patient. Non-fatal pulmonary embolism occurred in two patients in the immediate post operative period. *Conclusion:* The data presented here confirm that the laparoscopic Modified Toupet operation is both safe and effective in the treatment of refractory GERD. Post operative LES function normalised in virtually all patients who were evaluated. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux Laparoscopic surgery: Therapy } "Laparoscopic Modified Toupet Operation for the Treatment of Gastro Esophageal Reflux Disease"

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"P P 23 0622" P 23 0622 **The Results of Aggressive Surgery for Gastrooesophageal Leaks after Oesophagectomy**

\*M.T. Hallissey, J.G. Temple

Dept of Surgery, Queen Elizabeth Hospital, Birmingham UK The mortality following gastro-oesophageal leakage after oesophageal resection is recognised to be high with rates of over 50% being reported. From 1991, a policy of immediate surgical intervention has been adopted by our unit, the aim being to re-operate on all cases within 12 hours of evidence of leakage. This study assesses the results of this approach on mortality and the success rate for re-establishing gastrointestinal continuity. Between July 1991 and April 1996, 10 patients have developed clinical evidence of a GI tract leak in the chest. All had undergone potentially curative oesophageal surgery, stage I–III. Primary surgery was an Ivor-Lewis resection in 7 cases and a 3 stage McKeown's resection in 3 cases. The cause of leakage was necrosis of the gastric staple line in one case, gastric remnant necrosis in 2 cases and anastomotic leakage in 7 cases. The gastric staple line leakage was treated by resection and primary repair with thoracic lavage. The remaining cases were all treated by exteriorisation, forming a cervical oesophagostomy and gastrostomy, with thoracic lavage. There was a single death from multi-system failure following salvage surgery in a patient undergoing exteriorisation. Reconstruction was attempted 3 months following discharge after salvage surgery. Reconstruction with a substernal colonic interposition was successful in 7 of the 8 cases. The failure was a result of necrosis of the colonic graft at 10 days. There were no deaths in this group. There have been 2 deaths during follow up, one at 11 months and one at 18 months following salvage surgery, both from recurrent disease. The remaining patients are well at a follow up of between 6 and 34 months. Aggressive surgical intervention can salvage 90% of patients following leakage after oesophagectomy. Gastrointestinal continuity can be restored in 88% of survivors. This supports the value of early intervention in patients with leakage following oesophageal surgery. Clinical practice: Management strategy Oncology, specific: Oesophagus } "The Results of Aggressive Surgery for Gastrooesophageal Leaks after Oesophagectomy"

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## "P P 23 0623" P 23 0623 **Posterior Hemifundoplication for Gastro-Oesophageal Reflux — Comparison of Laparoscopic and Open Approach**

\*P. Jagot, A. Sauvanet, B. Maignien, G. Cargill, J. Belghiti, F. F\ 'e9k\ 'e9t\ 'e9

Digestive Surgery, Hopital Beauton, 100 Bd Du Gal Leclerc, 92110 Clichy, France In experienced hands, laparoscopic fundoplication can be performed with safety and with good immediate results. Some authors reported an higher rate of postoperative dysphagia after laparoscopic approach. The aim of this study was to compare results of 270\ 'b0 posterior fundoplication after laparoscopic and open approach. *Patients and Methods:* Sixty-three patients operated for a laparoscopic posterior hemifundoplication from 1992 to 1995 were compared retrospectively with 118 patients operated through laparotomy from 1989 to 1991. These 2 groups had similar clinical, radiological, endoscopic, pH-metric and manometric features. Of 63 laparoscopic procedures attempted, 53 (84%) were completed laparoscopically and were analysed for functional results. *Results:* Operating time was significantly longer in the laparoscopic group (142 – 48 min vs 112 – 51 min,  $p < 0.05$ ). No patient died postoperatively. Postoperative course was uneventful in 60/63 (95%) patients after laparoscopy and in 99/118 (84%) after laparotomy (NS). The period of hospitalization was shorter for the laparoscopic group (4.5 – 2 vs 10 – 4 days,  $p < 0.05$ ). The median follow-up was superior to 12 months in both groups. Two patients (4%) after laparoscopy and 5 patients (4%) after laparotomy showed clinical or pH-metric evidences of reflux recurrence. More than one month after the procedure, 7/53 patients (13%) in the laparoscopic group and 4/118 patients (3%) in the laparotomy group complained dysphagia ( $p < 0.05$ ). *Conclusion:* these results suggest that laparoscopic 270\ 'b0 posterior fundoplication is as effective to treat the gastro-oesophageal reflux as the open procedure, shorten the hospitalization period but is more frequently associated with postoperative dysphagia. Longer follow-up and reduction of incidence of postoperative dysphagia are mandatory before considering laparoscopic approach as the gold standard for anti-reflux surgery. Oesophageal gastric duodenal disorders: EG Reflux }" "Posterior Hemifundoplication for Gastro-Oesophageal Reflux / Comparison of Laparoscopic and Open Approach"

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"P P 24 0625" P 24 0625 **Corrosive Esophagitis and Esophageal Cancer. Definitions of Predictive Signs of Cancer by Long-Term Endoscopic and Pathologic Evaluation** E.G.H. Moura,

\*F. Maluf Filho, R.S. Azzam, P. Sakai, S. Ishioka, K. Iriya, I. Cecconello, H.W. Pinotti

Department of Gastrointestinal Endoscopy and Digestive Surgery, Hospital das Clínicas, São Paulo University, São Paulo, Brasil

*Purpose:* Corrosive esophagitis is a well-known high-risk condition for squamous cell carcinoma of the esophagus. The prognosis of this association is commonly poor due to difficult and late diagnosis. We sought to establish predictive signs of epidermoid cancer occurrence at caustic esophageal stenosis. *Method:* Thirty-seven patients with a previous history of lye ingestion dating from ten or more years were prospectively evaluated by a five-year protocol. They underwent to yearly upper GI series, endoscopic examinations associated to chromoscopy with a 3% Lugol solution. Exfoliative cytology and biopsies were oriented to all negative and low stained areas. Mucosal abnormalities and dilation difficulty were graded by the same operator. The cytologic smears were considered negative or positive for malignant cells. Pathologic findings were described as chronic esophagitis, suprapapilar atrophy and squamous cancer by the same pathologist. *Results:* During the five-year follow-up period, cancer was found in 6 patients (16.2%) staged as early in two and advanced lesions in four cases. The longer the postingestion period (11 to 57 years, mean = 31.6 y), the greater the chance of cancer occurrence. Some endoscopic and histopathologic findings were statistically proved to be predictive for cancer occurrence: I – a difficult dilation of a stenosis covered by an irregular mucosa and II – the finding of suprapapilar atrophy. *Conclusions:* The endoscopic and histopathologic findings above mentioned at stenotic caustic esophageal area aging ten or more years demand close follow-up. These findings rise again the question of preventive surgical approach for these group of patients. Endoscopy, specific: Oesophagus Oncology, specific: Oesophagus Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux } "Corrosive Esophagitis and Esophageal Cancer. Definitions of Predictive Signs of Cancer by Long-Term Endoscopic and Pathologic Evaluation"

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**"P P 25 0629" P 25 0629 RIBA Positive, PCR Negative Irish Anti-D Hepatitis C Patients have Minimal Liver Inflammation and Fibrosis, Not Predicted by Number of Positive RIBA Bands**  
**N. Kieran, G. Clarke, P. MacMathuna, A. Sullivan, G. Callagy, J.C. O'Keane, J. Crowe**

Liver Unit, Mater Misericordiae Hospital, Dublin 7 Of 1013 RIBA positive anti-D associated chronic hepatitis C (CHC) Irish women, 438 were PCR positive and have surprisingly mild disease. However, the disease status of the RIBA positive, PCR negative patients is thus uncertain (? immune, carriers or low grade inflammation with silent fibrosis) and was the subject of this investigation. 23/74 RIBA positive persistently PCR negative CHC patients referred to our unit were biopsied because of elevated ALT (4) or florid symptoms dating from inoculation (23). *Results:* Histologic activity index\* (Range 1–18) RIBA 1 5, 1, 0, 1 BANDS 2 3, 2, 2 (F), 0, 4 (F), 2 (F), 0, 4 (F), 1, 2, 0 3 0, 2, 1, 2, 2, 5 (F), 2 4 2, 3, 2, 3 No bile duct damage, lymphoid follicles or aggregates were observed. Only 3/23 patients had mild peri-portal fibrosis (F), 2 of these had steatohepatitis with obesity (1) and impaired glucose tolerance (1) suggesting dual pathology. *Conclusions:* (1) RIBA positive, PCR negative anti-D/CHC patients have minimal inflammatory activity and fibrosis. (2) Elevated ALT and fibrosis may be associated with dual pathology (non-alcoholic steato hepatitis) in CHC, possibly a synergistic effect. (3) Number or type of RIBA bands positive is not a predictor of inflammatory activity. Liver and bile ducts, 1: Hepatitis viral, diagnosis } "RIBA Positive, PCR Negative Irish Anti-D Hepatitis C Patients have Minimal Liver Inflammation and Fibrosis, Not Predicted by Number of Positive RIBA Bands"

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"P P 25 0630" P 25 0630 **Interferon-Ribavirin Combination Therapy for Chronic Hepatitis C, Type 1b in a Unique Irish Cohort 18 Years Post Inoculation** G. Clarke, A. Sullivan, P. MacMathuna, G. Callagy, P. Kelly, J. Crowe

Liver Unit, Mater Misericordiae Hospital, Dublin 7 *Introduction:* In 1977 anti-D serum contaminated by Hepatitis C was given to women subsequently identified by a national screening programme which revealed 438 to be PCR positive for RNA of Hepatitis C Type 1b. Ninety four were referred to this institution, of these ten had moderate inflammatory activity (Modified Knodell Activity Index (KAI) 8 – 1.4) bridging fibrosis and mean ALT of 77 (42–176) and were selected for treatment. *Methods:* We chose 6 months dual therapy consisting of Interferon 3 Mu  $\times$  3 weekly and Ribavirin 400 mgs  $\times$  2 daily, in an attempt to increase efficacy over interferon monotherapy in this group with adverse prognostic indicators (Genotype 1b and long disease duration). *Results:* Two of ten withdrew because of hyperthyroidism (1) and depression (1). Seven of eight patients (88%) responded with normalisation of ALT and negative PCR. All eight showed improved histology (KAI 4 – 1.5), fibrosis was unchanged. Adverse reactions in treated group included marrow suppression (1) and thyrotoxicosis (1). At six months follow up 4 of 7 patients remain in remission with negative PCR and normal ALT. Three have relapsed (PCR positive, mean ALT 87 (50–150).) *Conclusions:* Despite adverse prognostic indicators in this homogenous group with CHC genotype 1b and long disease duration, dual therapy with Ribavirin and low dose Interferon achieved therapeutic responses comparable to prolonged high dose Interferon therapy in patients with more susceptible genotypes Liver and bile ducts, 1: Hepatitis, viral, treatment } "Interferon-Ribavirin Combination Therapy for Chronic Hepatitis C, Type 1b in a Unique Irish Cohort 18 Years Post Inoculation"

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"P P 25 0631" P 25 0631 **Absence of Correlation between HCV NS5A Mutations and Response to Alpha Interferon in French Patients with Chronic Hepatitis C** Gio Squadrito, F. Leone, B. Nalpas<sup>2</sup>, P. Berthelot<sup>2</sup>, S. Pol<sup>2</sup>, C. Brechot

<sup>1</sup> INSERM U370, Paris, France

<sup>2</sup> Liver Unit, CHU Necker, Paris, France

<sup>3</sup> Dept. Internal Medicine, University of Messina, Italy

<sup>4</sup> Dept. Internal Medicine, University of Novara, Italy *Objectives.* It has been recently suggested that in patients with chronic HCV-1b infection there is a correlation between response to IFN and mutations in NS5A<sub>2209–2248</sub> gene. The aim of our study was to examine whether the NS5A amino acid sequence before treatment could be correlated to response to IFN in patients infected with genotypes associated to both low (1b) and high (3a) response rates. *Methods.* We retrospectively analyzed 37 patients with chronic HCV infection, 19 infected with genotype 1b and 18 with 3a, who had received from 3 to 6 MU of IFN for 6 to 12 months. Eleven patients were long term responders (LTR) and 26 were non-responders (NR). We amplified and directly sequenced, from pretreatment serum samples, the amino acid sequence of NS5A that was compared with the published sequence for HCV-J and NZL1. HCV RNA quantitation was analyzed by Branched DNA assay (Quantiplex<sup>®</sup> 2.0). *Results. Genotype 3a:* One of 7 LTR and none of 11 NR showed amino acid mutations in NS5A. *Genotype 1b:* All 4 LTR and 10 of 15 NR showed mutations in NS5A. Among the 14 patients with mutation in NS5A, 9 had 1 mutation and 5 had 2 mutations. Thirteen of 19 amino acid changes occurred at codon 2218. There was no significant difference of baseline serum HCV RNA levels between patients infected with the HCV 1b wild type and the NS5A mutated genome (49.3 – 62.37 and 31.47 – 36.55  $\times 10^5$  genomes eq/ml, respectively). *Conclusion.* In contrast with previous studies in Japan there is no apparent correlation in our patients between NS5A sequence and response to IFN; among patients infected with genotype 1b, mutation at codon 2218 is the most prevalent but its implication is unclear; NS5A mutations do not correlate with viral load. } "Absence of Correlation between HCV NS5A Mutations and Response to Alpha Interferon in French Patients with Chronic Hepatitis C"

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"P P 25 0632" P 25 0632 **Tauroursodeoxycholic Acid for the Treatment of HCV-Related Chronic Hepatitis: A Multicenter, Placebo-Controlled Study**

\*A. Crosignani, G. Budillon, C. Del Vecchio Blanco, F. Fatti, G. Ideo, G. Raimondo, R. Stabilini, M. Podda

Milano, Monza, Napoli, Messina, Mantova, Italy Tauroursodeoxycholic acid (TUDCA) has physicochemical and metabolic properties which favour its use as an alternative to ursodeoxycholic acid for chronic cholestatic liver disease. TUDCA may prove of benefit also for necroinflammatory liver disease, especially for HCV-related chronic hepatitis in which bile duct damage is frequently seen at histology. To evaluate the effects of TUDCA administration on serum liver enzymes related to cytolysis and cholestasis, 150 patients with HCV-related chronic hepatitis were selected in 6 different centers and randomly allocated to double-blind treatment with placebo, TUDCA 500 mg/day or TUDCA 750 mg/day for 6 months. Blood samples were taken at entry and after 30, 90 and 180 days of treatment and serum liver biochemistry was evaluated in the same laboratory. Patient characteristics (gender, age, severity of the disease at histology) were comparable in the three groups. A consistent and progressive decrease in serum liver enzymes was observed in patients treated with TUDCA. Values (means – S.D.) at baseline and after 180 days of treatment are reported in the table. Baseline Treatment Placebo 67 – 33 79 – 43 AST TUDCA 500 mg 68 – 34 47 – 18\* (IU/L) TUDCA 750 mg 75 – 33 47 – 20\* placebo 88 – 49 103 – 41 ALT TUDCA 500 mg 83 – 42 52 – 28\* (IU/L) TUDCA 750 mg 90 – 39 56 – 31\* placebo 71 – 52 73 – 54 { g } -GT TUDCA 500 mg 68 – 50 47 – 38\* (IU/L) TUDCA 750 mg 66 – 41 41 – 20\*\* p < 0.001 vs. placebo. In conclusion, TUDCA may be beneficial in patients with HCV-related chronic hepatitis. Long-term studies with clinically relevant end-points are warranted. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Tauroursodeoxycholic Acid for the Treatment of HCV-Related Chronic Hepatitis: A Multicenter, Placebo-Controlled Study"

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"P P 25 0633" P 25 0633 **Comparison Between Two Different Regimens of Alfa INF Treatment in Chronic Hepatitis C**

\*B. Paris, M. Bonelli, F. Negrini, E. Marzo, S. Signorelli, M. Girola

Gastroenterology and Third Department of Internal Medicine, Ospedali Riuniti, Bergamo, Italy. INF alfa recombinant is the drug of choice for treatment of chronic hepatitis C. However a sustained biochemical and virological response to standard therapy (3 MU thrice weekly – TIW – for six months) is seen in no more than 20–25% of patients. Predictors of poor response appear to be presence of cirrhosis, genotype 1b infection and high levels of viraemia pretreatment, but doubts concerning influence of dosage and duration of treatment still remain. *Aim of the study.* To assess the efficacy of two schedules (3 vs 6 MU) of INF 2a in the treatment of chronic hepatitis C. *Patients and methods.* 46 pts. (32 men mean age 46 + 5 years) were randomized to receive 3 or 6 MU of INF TIW for six months. All cases had chronic hepatitis histologically proven without cirrhosis. Sustained response (SR) was defined as normalization of ALT levels and disappearance of HCV-RNA by PCR 12 months after stopping therapy. *Results.* The 2 groups of pts. were homogeneous concerning age, sex, ALT levels, distribution of genotype 1b and histologic lesions. The follow-up was at least 12 months for all patients. In the group A (23 pts. 3 MU INF) we had a SR in 5/23 (21.7%) while in group B (23 pts. 6 MU INF) we found a SR in 9/23 (39%) ( $p < 0.05$ ). In both groups INF was well tolerated and all pts. completed the study. *Conclusion.* The sustained response to INF is statistically more effective in pts. treated with 6 MU for 6 months than with 3 MU for the same period. }" "Comparison Between Two Different Regimens of Alfa INF Treatment in Chronic Hepatitis C"

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"P P 25 0634" P 25 0634 **The Influence of Antiviral Therapy with Interferon Alfa-2A on the Levels of Oncomarker CA 19-9 in Chronic Viral Hepatitis C**. V. Gorbakov, O.V. Rumyantsev, S.V. Plyusnin, V.T. Ivashkin

Burdenko Main Military Hospital, Moscow, Russia *Aim of the study:* to assess the levels of oncomarker CA 19-9 in patients with chronic viral hepatitis C (HCV) and their changes during the treatment with interferon  $\alpha$ -2a. *Patients and methods:* 53 patients with HCV have undergone clinical, laboratory and morphological (liver biopsy) examination. All patients received antiviral treatment with interferon  $\alpha$ -2a (Roferon-A, Hoffmann-La Roche, Switzerland) during 6 months (6 mln ME intramuscularly tiw during the first 3 months, 3 mln ME tiw during consequent 3 months). *Results:* Blood levels of the oncomarker CA 19-9 were increased in 52.8% patients with HCV (normal – 37 U/ml). The carbohydrate antigen CA 19-9 is used for laboratory diagnose of pancreatic malignancies. In patients with benign pancreatic neoplasm, CA 19-9 is increased only in 12% of cases. Mean ( $\pm$  SD) level of CA 19-9 in HCV patients was 101.0 – 11.0 U/ml that is over 3-fold higher than the upper normal range. In patients with morphologically verified chronic persistent hepatitis (CPH) (n = 25) the mean CA 19-9 level was 65.2 – 10.3 U/ml, in those with chronic active hepatitis (CAH) (n = 23) 145.0 – 20.6 U/ml, in those with CAH and cirrhotic transformation and liver fibrosis (n = 25) 119.0 – 34.3 U/ml. Treatment with Roferon-A resulted not only in normalisation of ALT levels and other liver test, but also led to changes of CA 19-9 levels. From 1 to 4 months after the start of the treatment the increased levels of carbohydrate antigen were found only in 18.9% of patients (mean, 54.6 – 16.7 U/ml). Patients with CPH had the mean CA 19-9 level of 60.3 – 33.1 U/ml, those with CAH – 43.9 – 6.6 U/ml, those with CAH and cirrhotic transformation – 62.3 – 14.1 U/ml. *Conclusions:* 1. Increased blood levels of CA 19-9 are characteristic for 52.8% of patients with chronic viral hepatitis C. 2. The increase of carbohydrate antigen levels correlates with activity of pathological process in the liver. 3. Treatment with interferon  $\alpha$ -2a (Roferon-A) results in normalisation or significant reduction of CA 19-9 levels in most of patients with all morphological types of hepatitis. Liver and bile ducts, 1: Hepatitis, viral, treatment } "The Influence of Antiviral Therapy with Interferon Alfa-2A on the Levels of Oncomarker CA 19-9 in Chronic Viral Hepatitis C"

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"P P 25 0635" P 25 0635 **Interferon Gamma Deficiency in Pathogenesis of Chronic Hepatitis C (CHC)**

\*N. Osna, G. Silonova, M. Ponomareva, N. Vilgert, L. Viksna, D. Gardovska, A. Sochnev

Latvian Medical Academy, Riga, Latvia

THE AIM of our work is to study IFN $\gamma$  production capacity of peripheral blood cells in CHC and to analyse the influence of rIFN $\alpha$  therapy on this parameter. Twelve adult patients and 10 children (anti HCV+, with clinical, biochemical and morphological features of CHC) were treated by rIFN $\alpha$  (2–3 MU thrice a week, 24 weeks). IFN $\gamma$  was induced at pre- and posttreatment level in whole peripheral blood culture by PHA (24 and 96 hours of incubation) and tested in ELISA. It was shown that IFN $\gamma$  production capacity was decreased in CHC patients versus healthy donors ( $p < 0.05$ ). After three months of IFN $\alpha$  therapy we saw an enhancement of spontaneous and early (24 hours) induced IFN $\gamma$  only in responder group (patients that have responded to rIFN $\alpha$  therapy by ALT normalisation). This effect was prolonged till 6 months of the therapy and did not concern IFN $\gamma$  induced in 96 hours. We did not find such dynamics in the non-responder group. If we accept that 24 h induced IFN $\gamma$  is the predominant product of natural killers (NK) cells, and 96 h induced IFN $\gamma$  are produced by T-cells, our results means that rIFN $\alpha$  therapy activates IFN $\gamma$  production mainly at NK cells level, and this factor corresponds to the therapy outcome. We have analysed possible causes of defect 96 h induced IFN $\gamma$  production. In children but not in adult group impaired IFN $\gamma$  level was restored by combination of PHA with rIL-2. We also have found that auto-serum possessed IFN $\gamma$  downregulative properties especially after rIFN $\alpha$  treatment course. We conclude that IFN $\gamma$  deficiency is of pathogenic meaning, and activation of IFN $\gamma$  production by NK cells during rIFN $\alpha$  treatment is an important factor in responder status establishment in CHC.

Immunology and microbiology: Host defense mechanisms  
Immunology and microbiology: Inflammation  
Liver and bile ducts, 1: Hepatitis, viral, treatment }

"Interferon Gamma Deficiency in Pathogenesis of Chronic Hepatitis C (CHC)"

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"P P 25 0636" P 25 0636 **Response to HBV Vaccine in Relation to Anti-HCV and to Anti-HBc Positivity: A Study in Drug Addicts**

\*F. Minniti, L. Di Furia<sup>1</sup>, R. Bricolo<sup>1</sup>, R. Trivello<sup>2</sup>, L. De Marzi<sup>3</sup>, M. Miolo<sup>3</sup>, M. Chiaramonte

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<sup>2</sup> Dpt. of Hygiene, University of Padova, USSL 16 Padova

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<sup>3</sup> Public Health Laboratory, USSL 16 Padova Drug addicts is the group of young adults with the lowest response to HBV vaccine. It is, therefore, a good model to study the factors affecting the decrease of the response to HBV vaccine. HCV infection had been suggested to lower the vaccine response (Clin. Nephrol. 1994; 41: 113–116) while the role of antiHBc positivity is still debated. We studied 110 i.v. drug addicts (90 male, 20 female, mean age 29.5 – 6.3), all HIV negative, HBsAg and antiHBs negative and all vaccinated with the following protocol: Recombivax 10 100 µg i.m. at month 0, 1, 2. AntiHBs test was done between month 4 and 6. As usual, response to vaccine was considered positive when antiHBs was over 10 IU/L. Out of the 110, 73 were antiHCV+ve and 37 antiHBc+ve; 32 subjects were positive for both. The overall prevalence of the response to vaccine was 66.4%. We correlated the response either to positivity of antiHCV or antiHBc. Response in antiHCV+ve was 63.0% vs 72.9% in antiHCV{ - }ve (p = n.s.), response in antiHBc+ve was 51.4% vs 74.0% in antiHBc{ - }ve (p < 0.05) and in anti HCV+/antiHBc+ve was 50.0% vs 73.2% in anti HCV+/antiHBc{ - }ve (p < 0.05). *Conclusions.* In drug addicts we found an overall low response to vaccine. According to previous results, the fast protocol, used to increase the compliance, can affect the antiHBs titer but not the response. The response seems to be affected by positivity of antiHBc but not by HCV infection. These results suggest that antiHCV positive subjects can be successfully vaccinated, while the low response observed in some cases can be due to a latent HBV infection reflected by antiHBc positivity. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Response to HBV Vaccine in Relation to Anti-HCV and to Anti-HBc Positivity: A Study in Drug Addicts"

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"P P 25 0637" P 25 0637 **Interferon (IFN) Therapy Combined with Nonsteroid Antiinflammatory Drugs (AINS) Does Not Induce a Significant Increase of 2'5' Oligoadenylate Synthetase (2'5' AS) Activity in Patients with Chronic Hepatitis C**

\*M. Maynard<sup>1</sup>, S. Chousterman<sup>2</sup>, M. Baud<sup>3</sup>, T. Hicham<sup>1</sup>, L. Hamici<sup>1</sup>, J.P. Zarski

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<sup>3</sup> Laboratoire de Virologie M\edicale Mol\eculaire-Facult\e9 de M\edicine de Grenoble, France *Introduction:* Nonsteroid antiinflammatory drugs are cyclooxygenase inhibitors, which could increase IFN efficacy by an activation of the arachidonic acid metabolism pathway (epoxygenase). *The aim* of this study was to evaluate the changes of 2'5' AS levels on peripheral blood mononuclear cells (PBMC) in patients treated by the association of interferon and nonsteroid antiinflammatory drugs (tenoxicam) by comparison to IFN alone. The 2'5' AS is an intracellular enzyme induced by IFN. Double blind prospective study concerned 28 patients (20 males, 8 females) with histologically proved chronic hepatitis C. Mean age was 34.3 – 11.1 years. Patients were randomly divided in 2 groups: group 1 (n = 13): IFN a 2a 3 MIU/TIW/6 months plus Tenoxicam 20 mg Po per day; group 2 (n = 15): IFN a 2a 3 MIU/TIW/6 months. The 2 groups were similar for age, sex, basal ALT level, mode of contamination, duration of disease, serotype, quantitative viremia (MONITOR), Knodell score, response to therapy, and basal 2'5' AS levels. 2'5' AS activity was measured in PBMC by a radio active assay and expressed in UI/10<sup>7</sup> cells at D0, M3, M6, and M12. *Results:* In group 1, 2'5' AS level was not significantly increased at M3 (2.85 – 3.48 vs 1.13 – 2.26 at D0), M6 (2.19 – 2.85) and at M12 (0.82 – 0.81); on the other hand, in group 2, 2'5' AS level was significantly increase at M3 (6.08 – 5.44 vs 1.13 – 2.26 at D0: p < 0.05) but not at M6 (2.33 – 1.85) and M12 (1.09 – 0.77). Serotype and HCV RNA levels were not predictive parameters of 2'5' AS levels increase. *Conclusion:* Our results suggest that in patients with chronic hepatitis C, IFN therapy significantly increased 2'5' AS levels. This increase is temporary and not find with IFN/nonsteroid antiinflammatory drugs combination. Liver and bile ducts, 1: Hepatitis, viral, treatmentLiver and bile ducts, 1: Hepatitis viral, diagnosisImmunology and microbiology: Host defense mechanisms }" "Interferon (IFN) Therapy Combined with Nonsteroid Antiinflammatory Drugs (AINS) Does Not Induce a Significant Increase of 2'5' Oligoadenylate Synthetase (2'5' AS) Activity in Patients with Chronic Hep"

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## "P P 25 0638" P 25 0638 Hepatitis C Virus (HCV) Genotypes and Response to Interferon Alpha (IFN) Therapy in Morocco

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<sup>4</sup> Institut Pasteur Casablanca, Maroc  
The aim of this study is to explore the distribution of HCV genotypes in Morocco and to evaluate its effects on treatment response to IFN alpha in chronic active hepatitis C (CAH). *Methods:* we studied serum samples from 44 patients (pts) with chronic hepatitis C evaluated histologically by Knodell and Metavir scores (serum anti HCV positive tested by Liatek third generation and HCV ARN detected by nested PCR). HCV genotyping was performed by reverse hybridation line probe assay (INNO LiPA HCV) according to Simmonds classification. Of the 44 pts, 26 pts (20 CAH, 6 active cirrhosis) (17 men/9 women) were treated with IFN at the dose of 3 MU three times a week for 6 (n = 15), 12 (n = 8), 18 (n = 2) or 24 months (n = 1). Three groups were defined at the end of therapy according to biochemical response (rB) (normal amino alanine-transferase (ALT)) and histological response (rH): Responders (RS): rB + rH; Non responders (NR): no rB + no rH; Intermediate responders (IR): rB + no rH or rH + no rB Results: RS (n = 12) IR (n = 5) Type 1a: (n = 3) 1/3 (33.3%) 1/3 1/3 (33.3%) Type 1b: (n = 24) 7/16 (43.7%) 2/16 7/16 (43.7%) Type 2: (n = 17) 4/7 (57.1%) 2/7 1/7 (14.3%) 3 pts RS (type 1a, 1b, 2) showed a relapse (increase of ALT) more than 6 months after the end of therapy. *Conclusions:* 1) Only HCV types 1a, 1b and 2 were identified in moroccan pts with predominance of type 1b; 2) Type 2 seems associated with a better response to IFN than type 1b which was found in 77.7% of NR. 3) Predictive factors for a favorable response to IFN (46%) were also absence of cirrhosis and lower rate of serum ferritin. No difference of age, Knodell score and pretreatment ALT was found between RS and NR. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment Hormones and receptors: Molecular biology } "Hepatitis C Virus (HCV) Genotypes and Response to Interferon Alpha (IFN) Therapy in Morocco"

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## "P P 25 0639" P 25 0639 How Do Patients with Mild Chronic Hepatitis C Respond to Interferon (IFN) Therapy?

\*L. Serfaty<sup>1</sup>, O. Chazouillères<sup>1</sup>, J.M. Dauchot<sup>1</sup>, A. Loria<sup>1</sup>, C. Legendre<sup>2</sup>, R. Poupon<sup>1</sup>

<sup>1</sup> Unité d'Hépatologie, Hospital St-Antoine, Paris, France

<sup>2</sup> Service d'anatomopathologie, Hospital St-Antoine, Paris, France

The influence of histological activity on efficacy of IFN in patients with non cirrhotic chronic hepatitis C is debated. The aim of this study was to compare biochemical and virological responses to IFN in patients with mild hepatitis or with moderate to severe hepatitis. *Methods:* Between 1990 and 1993, 192 patients with non cirrhotic chronic hepatitis C were treated with IFN alfa 2 recombinant 3 MU 3/week for 6 months in our institution. 57 had mild hepatitis (MiH), defined by Knodell score  $\leq 4$ , 135 had moderate to severe hepatitis (SH). Biochemical response was classified as non response (NR) (i.e., elevated ALT at the end of treatment), response with relapse (RR) (i.e., normal ALT at the end of treatment and elevated ALT thereafter) or sustained response (SR) (i.e., ALT still normal one year after the end of treatment). Virological response was defined as PCR negativity. HCV genotype was determined in 67 patients using InnoLipa technic. Mean follow-up was 21 – 12 months. *Results:* Pretreatment characteristics of patients with MiH or SH were as follows: age (37 – 10 vs 43 – 13 yrs,  $p < 0.05$ ), sex ratio (1.1 vs 1.3), history of blood transfusion (32% vs 43%) or IVDU (41 vs 35%), ALT levels (73 – 46 IU/l vs 101 – 98 IU/l,  $p < 0.05$ ), HCV genotype (1a, 1b, 2a, 3a, others: 29, 29, 6, 18, 18 vs 18, 36, 8, 18, 20%). Biochemical response was not significantly different between the 2 groups: NR, RR, SR = 37, 37, 26% in the MiH group vs 45, 40, 15% in the SH group. Virological response was also identical at 3 and 6 months of treatment (53 vs 48%, 40 vs 42%). Among the 35 patients with a sustained biochemical response, the percentage of patients with negative PCR one year after the end of treatment was not significantly different in patients with MiH or SH (55% vs 83% respectively,  $p > 0.05$ ). *Conclusion:* this large cohort study shows that biochemical or virological responses to IFN are not significantly better in patients with mild hepatitis than in patients with moderate to severe hepatitis. Taken together with the generally good prognosis of the natural course of mild hepatitis C, this relatively low efficacy makes questionable the standart IFN therapy in these patients. } "How Do Patients with Mild Chronic Hepatitis C Respond to Interferon (IFN) Therapy?"

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"P P 25 0640" P 25 0640 **Prevalence of Anti-Thyroid Autoantibodies before and after Interferon Treatment in Patients with HCV Infection and B-Thalassaemia Major in Greece** K. Mimidis,

\*K. Goritsas, P. Matsouka, V. Margaritis, C. Lambropoulou-Kar'etza

Department of Internal Medicine, University Hospital of Patras, Patras, Greece The prevalence of anti-thyroid autoantibodies varies in reports from different countries. A high prevalence of antithyroid antibodies in chronic hepatitis C especially after IFN treatment is already reported. We studied the prevalence of antimicrosomal antibodies in Greece in multitransfused thalassaemic patients and in otherwise healthy patients with chronic hepatitis C. Epidemiologic data in general population of our region (SW Greece) report a prevalence for anti-thyroid antibodies of 12%. *Patients-Method:* 25 patients with chronic HCV infection (9 males and 16 females; age 54 – 2 years, mean – SD) and 24 patients (9 males and 15 females; 24 – 2.1 years, mean – SD) with chronic HCV infection and  $\beta$ -thalassaemia major, transfused regularly in monthly intervals were included in the study. All patients were treated with  $\alpha$ 2 $\beta$  IFN 3 MU three times/week for at least 6 months. HCV diagnosis was made by ELISA-3 Abbot for HCV and RT-PCR for HCV. Liver biopsy was performed in all patients. Thyroid function and anti-thyroid peroxydase antibodies were measured by RIA in all patients at diagnosis, every three months during IFN therapy and 6 months after withdrawn of IFN. *Results:* Before IFN treatment 4 patients (3 females, 1 male) out of total 49 (8.16%) presented with an increased autoantibody titer (NS compared with the prevalence in general population in our region). None of those 4 patients was thalassaemic. After IFN treatment only one female patient with thalassaemia (4.1%) and the previous 4 patients presented an increased autoantibody titer. Subclinical hyperthyroidism after IFN therapy presented only one non thalassaemic patient. *Conclusion:* 1) Prevalence of autoantibody in Greek patients with HCV infection does not differ from that observed in general population. 2) Patients with  $\beta$ -thalassaemia major had a nihil prevalence of anti-thyroid antibodies probably because of their young age. 3) IFN treatment did not influence the thyroid function in anti-thyroid autoantibody negative patients. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Prevalence of Anti-Thyroid Autoantibodies before and after Interferon Treatment in Patients with HCV Infection and B-Thalassaemia Major in Greece"

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"P P 25 0641" P 25 0641 **Udca, Alone or in Combination with Interferon- $\alpha$ , in the Management of Chronic HCV Infection**. H. Senturk, O. Uzunalimoglu, Y. Batur, I. Simsek, A. Mert, H. Cetinkaya, G. Ersoz, F. Tabak, H. Akbaylar, M. Akdogan, A. Dokmeci, A. Sonsuz, S. Ozenirler, E. Avsar, N. Tozum

Hepatitis Study Group, Turkey Ursodeoxycholic acid (UDCA) has a controversial role in the treatment of chronic hepatitis C virus (HCV) infection. We studied its impact, alone or in combination with Interferon- $\alpha$  (Intron, Schering & Plough), on chronic HCV infection. The diagnosis was based on: 1-The presence of ALT elevation, in the preceding six months, 2-Presence of Anti-HCV antibodies and HCV-RNA by PCR in the circulation, 3-Chronic hepatitis in liver biopsy. Response was defined as complete normalization of ALT. Sustained meant no flare in the six months period following treatment. In total, 107 patients were randomized into three treatment arms: 1-UDCA alone 250 mg bid (14), 2-UDCA 250 mg bid + Ifn- $\alpha$  3 MU tiw (45), 3-Ifn- $\alpha$  alone 3 MU tiw (49). The treatment was continued for six months. At the end of six months the responders continued the same treatment for another six months. The nonresponders of the groups were crossed-over as following: 1-UDCA was replaced by Ifn- $\alpha$  3 MU tiw. 2-The dose of Ifn- $\alpha$  was increased to 6 MU tiw. 3-UDCA 250 mg bid was added to the treatment. All the nonresponders received these alternative treatments for six months. All the responders to any type of treatment were followed-up for another six months untreated. The enrollment to UDCA group was stopped early, because only 1/14 patient normalized ALT at the end of three months. However 12/14 from this group completed six months and then crossed-over as planned. 39/45 from the second and 45/49 from the third group completed treatment. 1/12 of UDCA patients responded which was not sustained. Overall sustained response rate did not differ between Ifn- $\alpha$  and Ifn- $\alpha$  + UDCA groups (7/39, 18% vs. 9/45, 20%). None of the Ifn- $\alpha$  nonresponders achieved sustained response with switch to combination treatment. Only 1/15 nonresponders from combination group achieved sustained response with the dose escalation of Ifn- $\alpha$ . It was concluded that UDCA alone is ineffective in chronic HCV infection. Combination with Ifn- $\alpha$  is not additive to the latter. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Udca, Alone or in Combination with Interferon- $\alpha$ , in the Management of Chronic HCV Infection"

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**"P P 25 0642" P 25 0642 Chronic Hepatitis C And Autoimmunity. Good Response to Immunosuppressive Treatment A. Tran<sup>1</sup>, S. Benzaken<sup>2</sup>, G. Yang<sup>1</sup>, P. Rampal<sup>1</sup>**

<sup>1</sup> Liver Unit, Archet Hospital, Nice, France

<sup>2</sup> Department of Immunology, Archet Hospital, Nice, France The link between autoimmunity and hepatitis C virus infection remains controversial. Some rare patients with chronic active hepatitis C present features of autoimmune liver disease. The choice of treatment is very difficult: Interferon-alpha may exacerbate the autoimmune component while corticoids may enhance viral replication. We describe 3 patients with chronic hepatitis C and features of autoimmune liver disease treated by azathioprine (2 mg/kg/day) and prednisone (1 mg/kg/day). The dose was then adjusted. The follow-up was 4, 2 and 1 years in patients 1, 2 and 3, respectively. Treatment was safe and efficacious (See table). Data Patient 1 Patient 2 Patient 3 Age (yrs) 67 69 70 Sex female female male HCV RNA (RT-PCR) positive positive positive Contamination transfusion transfusion unknown Genotype 3a 3a 1b Liver biopsy cirrhosis cirrhosis cirrhosis Before After Before After ALT (5–40 IU/l) 52 17 68 17 110 25 Gammaglobulin (9–17 g/l) 23.5 15.3 29.2 10.8 24.9 17.4 Anti-LKM antibody (ab) Neg Neg Neg Neg Neg Neg Anti-nuclear ab Neg Neg Neg Neg 1/10<sup>4</sup> 1/10<sup>3</sup> Anti-mitochondrial ab Neg Neg 1/10<sup>3</sup> 1/200 Neg Neg Anti-smooth muscle ab 1/600 1/50 Neg Neg Neg Neg Knodell's score 12 8 17 12 16 In conclusion, we recommend that these patients with chronic hepatitis C and features of autoimmune liver disease be treated by immunosuppressive therapy first. Interferon therapy should be reserved for those patients who fail to respond. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Chronic Hepatitis C And Autoimmunity. Good Response to Immunosuppressive Treatment"

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"P P 25 0643" P 25 0643 **Interferon Therapy in HBV Precore Mutant Related Chronic Liver Disease in India** R.C. Guptan, V. Thakur,

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*Background:* About 15% of Indian patients with HBV related chronic liver disease (CLD) have infection with precore mutant forms. These patients have an aggressive course. Some success with interferon (IFN) therapy is reported from the West. IFN was found effective by us (J. Hepatol. April, 1996) in Asian Indians with CLD due to wild type HBV. IFN therapy has not been evaluated in CLD due to mutants in Asian patients. *Material and Methods:* 18 biopsy proven CLD patients (age 38.2 – 12 yr, M:F:: 17:1) with mutations at 1896 and 1898 position, HBsAg+ve, HBeAg { - } ve, HBeAb+ve, HBVDNA+ve), ALT levels > 2 { \b4 } N and negative for hepatitis C and auto immune markers were included. IFN (INTRON-A) was given as 3 MU, AD, for 4 mo. Serial serology and repeat liver biopsy was done after completion of therapy and hepatic activity index (HAI) was calculated. HBVDNA was done by both Dot-Blot Hybridization (detection limit < 1 pg/ml) and PCR at base line and 4 mo. Success of IFN was defined as normalization of ALT and loss of HBVDNA by dot-blot. *Results* INF therapy was successful in 12 (75%) patients. The mean ALT decreased from baseline in responders (36.5 – 12 vs. 82.6 – 22 IU/L, p < 0.05), while it remained high (72.2 – 26 IU/L) in non-responders. HAI decreased insignificantly (15 – 6 vs. 11 – 8.4). 12 patients became HBV DNA negative by dot blot at 4 mo but none became PCR negative. During 13.2 – 6.2 mo follow-up, 7 (58.3%) responders relapsed. 2 (11.1%) patients died; 1 of hepatoma and the other of coma. In 3 (16.6%) patients, IFN was rescheduled due to thrombocytopenia. *Conclusions* (i) IFN therapy is beneficial in precore mutant related CLD (ii) Despite HBVDNA clearance by dot-blot in 75% patients, low level viremia (PCR+ve) persists leading to high relapse. Combination of drugs needs evaluation. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Interferon Therapy in HBV Precore Mutant Related Chronic Liver Disease in India"

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"P P 25 0644" P 25 0644 **Clinical Study of the Efficacy of Interferon Therapy for Chronic Hepatitis CM. Takase, Y. Ishizuka, K. Uchiyama, H. Mutsukawa, T. Kawai, M. Nakagawa, Y. Nishizato<sup>1</sup>, T. Saito<sup>2</sup>**

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<sup>2</sup> The Fourth Dep. of Internal Medicine, Tokyo Medical College *Objectives:* The therapeutic effects of interferon (IFN) therapy for chronic hepatitis C were investigated according to hepatitis C virus (HCV) subtype, HCV-RNA quantity, and histodiagnosis. HCV core antibody (C22-3) level was quantitatively determined before and after IFN therapy to investigate the correlation of the level with HCV-RNA and the usefulness of the antibody level for evaluating the efficacy of IFN therapy. *Methods:* The subjects were 35 patients who had tested positive in a blood HCV-RNA determination. Three periods of administration of r-IFN a 2a at a daily dose of 9 MU were used (total dose, 774, 846 and 918 MU). The case in which alanine amino transferase (ALT) was normalized within 6 months after the administration period and the ALT level remained normal for at least the next 6 months was regarded as complete response (CR). Viral fluctuation (fate) was also investigated by determining HCV-RNA at the end of administration and 6 months after the administration period. HCV subtypes were determined according to the method of Okamoto et al., and HCV-RNA quantity according to the competitive RT-PCR method. The histodiagnosis followed the European classification. *Results:* CR was observed in 48.6%. As a result of assessing the background factors in the CR group, HCV-subtypes 2, 3 and 4 were observed in 33.3%, 77.8% and 50.0%, respectively. The HCV-RNA quantity was  $10^5/50$  ul or more in 31.6% and less than  $10^5/50$  ul in 68.8%. According to histodiagnosis, CAH2A and CAH2B were observed in 54.5% and 38.5%, respectively, in the CR group. The C22-3 antibody titer decreased to 68.2% and 56.8% at the end of administration and at 6 months after the administration period, respectively, as compared with the level before IFN therapy, in the patients who showed a change in HCV-RNA to a negative level at the end of administration and 6 months after the administration period. In the patients who showed no change in HCV-RNA to a negative level, the antibody titer decreased to 78.7% at the end of administration, and it tended to increase thereafter. *Conclusions:* 1. IFN therapy showed low efficacy in the patients with HCV-subtype 2, HCV-RNA quantity of  $10^5/50$  ul or more, and who showed advanced histological findings of the liver. 2. The quantitative level of C22-3 antibody is useful as an indicator for estimating viral fluctuation (fate), and the continuous decrease in the C22-3 antibody level starting from the end of administration, which suggested the elimination of HCV-RNA. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Clinical Study of the Efficacy of Interferon Therapy for Chronic Hepatitis C"

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"P P 25 0645" P 25 0645 **HCV Carriers with Normal ALT: Response to Interferon (IFN) Treatment**

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<sup>2</sup> I Dept. of Pathology, Hospital of Brescia, Italy

<sup>3</sup> Blood Transfusion Service, Hospital of Chiari, Italy The efficacy of interferon treatment in HCV carriers with normal ALT levels is still debated. *Methods:* 19 consecutive subjects with normal ALT, positive for anti-HCV and HCV-RNA (mean age 50.8 – 9.5; M:F 11:8) underwent monthly monitoring of ALT activity for 8–18 months. ALT levels were persistently normal (< 40 IU/l) in 12 cases, whereas occasional elevations < 1.5-fold N.V. were detected in 7 cases. Liver biopsy detected CAH in 18 and CLH in 1 (median Knodell score = 6, range 2–8). Patients were randomized to receive IFN alpha 2b 3 MU t.w. for 12 months (n. 10, group 1) or no treatment (n. 9, group 2). The response treatment was monitored with monthly ALT and HCV-RNA determinations. In case of HCV-RNA persistence treatment was suspended after 6 months. Subjects of group 1 and 2 did not differ significantly for age, sex, Knodell score (median 5 vs 6), HCV genotype (type 1 n. 2, type 2 n. 8; vs type 1 n. 5, type 2 n. 4), HCV-RNA titer (median 8.15 log copies/ml vs 7.5). n. of subjects with occasional ALT elevation (4 vs 3). *Results:* during IFN therapy 5 patients in group 1, but none in group 2, cleared serum HCV-RNA. ALT flare-up was observed in 2 patients, but ALT levels returned normal in few months. After stopping therapy 3/5 had immediate re-appearance of viremia and transient ALT increase. The 2 remaining patients were still HCV-RNA negative after 9 months of post-treatment follow-up. They had a pretreatment viral titer of 7.1 and 5 log copies/ml and were infected with genotype 2c. Total Knodell score were 4 and 8. These results show that in HCV carriers with persistently normal or near normal ALT: 1) interferon treatment induced clearance of HCV-RNA until 9 months post-IFN in 2/10 patients, both infected with genotype 2; 2) transient ALT flare-up may be detected 3) clearance of HCV-RNA during treatment is not predictive of sustained response. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "HCV Carriers with Normal ALT: Response to Interferon (IFN) Treatment"

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"P P 25 0646" P 25 0646 **Hepatitis C Virus-Positive (HCV) Chronic Active Hepatitis (CAH): A Randomized, Controlled Trial of IFN – Colchicine**

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<sup>1</sup> Cattedra di Gastroenterologia, Universit  di Pisa, Italia Fibrosis in pts with CAH is a frequent occurrence also in long term responders to IFN; colchicine (C) has been used as antifibrillogenic drug. We have therefore planned a randomized trial of IFN – C [IFN 6 MU {b4} 3 months, 3 MU {b4} 3 months (Roferon A, Roche) – C 1 mg for 5 days/week for 1 year] trying to improve the overall outcome of IFN alone. We report the results at 2 years of the 85 pts with antiHCV+ CAH enrolled (IFN: 42; IFN + C: 43). *Results:* the 2 groups were balanced for all parameters (age, sex, ALTs levels, duration of disease) except than more severe CAH (HAI > 9), more genotype 1b and baseline higher PIIP (indirect index of collagen deposition) were present in IFN + C group. Longterm response (LTR) was significantly higher in IFN (9.5%) vs IFN + C (4.5%) treated pts. PIIP decrease in both groups was significant at month XII vs baseline ( $p < 0.05$ ) but not between the 2 groups. HAI decrease at month XII in both groups was not significant. Presence of genotype 1b was the only parameter associated, at multivariate analysis, with non response. Comparison of the subgroup, in the IFN + C (n. 14), characterized by more severe cases with the totality of IFN-treated patients demonstrated a rate of LTR in IFN + C pts similar to that of IFN-treated patients (IFN vs IFN + C: 9.5 vs 7.0%) and a significantly higher decrease of HAI score ( $p < 0.05$ ). *Conclusions:* 1. genotype 1b is a strong predictor of non response to IFN; 2. PIIP decrease may be a consequence of the antiviral-antiinflammatory activity of IFN; 3. the association with colchicine does not improve the overall response of IFN in unselected CAH; however, it improves the rate of long term response and the histological activity score in patients with more severe disease. (Supported by grant 40% Virus). Liver and bile ducts, 1: Hepatitis, viral, treatment Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Hepatitis C Virus-Positive (HCV) Chronic Active Hepatitis (CAH): A Randomized, Controlled Trial of IFN ± Colchicine"

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## Three Versus Five Million Units Interferon Recombinant $\alpha$ 2b in the Treatment of Chronic Hepatitis C: A Randomized Study

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**Background** – Interferon (IFN) therapy is effective in HCV-related chronic liver disease but doubts concerning dosage and duration of treatment still remain. **Aim** – To assess the efficacy of 2 schedules (3 vs 5 MU) of IFN- $\alpha$  2b in the treatment of chronic hepatitis C. **Patients and Methods** – Thirty patients (19 men, mean age 38 – 7 y) were randomized to receive 3 or 5 MU of IFN (interferon alpha 2b, Intron-A<sup>®</sup>, Schering-Plough, NJ) thrice weekly (TIW) for 1 year. All cases had chronic hepatitis histologically proven and no one had cirrhosis. Complete response was defined as normalization of aminotransferases at the end of treatment, and complete sustained response as normalization of aminotransferases at the end of follow-up. Serum HCV RNA was tested by bDNA (Quantiplex<sup>®</sup> HCV RNA, Chiron Cooperation, Emeryville, USA). **Results** – The two groups of patients were homogenous, concerning age, sex, ALT levels and histologic lesions. At the end of treatment, all patients were followed-up for 12 months. IFN was well tolerated, and all patients completed the treatment. **Table 1. IFN dosage, HCV titer and response to interferon treatment**

Patients, n	IFN	Histologic lesions	Mean HCV titer*	CR (%)	SR (%)
15	3 MU	mild/moderate CAH (n = 12)	24 – 4	7/12 (58.3)	4/12 (33.3)
15	5 MU	mild/moderate CAH (n = 11)	21 – 5	7/11 (63.6)	6/11 (54.5)

severe CAH (n = 3) 36 – 5 0/3 (0) 0/3 (0) severe CAH (n = 4) 38 – 7 0/4 (0) 0/4 (0) CR = complete response; SR = sustained response; \*mean – SD; \*\* p < 0.05 **Conclusions** – (1) The response to interferon is statistically more effective in patients treated with 5 MU TIW for 1 year than with 3 MU; (2) HCV RNA levels seem to be predictors of subsequent response to IFN in Portuguese patients with chronic HCV infection. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Three Versus Five Million Units Interferon Recombinant  $\alpha$  2b in the Treatment of Chronic Hepatitis C: A Randomized Study"

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"P P 25 0648" P 25 0648 **Virological Characteristics and Effect of Interferon Therapy in Anti-HCV Positive Patients with Normal Transaminases Levels**

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Chronic HCV infection in patients with persistently normal ALT activity is under investigation.  
*Aim* – To assess the level of viremia, HCV genotype, histological activity and the effect of interferon recombinant alpha 2b in these patients, compared with a control group.  
*Methods* – We have studied 14 patients with persistently normal ALT levels. HCV RNA was quantified by bDNA (Quantiplex HCV RNA, Chiron Corporation, Emeryville, USA), and HCV genotype by LIPA. The levels of viremia and HCV genotype of these patients were compared with a homogeneous control group of 20 patients with chronic hepatitis C histologically proven but with elevated ALT values. Eleven (78.6%) of the 14 patients were treated by IFN 3 MU TIW for 6 months and were evaluated at the end of treatment, and six months later.  
*Results* – In the treated group thirteen (92.8%) patients had chronic hepatitis and 1 (7.2%) had minimal lesions; in the control group, 17 (85%) patients had chronic hepatitis and 3 had minimal lesions.  
Table 1. Levels of viremia and genotypes in patients (n = 14) and controls (n = 20) ALT levels\* HCV RNA Genotype (%) CR (%) SR (%) (UI/L) (Eq/ml {b4} 10<sup>5</sup>)  
Treated group (n = 14) 19 – 8 21 – 3 1a (36) 9/14 (64) 3/9 (33) 1b (50) 3a (14)  
Control group (n = 20) 124 – 11 38 – 5 1a (35) 12/20 (60) 7/12 (58) 1b (65)\*mean – SD  
*Conclusions* – In HCV carriers with persistently normal ALT activity: (1) HCV genotypes are not significantly different, but the level of viremia is lower when compared to patients with abnormal ALT activity; (2) histological liver injury is frequent; (3) IFN lowers levels of viremia, but fails HCV eradication. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Virological Characteristics and Effect of Interferon Therapy in Anti-HCV Positive Patients with Normal Transaminases Levels"

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"P P 25 0649" P 25 0649 **Pretreatment Low Serum HCV-RNA Levels with a Branched DNA Assay Predict Response to Interferon-Beta Treatment in Chronic Hepatitis C**

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The aim of this study is to evaluate whether initial HCV-RNA titer, HCV genotype and histological findings predict response to natural IFN-beta in chronic hepatitis C (CHC). *Method:* Thirty six patients with CHC (male 19 and female 17, mean age 46.4 years) were treated with natural IFN-beta 6 MU/day for 8 weeks. Complete response (CR) was defined as persistence of normal ALT levels after the end of treatment and as clearance of HCV RNA (by RT-PCR) at the end of treatment, 3 month and 6 month after the cessation of the treatment. HCV-RNA genotyping was performed using specific PCR primers according to the method of Okamoto, and HCV-RNA quantitation was performed using branched DNA (b-DNA) assay. Liver biopsy specimens were scored according to the Desmet's grading method. *Results:* HCV genotype 1b 2a 2b CR rate 23% (3/13) 58% (11/19) 50% (2/4) HCV-RNA (mEq/ml) < 0.5 0.5–1.0 1.0 < CR rate 84% (14/19) 0% (0/4) 15% (2/13) Grading minimal mild moderate severe CR rate 50% (5/10) 53% (9/17) 25% (2/8) 0% (0/1) Staging score 0 score 1 score 2 score 3 score 4 CR rate 0% (0/0) 58% (7/12) 39% (7/18) 33% (2/6) 0% (0/0) Analysis of the 19 patients with low serum HCV-RNA levels (< 0.5 mEq/ml) were as follows: HCV genotype 1b 2a 2b CR rate 75% (3/4) 77% (10/13) 50% (1/2) Staging score 0 score 1 score 2 score 3 score 4 CR rate 0% (0/0) 86% (6/7) 67% (6/9) 66% (2/3) 0% (0/0) *Conclusions:* These data suggested that pretreatment low serum HCV RNA levels (< 0.5 mEq/ml) determined by b-DNA assay were regarded as most important predictor of response to IFN-beta treatment in chronic hepatitis C. Consideration of this factor will provide more rational criteria to select patients for IFN-beta treatment. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Pretreatment Low Serum HCV-RNA Levels with a Branched DNA Assay Predict Response to Interferon-Beta Treatment in Chronic Hepatitis C"

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## "P P 25 0650" P 25 0650 Interferon (IFN) Therapy in HCV Chronic Liver Disease: Is Old Age a Contraindication?

\*U. Lorenzoni, A.R. Floreani, A. Vian, S. Lobello, R. Naccarato, M. Chiaramonte

Dept. of Gastroenterology, Padua University, Italy Elderly people are considered poor candidate for IFN treatment, because of a suspected higher risk of adverse effects and/or a higher prevalence of non responders. *Aim:* To evaluate the response to IFN in a selected population of old patients compared to adult controls. *Material and Methods:* We retrospectively evaluated 166 chronic HCV hepatitis patients enrolled in IFN treatment protocols since 1990: a) N. 25 were > 60 yr old (14 M, 11 F; mean age 61.6, range 60–67); b) N. 141 were < 60 yr. old (104 M, 37 F; mean age 43.2, range 24–59). The following variables were correlated to the response: gender, serum ferritin, { g }GT, ALT, HCV genotype and liver histology. The statistical analysis was done by T-Student's test for unpaired data. *Results:* Sustained response (12–48 months of follow-up after the therapy) was observed in 7/25 (28%) of aged compared to 43/141 (30.4%) of adult patients (p = n.s.). Short term response (with relapse after treatment) was observed in 6/25 (24%) of aged and in 48/141 (34%) of adults (p = n.s.). Univariate analysis demonstrated that liver cirrhosis and high levels of both ferritin and { g }GT were correlated with non-response to treatment in both groups. However, liver cirrhosis was more frequent in aged compared to adults (13/25, 52.0% vs 26/141, 18.4%; p < 0.001), while { g }GT, ferritin and 1b genotype were not statistically different in the two groups. Major side effects were more frequent in older patients than in adults (28.0% vs 14.2%, p < 0.01). *Conclusions:* Selected elderly subjects with HCV chronic hepatitis, in spite of the higher prevalence of cirrhosis, might have the same probability of sustained response compared to adults. However, attention must be paid in monitoring the major adverse effects. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Interferon (IFN) Therapy in HCV Chronic Liver Disease: Is Old Age a Contraindication?"

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## "P P 25 0651" P 25 0651 Can Pretreatment Characteristics Predict Short Term Non-Response to Interferon Therapy in Chronic Hepatitis C?

\*R. Testa, E. Giannini, A. Picciotto, S. Cagliaris, D. Risso<sup>1</sup>, P.B. Lantieri<sup>1</sup>, L. Arzani, S. Alvarez, G.L. Guido, N. Campo, L. Faraldi<sup>2</sup>, G.C. Icardi<sup>2</sup>, G. Lapertosa<sup>3</sup>, G. Celle

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<sup>1</sup> Institute of Medical Statistics, University of Genoa, Italy

<sup>2</sup> Institute of Hygiene, University of Genoa, Italy

<sup>3</sup> Institute of Pathological Anatomy, University of Genoa, Italy Predictors of a sustained response to interferon (IFN) therapy in chronic hepatitis C were identified in several trials. About 50% of patients have no response during IFN therapy and this failure is very expensive. Aim of our study was to identify possible predictors among biochemical, virological, pharmacokinetic and histological pretreatment variables of a non-response during IFN therapy. 50 patients (41 M and 9 F, mean age 46 – 12) with chronic hepatitis HCV RNA positive were treated with IFN { a }2b recombinant or lymphoblastoid (9 MU weekly for six months). Pretreatment were evaluated ALT, AST, { g }GT, alkaline phosphatase, bilirubin, albumin, protrombin activity, gammaglobulin (GGL), prolylhydroxylase, procollagen III peptide, bile acids, viral genotype, monoethylglycinexylidide formation (MEGX, lidocaine metabolite), histological activity index (HAI) with partial scores (fibrosis, necrosis + inflammation, biliary duct damage, steatosis) and were related to short term response (ALT and AST normalization both at 3rd and 6th month). 24 patients were responders and 26 non responders. Significant differences between responders and non responders were found for { g }GT (mean – SD U/l 37 – 18 vs 78 – 61, p = 0.0007), GGL (g/dL 1.4 – 0.4 vs 1.7 – 0.7, p = 0.042), HAI (6.5 – 3.0 vs 9.5 – 4.2, p = 0.0075), necrosis + inflammation (5.5 – 2.4 vs 7.5 – 3.1, p = 0.0109) and fibrosis (0.5 – 0.8 vs 1.2 – 1.2, p = 0.05). Multivariate logistic analysis showed that only increased { g }GT is an independent predictor of non-response (p = 0.0254), and that in combination with decreased MEGX formation at 60 min, high HAI and genotype 1 allows to calculate a probability index of non response (0.26 error, p = 0.0008). Non response probability { \b3 } 0.50 showed a 0.75 SP, 0.73 SS and 0.76 PPV, while a probability { \b3 } 0.70 showed a 0.92 SP, 0.50 SS and 0.87 PPV. A high pretreatment risk of non response can suggest to modify IFN dose or to combine it with other drugs. Liver and bile ducts, 1: Hepatitis, viral, treatment } "Can Pretreatment Characteristics Predict Short Term Non-Response to Interferon Therapy in Chronic Hepatitis C?"

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## "P P 26 0652" P 26 0652 Apolipoprotein E Polymorfism in Primary Sclerosing Cholangitis (PSC)

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Department of Medicine Helsinki, Tampere and Turku University Hospitals, Finland

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Department of Radiology of Helsinki University Hospital, Finland PSC is a non-suppurative inflammation of intra- and extrahepatic bile ducts of uncertain origin leading to chronic cholestatic liver disease. No effective medical treatment has so far been available. Ursodeoxycholic acid (UCDA) has widely been used in patients with PSC, although there is no proven efficacy of the treatment. Apolipoprotein E (Apo E) polymorfism has been shown to regulate the absorption of intestinal cholesterol and bile acids. Moreover, apo E polymorfism has been demonstrated to affect the treatment response to UCDA in primary biliary cirrhosis. *Aim of the study.* To evaluate the apo E polymorfism in PSC patients and compare it in healthy finnish population. *Patients and methods.* The study population consisted of 67 patients with PSC. The diagnosis was based on ERCP and liver histology. Apo E phenotyping was determined by isoelectric focusing. Liver enzymes and bilirubin were measured by routine lab methods. *Results.* The relative frequencies of apolipoprotein E phenotypes in healthy controls (n = 615), in PSC (n = 67) and in primary biliary cirrhosis (n = 88) are shown in the table 1. The apo E2 phenotype was 4.6 times higher in PSC than in controls and about two times higher than in PBC. The effect of apo E phenotype on the clinical manifestations (extent of the disease judged by ERCP, S-ALP, S-bilirubin and bile acids) of PSC was further analyzed, showing no clinically significant differences between the different apo E phenotypes, although patients with apo E2 tend to have more cholestatic disease. *Table 1. Apolipoprotein E polymorfism in PSC*

Apo E phenotype	Controls	PSC	PBC
E2	4.1%	18.8%*	9.7%*
E3	73.3%	59.4%*	73.3%
E4	22.7%	21.7%	17.0%*

\*p < 0.01 *Conclusions.* Apo E2 phenotype is significantly higher and apo E3 lower in PSC than in healthy controls or in PBC. Patients with apo E2 tend to have more cholestatic disease. The effect of apo E phenotype on the treatment response to UDCA is to be determined. Liver and bile ducts, 2: Bile formation, cholestasis }" "Apolipoprotein E Polymorfism in Primary Sclerosing Cholangitis (PSC)"

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"P P 26 0653" P 26 0653 **Antiendomysial and Antigliadin Antibodies in Patients with Autoimmune Liver Diseases**

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<sup>1</sup> Division of Gastroenterology, Mayo Clinic, Rochester, Minnesota, USA Serum antiendomysial (EmA) and antigliadin antibodies (AGA) proved to be reliable markers of coeliac disease (CD). The reported association of CD with autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC) prompted us to perform an antibody screening for gluten sensitive enteropathy in a large series of patients with autoimmune liver disorders. Sera from 181 patients with AIH (157 type 1 – ANA/SMA+ – and 24 type 2 – LKM/LC1+) and 62 with PBC were tested for IgA EmA on human umbilical cord (EmA-HUC) by IFL and for IgG and IgA AGA by ELISA. As control group, sera from 80 patients with HCV chronic hepatitis (CH) (of whom 53 LKM/LC1+) and from 30 with HBV CH were studied. IgA EmA-HUC were positive only in 8 AIH patients (5 females and 1 male with AIH type 1 and 2 females with AIH type 2). IgA AGA were detected in 6 out of the 8 EmA-HUC positive cases, but were also present in other 2 cases of AIH type 2 and in one with HCV CH. IgG AGA were positive in 15% of the 243 patients with autoimmune liver disorders (16 AIH type 1 and 9 type 2 and 11 PBC) and in 13% of the 110 with HCV and HBV CH. It is generally acknowledged that IgA EmA-HUC display a 100% positive predictive value for CD, whereas IgA and especially IgG AGA can be also found in patients without a gluten-induced intestinal damage. The 2 women with AIH type 2, positive for both IgA EmA-HUC and AGA, underwent duodenal biopsy showing a subtotal villous atrophy consistent with the diagnosis of CD. On the basis of these data at least 2 (8.3%) of the 24 patients with AIH type 2 are affected by CD, but we can also presume that the results of duodenal biopsy, which is still in progress, will definitely confirm CD diagnosis in the 6 (3.8%) AIH type 1 cases with IgA EmA-HUC. The high prevalence of IgG AGA in both autoimmune and viral liver diseases is likely to be related to an impaired hepatic clearance of dietary antigens which, passed through the intestinal barrier, evoke an enhanced IgG class antibody synthesis. Therefore, AIH type 1 and 2 can be regarded as a high risk condition for CD and all AIH patients should be screened by means of IgA EmA-HUC and AGA for excluding the coexistence of gluten-sensitive enteropathy. Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption syndromes Liver and bile ducts, 1: Chronic non viral hepatitis } "Antiendomysial and Antigliadin Antibodies in Patients with Autoimmune Liver Diseases"

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"P P 26 0654" P 26 0654 **Hydroxylysylpyridinoline in Bile — A Marker for Primary Sclerosing Cholangitis and Primary Biliary Cirrhosis?**

\*A. Gillessen<sup>1</sup>, Y. Acil<sup>2</sup>, J. Brinckmann<sup>3</sup>, P.K. Møller<sup>2</sup>, W. Domschke<sup>1</sup>

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Hydroxylysylpyridinoline (HP) is a non-reducible cross-link molecule of mature collagen. This degradation product is found in serum and urine and has been evaluated as a marker for the catabolism of collagen fibres mainly from skeletal tissues. Recently a possible value of HP as measured in serum for the assessment of fibrotic liver diseases was described. In primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) fibrogenesis takes place next to the bile ducts. Consequently it was tempting to investigate concentrations of HP in the bile. We analyzed bile samples from 10 patients with PBC (5) or PSC (5) and 10 controls. The bile was obtained free of contrast medium during ERCP examination. The total amount of HP was measured by fluorometry after reversed-phase high-performance liquid chromatography (HPLC) of hydrolyzed bile. Bile of normal controls contained no measurable HP in 9 of 10 cases. fifty-five pmol HP/ml bile were found in one normal patient. HP concentrations in bile of all patients with PBC were measured to be between 34–75 pmol/ml (mean 52.6 pmol/ml). In bile of 4 PSC-patients, HP values between 20–98 pmol/ml (mean 51.25 pmol/ml) were obtained. One patient suffering from mild PSC had no detectable HP concentrations in bile. There was no significant difference between HP concentrations in any of these diseases. Hydroxylysylpyridinoline is only detectable in bile of patients with PBC or PSC, while normal controls have no measurable bile HP content. This clear difference was found in 9 of 10 patients in each group indicating a possible role of this marker for assessment of fibrotic activity in these diseases. Endoscopy, specific: Biliary Liver and bile ducts, 2: Bile formation, cholestasis Liver and bile ducts, 1: Cell biology, collagen, fibrosis } "Hydroxylysylpyridinoline in Bile / A Marker for Primary Sclerosing Cholangitis and Primary Biliary Cirrhosis?"

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"P P 26 0655" P 26 0655 **Clinical Significance of Different Antinuclear Antibody Patterns in the Course of Primary Biliary Cirrhosis**

\*T. Remmel, A. Piirsoo, A. Kõiveer, R. Uibo, V. Salupere

University of Tartu, Estonia *Aims:* The purpose of this study is to investigate the clinical significance of antinuclear antibodies (ANA) in primary biliary cirrhosis (PBC) patients. *Methods:* 69 patients with PBC were investigated. Control groups included 21 patients with autoimmune hepatitis, 26 with alcoholic liver disease, 13 with systemic connective tissue disease and 27 healthy persons. ANA was detected by an immunofluorescence method on rat liver tissue sections and HEp-2 cells at serum dilution 1/40. *Results:* In 48 out of 69 PBC patients (70%) ANA was positive in HEp-2 cell line, but in rat liver tissue sections only 29% of patients had positive ANA reactions. Most frequent patterns were multiple nuclear dots (MND) in 42% and perinuclear in 16%. ANA were found in all five AMA negative PBC cases. AMA negative-ANA-positive (5 patients) and AMA positive PBC patients (64 patients) did not differ in clinical, laboratory and histological features from each other ( $p > 0.05$ ). ANA-negative patients had higher sedimentation rate ( $p < 0.05$ ), more frequently ascites ( $p < 0.05$ ) and variceal haemorrhages ( $p < 0.05$ ), but other clinical and laboratory features were similar ( $p > 0.05$ ). There were no more associated autoimmune diseases in ANA-positive group ( $p > 0.05$ ). Survival from the moment of developing first symptom(s) attributable to liver disease was longer in the ANA positive patients than ANA negative ones ( $p < 0.02$ ). There were no statistically significant differences in histological stages at the beginning of the study and in treatment regime and doses during the course of disease, between ANA-negative and ANA-positive patients group ( $p > 0.05$ ). *Conclusion:* In PBC patient's incidence of ANA, especially MND-ANA is a frequent immunological abnormality. All AMA-negative patients had ANA, but clinical, histological and laboratory features were similar. ANA positive patients have significantly better survival. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Clinical Significance of Different Antinuclear Antibody Patterns in the Course of Primary Biliary Cirrhosis"

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"P P 26 0656" P 26 0656 **High Prevalence of Coeliac Disease among Patients with Primary Biliary Cirrhosis**

\*W. Dickey, S.A. McMillan, M.E.C. Callender

Altnagelvin and Royal Victoria Hospitals, Regional Immunology Laboratory, Belfast City Hospital, Northern Ireland *Introduction:* Many published case reports describe coeliac disease (CD) in association with primary biliary cirrhosis (PBC). However, as CD is common (1:250–300 by screening) the link may be coincidental. We screened our PBC patients for CD to clarify the situation. *Methods:* Sera from patients with PBC (serum antimitochondrial antibodies and typical liver histology) were tested for IgA endomysial antibodies (EmA) by indirect immunofluorescence. No patient studied was taking a gluten-free diet (GFD) or immunosuppression. Patients who had EmA were invited to undergo endoscopic small bowel biopsy. *Results:* We studied 57 patients (52 female), aged 30–79 years (mean 57). Six (11%) had EmA. Four (7%) agreed to undergo small bowel biopsy which showed villous atrophy and inflammatory cells consistent with CD. Three patients were treated with GFD for at least 12 months with no improvement in liver biochemistry. *Conclusions:* The prevalence of CD among patients with PBC is at least 1:14. Although, as reported elsewhere, the liver disease does not respond to GFD, screening for CD is worthwhile. Both conditions are potent risk factors for metabolic bone disease and some of the symptoms reported by individual patients may be gluten sensitive. Intestinal disorders, absorption: Malabsorption syndromes Intestinal disorders, absorption: Gluten enteropathy Liver and bile ducts, 2: Bile formation, cholestasis } "High Prevalence of Coeliac Disease among Patients with Primary Biliary Cirrhosis"

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"P P 26 0657" P 26 0657 **Primary Biliary Cirrhosis (PBC) in Poland: Demography and Survival Model**

\*A. Habor, P. Krzeski, E. Butruk

Department of Gastroenterology, Medical Center for Postgraduate Education, Oncology Center, Warszawa, Poland

The incidence of PBC in Poland is not known. The aim of this study was to analyse the incidence and course of this disease in a representative group of the Polish population.

*Material and methods:* The incidence and prevalence of PBC during the period of 1983–1995 were investigated in four distant provinces of Poland representing 1/5 of the total Polish population. The data were collected by means of mail survey of specialist physicians and a review of clinical records of seven gastroenterology departments located in these provinces. The observed survival of PBC patients was compared with the predicted survival using Mayo model.

*Results:* Over 13-ys period, PBC was diagnosed in 136 patients. No case was diagnosed in a provincial or district hospital. The female: male ratio was 13:1. The familial incidence of PBC was 1.4%. There were only six asymptomatic cases of PBC. The mean annual incidence in four Polish provinces was 1.24/l mln (range: 0.79–1.70). In two urban provinces (Warszawa and Katowice) the incidence of PBC was higher than in predominantly rural provinces of Gdansk and Szczecin. The point of prevalence (Dec. 1995) for the whole analysed group was 10.82/l mln. The Mayo model used for our patients did not correlate with their actual survival. Therefore, we constructed our own model in which the age, serum bilirubin and serum cholesterol were selected for calculation of prognostic index.

*Conclusions:* 1. The incidence and prevalence of PBC in Poland is the lowest ever recorded. 2. The Mayo survival model could not be applied to our patients, an observation which suggests that an individual survival model should be constructed for each population.

*Clinical practice:* Epidemiology (non cancer) Liver and bile ducts, 2: Bile formation, cholestasis }

"Primary Biliary Cirrhosis (PBC) in Poland: Demography and Survival Model"

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"P P 26 0658" P 26 0658 **Anti-Calreticulin Autoantibodies: IgG- and IgM- Subclasses Differentiate between Autoimmune Hepatitis and Primary Biliary Cirrhosis**

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<sup>1</sup> Medical Clinic, D-72076 Tübingen, Germany *Introduction:* Autoantibodies against the multifunctional protein calreticulin (CR) have been detected in systemic lupus erythematosus, Sjögren's syndrome, the congenital heart block, and in alcoholic hepatitis. Recently we demonstrated anti-calreticulin auto-antibodies in primary biliary cirrhosis and autoimmune hepatitis. *Methods:* By a modification of the ELISA we measured IgG- and IgM-subclasses of anti-CR autoantibodies. *Results:* The following OD were obtained in the ELISA (mean – SD): n Total IgG IgM Controls 51 0.25 – 0.10 0.56 – 0.18 0.42 – 0.26 ALC 20 0.34 – 0.13 0.81 – 0.25 0.77 – 0.37 AIH 51 0.75 – 0.25 1.20 – 0.33 0.73 – 0.44 PBC 46 0.50 – 0.22 0.97 – 0.22 1.18 – 0.37 ALC = alcoholic liver cirrhosis AIH = autoimmune hepatitis PBC = primary biliary cirrhosis *Conclusions:* In AIH anti-CR autoantibodies mainly belong to the IgG subclass, whereas in PBC they are of the IgM class. Anti-CR autoantibodies prove to be a helpful new serological marker for the diagnosis and differentiation of autoimmune liver diseases. Liver and bile ducts, 1: Chronic non viral hepatitis Immunology and microbiology: Host defense mechanisms Immunology and microbiology: GI infections in adults } "Anti-Calreticulin Autoantibodies: IgG- and IgM- Subclasses Differentiate between Autoimmune Hepatitis and Primary Biliary Cirrhosis"

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## "P P 26 0660" P 26 0660 Autoantibodies in Chronic Hepatitis. Importance of the Autoimmune Etiology

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University Hospital "Infanta Cristina", Badajoz, Spain  
**Aims:** To investigate the presence of serum autoantibodies (AB) and viral markers in chronic hepatitis (CH) and to evaluate autoimmune etiology in our area.  
**Methods:** 225 patients with CH by histological assessment were evaluated retrospectively. Age, sex, history of alcoholism (in males > 80 g/daily, in females > 60 g/daily), past transfusion, intravenous drug use, liver enzymes, gammaglobulin, immunoglobulins, hepatitis B and C viral markers, antinuclear (ANA), antimitochondrial (AMA), smooth muscle (SMA) and liver/kidney microsomal type 1 (LKM1) antibodies were studied. Anti-HCV was determined by ELISA 2nd-3rd generation in 193 patients (85.78%) and by ELISA-1st generation in the others. HCV-RNA was done in 69 cases. AB were positive at titres 1:40. Scoring System for diagnosis of *Autoimmune Hepatitis (AIH)* defined by *The International Autoimmune Hepatitis Group (IAHG)* was applied in 170 patients.  
**Results:** The mean age of patients was 44.62 – 15.39 years and 148 (65.78%) were male. A history of alcoholism was found in 21.33% of patients, past transfusion in 32.89% and intravenous drug use in 9.33%. There were: 17.33%, HBsAg (+); 74.67%, anti-HCV (+); 1.33%, both markers (+) and 6.67%, neither. In 31.9% (67/210) there was at least one AB (+): ANA, 8.57%; AMA, 1.43%; SMA, 24.29% and LKM1, 1.18% (2/170). Only 7 cases (3.33%) had two AB (+). Titres 1:80 were found in 77.78% of ANA (+), 75.56% of SMA (+) and in 66.67% of AMA (+). Of patients with AB (+), 80.60% were anti-HCV (+); 11.94%, HBsAg (+) and 1.49% had both markers (+), without differences in relation to patients with AB (-). Only one patient (0.59%) had score of *definite* and two (1.18%) of *probable AIH*. In 3 patients (1.76%) score was close to a probable AIH and one of these with LKM1 (+) and RNA-HCV (+) was diagnosed of AIH after a bad response to interferon and a good response to steroids when other autoimmune disease was appeared.  
**Conclusions:** 1) AIH are rare in our area. 2) 95% of CH with AB (+) had positive viral markers, predominantly of HCV (> 80%). 3) Titres 1:80 were found in almost 80% of patients with AB (+). 4) No differences were found between AB (+) and AB (-) and positive and negative viral markers. 4) The criteria defined by IAHG for the diagnosis of AIH are very strict and may exclude cases which behave like AIH. This indicates that better diagnostic criteria of AIH are required. Liver and bile ducts, 1: Chronic non viral hepatitis  
Liver and bile ducts, 1: Hepatitis viral, diagnosis } "Autoantibodies in Chronic Hepatitis. Importance of the Autoimmune Etiology"

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"P P 27 0661" P 27 0661 **Incidence of Viral Replication in Chronic Infection with Hepatitis B Virus in Children**

\*P. Grigorescu-Sido, R. Manasia, C. Lazar, L. Jebeleanu, P. Florescu, C. Skorka

1st Pediatric Clinic, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj, Romania *The purpose of the study* was to ascertain the incidence of the cases with chronic HBV infection in their phase of viral replication in order to select them for interferon treatment. *Patients and methods.* The authors investigated 73 children (3–15 years) with: chronic active and persistent hepatitis (27 and 28 cases respectively); liver cirrhosis (9 cases) and persistent glomerulonephritis associated with HBV infection (9 cases). The diagnosis was made based on: clinical examination, the biochemical functional liver and/or renal tests, ultrasonography and liver and/or renal biopsy. Depending on the duration of the disease 4 groups were delimited: group I (< 1 year), group II (1–3 years), group III (3–5 years) and group IV (> 5 years) In all cases HBsAg, HBcAb, HBeAg and HBeAb were determined using the Elisa enzymatic method. *Results.* The first two markers were present in all cases. HBeAg — a marker of viral replication — was present in 38.3% of the cases showing an incidence dependent on the length of the course of the disease: 85%; 57% and 23% in groups I, II and III and absent in group IV. HBeAb were present in 56.1% of the group, their incidence increasing progressively with the duration of the disease: 10%; 36%; 78% and 100% respectively in the 4 groups; 5.5% of the cases (negative HBeAg, HBeAb) probably presented mutant forms of hepatitis B virus. *Conclusion.* The results obtained indicated spontaneous onset in time of seroconversion. However the persistence of HBsAg — indicating its inclusion in the liver cell genome — pleads for the institution of interferon therapy in all children with chronic HBV infection and with viral replication, from the moment the diagnosis is made. Liver and bile ducts, 1: Liver diseases, children } "Incidence of Viral Replication in Chronic Infection with Hepatitis B Virus in Children"

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"P P 27 0662" P 27 0662 **Autoimmune Phenomena in Children with Chronic HCV Hepatitis**

\*G. Verucchi, M. Lenzi<sup>1</sup>, L. Attard, P. Muratori<sup>1</sup>, S. Diotallevi, R. Miniero<sup>2</sup>, F. Guzzo, F. Bianchi<sup>1</sup>, F. Chiodo

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<sup>1</sup> Internal Medicine, University of Bologna, Italy

<sup>2</sup> Dep. of Clinical Pathology, S. Orsola Hospital, Bologna, Italy *Aim of the study:* to assess the prevalence of non organ (ANA, SMA, anti-LKM1, anti-LC1) and organ specific autoantibodies (anti-thyroid peroxidase and anti-thyroglobulin) in a retrospective series of children with HCV-related chronic hepatitis. *Patients and Methods:* 31 patients (15 males, 16 females) with a median age of 8.9 years (range 2–15) were evaluated. Eighteen patients had received blood or plasma transfusion, 10 were born from anti-HCV positive mothers, one had had major surgery and in two the way of infection was unknown. All patients were anti-HCV and HCV RNA positive, had abnormal ALT values and in 19 liver biopsy showed a picture of chronic hepatitis. Twelve patients were treated with alpha Interferon (3 MU thrice weekly for 12 mo). Sera were tested at a dilution of 1:40 on liver, kidney and stomach cryostat sections and on Hep-2 cell. Anti-LC1 antibody was tested by CIE with rat liver cytosol as source of antigen. Anti-thyroid peroxidase and anti-thyroglobulin antibodies were tested by a commercially available RIA. *Results:* non organ-specific autoantibodies were detected in 9 out of 31 patients (29%). Four had low titre SMA antibodies (13%) with non-actin specificity, 1 had ANA (3%) (speckled pattern), 4 had anti-LKM1 antibodies (13%) (all positive for 50 kD peptide in immunoblotting) and none of the 21 tested had anti-thyroid antibodies. No clinical and biochemical differences were present between autoantibodies positive and negative patients. No specific association was found between HCV genotypes and a particular autoantibody. Four out of the 12 patients who underwent interferon therapy developed low titre autoantibodies (3 SMA, 1 ANA) under treatment. *Conclusions:* these results demonstrate that the overall prevalence of non organ specific autoantibodies associated with HCV-related chronic hepatitis in children is similar to that observed in adults. The autoantibodies specificities typical of autoimmune hepatitis were never observed in these patients. However differently from what observed in adults anti-LKM1 reactivity was more frequently observed than other autoantibodies. Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment } "Autoimmune Phenomena in Children with Chronic HCV Hepatitis"

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"P P 27 0663" P 27 0663 **The Role of Dendritic Cells in the Bile Duct Destruction of Primary Biliary Cirrhosis**

\*T. Tamai, T. Shiro, T. Nakagawa, M. Wakabayashi, M. Imamura, T. Itou, A. Nishimura, T. Seki, K. Inoue, A. Okamura<sup>1</sup>

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*Aim:* Primary biliary cirrhosis (PBC) is an immune-mediated liver disease. Histopathologically, chronic non-suppurative destructive cholangitis (CNSDC) involving small intrahepatic bile ducts is the fundamental lesion in PBC. In this study, we investigated whether interdigitating cells (IDCs) or follicular dendritic cells (FDCs) could act as antigen presenting cells to induce CNSDC in PBC. *Materials and Methods:* The frozen tissues obtained from fifty cases of clinicopathologically confirmed PBC, by needle liver biopsy. Each sections were immunostained using a modification of the avidin-biotin-peroxidase complex method. To recognize dendritic cells was used both of the monoclonal antibodies, against FDCs (Dako) and IDCs (Serotec Ltd.). *Results:* In this study, FDCs were not found in the portal areas with and without lymphoid follicles in PBC. In contrast, IDCs infiltrated around the damaged bile ducts characterized by CNSDC within the portal areas. And IDCs within the portal areas were observed most frequently in the sections showing an earlier stage of the disease. Further some of these IDCs were observed to be in direct contact with the biliary epithelial cells. On the other hand, many of inflammatory cells infiltrated within the portal area were T lymphocytes, and the average number of CD4-positive and CD8-positive T cell subsets was almost even. Furthermore, CD8-positive T cells were found inside the basement membrane between biliary epithelial cells of damaged bile ducts. *Conclusion:* These results suggested that IDCs infiltrated around the bile ducts were considered to played an important role in a immune process induced CNSDC, at the initial stage of PBC. Liver and bile ducts, 1: Chronic non viral hepatitis } "The Role of Dendritic Cells in the Bile Duct Destruction of Primary Biliary Cirrhosis"

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"P P 27 0664" P 27 0664 **Peroxide Oxidation of Lipids and Prostanoids in Pathogenesis of Functional Disorder of Biliary System in Children and Adolescents** L.K. Parkhomenko,

\*L.A. Strashok

Department of Therapy of Adolescents Kharkov Post Graduate Medical Studies Institute, Ukraine At present the study of endogenic biologically active substances — prostanoids and their correlation with the starting mechanism of most pathological processes — by means of free radical oxidation of lipids is one of prospective directions of basic research in medicine. The goal of our research was the study of prostacyclin and thromboxan, general TBA active products of peroxide oxidation of lipids in children and adolescents with prime dyskinesia of biliary system. We have investigated 15 boys and 15 girls (10–18 years old). All the patients underwent thorough anamnestic, physical, endoscopic, ultrasonic, radioisotope, biochemical research with the aim of exclusion of accompanying organic pathology of digestive system. Prostanoids were under study with help of standart radioimmunologic sets of Hungarian Academy of Science Products of free radical oxidation in erythrocytes and plasma were defined with help of thiobarbituric acid test. All the patients regardless of sex had heightened contents of products of peroxide oxidation of lipids: in erythrocytes (14.94 – 1.81 nmol/mg of albumin,  $p < 0.01$ ), in plasma (6.73 – 1.08 nmol/mg of albumin,  $p < 0.01$ ) that testifies to the fact that penetrability of cytomembranes has increased. In boys changes in prostanoid system didn't reach statistically significant quantities. In girls there was revealed decrease of contents of prostacyclin (34.73 – 2.72 pg/ml,  $p < 0.01$ ) and increase of thromboxan level (243.76 – 76.28 pg/ml,  $p < 0.01$ ). There is an intimate relationship between the state of prostacyclin–thromboxan system and intensity of free radical oxidation of lipids that coincides with the data obtained. More clear-cut changes of prostanoids in girls are possibly peculiarity of proceeding of biliary pathology in adolescents and probably they are responsible for more frequent and clear-cut manifestation of biliary disorder exactly in females. Spectrum of changes of peroxide oxidation of lipids and prostanoids during biliary dyskinesia coincides with the one during atherosclerosis, hypertonicity and gallstones disease that probably reflects general biological reaction to a stress. Our results point to expediency of application of antioxidants and membrane stabilizers for functional disorder in biliary system, too. Liver and bile ducts, 2: Gallstones, formation, treatment }" "Peroxide Oxidation of Lipids and Prostanoids in Pathogenesis of Functional Disorder of Biliary System in Children and Adolescents"

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## "P P 27 0665" P 27 0665 Immunological Status of Children with Chronic Hepatitis C

\*T. Wozniakowska-Gesicka, D. Dworniak, J. Kups, M. Wisniewska, L. Bak-Romaniszyn, K. Zeman, I. Planeta-Malecka

Department of Pediatrics Polish Mother's Memorial Hospital, Łódź, Poland

Department of Infectious Diseases and Gastroenterology Military Medical University, Łódź, Poland HCV infection evokes a number of cellular and humoral immunological phenomena. Their effectiveness decides on the virus elimination and protects from chronic forms of HCV. The purpose of the study was the evaluation of immunological system in children with chronic hepatitis C. *Methods:* Investigations were performed in 20 children (8 girls, 12 boys) aged 3–6 years (mean 5.5 years) with anti-HCV antibodies and HCV-RNA in blood serum. ALT activity, total bilirubin level, leucoaggregation test, total complement activity (CH50) and C3, C4 components, T-lymphocytes subsets: CD3, CD4, CD8, CD19, CD4/CD8 ratio, NK cells (CD16), were estimated, moreover, IL-1, IL-2, IL-4 and TNF- $\alpha$  levels were determined. *Results:* ALT activity was increased significantly (185 – 96.65). Leucoggregation test value was decreased statistically insignificantly (2.02 – 0.67%). Total complement activity was statistically significantly decreased (37.63 – 10.14) and so were C3 component (60.11 – 12.55) and lymphocytes subsets: CD3 (60.0 – 6.25) and CD4 (34.25 – 6.78). Percentage of CD8 lymphocytes, NK cells and CD4/CD8 ratio were statistically significantly decreased. Mean IL-1 values showed significant increase (4.48 – 4.17 pg/ml). In 15 from 20 children concentration of IL-2 were below detectability threshold and in 5 from 20 of them TNF- $\alpha$  level was increased. *Conclusions:* The study results point to a potential engagement of the immunological system into processes to chronic hepatitis C. The observed changes may speak for immunological mechanisms defect. Immunology and microbiology: Host defense mechanisms Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Liver diseases, children } "Immunological Status of Children with Chronic Hepatitis C"

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"P P 27 0666" P 27 0666 **Cholelithiasis in Children: Clinical Analysis and Results of Bile Acids Therapy** F. Iwanczak,

\*A. Stawarski, B. Iwanczak

II Clinics of Pediatrics and Gastroenterology, Medical University, Wrocław, Poland The purpose of our study was clinical analysis of 24 children aged from 10 months to 16 years with gallbladder stones and 3 children aged 3, 5–12 years with choledochal stones. Next we analysed results of bile acids therapy in 15 children treated with ursodeoxycholic and/or chenodeoxycholic acids. In all children health and family history were collected, physical examination, biochemical tests (aminotransferase and alkaline phosphatase activity, cholesterol and bilirubin concentration in blood serum), ultrasonography and postprandial gallbladder emptying were done. Children with mild clinical symptoms, with cholesterol radiolucent stones no bigger than 20 mm in diameter, with normal anatomy and motility of the gallbladder and without inborn errors of the lipid metabolism were qualified to the therapy. Bile acids were administered in a daily dose of 10–15 mg/kg body weight twice a day or just once in the evening. The therapy lasted from 2 to 12 months. During therapy children were controlled every other month. In 20% of patients no symptoms were observed in the course of the disease. The following symptoms were observed for the remaining group of patients: abdominal pain (85%), nausea (78%), vomiting (64%), meteorism and constipation (50%). The symptoms of the disease were observed for a period from 1 month to 8 years. After bile acids therapy in 6 children gallbladder stones dissolved, in 7 patients stones did not dissolve. However, complete or partial recovery of clinical symptoms was observed and higher values for the activity of aminotransferase and the concentration of serum bilirubin were back to normal. Bile acids were well tolerated. Our own experience confirms good therapeutic effects of bile acids in children with gallstones. Therapeutic results depend on the appropriate selection of patients. Liver and bile ducts, 2: Gallstones, formation, treatment } "Cholelithiasis in Children: Clinical Analysis and Results of Bile Acids Therapy"

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"P P 27 0667" P 27 0667 **Long-Term Follow-Up of Low Dose Versus High Dose Ursodeoxycholic Acid (UDCA) in Cholestasis Related to Cystic Fibrosis (CF)**

\*P.C. Van de Meeberg, G.P. VanBerge Henegouwen, Dutch CF-UDCA trial group

Department of Gastroenterology, University Hospital Utrecht, The Netherlands UDCA improves liver biochemistry in CF related cholestasis. Since bile salt malabsorption may complicate the disease, high dose UDCA has been recommended. We studied the long-term biochemical response during low dose and high dose UDCA. CF patients with cholestasis (GGT > 150% normal), aged > 5 yrs were randomized for low dose (10 mg/kg/day, n = 16, 18.3 – 2.0 yrs, M/F = 11/5) or high dose (20 mg/kg/day, n = 15, 18.5 – 2.7 yrs, M/F = 11/4) UDCA. In both groups 1 patient was classified as child B, all others as Child A. Improvement of biochemical parameters was evaluated after 3 (n = 31) and 12 months (n = 21: 12 low dose, 9 high dose). Liver enzymes were comparable between groups at base-line, whereas the majority of patients had a normal bilirubin level. In both groups, 1 patient dropped out because of severe pruritus. One patient (low dose) died from liver failure, 7 patients have not yet completed 12 months follow-up.

*Results:* Decrease from base-line (mean – SEM) 3 months 12 months 10 mg/kg 20 mg/kg 10 mg/kg 20 mg/kg APh\* 38.6 – 9.7 42.9 – 7.0 39.1 – 8.4 44.5 – 8.7 GGT 50.3 – 5.0 68.4 – 4.1<sup>186</sup> 54.7 – 4.5 69.8 – 6.8<sup>186</sup> AST 25.5 – 5.8 33.8 – 6.5 35.5 – 8.3 36.1 – 7.5 ALT 41.1 – 7.1 46.2 – 9.0 48.1 – 6.2 45.7 – 17.7\* APh: only patients older than 18 yrs included. <sup>186</sup>p < 0.02 (high dose vs low dose, Mann-Whitney-U test). *Conclusion:* During long-term treatment liver enzymes improve slightly better with high dose UDCA in CF-related cholestasis. Liver and bile ducts, 2: Bile formation, cholestasis Liver and bile ducts, 1: Liver diseases, children } "Long-Term Follow-Up of Low Dose Versus High Dose Ursodeoxycholic Acid (UDCA) in Cholestasis Related to Cystic Fibrosis (CF)"

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## "P P 27 0668" P 27 0668 Polyunsaturated Fatty Acid Status of Cholestatic Infants in a Longitudinal Study

\*P. Socha, B. Koletzko, J. Pawlowska, E. Swiatkowska, A. Stolarczyk, J. Socha

Child Health Centre, Warsaw, Poland

Kinderpoliklinik, L-M University, Munich, Germany No information is available on the development of polyunsaturated fatty acid (PUFA) status in children with cholestasis with increasing age. Therefore, we performed a long term follow up study in 28 infants (initial age 2.15 – 0.98 months, mean – SD) with cholestasis (12 extrahepatic and 16 intrahepatic). We determined fatty acid composition of plasma phospholipids [% wt/wt] at baseline and then twice at random time intervals (about 1.7 mon.): at the age of 3.8 – 1.8 mon. in all infants and at the age of 5.6 – 1.5 mon. in a subgroup of 14 patients. The total bilirubin levels decreased during the course of the disease: from 10.6 – 4.4 to 6.1 – 4.8 at the 1st control ( $P < 0.001$ ) and to 5.3 – 5.4 at the 2nd control ( $P < 0.05$ ). Compared to the fatty acid profile of 12 age matched controls, low levels of PUFA were detected in cholestatic patients already at the beginning of the study (29.2 vs. 37.2 in controls,  $P < 0.001$ ). Changes of linoleic acid (LA, 18: 2{ w}-6),  $\alpha$ -linoleic acid (ALA, 18: 3{ w}-3), ratios arachidonic acid (AA, 20: 4{ w}-6)/LA and docosahexaenoic acid (DHA, 22: 6{ w}-3)/ALA during the study are shown in the table (values expressed as means):

Baseline	Mean age 3.8	Baseline	Mean age 5.6	(N = 28)	(N = 28)	(N = 14)	(N = 14)		
LA	14.6	16.9, $P < 0.05$ .	13.2	17.2, $P < 0.05$	ALA	0.11	0.17, $P < 0.01$	0.12	0.23, $P < 0.05$
AA/LA	0.6	0.5, n.s.	0.61	0.40, $P < 0.05$	DHA/ALA	22.9	11.6, $P < 0.01$	18.0	9.6, $P < 0.05$

AA, DHA and PUFA content did not change significantly during the study. *Conclusions:* 1. Cholestatic infants have a high risk of essential fatty acid deficiency. 2. ALA and LA levels increase during the course of the disease which can be explained by therapeutic intervention with improved bile flow and reduced bilirubin levels. 3. Hepatic conversion of LA and ALA to AA and DHA, respectively, seems to be increasingly impaired with progressive liver dysfunction. Liver and bile ducts, 1: Liver diseases, children Nutrition: Nutrition: children Liver and bile ducts, 2: Bile formation, cholestasis } "Polyunsaturated Fatty Acid Status of Cholestatic Infants in a Longitudinal Study"

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"P P 27 0669" P 27 0669 **High Infection Rate with Hepatitis E Virus among Young Children** Rakesh Aggarwal, Hansa Shahi, Sita Naik, S.K. Yachha,

\*S.R. Naik

Departments of Gastroenterology and Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226 014, India *Objective:* Hepatitis E virus (HEV) infection is common in India. However the frequency of HEV infection among healthy adults and children in different age groups is not known. Such information is necessary to better understand the epidemiology of HEV infection in endemic areas. *Methods:* Sera from 20 healthy adults and 75 children in different age groups were tested for IgG anti-HEV antibodies using an enzyme immunoassay (Abbott Laboratories). *Results:* Age (yr) n Anti-HEV +ve Anti-HEV { - }ve %  
+ve 0-5 28 18 10 64% 6-10 22 13 9 59% 11-18 25 16 9 64% Adults 20 10 10 50% *Conclusions:* Our data show that IgG anti-HEV antibodies were present in 64% of children in the 0-5 year age group and that their prevalence did not increase with age even upto adulthood. These prevalence rates are higher than those in other geographic areas. No such data have been reported from other endemic areas. Thus our data suggest that in endemic areas, HEV infection is common in children and occurs quite early in life. Occurrence of large epidemics despite frequent exposure in childhood may suggest that infection in early childhood may not provide lifelong immunity as occurs with hepatitis A. *Clinical practice:* Epidemiology (non cancer) Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Liver diseases, children } "High Infection Rate with Hepatitis E Virus among Young Children"

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"P P 27 0670" P 27 0670 **Serum Insulin-Like Growth Factor II in Children with Chronic Liver Diseases** A. Abdalla, F. El-Shennawy, A. Shaltout, H. Shafeik

Paediatric Gastroenterology Unit and Clinical Pathology Department, Mansoura University, Mansoura, Egypt *Aims:* our aims were to assess the serum levels of insulin-like growth factor II (IGF-II) in children with chronic liver diseases and to find if there is any correlation between such levels and clinical, laboratory and pathological parameters. *Methods:* 28 patients and 15 controls were the material of this study. Patients were classified histopathologically into: group I (15 cases with liver cirrhosis) and group II (13 cases with chronic active hepatitis, CAH). Serum IGF-II was measured in all patients and controls using immunoradiometric assay. *Results:* Serum levels of IGF-II was found to be significantly decreased in children with chronic liver diseases compared to controls (group I Vs control,  $P < 0.05$  and group II Vs control  $P < 0.05$ ). However, no significant difference was found between cirrhotic and CAH cases ( $P > 0.05$ ). No significant correlation was found between serum levels of IGF II and clinical, laboratory or pathological features of children with chronic liver diseases. Cirrhotics and CAH cases could be correctly classified (100%), according to discriminating functional analysis utilising some of the clinical and laboratory variables assessed. *Conclusions:* serum IGF-II levels was found to be decreased significantly in children with chronic liver diseases. However, no significant correlation was found between serum IGF-II levels and clinical, laboratory or pathological feature of those children. Liver and bile ducts, 1: Cell biology, collagen, fibrosis Liver and bile ducts, 1: Liver diseases, children } "Serum Insulin-Like Growth Factor II in Children with Chronic Liver Diseases"

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**"P P 28 0679" P 28 0679 Study of the Role of Direct Intra-Variceal Pressure Measurement in Prediction of Variceal Bleeding S. Sheir Baddar,**

\*M. Osman, S. Shalaby, T. Zaki

Internal Medicine Department, Ain Shams University, Cairo, Egypt This study included fifty patients with portal hypertension and oesophageal varices, proved by clinical examination, ultrasonography, and laboratory investigations. There were 28 patients with history of upper gastrointestinal bleeding (bleeders) and 22 patients non-bleeders. According to Child's classification, there were 22 patients of Child A, 11 patients of Child B and 17 patients of Child C. Intra-oesophageal variceal pressure (IOVP) was measured for all patients and it was found to be significantly higher in bleeders than non-bleeders and IOVP  $>/18$  mmHg was found to be ""risk value"" for predicting variceal bleeding. IOVP was found to be significantly higher in patients with large varices (3rd-degree) than those patients with 2nd-degree varices and in 80.7% in those with 3rd- degree varices. IOVP was found to be significantly higher in patients with endoscopic red color sign and in Child C than Child B and A. Serum bilirubin was significantly higher in bleeders than non-bleeders and there was significant correlation between serum bilirubin and IOVP. Serum albumin, prothrombin time, platelet count and ascites were not significantly correlated to IOVP or variceal bleeding. The congestion index of the portal vein (measured by Color Doppler) was significantly correlated with IOVP. We concluded that IOVP is considered a very reliable and accurate parameter in predicting variceal bleeding in portal hypertensive patients. } "Study of the Role of Direct Intra-Variceal Pressure Measurement in Prediction of Variceal Bleeding"

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"P P 28 0681" P 28 0681 **Hemodynamic Changes in Intrahepatic Portal Vessels after Percutaneous Ethanol Injection of Hepatocellular Carcinoma under General Anesthesia**

\*L. Tarantino, A. Giorgio, G. de Stefano, A. Perrotta, V. Aloisio, F. Esposito

US Department, D. Cotugno Hospital, Naples, Italy *Background:* Thrombosis of intrahepatic portal vessels (IPV) and ischemic necrosis of liver parenchyma after Percutaneous ethanol injection (PEI) of Hepatocellular Carcinoma (HCC) have been reported. We evaluated intrahepatic hemodynamic changes in HCC patients treated with PEI. *Patients and methods:* From January to April 1996, 35 patients (21 male; age 49–80) with 62 HCC nodules underwent 42 sessions of PEI under general anesthesia (u.g.a). Amount of ethanol injected per session ranged 7–55 ml (mean: 29 ml). A baseline echo-color-doppler the day before treatment and a control examination within 6–10 days after the treatment were performed on all fasting patients and in supine position. Patency and blood flow direction were evaluated in main, right and left portal vein, in segmental portal vessels and in hepatic veins. *Results: Baseline echo-doppler examination* showed: absence of thrombosis in all patients; hepatopetal flow in IPV in 33/35 patients; reverse flow in the segmental portal branch related to the segment where the tumor was located (VII and VI respectively) in 2/35 (5.7%) patients; patency of paraumbilical vein with hepatofugal flow in 3/35 (8.5%) patients; continuous flow in hepatic veins in 28/35 (80%) patients and triphasic flow pattern in 7. *The post-treatment echo-color-doppler* showed: partial non neoplastic thrombosis (proved by fine needle biopsy) of right portal vein in one patient; reverse flow in the segmental portal branch related to the segment where the treated tumor was located in 5/35 (14.3%; 3 more than before PEI treatment) in one case there was clear evidence of periferic artero-portal shunt at echo-color-doppler. In another patient (who received 40 ml ethanol and had already been treated with 70 ml ethanol 35 days before) echo-color doppler showed reverse flow in right portal vein, in all portal vessels of the right lobe and in segmental portal vessels of the left lobe together with hepatopetal flow in main portal vein and in left portal vein which drained in a large patent paraumbilical vein with hepatofugal flow; this last patient started showing a severe liver failure 5–10 days after the treatment and died one month later. In the other patients echo-color-doppler did not show any change in hepatic vein flow and in portal vessels. *Conclusions:* PEI of HCC can cause reverse flow in intrahepatic portal vessels probably due to diffuse thrombosis of the thin intralobular vessels or periferic portal vessels. Moreover, already pre-existing peritumoral and/or intrahepatic (cirrhosis-related) artero-portal shunts can play a role. Liver and bile ducts, 1: Cirrhosis: portal hypertension Oncology, specific: Liver, biliary Radiology and ultrasound: Therapy } "Hemodynamic Changes in Intrahepatic Portal Vessels after Percutaneous Ethanol Injection of Hepatocellular Carcinoma under General Anesthesia"

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"P P 28 0682" P 28 0682 **Changes of Portal Hemodynamics in Patients with Liver Cirrhosis**

\*T. Nakajima, H. Yoshioka, K. Ohnishi, K. Fujiwara, M. Nakajima<sup>1</sup>

The Third Department of Internal Medicine, Saitama Medical School, Moroyama, Japan

<sup>1</sup> Department of Clinical Laboratory, Saitama Medical School, Moroyama, Japan We evaluated at regular interval changes in portal hemodynamics by Doppler's methods in patients with liver cirrhosis. The subjects consisted of 45 patients with liver cirrhosis in whom portal blood flow was could by Doppler's methods for 5 years. None of them had bleeding of esophageal varices, operation of the abdomen and treatment of portal hypertension. Blood flow was measured in the main portal vein (MPV), left branch (LPV) and right branch (RPV) at 12-month intervals. At each site, mean velocity, cross section area (CSA) and flow volume were measured. The CSA in the MPV was  $1.03 - 0.32 \text{ cm}^2$  at the beginning of observation but significantly increased to  $1.11 - 0.30$  after 2 years ( $p < 0.05$ ). The velocity in the MPV was  $15.8 - 4.4 \text{ cm/sec}$  at the beginning but significantly decreased to  $14.9 - 4.4$  after 1 year ( $p < 0.05$ ). The flow volume in the MPV was  $931 - 265 \text{ ml/min}$  at the beginning but significantly decreased to  $899 - 187$  after 1 year ( $p < 0.05$ ) with significantly changes in the subsequent year ( $p < 0.01$ ). Similar findings were obtained at the other sites in terms of CSA, velocity and flow volume. The patients with liver cirrhosis showed an increase in the CSA, a decrease in the velocity and a decrease in the flow volume of portal system with the course. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis } "Changes of Portal Hemodynamics in Patients with Liver Cirrhosis"

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"P P 28 0683" P 28 0683 **The Impact of Spironolactone on Portal Vein Pressure and Portal-Systemic Shunt in Cirrhotic Dogs Induced by Common Bile Duct Ligation**

\*J.Y. Wang, X.F. Lin, F.Z. Chen, X.F. Chen

Shanghai Medical University, Shanghai, China *Aim:* The impact of spironolactone on portal vein pressure and portal-systemic shunting were assessed in cirrhotic dogs induced by common bile duct ligation in order to investigate the effects of this drug on reducing portal hypertension and its mechanism. *Material and Methods:* 20 dogs were studied. Eight weeks after common bile duct ligation, blood sample was collected for testing plasma renin activity (PRA), plasma concentration of aldosterone, and AT-II. A cannula was inserted through mesenteric vein into portal vein to measure portal vein pressure. After injection of Indocyanine green (ICG) (0.6–0.8 mg/kg) into femoral vein, blood sample was collected in 5, 8, 11, 14, 17 sec. from femoral artery and hepatic vein to measure the ICG concentration and calculate extraction rate (ER), intrinsic clearance estimated hepatic blood flow (EHBF) and plasma volume (PV). Heart to Liver ratio (H/L) was tested by using <sup>99m</sup>Tc-MIBI per rectum to estimate the degree of portal-systemic shunt. After administration of spironolactone for 4 weeks (2 mg/kg/day), the above studies were repeatedly performed. *Results:* After eight weeks ligation, cirrhosis developed and confirmed pathologically. The portal vein pressure was 0.1368 – 0.37, 2.587 – 0.51 and 2.42 – 0.47 Kpa respectively before ligation, 8 weeks after ligation and 4 weeks after given spironolactone. H/L was decreased from 0.33 – 0.06 to 0.30 – 0.08, while the liver experienced a progressively pathological change. There was a significant reduction in plasma volume (from 569 ml to 549 ml), but no remarkable change in EHBF. The PRA and aldosterone level elevated. *Conclusion:* The results suggest that chronic administration of spironolactone could reduce portal vein pressure, relief portal-systemic shunt. It is effective in treating portal hypertension. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "The Impact of Spironolactone on Portal Vein Pressure and Portal-Systemic Shunt in Cirrhotic Dogs Induced by Common Bile Duct Ligation"

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## "P P 28 0684" P 28 0684 **Reverse Flow in Intrahepatic Portal Vessels and Liver Function Impairment in Cirrhosis**

\*L. Tarantino, A. Giorgio, G. de Stefano, N. Mariniello, A. Perrotta, V. Aloisio, F. Esposito

US Department, D. Cotugno Hospital, Naples, Italy Prevalence of Reverse Flow (RF) in extrahepatic portal vessels has been reported in 8.3% of cirrhotic patients and a significant correlation has been found with Child class. Few reports have been published about RF in intrahepatic portal vessels (IPV). We evaluated the prevalence of RF in IPV patients with different chronic liver diseases and its correlation with Child class and short term survival. *Patients and methods:* 45 patients with chronic active hepatitis (ECA) (17–56 years; 30 males) and 134 cirrhotic patients (26–72 years; 109 males) underwent Echo-Color-Doppler for evaluation of flow direction in segmental IPV, right and left portal vein (RPV, LPV) portal vein (PV), splenic vein (SV), superior Mesenteric Vein (SMV) and porto-systemic shunts (paraumbilical, spleno-renal, left gastric vein). Patients with hepatocellular carcinoma and complete thrombosis of portal vein were excluded. All patients were followed-up for 3–8 months. *Results:* ECA: hepatopetal flow in all portal vessels without portosystemic shunts in 44/45 patients. 1/45 (2.3%) showed RF in the SV with spontaneous spleno-renal anastomosis. Cirrhosis: 1) 111/134 (82.8%) cases (32 Child A, 59 Child B, 20 Child C) showed hepatopetal flow in all portal vessels. 9/111 (8.1%) showed a patent paraumbilical vein with hepatofugal flow. 2) 9/134 (6.7%) patients (2 Child A, 6 Child B, 1 Child C) showed RF only in the SV together with spleno-renal anastomosis. 3) 2/134 patients (1 Child B, 1 Child C) showed alternating ("back and forth") flow only in IPV, RPV and LPV with continuous hepatopetal flow in PV. 4) 9/134 (6.7%) showed RF in IPV (3 Child B, 4 Child C): in 4 cases RF was limited to LPV and related segmental portal vessels or to 1–2 segmental portal vessels together with hepatopetal flow in PV; the other 5 patients showed RF in all IPV and in main PV associated with hepatofugal flow through a large left gastric vein and large esophageal varices in 2 cases and through the splenic vein with spleno-renal anastomosis in 3 cases. In no case RF in SMV were observed. 3/9 (33%) patients died for liver failure in group 4 (all Child C) and 1/111 (0.9%) patient died for rupture of esophageal varices in group 1 within 2, 4, 4 and 4 months respectively ( $p < 0.001$ ). Prevalence of RF in 1 or more portal vessels in Child C patients (8/29: 27.5%) were significantly higher than in Child B patients (9/67: 13.5%) and in Child A patients (2/34: 6%) ( $p < 0.02$ ). Prevalence of RF only in IPV was significantly different between Child B patients (4/61: 6.5%) and Child C patients (7/28: 25%) ( $p < 0.05$ ). *Conclusions:* RF in IPV is a late event in cirrhosis with advanced liver function impairment and often indicates a poor prognosis. RF only in extrahepatic portal vessels can be observed in well compensated cirrhotic patients and also in non cirrhotic patients. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Chronic non viral hepatitis Radiology and ultrasound: Diagnosis } "Reverse Flow in Intrahepatic Portal Vessels and Liver Function Impairment in Cirrhosis"

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## "P P 28 0685" P 28 0685 "Congestion Index" of the Portal Vein Determined in Patients with Different Stages of Chronic Liver Disease

\*M. Trajkovska, V. Serafimoski, M. Neshkovski, M. Miloshevski, D. Trajanovski, D. Orovchanec, V. Chalovska

Clinic of Gastroenterohepatology, Medical Faculty, Skopje, Republic of Macedonia To evaluate the portal blood flow in different stages of chronic liver disease, we used the "congestion index" – CI. Congestion index is used to determine the ratio between the cross-sectional area (cm<sup>2</sup>) and the blood flow velocity (cm/sec) of the portal vein, detected by Duplex-Doppler system. We studied a portal blood flow of 34 pts with liver cirrhosis (LC), 11 pts with chronic active hepatitis (CAH), 7 pts with chronic persistent hepatitis (CPH) and in 21 healthy normal volunteers (HV). The cross sectional area (CSA) of the portal vein in pts was as follows: LC 1.09 – 0.40, CAH 1.03 – 0.44, CPH 0.98 – 0.42 and in HV 0.71 – 0.19. There was a statistically significant difference between the CSA of the control group, and the CSA of the pts with LC ( $p < 0.005$ ) and pts with CAH ( $p < 0.005$ ). Mean blood flow velocity was as follows: 10.67 – 3.17 in pts with LC, 11.88 – 4.44 in pts with CAH, 13.9 – 3.51 in pts with CPH and 21.26 – 5.12 in HV. There was a statistically significant difference between the mean blood flow velocity of the control group and the pts with LC ( $p < 0.005$ ), pts with CAH ( $p < 0.005$ ) and pts with CPH ( $p < 0.005$ ). The CI was as follows: 0.132 – 0.145 cm<sup>4</sup> sec in pts with LC, 0.104 – 0.075 cm<sup>4</sup> sec in pts with CAH, 0.073 – 0.031 cm<sup>4</sup> sec in pts with CPH and 0.030 – 0.01 cm<sup>4</sup> sec in HV. There was a statistically significant difference between the CI from the normal subjects and the indices obtained from patients with CPH, CAH and LC. Our results showed that the "congestion index" is very sensitive in detecting the changes of the portal blood flow in terms of pathophysiological haemodynamics in pts with different stages of chronic liver disease. Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy Liver and bile ducts, 1: Hepatitis viral, diagnosis } " "Congestion Index" of the Portal Vein Determined in Patients with Different Stages of Chronic Liver Disease"

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"P P 28 0686" P 28 0686 **Monitoring of Hepatic Hemodynamics by Pulsed Doppler in Hepatic-Portoentero-Stomied Children for Biliary Atresia** M. Sugai, R. Hada, M. Endoh, H. Kobori, D. Seito, Y. Toyoki, M. Konn

Department of Surgery, Hirosaki University School of Medicine, Hirosaki, Japan *Aim:* To examine the hepatic hemodynamics in hepatic-portoenterostomied biliary atresia (BA) patients to predict the prognosis. *Methods:* The patients consisted of 5 boys and 5 girls who had undergone either Kasai original or Suruga-II hepatic portoenterostomy at the age of 36 to 81 day. Age- and gender-matched children without hepatobiliary diseases were served as normal controls. At a fasted condition, flow velocity and Doppler wave form in the right hepatic vein, portal venous trunk and splenic vein were determined with a duplex Doppler equipment (TOSHIBA-270A) with a 3.75 MHz transducer (convex or sector). *Results:* Wave forms were classified according to follows: *type 1*, pulsatile flow with reversed phase; *type 2*, pulsatile flow without reversed phase; and *type 3*, continuous flow with/without fluttering. The mean portal venous flow velocity was 16.6 – 3.7 for the patients versus 19.4 – 4.4 cm/s for the controls. The portal venous flow was hepatofugal with *type 3* wave form in all patients, while it was hepatofugal but with *type 1* wave form in the controls. The mean hepatic venous flow velocity was 17.7 – 2.9 for the patients versus 22.7 – 6.7 cm/s for the controls ( $p < 0.01$ ). The hepatic venous flow was hepatofugal in all patients and the wave forms recorded were *type 3* for 4 patients (2/4 with a minimal fluttering) and *type 1* or 2 for 6 patients. Of the 4 patients with *type 3* hepatic venous wave form, 2 had portal hypertension featured with hepatomegaly, splenomegaly and hypersplenism. The splenic venous flow velocity determined in 4 patients, in whom the vein was dilated to more than 10 mm in diameter, ranged from 12 to 13 cm/s. *Discussion and Conclusion:* Flow velocity in the portal or right hepatic vein slightly decreased in the postoperative patients with BA. The direction of flow was hepatofugal in both veins. Wave form of right hepatic venous flow may be of a clinical importance in estimating the hepatic parenchymal condition for *type 3* wave form (continuous flow pattern with a minimal fluttering) indicating decreased compliance of the vein was registered in 2 of 4 patients with portal hypertension. Duplex Doppler can be a non-invasive method to estimate hepatic hemodynamics in the follow-up of postoperative patients with BA. Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 2: Biliary cysts, atresia: children Radiology and ultrasound: Diagnosis } "Monitoring of Hepatic Hemodynamics by Pulsed Doppler in Hepatic-Portoentero-Stomied Children for Biliary Atresia"

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"P P 28 0687" P 28 0687 **Expression and Distribution of Nitric Oxide Synthase in Patients with Portal Hypertensive Gastropathy (PHG)**

\*K.B. Hahm, K.J. Lee, Y.S. Moon, Y.S. Kim, H.K. Kang, J.H. Kim, S.W. Cho

Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea Nitric oxide (NO) is associated with hyperdynamic circulation and development of collaterals in portal hypertension. However, still controversies exist in the involvement of NOS in the pathogenesis of PHG. The distribution and expression of NO synthase (NOS) have not been explored in detail in patients with portal hypertension. The aim of this study was to investigate whether NOS is activated in the PHG. The subjects composed of 19 patients, admitted due to complications of PHG; hematemesis or melena, and 19 normal controls showing normal looking gastric mucosa at endoscopy (*H. pylori* (-)). Obtaining 4–5 pieces of mucosal biopsied tissues, cNOS and iNOS activities were measured by measuring the conversion of <sup>14</sup>C-arginine to <sup>14</sup>C-citrulline, respectively. Western blotting and immunohistochemical staining were performed using antibody, eNOS and iNOS from Affinity Bioreagent Co. (1:250, 1:500 dilutions). MPO activities were measured according to the method by Bradley. The cNOS activities were significantly elevated as compared to those of normal controls (0.98 – 0.14 vs. 0.12 – 0.02,  $P < 0.01$ ). However, iNOS activities were not differed each other between PHG and normal controls. MPO activities were significantly elevated in PHG than normal controls (0.06 – 0.03 vs. 0.018 – 0.009,  $P < 0.001$ ). The cNOS activities were correlated with Child classification grade and total bilirubin levels. In 80% of the PHG, strong cNOS staining was noted in the endothelium of congested, dilated lamina propria capillaries and gastric glands, whereas positive iNOS staining was observed in only 20% of PHG. The results of immunostaining were correlated with the results of western blottings. In conclusion, NOS didn't show causative role in the development of PHG in portal hypertension. Increased cNOS activities and expressions seemed to be the consequence of shear forces of portal hyperdynamic circulation. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Expression and Distribution of Nitric Oxide Synthase in Patients with Portal Hypertensive Gastropathy (PHG)"

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## "P P 28 0688" P 28 0688 Evaluation of Haemodynamic Parameters of Portal Vein as Indicators of Portal Hypertension — An Echo Doppler Study

\*O. Chira<sup>1</sup>, R. Badea, A. Ban, A.S. Chira

<sup>1</sup> Inst of Hyg&Public Hlth, Hlth Serv and Management, 3<sup>rd</sup> Medical Clinic, Cluj, Romania Over the past few years special attention has been paid to the haemodynamic parameters of the portal vein in the assessment of portal hypertension. The aim of this study was to evaluate the maximum velocity in the portal vein and the congestion index of the portal vein, recorded by duplex-doppler ultrasonography, in patients with various degrees of liver fibrosis. In 75 patients with liver disease who underwent liver biopsy, the cross sectional area, mean and maximum velocity in the portal vein were recorded with Toshiba Sal 140. The congestion index of the portal vein was calculated (CI = cross sectional area/mean velocity). Based on a semiquantitative evaluation of hepatic fibrosis according to Knodell's scoring system, we divided the patients into two groups: one with mild fibrosis (grade 1) and another with severe fibrosis (grade 3–4). We compared the above mentioned haemodynamic parameters in these two groups. The patients with extensive fibrosis: grade 4 (cirrhosis) had the maximum velocity in the portal vein which was significantly lower than patients with mild fibrosis (16.7 – 3.5 cm/s vs 25.7 – 7 cm/s; p = 0.001) and the congestion index of the portal vein was significantly higher (0.08 – 0.02 cm<sup>4</sup> s vs 0.03 – 0.01 cm<sup>4</sup> s; p = 0.001). When we compared patients with grade 1 fibrosis to those with grade 3 (bridging fibrosis) the difference remained statistically significant: 25.7 – 7 cm/s vs 18.6 – 3.7 cm/s; p = 0.001 for maximum velocity and 0.03 – 0.01 cm<sup>4</sup> s vs 0.06 – 0.02 cm<sup>4</sup> s; p = 0.001 for congestion index of the portal vein. We think that this haemodynamic parameters of portal vein could be good predictors for extensive fibrosis. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis } "Evaluation of Haemodynamic Parameters of Portal Vein as Indicators of Portal Hypertension / An Echo Doppler Study"

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## "P P 28 0690" P 28 0690 Postprandial Portal and Splenic Flow is Related to the Severity of Portal Hypertension in Chronic Liver Disease

\*D. Ludwig, C.M. Korbel, B. Schiefer, K. Schwarting, E.F. Stange

Dept. of Medicine I, University of L'fbeck, Germany  
The purpose of this study was to determine if the combined analysis of portal and splenic flow in the postprandial state is related to the severity of portal hypertension in cirrhotic patients. In 113 patients with chronic liver disease portal and splenic flow were measured by Dopplersonography. Flow and cross-sectional area were assessed before and 30 minutes after a standardized liquid meal (Fresubin 5 ml/kgbw). Measurements were compared to parameters reflecting the severity of liver disease (Child-Pugh-Score) and portal hypertension (esophageal varices (EV), stigmata of bleeding (BS), portal hypertensive gastropathy (PHG)). Healthy volunteers (n = 12) and patients without liver disease (n = 8) served as controls. Baseline portal (BPF) and splenic (BSF) flow were equal in the control group (BPF 13.8 – 4.2 cm/s, BSF 13.8 – 3.4 m/s). The postprandial increase of portal flow (PIPF) exceeded the increase of splenic flow (PISF) significantly (PIPF 1.65 – 0.29, PISF 1.15 – 0.2; p < 0.05). BPF was lower in cirrhotic patients but not significantly different compared to the control group. In most patients with esophageal varices (82.5% with I–II, 100% with III) BSF exceeded BPF whereas in 90% of controls BSF was lower than BPF. PIPF was inversely related to the severity of liver disease (Child's score, p < 0.002) and portal hypertension (esophageal varices, p < 0.02; bleeding vs. non-bleeding, p < 0.0005; PHG, p < 0.002). In contrast to the controls, postprandial splenic flow decreased in most cirrhotic patients. The maximal reduction of splenic flow was observed in severe cirrhosis (Child C, p < 0.005; EV III, p < 0.005; severe PHG, p < 0.001). Patients with chronic liver disease and a splenic flow exceeding portal flow have a high prevalence (> 80%) of esophageal varices. The postprandial increase in portal flow is related negatively, the decrease in splenic flow positively to the severity of liver cirrhosis and portal hypertension. Liver and bile ducts, 1: Cirrhosis: portal hypertension  
Radiology and ultrasound: Diagnosis } "Postprandial Portal and Splenic Flow is Related to the Severity of Portal Hypertension in Chronic Liver Disease"

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"P P 28 0691" P 28 0691 **Hemodynamic Alterations in Decompensation of Liver Cirrhosis and Portal Hypertension** K. Boulanov

Institute of Clinical and Experimental Surgery, Kiev, Ukraine Alterations in splanchnic hemodynamics play key role in the natural course of liver cirrhosis and portal hypertension. The aim of the study was to evaluate results of serial determination of hemodynamics in 90 cirrhotic patients subjected to surgical treatment. Measurements were performed using duplex system, dynamic scintigraphy, venous phase of superior arteriomesentericography and direct portomanometry and included the following parameters: splenic arterial flow (SAF), splenic venous flow (SVF), portal venous flow (PVF), hepatic arterial flow (HAF), portal congestive index (PCI), hepatoportal index (HPI), degree of portal perfusion (DPP), portal pressure (PP). Results given in the table are means. Normal Child A Child B Child CN 30 30 30 30 SAF ml/min 189.5 349.8\* 283.8\*# 232.3# SVF ml/min 206.2 949.0\* 616.8\*# 595.0\*# PVF ml/min 916.8 883.3 542.2\*# 459.0\*# HAF ml/min 210.0 174.0 100.3\*# 69.9\*# PCI cm.s 0.04 0.10\* 0.16\* 0.18\*# HPI % 66.2 45.5 30.5\* 18.5\*# PP mmHg 8.7 32.8\* 25.3\*# 21.4\*# DPP 1.0 1.3 2.7\*# 3.2\*# \*P < 0.05 compared with normal, #P < 0.05 compared with group A These results suggest, that major hemodynamic alterations responsible for decompensation of liver cirrhosis and deterioration of functional hepatic reserve are the following: change of hyperdynamic state of splenic circulation into congestive, gradual reduce of total and effective hepatic inflow and decrease of portal pressure. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis } "Hemodynamic Alterations in Decompensation of Liver Cirrhosis and Portal Hypertension"

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"P P 28 0693" P 28 0693 **Role of Sensory Neurons and Nitric Oxide in the Control of Hepatic Blood Flow**

\*K. Czarnobilski, R. Sendur, M. Zejc-Bajsarowicz, J. Biernat, W.W. Pawlik

Inst. of Physiol., Jagiellonian Univ. Med. School, Krakow, Poland An evidence exists that sensory nerve terminals (C-fibers) which contain different vasodilator peptides are found in the liver vasculature. In the present study the acute utilizing of neurotoxin-capsaicin (CAP) was used to explore the role of C-fibers in the maintenance of hepatic blood flow. The mediatory role of endogenous nitric oxide (NO) in the regulation of hepatic vasculature tone was also determined. Experiments were performed on rats under nembutal anesthesia. Hepatic blood flow (HBF) was registered continuously by Laser Doppler flowmeter (Periflux 4001 Master). Portal blood flow (PBF) was measured ultrasonically (Transonic System 206T). Systemic arterial pressure (AP) was measured with a strain gauge transducer. Topical application of CAP (0.5 mg) to periarterial nerves located in the hepatic porta evoked an initial vasodilation (at 8 minute HBF and PBF increased 77 – 6 and 48 – 4% respectively, while blood pressure decreased (19 – 3%). The apparent vasodilation was succeeded by vasoconstriction (at 30 min, HBF and PBF were decreased 31 – 5 and 55 – 3% respectively from control). Inhibition of NO synthase by N-nitro-L-arginine (L-NNA) (15 mg/kg i.v.) decreased HBF by 38 – 7 and PBF by 29 – 7% respectively and increased AP by 28 – 4%. Pretreatment of the animals with L-arginine (L-Arg) (100 mg/kg i.v.) was without any hemodynamic effects. However L-Arg reversed all circulatory effects of L-NNA. We conclude that acute responses to CAP of the hepatic circulation reflect release of peptide neurotransmitters (initial vasodilation) and their subsequent depletion (late vasoconstriction). These findings also suggest that primary sensory afferent nerves are physiological modulators of blood flow and vascular tone in the liver. The results presented also emphasize an important role of endogenous NO as a tonic vasodilator of hepatic vasculature. Intestinal disorders: Splanchnic circulation, ischemia Hormones and receptors: Receptor characterization } " "Role of Sensory Neurons and Nitric Oxide in the Control of Hepatic Blood Flow"

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"P P 28 0696" P 28 0696 **Evaluation of Portal System by Color Doppler Ultrasonography in Patients with Liver Cirrhosis** Vedat G\ 'f6ral, Fesih Araz, Arslan Bilici, Fikri Canoru\ 'e7

Dicle University School of Medicine, Division of Gastroenterology, Diyarbakir, Turkey Portal hypertension is the most important complication of liver cirrhosis. The development of portal hypertension usually becomes evident by the appearance of splenomegaly, ascites, encephalopathy, and/or esophageal varices. *Aim:* In this study, portal system was evaluated by color Doppler ultrasonography in liver cirrhosis. *Methods:* All patients were postnecrotic (HBV, HDV, HCV) cirrhosis. Portal system was evaluated by color Doppler ultrasonography (Toshiba SSA-270) in 40 cases (13 female, 27 men, mean age 42.7 years) with decompensated liver cirrhosis. 30 healthy persons were taken as control groups (9 female, 21 men, mean age 40.2 years). In both groups, diameter of portal and splenic vein, portal vein flow direction (hepatopedal or hepatofugal), portal vein thrombosis were investigated. In addition, all collateral veins were investigated in patients with liver cirrhosis. *Results:* Portal vein diameter was between 7–23 mm (mean 13.5 mm) in all cases and portal vein thrombosis couldn't find in any cases. PV flow direction was hepatopedal in 39 cases. Paraumbilical vein (PUV) was established in 22 cases (55%), left gastric vein was established in 11 cases (45%). Retroperitoneal collaterals in 17 cases (40.5%), LGV in 11 cases (27.5%), renal vein collaterals in 15 cases (37.5%), peripancreatic collaterals in 1 case (2.5%), perigastric collaterals in 4 cases (10%) were established in cases with liver cirrhosis. At the 30 healthy persons, PV diameter was between 7–12.5 mm (mean 9.5 mm), splenic vein diameter was between 3–12.5 mm (mean 5.5 mm). There was a meaningful different between liver cirrhosis and healthy persons ( $p < 0.001$ ). *Conclusion:* These results conclude that ultrasonography gives very useful informations about portal hypertension. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis Clinical practice: Management strategy } "Evaluation of Portal System by Color Doppler Ultrasonography in Patients with Liver Cirrhosis"

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## "P P 28 0697" P 28 0697 Pulmonary Circulation Time in Patients with Chronic Liver Disease

\*M. Ohsuga, H. Homma, X.J. Zhang, T. Nagano, H. Komeichi, H. Terada, T. Sekiyama, K. Satomura, Y. Katsuta, T. Aramaki

First Dept. of Int. Med., Nippon Medical School, Tokyo, Japan The hepatopulmonary syndrome (HPS) is an clinical entity characterized by abnormalities of arterial oxygenation in patients with chronic liver disease without cardiopulmonary disorders. The pathophysiology of this syndrome is thought to involve intrapulmonary vascular dilatation. We measured pulmonary circulation time (PCT) using contrast echocardiography and evaluated the relationship between PCT and arterial  $pO_2$  ( $p_aO_2$ ). *Patients and Methods:* 21 patients with chronic liver disease (cirrhosis  $n = 14$ , chronic hepatitis  $n = 7$ , age 27–77 yrs) were studied. PCT was measured by contrast-enhanced echocardiography using Albutex<sup>®</sup> (human serum albumin-micro air bubble complex, mean diameter 4  $\mu$ m). PCT was defined as the time lag of opacification between right and left atrium observed in video-records. Cardiac output (CO) was also determined by doppler echocardiography.  $p_aO_2$  was measured in supine and sitting position. *Results:* Patients were divided into two groups; PCT < 4 sec. (S-PCT,  $n = 7$ , mean – S.D. 2.8 – 1.0 sec.) and PCT  $\geq$  4 sec. (NS-PCT,  $n = 14$ , 5.2 – 0.6 sec).  $p_aO_2$  in supine position in S-PCT was significantly lower than in NS-PCT (83.9 – 5.6 mmHg vs 95.6 – 12.4,  $p < 0.05$ ). In S-PCT,  $p_aO_2$  in sitting position was significantly decreased than in supine position (77.8 – 8.0 vs 83.9 – 5.6,  $p < 0.05$ ). No significant change in  $p_aO_2$  was observed between two positions in NS-PCT. PCT significantly correlated with  $p_aO_2$  in sitting position ( $r = 0.56$ ,  $p < 0.01$ ). PCT also significantly correlated with CO ( $r = -0.62$ ,  $p < 0.01$ ). *Conclusion:* Orthodeoxia was observed in patients with S-PCT. Thus PCT may detect potential HPS. Clinical practice: Quality assurance Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Diagnosis } "Pulmonary Circulation Time in Patients with Chronic Liver Disease"

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## "P P 28 0698" P 28 0698 Portal Hypertensive Colopathy — A Prospective Study

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The term Portal Hypertensive Gastroenteropathy was chosen to describe the spectrum of gastrointestinal mucosal changes associated with Portal Hypertension (PH). The aims of our study were: to detect the prevalence of Portal Hypertensive Colopathy (PHC) in patients with PH; to describe the colonoscopic and histological features and to correlate such findings with a variety of clinical, biochemical and endoscopic parameters. *Patients and methods:* thirty patients with PH and with clinical indication for colonoscopy were studied prospectively. The study included anamnesis, laboratory data, abdominal ultrasonography, upper gastrointestinal endoscopy, colonoscopy and biopsies, when possible. *Results:* nineteen of the 30 patients (63%) with PH had colonoscopic findings suggestive of PHC. Seven of these 19 patients had also varices of the rectum and/or sigma. We didn't find any correlation between the severity and extension of the lesions and Child-Pugh classification. We performed biopsies in 16 patients and in 15 dilatation and capilar congestion were found, associated with a chronic inflammatory infiltrate in 12. PHC was associated with Portal Hypertensive Gastropathy (PHG) in 13 patients, with esophageal varices in 15 and with gastric varices in 5. Thirteen patients had had upper gastrointestinal hemorrhage, but only 3 had been previously submitted to variceal sclerotherapy. *Conclusions:* PHC is found in approximately 2/3 of patients with PH and it is not always associated with PHG or with esophageal varices. This entity must be included in the differential diagnosis of lower gastrointestinal hemorrhage and ferropenic anaemia in patients with PH. The gravity and extension of lesions have no correlation with the severity of hepatic insufficiency. Liver and bile ducts, 1: Cirrhosis: portal hypertension

Endoscopy, specific: Colon, rectum } "Portal Hypertensive Colopathy / A Prospective Study"

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"P P 28 0699" P 28 0699 **Plasma Interleukin-8 Levels in Patients with Post-hepatic Cirrhosis: Relationship to Severity of Liver Disease, Portal Hypertension and Hyperdynamic Circulation**

\*H.J. Liu, C.P. Li, F.Y. Lee, Y.T. Tsai, H.C. Lin, R.H. Lu, H.M. Cheng, T.F. Wang, S.S. Wang, S.D. Lee

The 807 Military General Hospital and Division of Gastroenterology, Veterans General Hospital-Taipei, Taiwan, ROC

*Background/Aims:* This study investigated plasma interleukin-8 (IL-8) levels in patients with post-hepatic cirrhosis and correlated it with the severity of liver diseases and hemodynamic parameters. *Methods:* Plasma IL-8 levels were determined by ELISA and hemodynamic studies were performed using Swan-Ganz catheterization. *Results:* Plasma IL-8 levels were significantly higher in 57 post-hepatic cirrhotic patients (7.5 – 1.8 pg/ml,  $p < 0.005$ ) than those in 41 healthy subjects (2.0 – 0.2 pg/ml). Elevated plasma IL-8 levels (plasma IL-8 level  $> 5$  pg/ml) were found in up to 30% of the cirrhotic patients. In cirrhotic patients, the plasma IL-8 levels progressively increased in relation to the severity of liver dysfunction (Pugh's class A/B/C = 4.5 – 1.0/4.9 – 1.4/20.5 – 8.3 pg/ml,  $p < 0.005$ ). A significant correlation was observed between plasma IL-8 levels and serum bilirubin levels ( $r = 0.72$ ,  $p < 0.001$ ). There were no differences in the hepatic venous pressure gradient (15.4 – 1.1 vs 15.1 – 0.9 mmHg,  $p > 0.05$ ) and systemic vascular resistance (1119 – 118 vs 1199 – 54  $\text{dyne}\cdot\text{s}\cdot\text{cm}^{-5}$ ,  $p > 0.05$ ) between cirrhotic patients with and without elevated plasma IL-8 levels. In addition, plasma IL-8 levels did not correlate with hepatic venous pressure gradient ( $r = 0.26$ ,  $p > 0.05$ ) and systemic vascular resistance ( $r = -0.24$ ,  $p > 0.05$ ). *Conclusions:* These results demonstrate that plasma IL-8 levels are increased in patients with post-hepatic cirrhosis. The severity of liver cirrhosis is an important factor for the occurrence of enhanced IL-8 levels. IL-8 does not play a role in the hyperdynamic circulation observed in patients with post-hepatic cirrhosis. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Plasma Interleukin-8 Levels in Patients with Post-hepatic Cirrhosis: Relationship to Severity of Liver Disease, Portal Hypertension and Hyperdynamic Circulation"

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"P P 28 0700" P 28 0700 **Long-Term Follow-Up of Intrahepatic Portal Flow Change in Normal Volunteers and Patients with Chronic Liver Diseases**

\*Z.Y. Lin, J.H. Wang, M.L. Yu, S.N. Lu, S.C. Chen, W.L. Chuang, M.Y. Hsieh, J.F. Tsai, L.Y. Wang, W.Y. Chang

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The summation of portal blood flow (SPBF), measured from the left umbilical portion and the right anterior branch by Doppler, was applied to investigate the long-term intrahepatic portal flow change in normal volunteers and patients with chronic liver diseases. Serial SPBF measurements were performed in 14 normal volunteers and 25 patients with chronic liver diseases. The duration of follow-up for patients and volunteers were 13.9 – 6.36 months and 17.89 – 4.51 months (mean – SD) respectively. The SPBF result obtained when both AST and ALT were within their normal limits was used as a baseline to compare with the subsequent data. Each SPBF result was compared with baseline and the coefficient of variation (CV) > 11% was defined as significant change of the SPBF. All volunteers and 20 patients showed constant or decreased SPBF results. The remaining 5 patients showed increased SPBF on serial follow-up. Among them, one with cirrhosis and one with chronic hepatitis C showed mild increase of the SPBF (CV range: 11–14%), one with chronic hepatitis B underwent seroconversion of HBeAg (+) to anti-HBe (+) showed moderate increase of the SPBF (CV = 18.65%), one with acute exacerbation of chronic hepatitis B during follow-up showed fluctuant increase of SPBF (CV range: 14.24–20.65%), and the remaining one chronic hepatitis C patient with persistent elevation of both AST and ALT for 22 months showed most remarkably progressive increase in SPBF (CV value increased from 17.47% to 49.25%). In conclusion, Doppler SPBF measurement can be applied in long-term follow-up study. Persistent inflammation of the liver may cause progressive increase of the SPBF which may be the early clue in the producing portal hypertension. Liver and bile ducts, 1: Cirrhosis: portal hypertension

Radiology and ultrasound: Diagnosis }

"Long-Term Follow-Up of Intrahepatic Portal Flow Change in Normal Volunteers and Patients with Chronic Liver Diseases"

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## "P P 29 0701" P 29 0701 **The Laparoscopic Cholecystectomy Associated with Operation for Hernia or Incisional Hernia**

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First Surgical Clinic, University of Medicine and Pharmacy Timisoara, Romania  
The association of cholelithiasis with hernia or incisional hernia poses a problem for the surgeon in evaluating whether laparoscopic cholecystectomy, a classic cholecystectomy followed by hernia or incisional hernia operation or a simultaneous operation is the preferred approach for this particular condition. The best choice is especially difficult, by the paucity of data on laparoscopic techniques in this situation. In the First Surgical Clinic Timisoara in the period 1.01.94–15.01.96 we performed 296 laparoscopic cholecystectomies (L.C.) and we found at 7 cases the association of cholelithiasis with hernia: { - } 2 cases with infraumbilical incisional hernia (one of these was a giant one); { - } 4 umbilical hernias, { - } 1 epigastric supraumbilical hernias. The 7 patients were females, age between 31–68. We choosed the solution of simultaneous operation: L.C. and operation for hernia. Under general anesthesia we performed an incision at the niveau of the hernia, we isolated the peritoneal sack. Through a direct cutdown onto the peritoneum we controlled the presence of adherence and we prevented a visceral injury and as in a open laparoscopy we inserted laparoscopic port. A purse string suture is placed around the fascia and peritoneum in order to prevent excessive CO<sub>2</sub> leak. We inserted the laparoscope and the other 3 additional ports. In the case of under-umbilical hernia we reduced the peritoneal sack with separate suture. In the cases of umbilical hernia we introduced the first port through the umbilical sack. At the epigastric hernia we introduced the first port through the epigastric hernia and the 2-nd port infraumbilical. We performed normally the laparoscopic cholecystectomy and we finished by repairing the abdominal wall, closing the fascial defect. In 1 incisional hernia we performed a parietal aloplastia with net. The postoperative evolution was good in all the cases. Liver and bile ducts, 2: Gallstones, formation, treatment  
Laparoscopic surgery: Therapy  
Clinical practice: Management strategy } "The Laparoscopic Cholecystectomy Associated with Operation for Hernia or Incisional Hernia"

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"P P 29 0702" P 29 0702 **Comparison between Ultrasonographic Diagnosis and Intraoperative and Histological Findings in Patients with Laparoscopic Cholecystectomy**

\*P. Georgiev, E. Belokonski, K. Vassilev, S. Handjiev, K. Daiev

Military Medical Academy, Sofia, Bulgaria Since 1992 laparoscopic cholecystectomy is a method of choice for treatment of the symptomatic cholelithiasis. Ultrasonography is a basic method for exact diagnosis and indications for operative treatment. The aim of this study was the comparison between the preoperative ultrasonographic diagnosis and intraoperative and histological findings. We used Braghetto's classification to divide our patients according to the ultrasonographic diagnosis to 4 groups: I. Usual chronic calculous cholecystitis: 368 patients. II. Acute calculous cholecystitis type II A with thickness of gallbladder wall < 5 mm: 21 patients. type II B with thickness of gallbladder wall > 5 mm: 15 patients. III. Scleroatrophic chronic cholecystitis: 46 patients. There is the high level of coincidence of the preoperative ultrasonographic diagnosis with videoendoscopical and histological findings. Our experience demonstrated that patients with cholecystitis type II B and type III had need from the prolongation of the operative time, between them the frequency of complications is higher, more frequent is the conversion to open cholecystectomy. Braghetto's classification proposes the possibility for determination of course of surgical intervention and estimation of probability for conversion and intraoperative and postoperative complications. Liver and bile ducts, 2: Gallstones, formation, treatment Laparoscopic surgery: Therapy Radiology and ultrasound: Diagnosis } "Comparison between Ultrasonographic Diagnosis and Intraoperative and Histological Findings in Patients with Laparoscopic Cholecystectomy"

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"P P 29 0705" P 29 0705 **The Use of Ultrasound Surgical Destructor-Aspirator in the Laparoscopic Cholecystectomy**

\*A.I. Nikitenko, E.G. Nikitenko, A.M. Zhelannov

Central Hospital of the Nizhny Novgorod Region, N. Novgorod, Russia The purpose of the ultrasound surgical destructor-aspirator (USDA) is to explore Calots triangle by fragmentation and aspiration of the fatty tissue without damaging the nerves, vessels, and cystic duct. The serosa of the Calots triangle is cut via electrocautery with the sharp-angle hook dissector. Then the cystic duct and artery are efficiently exposed by the USDA. Laparoscopic cholecystectomy with USDA was performed successful in 45 cases including 17 cases with an acute cholecystitis. Using USDA the stones in the gall bladder were destructed and gall bladder was removed without wound distension. The USDA is suitable for skeletonizing the cystic duct and cystic artery, and the procedure is perfectly safe. Laparoscopic surgery: Therapy } "The Use of Ultrasound Surgical Destructor-Aspirator in the Laparoscopic Cholecystectomy"

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"P P 29 0706" P 29 0706A **Comparison of N<sub>2</sub>O and CO<sub>2</sub> Pneumoperitoneums during Laparoscopic Cholecystectomy, with Special Reference to Postoperative Pain**

\*P. Aitola, I. Airo, S. Kaukinen, P. Ylitalo

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Department of Pharmacology, Clinical Pharmacology and Toxicology, University of Tampere, Tampere and Diaconess Institute, Helsinki, Finland Nitrous oxide (N<sub>2</sub>O) pneumoperitoneum has been shown to be less pain provoking than carbon dioxide (CO<sub>2</sub>) pneumoperitoneum during diagnostic laparoscopy under local anaesthesia. There are no reports of whether N<sub>2</sub>O has that benefit also on major surgical laparoscopic procedures under general anaesthesia. In the present study we compared the effects of N<sub>2</sub>O and CO<sub>2</sub> pneumoperitoneums on postoperative pain and on cardiorespiratory variables during laparoscopic cholecystectomy. Forty patients scheduled for laparoscopic cholecystectomy due to symptomatic cholelithiasis were randomised to either N<sub>2</sub>O or CO<sub>2</sub> pneumoperitoneum groups. Heart rate, blood pressure, pulse oximetry and end tidal CO<sub>2</sub> were continuously monitored during the operations. Arterial blood gases were analysed three times during the procedures. Serum cortisol, epinephrine and norepinephrine concentrations were measured before insufflation, at the end of and 8 hours after the operations. The intensity of postoperative pain was measured using visual analogue pain scale. No differences between the two groups in baseline or perioperative blood pressures, heart rates or pulse oximetry values were found. The patients in the CO<sub>2</sub> group had significantly lower pH values than the patients in the N<sub>2</sub>O group at the end of the operation. In the CO<sub>2</sub> group a respiratory acidosis developed as seen in significantly increased arterial and end tidal CO<sub>2</sub> values and decreased pH. No differences between the groups in serum cortisol or epinephrine levels were found. At the end of and after the operations norepinephrine levels were higher in the N<sub>2</sub>O group than in the CO<sub>2</sub> group. The patients in the N<sub>2</sub>O group required less anaesthetic agent (enflurane) during the operations and had significantly lower pain scores one hour, six hours and the next morning 23 and 24 hours postoperatively. Patients operated with N<sub>2</sub>O pneumoperitoneum had no side-effects of CO<sub>2</sub> and were less painful postoperatively than those operated with CO<sub>2</sub>. Nitrous oxide is a good alternative for CO<sub>2</sub>, especially when prolonged laparoscopic operations are performed on patients with chronic cardiopulmonary diseases. Laparoscopic surgery: Therapy } "A Comparison of N<sub>2</sub>O and CO<sub>2</sub> Pneumoperitoneums during Laparoscopic Cholecystectomy, with Special Reference to Postoperative Pain"

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"P P 29 0707" P 29 0707 **6 Years of Laparoscopic Cholecystectomy: Results on 1778 Patients** D. Lomanto, A. Paganini<sup>1</sup>, F. Carlei<sup>2</sup>, M. Nardovino<sup>3</sup>, M. Guerrieri, F. Giacobuzzo, M. Sottili, P. Lepiane, A. Cicalese, Meli E. Zarba, E. Lezoche<sup>1</sup>

II Clinica Chirurgica, Universit  degli Studi "La Sapienza", Roma

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<sup>1</sup> Patologia Chirurgica, Universit  di Ancona

<sup>2</sup> Dipartimento Medicina Sperimentale, L'Aquila *Aim of the Study:* Laparoscopic cholecystectomy is today the standard therapy for gallstones disease. Improved experience with this technique allows to achieve better results. Aim of this study was to analyse our large series to evaluate the results achieved. *Methods:* Between 1991 and 1996 1778 patients were submitted to laparoscopic cholecystectomy for gallbladder lithiasis. Preoperative imaging study consisted of US in all cases, i.v. cholangiography in 134 cases and ERCP in 81 cases. The lithiasis was complicated by acute cholecystitis (39 cases), empiema (16 cases), hydrops (24 cases) and adenomioma (5 cases). 565 patients had been submitted to previous laparotomies (25 upper abdomen, 540 lower abdomen). 1724 (97%) of pts underwent IOC A bile duct lithiasis was associated in 165 cases (9.3%) whose 4.2% unsuspected. *Results:* Intraoperative complications occurred in 65 cases (3.6%): most common were bleeding (18 cases) and loss of small stones (43 cases) but we also observed a small bowel lesion, a diaphragm lesion and two lesions of biliary tract (1 choledocus and 1 common hepatic duct). Our conversion rate was 1.4% (25 cases) and it was due to bleeding (10 pts), visceral lesions (4 pts), cholecystitis (2 pts), multiple visceral adhesions (5 pts) and bile duct lithiasis (4 cases). Postoperative complications were 71 (3.9%): 15 parietal abscesses, 22 parietal hematomas, 6 incisional hernias through umbelical port, 15 subhepatic bile collections, 8 intraperitoneal bleeding and 5 residual VBP lithiasis. We also report a case of mortality due to cardiogenic shock. *Conclusions:* Laparoscopic cholecystectomy performed in experienced centers can achieve optimal results in terms of morbidity, in-hospital stay and recovery to normal activities of the patients shorter than open cholecystectomy. Laparoscopic surgery: Therapy Liver and bile ducts, 2: Gallstones, formation, treatment } "6 Years of Laparoscopic Cholecystectomy: Results on 1778 Patients"

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"P P 29 0709" P 29 0709 **Bile Duct Injury during Cholecystectomy in the Era of Laparoscopy**

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Department of Digestive Surgery, Hospital Beaujon, University Paris VII, Clichy, France  
The development of laparoscopic cholecystectomy (LC) has been associated with a rise in the incidence of bile duct injury (BDI). The aim of this study was to assess the changes in the presenting features and management of BDI in the era of LC. *Methods:* All BDI cases (primary or secondary referral) treated at our center since January 1979 have been included for analysis. *Results:* Between 1979 and 1989, 31 patients (average: 2.8 per year) were treated for BDI after cholecystectomy vs 39 patients from 1990 to 1995 (average: 6.5 per year). Of these most recent 39 patients, 16 (41%) have had an open cholecystectomy (OC) and 23 (59%) have had a LC. In 12 (31%) patients, the BDI was discovered during the operation: 6 (38%) during OC and 6 (26%) during LC. The presenting features in the 27 patients in whom BDI was not discovered at the time of surgery were as follows: n Septic Biliary Biliary Emergency syndrome fistula ascites reoperation OC 10 1 (10%) 3 (30%) 1 (10%) 3 (30%) LC 17 8 (47%) 4 (24%) 8 (47%) 12 (71%) Of the 18 (46%) patients undergoing an angiography, 9 (50%) had a lesion of the hepatic artery or of the portal vein; 4 (45%) after OC vs 5 (66%) after LC. The type of biliary lesion according to Bismuth's classification was identical in the both groups. Endoscopic treatment was not attempted in any case after OC but was attempted in 9 (39%) cases after LC. Seven (78%) of these patients were finally operated. Roux-en-Y hepaticojejunostomies was performed in 11 patients (69%) after OC and 16 (70%) after LC. *Conclusion:* this study confirms an increase in the incidence of BDI in patients undergoing laparoscopic cholecystectomy although 40% are still related to open cholecystectomy. Bile duct injury after laparoscopic cholecystectomy are diagnosed later, notably through septic and peritoneal complications, and are more frequently accompanied by vascular lesions. But these findings and the attempt of percutaneous or endoscopic treatments do not seem to have changed the type of reparation. Laparoscopic surgery: Therapy } " Bile Duct Injury during Cholecystectomy in the Era of Laparoscopy"

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"P P 29 0710" P 29 0710 **Incidence of Bile Duct Stone Disease Occurring after Prophylactic Cholecystectomy Incorporated in Curative Gastrectomy for Cancer** H. KOBORI, R. HADA, Y. SUGIYAMA, N. WAJIMA, M. SUGAI, D. SEITO, Y. MIKAMI, H. SUZUKI, M. KONN

Department of Surgery, Hirosaki University School of Medicine, Hirosaki, Japan *Background and Aim:* We reported a 6 to 10 times higher incidence of gallstone disease in curatively gastrectomized patients for cancer (Dig Surg 6: 39–45, 1989, Gastroenterology 104: A362, 1993). One possible factor for this lithogenesis is impaired gallbladder (GB) motility brought about by vagal denervation (Dig Surg 6: 39–45, 1989), and another possible factor to be altered GB bile composition related to bile infection (Gastroenterology 104: A371, 1993, 106: A340, 1994). Since 1989, we have employed concomitant cholecystectomy for its prophylaxis, especially when total gastrectomy or a duodenum-bypassing subtotal gastrectomy plus hepatoduodenal lymph node dissection were performed. A follow-up study has indicated that the prophylactic cholecystectomy is effective. However, the possibility of increasing incidence of bile duct stone disease after prophylactic cholecystectomy remained to be settled. *Methods:* We performed a follow-up study employing periodic ultrasound (per 6 months) on the incidence of bile duct stone in a series of 150 patients having undergone a curative gastrectomy for cancer and cholecystectomy. The patients consisted of 106 males and 44 females aged 60.0 – 10.3 y. Cholecystectomy in these patients had already been performed before gastrectomy in 9 patients (Group A), was concomitantly performed for biliary disease in 59 patients (Group B) or for prophylaxis in 77 patients (Group C) or for other reasons (Group D). The follow-up period (duration) was 44.4 – 36.0 for Group A, 53.4 – 33.7 for Group B, 33.2 – 23.0 for Group C and 16.3 – 10.4 mo for Group D, respectively. *Results:* Bile duct stone was diagnosed in only one of the 150 patients (1/150, 0.7%) and that in Group C (prophylactic cholecystectomized patients). The patient (62 y aged male) had undergone total gastrectomy, distal pancreatectomy, splenectomy and prophylactic cholecystectomy. A bile duct stone developed 39 mo latter. *Discussion and Conclusion:* The low incidence of bile duct stone (0.7%) demonstrated in the present study may verify the concomitant cholecystectomy as a sufficient means for the total prevention of gallstone disease occurring after curative gastrectomy for cancer. Liver and bile ducts, 2: Gallstones, formation, treatment } "Incidence of Bile Duct Stone Disease Occurring after Prophylactic Cholecystectomy Incorporated in Curative Gastrectomy for Cancer"

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"P P 29 0711" P 29 0711 **Can Preoperative Variables Predict Symptomatic Outcome after Cholecystectomy?** I.B. Andersen, L. Bardram, L. Borly, E. Christensen, H. Kehlet, L. Paloheimo,

\*L. Højgaard

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Cholecystectomy for symptomatic gallstone disease results in pain relief in most of the patients, but for 20–30% abdominal pain is present also after the operation, as the so-called postcholecystectomy syndrome. *The aim* of this study was to investigate whether preoperative variables could predict the symptomatic outcome after cholecystectomy. *Methods:* 102 patients were referred to elective cholecystectomy in a two year prospective study. Median age was 45 years, range 20–81. A preoperative questionnaire on pain, symptoms, history etc. was completed, and the questions on pain and symptoms were repeated postoperatively after 6 weeks and one year. Preoperative cholecystigraphy and sonography evaluated gallbladder motility, gallstones and gallbladder volume. CCK-profile was measured after meal stimulation. Bile, gallbladder and stones were analysed after the operation. Preoperative variables in patients with or without pain were compared statistically and significant variables were combined in a logistic regression model to predict the postoperative outcome. *Results:* 80 patients completed all questionnaires. Of the 80 patients 21 had abdominal pain after the operation, whereas 59 had no pain postoperatively. Patients with pain one year after cholecystectomy were characterized by preoperative presence of a high dyspepsia score, "irritating" abdominal pain and an introvert personality. Further by absence of "agonizing" pain and absence of symptoms coinciding with pain.  $\chi^2 = 47$ , d.f. 5,  $p < 0.000001$ . Of 18 patients predicted as having postoperative pain, 15 had this (PV<sub>pos</sub> = 0.83). Of 62 patients predicted as having no pain postoperatively, 56 had this (PV<sub>neg</sub> = 0.90). Overall 88.7% of the patients were classified correctly according to this reclassification. *Conclusion:* In this prospective study on postoperative outcome after cholecystectomy preoperative symptoms were able to predict abdominal pain after cholecystectomy. Since reclassification gives too optimistic results, the model should be validated in independent patients. Liver and bile ducts, 2: Gallstones, formation, treatment } "Can Preoperative Variables Predict Symptomatic Outcome after Cholecystectomy?"

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"P P 29 0712" P 29 0712 **Hepatectomy for Metastatic Liver Tumors from Colorectal and Gastric Cancers**

\*S. Miyagawa, S. Kawasaki

First Department of Surgery, Shinshu University, School of Medicine, Matsumoto, Japan *Purpose:* Long-term survival after hepatectomy was examined between patients with metastatic liver tumors from colorectal and gastric cancers. *Methods:* Between January 1990 and February 1996, 50 patients underwent hepatectomy for metastatic liver tumors from colorectal cancer (colon group) and 16 from gastric cancer (gastric group). *Results:* The mortality rate within 30 postoperative days was zero, although one patient died from cerebral bleeding in the hospital (1.5%). In the colon group, hepatectomy was performed synchronously with removal of the primary lesion in 8 patients (16%) and metachronously in 42. The mean number of resected liver tumors was 3 ranging from 1 to 17. Repeated hepatectomy for recurrent liver tumors was performed in 10 patients (20%) (two times in 8 patients and three times in 2). On the other hand, in the gastric group, hepatectomy was carried out synchronously in 8 patients (50%) and only one patient (6.3%) underwent repeated hepatectomy for recurrent liver tumor. The colon group had a higher percentage of repeated hepatectomy than the gastric group, but not significantly ( $p = 0.199$ ). In the colon group, the cumulative 1-yr survival rate after initial hepatectomy was 86.8%; 2-yr rate 75.9%; 3-yr rate 65.7%; and 5-yr rate 65.7%, respectively, although in the gastric group, 1-yr, 2-yr and 3-yr survival rates were 65.0%, 27.9% and 0%, respectively. Significantly longer survival after initial hepatectomy was observed in the colon group ( $p = 0.0012$ ). *Conclusion:* Hepatectomy can provide long term-survival for patients with metastatic liver tumors from colorectal cancer. Oncology, general: Therapy Oncology, specific: Liver, biliary } "Hepatectomy for Metastatic Liver Tumors from Colorectal and Gastric Cancers"

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## "P P 29 0713" P 29 0713 Surgical Treatment of Liver Echinococcosis: Our Experience

\*B. Bakula, I. Zoricic, N. Makek, T. Anic, Z. Perko

University Dept of Surgery, Sveti Duh General Hospital, Zagreb, Croatia Between January 1991 and March 1996 we operated 94 patients with liver echinococcosis. There were 79 (84%) females and 15 (16%) males. Average age was 39.2 years (SD – 16.5 years). Diagnosis was made by ultrasound, computerized tomography and serological testing. More common the right liver lobe has been affected (70.7% vs. 29.3%). Partial pericystectomy with drainage was the most common operation, performed in 44 (46.7%) cases. Partial pericystectomy with choledochotomy, "T-tube" drainage and suturing of open biliar ducts were performed in 10 (10.6%) patients, where cysts were centrally situated or biliary leakage was seen. Liver resections were done in patients with liver parenchyma destruction, multiple cysts or inadequate drainage openings: right hepatectomy, left hepatectomy and atypical resections in 9 (9.6%), 7 (7.4%) and 17 (18.1%) cases respectively. In one patient marsupialization was performed because of his bad condition and cyst infection. Six (6.4%) patients had secondary peritoneal echinococcosis, so besides liver procedures, total pericystectomies of these cysts were done, too. Nine patients were reoperated because of recidive of the disease, and one patient was reoperated four times. During postoperative course we did not have heavily complications. In eight (8.5%) patients abdominal collections have occurred, and ultrasound puncture and drainage were performed. In one case relaparotomy, drainage, suturing of the biliar duct and "T-tube" drainage were necessary due to subhepatic abscess. It could be concluded that liver echinococcosis can be managed with partial pericystectomy in the majority of cases, with good curative effects and low postoperative complications course. Choledochotomy with "T-tube" drainage is additional method for centrally situated cysts or evident biliar leakage, and liver resections for a large degree parenchyma destruction or inadequate drainage openings. Immunology and microbiology: Inflammation Clinical practice: Management strategy } "Surgical Treatment of Liver Echinococcosis: Our Experience"

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## "P P 29 0714" P 29 0714 Immunohistochemical Investigation in Occurrence of Endocrine Cells and Lysozyme in Chronic Cholecystitis

\*M. Onda, Y. Ozawa, T. Honjo, T. Okuda, Y. Sumiyama

Third Department of Surgery, Toho University, School of Medicine, Tokyo, Japan *Aim:* We investigated the functional significance of the occurrence of endocrine cells and lysozyme in cholelithiasis tissue by using the histochemical and immunohistochemical methods to clarify the etiology of chronic cholecystitis. *Materials and Methods:* The subjects consisted of 120 cases chronic cholecystitis surgically removed in our department and we selected 100 cases to show histologic evidence of metaplasia for study. Of the 120 patients, 53 were men and 67 were women, they ranged in age from 34 to 88 years, mean, 56.2 years. All specimens were fixed in 10 per cent neutral buffered formaldehyde immediately after cholecystectomy, embedded in paraffin and sectioned at 5 μm. Grimelius reactions were used to bring out the argyrophil cells. Special mucin stainings were applied to identify the periodic acid-Schiff (PAS) followed by alcian blue. For the immunohistochemical demonstration, we used an streptoavidin-biotin immunoperoxidase procedure (SAB) by monoclonal antibody. *Results:* In normal gallbladder mucosa, endocrine cells and lysozyme were not demonstrated. In chronic cholecystitis, non-metaplastic group in 20 cases also were not observed these cells. The expression rate of the occurrence of endocrine cells and lysozyme of metaplastic group were found in 48 (48%) and 63 (63%) of 100 cholecystitis, respectively. These cells were apparently formed by the metaplastic differentiation. The endocrine cells were found more abundantly in the body and fundus region than in the neck region. Among the hormones determined immunohistochemically, serotonin was detected most frequently followed by cholecystokinin, somatostatin, gastrin and pancreatic polypeptide. Various hormone-containing cells showed a high correlativity between the development of metaplasia and degree of cholecystitis. These cells were apparently formed by the metaplastic differentiation. And lysozyme also showed a close relationship to the metaplasia. *Conclusions:* It was recognized a strong correlation between endocrine cells and degree of metaplasia and cholecystitis. And it is suggested that endocrine cells has strongly influence on the occurrence and development of chronic cholecystitis. Therefore, there is much hope to the clinical application of hormone therapy in the treatment of cholecystitis. Oncology, specific: Endocrine Oncology, specific: Liver, biliary } "Immunohistochemical Investigation in Occurrence of Endocrine Cells and Lysozyme in Chronic Cholecystitis"

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"P P 29 0715" P 29 0715 **Differences in Pain and Dyspepsia after Cholecystectomy for Acute Cholecystitis and Symptomatic Gallstone Disease**

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<sup>5</sup> Odense University Hospitals Abdominal pain occurs in 20–30% of patients after cholecystectomy. The main cause of this pain remains unclear. Patients with acute cholecystitis (AC) could perhaps be expected to benefit more from surgical treatment than patients operated due to uncomplicated gallbladder stone disease (UGSD), as the necessity to operate is more unquestionable in patients with AC. *Purpose:* To compare pain and dyspepsia after cholecystectomy for AC with pain and dyspepsia after cholecystectomy for UGSD. *Methods:* All patients (223 women, 122 men) cholecystectomized for AC at 4 Danish University hospitals during the period from 1986 to 1990, and a control group of age and sex-matched patients (213 women, 83 men) cholecystectomized for UGSD, were invited to participate in a questionnaire concerning the occurrence of abdominal pain and dyspepsia before and after cholecystectomy. *Results:* 534 patients (83%) completed the questionnaire. Complaints of abdominal pain were found in 37% with equal frequency in the AC and UGSD group (37% vs 38%). Women suffered more often from abdominal pain after cholecystectomy than men (42% vs 29%, OR = 1.75). Although more than one third complained of abdominal pain after cholecystectomy, 93% were improved or cured by the operation and this occurred more often in UGSD than AC (95% vs 89%) (P = 0.02). In general cholecystectomy reduced nausea (P < 0.0001) and vomiting (P < 0.0001) but aggravated flatulence (P < 0.0001). Abdominal pain was significantly correlated to dyspepsia after cholecystectomy in both groups. *Conclusion:* Pain occurs with equal frequency in AC and UGSD after cholecystectomy. Liver and bile ducts, 2: Gallstones, formation, treatment } "Differences in Pain and Dyspepsia after Cholecystectomy for Acute Cholecystitis and Symptomatic Gallstone Disease"

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"P P 29 0716" P 29 0716 **Therapeutical Approach to Acute Cholecystitis** D. Lomanto, A. Paganini<sup>2</sup>, F. Carlei<sup>1</sup>, M. Guerrieri<sup>2</sup>, M. Nardovino<sup>1</sup>, G. Dalsasso, F. Giacobuzzo, Meli E. Zarba, E. Lezoche<sup>2</sup>

<sup>1</sup> II Clinica Chirurgica, University of Rome "La Sapienza", INI Canistro (AQ)

<sup>2</sup> Patologia Chirurgica Università di Ancona, Italia *Purpose of the Study:* Laparoscopic cholecystectomy (LC) is the gold standard for uncomplicated cholelithiasis: more debated are indications and timing in acute cholecystitis (AC). Aim of our study was to evaluate results of LC in patients with present or previous acute cholecystitis. *Methods:* Between 1991 and 1995 1778 pts. were submitted to LC for symptomatic cholelithiasis. Of these 158 pts. (8.9%) were admitted with the diagnosis of AC identified by clinical, lab and ultrasonographic signs. 5 of these presented with signs of cholangitis and in four of them common bile duct stones were demonstrated. Among the AC group, 39 pts. underwent LC within 48 hours from the clinical onset of symptoms (Group A). 119 patients, including elderly or high risk pts as well as pts. referred to us more than 48 hours after the onset of symptoms and pts. treated in the first two years of this study, underwent medical treatment and surgery was delayed of 5–7 weeks (Group B). *Results:* Conversion rate was 7.7% in Group A and 0 in Group B. Mean operative time was significantly shorter in Group B (49.2 minutes vs. 78.5 of Group A). In both groups no common bile duct injuries were observed. Morbidity was 8.3% in group A (2 port site infections and 1 hemoperitoneum, treated conservatively) and 4.2% in Group B (3 port site infections, 1 parietal hematoma and 1 biloma, treated conservatively). No mortality was observed. Mean postoperative hospital stay was 4.2 and 2.5 days respectively in Group A and B. *Conclusion:* Our results suggest that LC can be safely performed by skilled surgeons within 48 hours from the clinical onset of symptoms in no high risk patients. In high risk patients a delayed operation seems justified, as far as cholangitis is not present. Liver and bile ducts, 2: Gallstones, formation, treatment Laparoscopic surgery: Therapy } "Therapeutical Approach to Acute Cholecystitis"

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"P P 30 0717" P 30 0717 **Prognostic Factors of Liver Excretory Function in Patients Undergoing Biliary Decompression for Obstructive Jaundice**

\*C.Y. Chen, S.C. Shiesh, X.Z. Lin

National Cheng Kung University Hospital, Tainan, Taiwan *Aim:* We conducted this study to identify the predictors of recovery of liver excretory function in patients with obstructive jaundice. *Materials and Methods:* Twelve consecutive patients were recruited, with mean age 60.6 – 9.9 y-o, male 9, female 3. The underlying diseases were common bile duct stone: 4, and biliary malignancy: 8. They received nasobiliary drainage (NBD, 4) or percutaneous transhepatic choledochal drainage (PTCD, 8) according to clinical indications. Serum and bile were collected for biochemistry tests. The recovery of liver function was evaluated by indocyanine green retention test (ICG R<sub>15</sub>). Patients with a ICG R<sub>15</sub> reduction ratio less than 50% were considered as poor recovery (group 1, n = 6) while a good recovery was thought if the reduction ratio higher than 50% (group 2, n = 6). The clinical parameters were compared between two groups. *Results:* Sequential change of serum & biliary content are as follows: Day 0 Day 3 Day 6 Gr. 1 Gr. 2 Gr. 1 Gr. 2 (Biliary) Bile acid 5.8 – 5.7 24.4 – 23.9\* 1.0 – 0.9 5.2 – 2.2\ '86 2.1 – 2.5 7.2 – 3.1\* Bil – T 49 – 76 53 – 77 16 – 8 78 – 30\ '86 33 – 39 55 – 33 Volume/day – – 1158 – 349 701 – 286 1108 – 251 595 – 249\* (Serum) Ap 585 – 276 348 – 289\* 437 – 257 262 – 195 343 – 205 201 – 96\* Bil – T 19.0 – 6.7 11.7 – 5.9 11.4 – 3.6 4.4 – 1.5\* 9.5 – 2.5 3.2 – 0.9\ '86 \*p < 0.05; \ '86 p < 0.01 by Mann-Whitney U test The ICG reduction ratio was significantly correlated with the bile volume and the concentration of bile acids ( { g } = { - } 0.8 & { g } = 0.74 respectively, p < 0.01). *Conclusion:* Post-obstructive cholerisis and thin bile (low concentration of biliary bile acid) are bad prognostic factors for recovery of liver function. Both conditions are sequel of prolonged obstruction and a longer time for recovery is expected. Liver and bile ducts, 2: Bile formation, cholestasis Endoscopy, specific: Biliary }" "Prognostic Factors of Liver Excretory Function in Patients Undergoing Biliary Decompression for Obstructive Jaundice"

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"P P 30 0718" P 30 0718 **Role of Atrial Natriuretic Peptide on the Pathogenesis of Renal Dysfunction in Patients with Obstructive Jaundice**

\*F.J. Padillo, J.M. Gallardo, M. Rodriguez, A. Naranjo, P. Montilla, F. Infante, G. Miñero, C. Pera, A. Sitges-Serra<sup>1</sup>

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<sup>1</sup> Hospital del Mar; Barcelona, Spain *Purpose of the Study:* To investigate the sodium regulating hormones status and the role of the atrial natriuretic peptide (ANP) on the pathogenesis of the extracellular water (ECW) depletion and renal dysfunction in patients with obstructive jaundice (OJ). *Methods:* Forty two patients with OJ were evaluated. There were 21 women and 21 men with a mean age of 69 yrs (range 38–90). Fourteen patients had benign conditions and 28 periampullary tumors. Plasma ANP, Aldosterone (Ald) and Renin (Ren) concentrations were measured by radioimmunoassay. Extracellular water (ECW) was determined using tetrapolar bioimpedance. Fractional sodium excretion (FNaEx) and creatinine clearance (CrCl) were also measured. A control group (CG) of 14 healthy subjects matched for age (mean age 64 yrs; range 37–84) and sex (6 women and 8 men) were used as controls for hormonal measurements. *Results:* Ninety one percent of OJ patients had elevated ANP (> 60 pg/ml) vs 7% in CG (p < 0.001). Mean values were 119 – 46 pg/ml in OJ group vs 40 – 16 in CG (p < 0.001). Plasma Ald concentrations compared with CG was 156 – 72 vs 43 – 21 pg/ml (p < 0.001). Forty seven percent of OJ patients had elevated Ald concentrations (> 160 pg/ml) (p < 0.001). CrCl was 95 – 65. Twenty eight percent of patients had low CrCl (< 50 ml/min). FNaEx was 0.63 – 0.49. Patients with CrCl < 50 ml/min had higher Fractional sodium excretion (0.84 vs 0.55; p = 0.15). Sixty five percent of patients had ECW lower than 22% body weight. Plasma Renin concentrations was also higher in OJ patients than CG (41 – 54 vs 16 – 9 uU/ml; p < 0.01). *Conclusion:* The present study reports that plasma ANP is increased in patients with obstructive jaundice. Endocrine and extracellular water alterations could be related to renal dysfunction. These findings are relevant to the perioperative management of patients with obstructive jaundice. Liver and bile ducts, 2: Bile formation, cholestasis } "Role of Atrial Natriuretic Peptide on the Pathogenesis of Renal Dysfunction in Patients with Obstructive Jaundice"

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"P P 30 0719" P 30 0719 **Polypeptides from Red Cell Membranes: Electrophoresis Reveals Effects of Biliary Obstruction with High Bilirubin Levels in Rats**

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<sup>2</sup> Dept. of Pathology, Hospital C. Fraga F<sup>o</sup>, Fac. Medicina, Univ. Fed. do Rio de Janeiro, RJ, Brazil

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Experimental biliary obstruction in Wistar rats leads to differences in the polypeptides of the red cell membranes that can be detected by polyacrylamide gel electrophoresis in the presence of sodium dodecyl sulfate. Here we compare the pattern obtained in ghosts from normal rats and rats with high bilirubin levels in plasma, 5–11 days after experimental biliary duct obstruction. Ghost membranes from normal human subjects were also examined. After surgery, rats with coluria were sacrificed and biochemical tests for bilirubin, transaminase and amylase in plasma and an analysis of biliary/digestive tract histopathology were performed. Ghost membranes were solubilized and the polypeptides were separated on 7.5% polyacrylamide gels (stacking gel 4.9%) according to Laemmli (Nature 227: 680, 1970), and stained with Coomassie blue. The operated rats exhibited coluria, colangitis, ductal dilatation with cystus, and pancreatitis; and in liver, portal fibrosis with ductal proliferation. The biochemical results were consistent with the obstruction: high levels of bilirubin and of all the enzymes tested. Electrophoresis of ghosts revealed differences from normal rats between 75 and 25 kDa. At 53 kDa, a prominent band (designated 4.6) was found in normal rats between the bands 4.9 and 4.2, but disappeared with prolonged biliary obstruction. This band is not found in humans. Band 6 (35 kDa), present in humans, is absent from normal rats but appears after prolonged biliary obstruction. The intensity of bands 7 and 8 (29 and 25 kDa) increases in operated rats. Partial reversal of this profile was observed when the obstruction reversed spontaneously. We conclude that biliary obstruction with high bilirubin levels can affect red cell membrane polypeptides, depending on the severity and duration of the obstruction. *Support: CAPES, FUJB, UFRJ.* Liver and bile ducts, 2: Bile formation, cholestasis Liver and bile ducts, 2: Biliary cysts, atresia }"  
"Polypeptides from Red Cell Membranes: Electrophoresis Reveals Effects of Biliary Obstruction with High Bilirubin Levels in Rats"

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"P P 30 0720" P 30 0720 **Factors Associated with Increased Biliary Pressure in Bile Duct Obstruction**

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Division of Gastroenterology, Samsung Medical Center, Seoul, Korea

<sup>1</sup> Department of Radiology, Samsung Medical Center, Seoul, Korea *Purpose:* Increased bile duct pressure is the major factor responsible for acute cholangitis and bacteremia. Therefore, prompt medical or surgical decompression of bile under high pressure should be accomplished as fast as possible. But, measurement of bile duct pressure is invasive. So, the present study was undertaken to find out the clinical factors to predict the increased biliary pressure in patients with bile duct obstruction. *Methods:* Thirty-three patients with bile duct obstruction underwent percutaneous transhepatic biliary drainage (PTBD). Intraductal pressure was measured as soon as bile duct puncture was performed. Bile cultures were performed in 24 patients and blood cultures were performed in 21 patients. Correlation of bile duct pressure and severity of pain, duration of symptom, fever, leukocytosis, serum bilirubin, serum alkaline phosphatase, or bile duct diameter were statistically analyzed. *Results:* Bacteremias were noticed in 5 of the 17 patients with positive bile culture. Bacteremia was associated with the increased biliary pressure. Bacteremia was demonstrated when the biliary pressure was 22 cmH<sub>2</sub>O or more. Biliary pressure was associated with the severity of pain and body temperature. Significant correlation was not found between the duration of symptom, leukocytosis, serum bilirubin, serum alkaline phosphatase, or bile duct diameter and biliary pressure. *Conclusion:* Increased biliary pressure in patients with bile duct obstruction is more likely to be associated with severity of pain and fever than leukocytosis, bilirubin level, alkaline phosphatase level, or bile duct diameter. Liver and bile ducts, 2: Bile formation, cholestasis } "Factors Associated with Increased Biliary Pressure in Bile Duct Obstruction"

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## "P P 30 0721" P 30 0721 Bilirubinate Conjugates in Common Duct Bile of Patients with Choledocholithiasis

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Department of Internal Medicine, Ulleval hospital, Oslo, Norway

<sup>1</sup> Department of Clinical Chemistry, Ulleval hospital, Oslo, Norway Common bile duct stones are mainly brown with Ca-bilirubinate as a major component. Deconjugation of bilirubinate glucuronides by bacterial betaglucuronidase seem to be of importance. Our aim was to analyse the composition of common bile duct stones and relate this to bilirubinate conjugates in common duct bile. *Material and methods:* Common bile duct stones and common bile duct bile were collected endoscopically from 56 patients (29 women) with mean age 75 years (range 50–95). The stones were dried and 5 mg of each stone was crushed and dissolved in N,N-dimethylformamide/dimethyl sulfoxide and cholesterol concentration was measured enzymatically on a Cobas Bio centrifugal analyser. Stones with < 50% cholesterol were considered pigment stones. Biliary pH was measured. Bilirubinate conjugates were analysed immediately by high performance liquid chromatography. A 25 minutes gradient on a C18 column and detection at 440 nm was used. Concentrations were calculated as area under the curve on a computer. *Results:* Forty-four stones (78%) were pigment stones. All 25 patients with duodenal diverticula had pigment stones ( $p < 0.01$ ). Total bilirubin % Bilirubin Biliary  $\mu\text{mol/l diglucuronide}^*$  pHPigment stones  $n = 44$   $613 - 472$   $59 - 12$   $7.95 - 0.45$  Cholesterol stones  $n = 12$   $504 - 311$   $67 - 8$   $7.96 - 0.46$  \*t-test,  $p < 0.025$  No significant differences were found for the other conjugates. *Conclusion:* The percentage of the main bilirubinate conjugate, bilirubin diglucuronide, is decreased in common duct bile of patients with pigmented compared to cholesterol stones. Liver and bile ducts, 2: Gallstones, formation, treatment } "Bilirubinate Conjugates in Common Duct Bile of Patients with Choledocholithiasis"

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## "P P 30 0722" P 30 0722 Symptomatic Gallstone Disease: Which Patients Should Have ERCP?

\*E. Trondsen, B. Edwin, O. Reiertsen, A. F\`e6rden, H. Fagertun, A.R. Rosseland

Surgical Dept., Central Hospital of Akershus, Nordbyhagen, Norway For selection of patients with symptomatic gallstone disease to ERCP, clinical indicators of common bile duct stones (CBDS) (history, biochemical tests, ultrasonography (USG)) are too sensitive and may result in a large frequency of negative ERCP. In the present study a discriminant function (DF) for the probability of CBDS (confining age, bilirubin, ALAT, GT) was tested prospectively, and also compared to ultrasonographic CBDS indicators. 192 patients were included, 32 proved to have CBDS, and 160 not. Blood sampling was done mean 1.7 days prior to cholecystectomy or ERCP. Ultrasonography (USG) was performed in 171 patients (25 with and 146 without CBDS), ERCP in 71 patients, and both procedures in 57 patients. Clinical criteria for CBDS was positive in 152 patients (79.2%), 21.1% of them actually had stones, and there were no false negatives (sensitivity 100%, specificity 25%). DF was positive in 50 patients (26.0%), 60% of them had CBDS, and there were two false negatives (sensitivity 93.8%, specificity 87.5%). At USG mean bile duct diameter was 4.8 mm in patients without CBDS and 8.4 mm in patients with CBDS. In patients with diameter 6 mm or less (normal range), nine had stones and 116 not, with diameter > 6 mm, 16 had CBDS, 30 had not. Sensitivity of USG was 68.0% and specificity was 79.5%. There was a correlation between diameter at USG and ERCP ( $p < 0.001$ ), but  $r$  was only 0.543. Clinical characterisation is most sensitive for CBDS detection, but has low specificity. DF is more specific and sensitive than USG, is easy to use, and seems efficient in selecting symptomatic gallstone patients to ERCP. Clinical practice: Management strategy Liver and bile ducts, 2: Gallstones, formation, treatment } "Symptomatic Gallstone Disease: Which Patients Should Have ERCP?"

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"P P 30 0724" P 30 0724 **Bacterial Biofilm Formation: Clinical Bacteriology and Sem Analysis** A. Basoli<sup>1</sup>, F. Fiocca<sup>1</sup>, M. Cristaldi<sup>1</sup>, E. Grasso<sup>1</sup>, G. Scopelliti<sup>1</sup>, M. Crovaro<sup>1</sup>, A. Domenicucci<sup>1</sup>, D. Apa<sup>1</sup>, L. Baldassarri<sup>2</sup>, R. Di Rosa<sup>3</sup>

<sup>1</sup> Istituto II Clinica Chirurgica, Universit\ 'e0 ""La sapienza"" , Roma

<sup>3</sup> Dip. Clinica Medica, Universit\ 'e0 ""La sapienza"" , Roma

<sup>2</sup> Dipartimento Ultrstrutture, Istituto Superiore Sanit\ 'e0 We studied basic mechanism of biliary stent clogging to investigate on factors involved in it. *Material and Methods:* In one year period 22 biliary stents (10 for transhepatic access) of different plastic materials (polyethylene, polyurethane and teflon) and different diameters (10–12 F) were explanted. They were cut, before transversally from the duodenal and the biliary extremities (5 mm), then lengthwise; two parts, dipped into PBS solution to be sonicated, therefore they were analyzed by quantitative microbiology. The others were immersed into gluteraldeide diluted 1:10, to be analyzed by scanning electron microscopy. 12 stents were substituted for dislocation or for charge therapy, while 7 were explanted due to occlusion (mean implantation time was 95.8 days, range 18–210) *Results:* microbiological analysis didn't reveal a bacterial colonization in 7 out of 22 stents (mean implantation time 12.8 days, range 2–24, median 8). Only one of these was removed because of blockage, and SEM revealed heavy deposit of organic material. During the whole period of implantation an antibiotic therapy was administrated. Cholangitis episodes occurred in four patients, while the other patients presented symptoms of jandice or cholestatis. 15 stents (mean implantation time 73.3 days, range 4–210, median 21) revealed: 14 *Enterococcus spp.*, 3 *E. clocae*, 2 *E. coli*, 2 *candida* and 1 *C. freundii*, *Bacillus*, *Veillonella*, *Corynebacterium. spp.*. SEM analysis provided indications in three cases that microorganism were present though culture had resulted negative. *Conclusion:* bacterial cells were attached to both the inner and outer stent surface enclosed into a fibbrillar matrix, suggesting that the first event of stent clogging is the development of an adherent bacterial biofilm. Microorganism of duodenal origin, *Enterococcus spp.* 64% mainly rapresened as component of the biofilm deposited on stent. Nevertheless in the case of stent with transhepatic access, biliary side risulted more early colonized then the duodenal side. We can speculate biliary stasis plays a fundamental role in the drainage failure. Liver and bile ducts, 2: Gallstones, formation, treatmentLaparoscopic surgery: Therapy }" **"Bacterial Biofilm Formation: Clinical Bacteriology and Sem Analysis"**

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"P P 30 0725" P 30 0725 **The Presence of CaCO<sub>3</sub> in the Gallbladder Stones Is a Marker for the Bile pH at which Cholelithogenesis Occurs** I.O. Rada, D. Silasi, M. Mracec, Domnita Rada, Liliana Ivanov, Doina Sîntimbreanu, F.C. Rada

University of Medicine and Pharmacy, Timisoara, Romania, str. Siret no. 6 Cholesterol cholelithiasis etiopathogeny remains an uncertain and controversial matter. We determined during surgical procedures the pH in the gallbladder, the common bile duct and the common hepatic duct using the pH meter Digital 100. The presence of cholesterol crystals was studied with a polarized light microscope and we analyzed the composition of gallbladder stone layers. *Results:* in all cases when the bile pH was above 8, we discovered cholesterol crystals or conglomerates. In all cholesterol stones we found precipitates or crystals of calcium carbonate. In layers of lighter colors of the stones the CaCO<sub>3</sub> concentration is increased up to 18% and the radioopacity more evident. *Conclusions:* bile alkalization disturbs colloid micelles by reducing the volume and making thinner the double electric layer that keeps the particles in suspension, favoring the sedimentation and conglomeration of cholesterol. Constant identification of CaCO<sub>3</sub> in all cholesterol stones resulting from HCO<sub>3</sub> ion and calcium under a pH level above 8 in bile – represents a marker of the moment of the cholesterol sedimentation. The phenomenon of bile alkalization (pH above 8) disturbs the stability of the colloid micelles and represents the initial moment of the lithogenesis. The conglomeration of the precipitate (cholesterol and CaCO<sub>3</sub>) can also involve biliary pigments resulting in layering of various colors and radioopacity of the gallbladder stones sections. Such gallstones implanted steril in a dog's gallbladder are dissolved and eliminated in several weeks. In humans bile acidification determines the same process that can be followed by ultrasonography. Liver and bile ducts, 2: Gallstones, formation, treatment Endoscopy, specific: Biliary Radiology and ultrasound: Diagnosis } "The Presence of CaCO<sub>3</sub> in the Gallbladder Stones Is a Marker for the Bile pH at which Cholelithogenesis Occurs"

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"P P 30 0726" P 30 0726 **Changes in the Excretion of Bile Acids into the Greater Circulation System with the Continuous Infusion of Bile Acids into the Portal Vein of the Rat: A Biochemical and Microautoradiographic Study**

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<sup>1</sup> Second Department of Internal Medicine, Osaka Medical College, Osaka, Japan

<sup>2</sup> Shionogi Corporation, Osaka, Japan *Purpose:* We continuously infused taurocholic acid (TCA) and <sup>3</sup>H-TCA into the portal vein of rat. We biochemically and microautoradiographically analyzed the process of its excretion into the greater circulation and the distribution of <sup>3</sup>H-TCA in hepatic lobe. We examined this basic research might become one test method in the evaluation of hepatic function. *Material and methods:* Male Sprague-Dawley rats weighing 250-300 g were used. We continuously infused 2 mM-TCA into the portal vein of rat over 30 minutes under the following condition. (the infusion speed of TCA was 10 ml/h, 15 ml/h, 20 ml/h) We sampled the venous blood of the rat at 5 minutes interval from the cannula inserted into the cervical vein to study the excretion of bile acids into the greater circulation system. We infused 2 mM-<sup>3</sup>H-TCA into the portal vein of rat under the 15 ml/h. The liver of rats were removed at 3, 6, 12 minutes after infusion, and we made frozen tissue samples. We microautoradiographically observed the continual changes in the distribution of the <sup>3</sup>H-TCA in hepatic lobe. *Results and discussion:* The following results were obtained. (1) When 2 mM-TCA was continuously infused through the portal vein, that the upper limit of infusion speed to which the hepatic cells were able to treat the TCA, and prevent its excretion into the greater circulation system, was 15 ml/h. (2) As <sup>3</sup>H-TCA was continuously infused through the portal vein, microautoradiographic study of TCA incorporation showed, the so-called gradient, in which the grain moves from the hepatic cells surrounding the portal vein, into the area near the central venous system. Further studies will be conducted involving an experimental model of hepatic injury. Liver and bile ducts, 2: Bile acids synthesis } "Changes in the Excretion of Bile Acids into the Greater Circulation System with the Continuous Infusion of Bile Acids into the Portal Vein of the Rat: A Biochemical and Microautoradiographic Study"

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"P P 30 0727" P 30 0727 **Treatment of Gallstones in the Elderly by Oral Bile Acids** G.I.S.Co. (Interdisciplinary Group for the Study of Cholelithiasis)

Italy An oral bile acids treatment of symptomatic uncomplicated gallstone disease in the elderly can be proposed as alternative approach to surgery, which presents in these patients a greater risk of mortality and morbidity as compared to young adult subjects. *Aim* of this study was to evaluate the clinical efficacy of two different treatment of gallstones in elderly subjects by means of bile acids (Tauroursodeoxycholic acid-TUDCA- and Chenodeoxycholic+Ursodeoxycholic acids - CDCA+UDCA). 124 elderly patients with symptomatic uncomplicated gallbladder stones were studied: 66 (11 male, 55 female, age range 65–90) were treated by, CDCA-UDCA (5 + 5 mg/Kg/day) and 58 (25 male, 33 female, 65–92) by TUDCA (500 mg/day) for 1 year. The diagnosis was made by Biliary US, Plain Abdomen X-ray and Oral Cholecystography. All subjects presented one or more episode(-s) of biliary pain in the six months prior the study; 44 were also affected by dyspepsia (27 in TUDCA, 17 in CDCA-UDCA group). Patients were followed-up clinically every 3 and by US every 6 months. 42/66 subjects in CDCA-UDCA (24 drops: 9 operations for pain or complications, 9 deaths unrelated to gallstones, 1 side effects, 5 follow-up unattended) and 38/58 in TUDCA (20 drops: 1 operation for pain or complications, 9 deaths unrelated to gallstones, 3 side effects, 7 follow-up unattended) group completed the study. 4 total and 2 partial dissolution in CDCA-UDCA and 8 total dissolution in TUDCA group were observed. In 51 patients of CDCA-UDCA and in 39 of TUDCA group symptoms could be followed-up: CDCA-UDCA: 38 had become asymptomatic, 4 had dyspepsia and all 9 still symptomatic were operated; TUDCA: 25 had become asymptomatic, 11 suffered from dyspepsia and 3 were still symptomatic (1 of whom operated). *Conclusions:* 1) Gallstones dissolution in the elderly by oral bile acids seems to be scarcely effective; 2) no difference between the two bile acids was observed; 3) during oral bile acid therapy the majority of elderly subjects with gallstones show an improvement of their symptoms Liver and bile ducts, 2: Gallstones, formation, treatment }" "Treatment of Gallstones in the Elderly by Oral Bile Acids"

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"P P 30 0728" P 30 0728 **Effect of the Combination of Chenodeoxycholic and Ursodeoxycholic Acid in Gallstone Dissolution** G.I.S.CO. (Interdisciplinary Group for the Study of Cholelithiasis)

Italy Combination of two bile acids (CDCA+UDCA) has been described as capable of dissolving cholesterol gallstone in more than 60% of cases. Recently a lower percentage of complete dissolution (21%) has been reported. *The aim* of this study was to evaluate the efficacy of the combination of CDCA+UDCA in dissolving cholesterol gallstone in a large number of symptomatic unselected patients and to compare the efficacy of two different types of drug administration (single dose at bedtime or two doses at meals). A total of 212 pts (71 male, 141 female, mean age 46.4 yrs, range 18–65) with radiolucent gallstone in a functioning gallbladder was enrolled in 9 centres in North East Italy. All received CDCA+UDCA (5 mg/kg/day each) for 12 months or until dissolution. The drug was randomly administered in a single dose at bedtime or in two doses at main meals. Follow-up was performed by clinical evaluation every 3 months and biliary ultrasound every 6 months. 151 pts completed the study; 1 died from causes not related to gallstones; 18 were operated because of severe biliary pain and/or complications; 11 stopped the treatment for adverse reactions; 31 dropped-out. Complete and partial dissolution were observed in 18.4% and 8.9% patients (intention to treat) or 25.8% and 12.6% (per protocol) respectively. The success of therapy was inversely related to the diameter of stone. No difference in dissolution was observed according to the different administration schedules (chi square = 0.015, p: ns) *In conclusion*: 1. the combination of CDCA+UDCA is effective in dissolving radiolucent gallstones in less than one fifth of unselected patients. 2. The drug administration schedule does not affect the results of the therapy. Liver and bile ducts, 2: Gallstones, formation, treatment } "Effect of the Combination of Chenodeoxycholic and Ursodeoxycholic Acid in Gallstone Dissolution"

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**"P P 31 0729" P 31 0729 Effect of Age, Cholecystokinin and Erythromycin on Gallstone and/or Biliary Sludge Formation in the Guinea Pig M.R. Mas, \dc. Ateskan, S. Nalbant, H. \d6zotuk, H. Erdem, F. Kocabalkan**

GATA Int. Med. Dept. Ankara/Turkey In this study we aimed to evaluate the effect of age, cholecystokinin and erythromycin treatment on gallstone and/or biliary sludge formation. Guinea pigs (30 1-mo-old and 30 3-year-old) were placed on a cholelithogenic diet for 4 weeks while 10 guinea pigs of each group remained on normal diet. Ten guinea pigs of each group received respectively: cholelithogenic diet and daily intraperitoneal injection of 0.9% saline (control group), cholelithogenic diet and daily intraperitoneal injection of CCK (0.5 nmol/kg), cholelithogenic diet and daily erythromycin stearat (2 mg/kg) by nasogastric tube. After 4 weeks guinea pigs were killed and gallbladders were examined for gallstones and/or biliary sludge. The concentrations of bile constituents were determined. We observed no gallstone and/or sludge in the 1-mo-old-group. In the 3-years-old group; control 9 out of 10, cholecystokinin 5 out of 10, erythromycin 4 out of 10. In two age groups cholelithogenic diet significantly reduced the concentrations of bile salts and increased the cholesterol concentration and increased bile protein in 3-yr-old group. Treatment with cholecystokinin and erythromycin didn't alter the bile salt concentrations in both and reduced cholesterol in 1-mo-old. The ratio of bile salts/bile cholesterol reduced in both. However, treatment didn't alter this ratio in 3-years-old group but increased in 1-mo-old group. We conclude that major factors in the increased incidence of gallstones and/or biliary sludge formation in aged guinea pigs are increased; concentrations of bile protein, bile cholesterol and reduced concentration of bile salts and ratio of bile salts/bile cholesterol. Treatment with CCK and erythromycin decreased the incidence by decreasing bile protein and increasing bile lesitin and probably by increasing gallbladder motility. Clinical practice: Management strategy Liver and bile ducts, 1: Hepatotoxicity, ethanol } "Effect of Age, Cholecystokinin and Erythromycin on Gallstone and/or Biliary Sludge Formation in the Guinea Pig"

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## "P P 31 0730" P 31 0730 Effects of Nitric Oxide Donors on Gallbladder Motility in Humans

\*T. Pawlik, S. Bednarz, P. Thor, J.W. Konturek

I Department of Internal Medicine and Institute of Physiology Jagiellonian University, Krak\`f3w, Poland Gallbladder emptying is controlled by complex nervous and humoral mechanisms. It has been previously reported that endogenous nitric oxide (NO) is a neurotransmitter in the gallbladder (GB). The inhibition of NO synthase results in the increase of the intraluminal pressure of GB and this effect can be reversed by the pretreatment with L-arginine (L-Arg). The aim of this study was to evaluate the effects of Glyceryl Trinitrate (GTN), Molsidomine (MO) and L-Arg as potential sources of NO on fasting GB volume and on GB emptying rate, which was induced by modified sham feeding (MSF) and standard meal. The healthy subjects (9 men and 8 women), age range 25–37 years participated in this study. GB volume was examined by means of an ultrasonographic method. Volumens were calculated as described by Everson and co. GB volumes were measured every 10 min for the first 45 min. there after at 15-min intervals up to a total observation period of 2 h. After recording of control values (26.3 + 4 cm<sup>3</sup>), 0.5 mg GTN was administered sublingually, or 4 mg MO orally or L-Arg (12.63 g of L-Arg in 300 ml of 0.9% NaCl) was infused i.v. over 90 min. It was found that the fasted GB volume was significantly increased after GTN by 22 + 2 and after MO by 25 + 6%. MSF-induced GB emptying was completely inhibited by GTN and MO. Whereas, postprandial GB emptying was reduced maximally by 35.6 + 3% (p < 0.1) after pretreatment with GTN and by 40.3 + 5% (p < 0.1) after MO. L-Arg was without any effect on resting or stimulated GB volume. The results of the study support the hypothesis that NO, released from GTN and MO (but not synthesized from L-Arg) is the biologically active messenger which relaxes GB at rest and inhibits its emptying during active contraction. These effects also indicate that long-term therapy with NO donors might reduce GB. motility and increase lithogenicity due to retention of bile in the GB. Motility, general: Receptors and signals } "Effects of Nitric Oxide Donors on Gallbladder Motility in Humans"

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## "P P 31 0731" P 31 0731 Contractile Function of Gallbladder Sludge and its Natural History

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The purpose of this study is to assess gallbladder function in patients with sludge and its natural history. The subjects were 42 patients with gallbladder sludge [SL], 47 patients with gallstone [GS] and in 15 normal [NL]. None of them had diabetes mellitus with neuropathy, liver cirrhosis, gastrectomy and total parental nutrition. Gallbladder volume was calculated using ellipsoid formula by ultrasonography. After obtaining the gallbladder fasting volume, they had standard fatty meal and were measured every 5 minutes for 90 min. All of subjects with no treatment were examined at 12-month intervals for 3 years. Informed consent was obtained from all of subjects. Fasting gallbladder volume was no significant difference among the three groups. Maximum gallbladder contractility (MGC) was SL 47.2 – 10.1%, GS 45.7 – 9.9 and NL 61.7 – 11.4. Differences among the three groups (by Student's t test) were significant by seen for SL vs. NL ( $p < 0.01$ ) and GS vs. NL ( $p < 0.01$ ). An evolution of gallbladder sludge into stone was observed in 8 patients (19%) and disappearance of gallbladder sludge was observed in 14 patients (33%) for 3 years. MGC between these two groups (46.0 – 8.1%, 53.8 – 7.5) was significantly different ( $p < 0.05$ ). These results suggested that natural history of the gallbladder sludge was affected by contractile function of the gallbladder. Liver and bile ducts, 2: Gallstones, formation, treatment  
Radiology and ultrasound: Diagnosis } "Contractile Function of Gallbladder Sludge and its Natural History"

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**"P P 31 0732" P 31 0732 Biliary Motility Disorders and Biochemical Patterns in the Patients with Diabetes Mellitus E.V. Beloborodova, V.G. Borodulin, L.V. Kireeva, T.V. Galuza, T.A. Milovanova, L.M. Pustovoytova**

Siberian State Medical University, Tomsk, Russia The aim of the work was to study motor activities of the biliary system and the biochemical composition of the bile in the diabetes mellitus. 83 patients were investigated with moderate degree of diabetes mellitus in clinically compensated stage, 63 patient had the 1 type (1st group) and 20 – 2 type (2nd group) of the disease. Average age was  $28 \pm 0.2$  and  $48 \pm 0.5$  correspondingly. 50% of all were males in both groups. Endoscopy, ultrasound scan, duodenal probe and dynamic hepatobiliscintiscanning were performed in the clinic. Clinical picture showed the following symptoms of biliary tract disorders; aches under the right ribs, bitter taste and dyspepsia. 80% of the first and 98% of the second groups had the reduction of gallbladder tone which was revealed by the raising of bladder bile portion and the 4th phase time bile excretion prolongation. Sphincter of Oddi hypertone was observed in the isolated cases in both groups (1 and 2). The most significant clinical signs were: reduction the bile acids and phospholipids reduced concentration in the bladder bile as well as cholatocholesterol coefficient which was more strongly marked ( $4.2 \pm 0.21$ ) in the 2nd group than ( $6.3 \pm 0.32$ ) in the first one. Hepatobiliscintiscanning data showed sharp reduction of contractile ability of gallbladder in all the patients in the 2nd group. During a 1.5 hour period of observation the gallbladder contraction has not been shown. 2/3 of the 1st group had hypomotor disorders moderate in character in both groups. Taking into account the significant bile production and secretion disorders in the patients with diseases mellitus it seems to be necessary to include to the therapeutical complex the remedies regulating biliary system activities. Liver and bile ducts, 2: Bile formation, cholestasis } "Biliary Motility Disorders and Biochemical Patterns in the Patients with Diabetes Mellitus"

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"P P 31 0733" P 31 0733 **The Prokinetic Drug Cisapride Improves the Caerulein-Induced Contraction and the Refilling of the Human Gallbladder** A. Szepes, L. Mad'elcsy, B. Velósy, J. Lonovics

First Department of Medicine, Albert Szent-Gy'f'orgyi Medical University, Szeged, Hungary

**Introduction:** Prokinetic effects of cisapride on the gastrointestinal tract have been studied extensively. Studies of its action on the well-functioning gallbladder (GB), however, are limited and the results are not unanimous. The aim of this study was to determine whether oral administration of cisapride could improve the caerulein-induced contraction of the human GB.

**Patients and methods:** GB diameters (GBD) were measured and GB volumes (GBV) were calculated by Dodd's formula by means of real-time ultrasonography in 7 gallstone-free patients with a normal caerulein-induced GB ejection fraction (GBEF > 35%). After an overnight fast, 1 ng/kg/min caerulein (Takus) was administered i.v. for 10 min. The GBD was measured after 0, 5, 10, 15, 20, 25, 30 and 60 min, and the GBEF and the refilling of the GB (GBR) were calculated. Within one week a single dose of 10 mg cisapride (Coordinax, Janssen Pharmaceutica) was administered orally in 10 ml of water to all patients, the GBD was measured after 0, 30, 60, 90 and 120 min and the cisapride-induced changes in the GBV were calculated. After 120 min, caerulein was administered i.v. and the determinations of GBEF and GBR were repeated.

**Results:** The mean caerulein-induced GBEF in the basic study was in the normal range (50.99 – 18.6%). Cisapride administration significantly increased the fasting GBV (45.0 – 21.7 vs. 33.6 – 15.9 ml,  $p = 0.02$ ). The caerulein-induced GBEF improved slightly, but significantly after cisapride administration as compared with the basic study: 60.42 – 18.3% and 50.99 – 18.6%, respectively ( $p = 0.003$ ). The cisapride administration enhanced GBR (229.8 – 55 vs. 163.3 – 24.5%,  $p = 0.015$ ).

**Conclusions:** The prokinetic drug cisapride increases the fasting GBV by approximately 36%, and causes a significant improvement in the caerulein-induced GBEF and GBR. (Supported by a grant from the Ministry of Social Welfare: ETT 609/1993/02). Motility, general: Functional GI disorders }

"The Prokinetic Drug Cisapride Improves the Caerulein-Induced Contraction and the Refilling of the Human Gallbladder"

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"P P 31 0734" P 31 0734 **Effects of Cisapride on Biliary Drainage in Patients with Sphincter of Oddi Dysfunction and with Normal Sphincter of Oddi Motility Measured by Quantitative Hepatobiliary Scintigraphy**

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Cisapride is a gastrointestinal prokinetic drug which enhances motility by directly stimulating the release of acetylcholine of the myenteric plexus. It has been shown that cisapride increases bile flow in animals by an inhibitory effect on the sphincter of Oddi (SO) motility, possibly mediated via non-adrenergic, non-cholinergic neurons. Recent human investigations by endoscopic SO manometry revealed that cisapride decreased the SO basal pressure in patients with biliary stones, but did not have a similar effect in healthy volunteers. The aim of the present study was to evaluate the effect of cisapride on the biliary drainage by quantitative hepatobiliary scintigraphy (QHBS). *Methods:* QHBS was performed in 11 cholecystectomized patients with dyspeptic symptoms. QHBS and SO manometry indicated that 5 patients had an SO dysfunction (SOD) of biliary type II and III, but the remaining 6 had a completely normal SO motility (control group). 140 MBq EHIDA was given intravenously, and digital images were obtained at one frame/min. for 90 min. Time-activity curves were generated from regions of liver parenchyma (LP), hepatic hilum (HH) and common bile duct (CBD). The time to peak activity (Tmax), and the half time of excretion (T1/2) were calculated. Next, cisapride (Coordinax, Janssen Pharmaceutica) was given at 3 {\\b4} 10 mg/day to all patients an ambulatory basis. 2 weeks later, QHBS was repeated in the presence of 10 mg cisapride given orally in 10 ml of water 60 min before EHIDA administration. *Results:* In the control group, all patients had normal biliary transit and the quantitative parameters were within the normal limits during the first QHBS study (LP: Tmax: 10.8 – 1.9, T1/2: 23.8 – 2.9; HH: Tmax: 15.2 – 3.2, T1/2: 25.0 – 4.5; CBD: Tmax: 23.2 – 6.6, T1/2: 28.6 – 8.1 min.). In the remaining 5 SOD patients biliary transit and quantitative parameters were increased (LP: Tmax: 14 – 2.3, T1/2: 31.5 – 11.6; HH: Tmax: 23.8 – 4.5, T1/2: 37.5 – 5.0; CBD: Tmax: 41.5 – 13.1, T1/2: 71.3 – 16.0 min.). Cisapride administration caused significant decreases in T1/2 over the HH and CBD both in the controls (22.6 – 4.1 and 23.2 – 6.8 min) and in the SOD patients (29.0 – 2.2 and 41.5 – 10.8 min). *Conclusion:* The QHBS results proved that the administration of cispride significantly accelerates biliary drainage by improving the transpapillary flow both in patients with an SO dysfunction and in patients with normal SO motility. (Supported by ETT 609/1993/02). Motility, general: Functional GI disorders }" "Effects of Cisapride on Biliary Drainage in Patients with Sphincter of Oddi Dysfunction and with Normal Sphincter of Oddi Motility Measured by Quantitative Hepatobiliary Scintigraphy"

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"P P 31 0735" P 31 0735 **Abnormal Postprandial Gallbladder Emptying in Type 2 Diabetics (NIDDM) is Related to Increased B-Glucose but not to Gastric Emptying Rate**

\*E. Jørgensen, N. Qvist, P. Thygesen, L. Rasmussen, S.A. Pedersen

Medical dept., Assens Hospital, Depts. of Surgical Gastroenterology, Medical Endocrinology & Clinical Physiology, Odense University Hospital, Denmark *Purpose:* To describe the relation of gallbladder emptying (GBE) to gastric emptying (GE), antroduodenal postprandial motor index (PMI), B-glucose and P-insulin in 8 healthy males and 8 patients with IDDM. *Methods:* Continuous antroduodenal pressure recordings. GBE and GE were measured scintigraphically. For GBE a continuous infusion of  $^{99m}\text{Tc}$ -Mebrofenine 40 MBq/h was used, and for the GE a standard meal (100 g omelet tagged with 40 MBq  $^{99m}\text{Tc}$ -sulphur colloid and 150 ml water mixed with 8 MBq  $^{111}\text{In}$ -DTPA) was ingested in phase I of MMC. P-insulin was measured by RIA. *Results:* In normals as well as in patients meal ingestion elicited gallbladder emptying after a short lag-phase, however in 3 out of 7 patients with NIDDM a reduced emptying rate and augmented residue at nadir was found. In this subgroup of patients the characteristics of GE and PMI were similar to those patients with normal GBE and the control group. B-glucose in the subgroup of patients with abnormal GBE was median 15.7 mmol/l (9.6–16.0) compared to a median value of 7.4 mmol/l (5.7–17.3) in the patients with normal GBE. The values for P-insulin were 10.1 p mol/l (7.7–14.8) and 14.1 (4.7–20.4), respectively. *Conclusions:* The abnormal gallbladder emptying in patients with NIDDM was related to elevated B-glucose but not to changes in GE. These findings indicate that hyperglucosemia may impair GBE. Motility, general: Receptors and signals Motility, specific: Stomach Nutrition: Nutrients and gut function }"  
"Abnormal Postprandial Gallbladder Emptying in Type 2 Diabetics (NIDDM) is Related to Increased B-Glucose but not to Gastric Emptying Rate"

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"P P 31 0736" P 31 0736 **Postprandial Gallbladder Kinetic in Normals, Type 1 (IDDM) and Type 2 (NIDDM) Diabetics**

\*E. Jørgensen, N. Qvist, P. Thygesen, L. Rasmussen, S.A. Pedersen

Medical dept., Assens Hospital, Depts. of Surgical Gastroenterology, Medical Endocrinology & Clinical Physiology, Odense University Hospital, Denmark *Purpose:* To compare the characteristics of gallbladder emptying (GBE) in normal persons (NP) (4 young and 4 elderly males) with the characteristics of GBE in otherwise healthy male diabetics (8 young IDDM and 8 elderly NIDDM) with a short disease duration and without late complications. *Methods:* GBE was measured by scintigraphy during 5 h using a continuous infusion of  $^{99m}\text{Tc}$ -Mebrofenine 40 MBq/h. The standard meal, which consisted of an omelet (100 g, 1400 kJ, 60% fat) and 150 ml water, was ingested in a MMC phase I. *Results:* The *pattern* and characteristics of GBE in NP was an *uninterrupted emptying* after a *lag-phase* (= time until 10% GBE) of *median* 11 min (octiles 6–19) with a *rate* of 0.80%/min (0.73–0.81) until the *nadir* was reached after 150 min (120–190) with a *residue* of 1% (0–12). There were no difference in GBE characteristics between the young and the elderly. In IDDMs the lag-phase exceeded 19 min in 6 (range 23–68), the GBE-rate exceeded 0.81%/min in 5 (range 0.82–1.60), the nadir was below 120 min in 3 (range 60–70) and the residue at nadir was above 12% in 5 (range 21–115). In NIDDMs the lag-phase exceeded 19 min in 7 (range 31–68), the GBE was below 0.73%/min in 4 (range 0.33–0.70) and was above 0.81%/min in 2 (range 0.82–0.91). The nadir did not differ from NP but the residue at nadir exceeded 12% in 7 (range 14–64). In 1 subject the gallbladder was non-functioning. *Conclusions:* In IDDMs and in NIDDMs the lag-phase was prolonged. In IDDMs an interruption of gallbladder emptying after 60–70 min took place in 3/8 individuals. In NIDDMs the emptying rate was reduced and the residue augmented at nadir in 3/7 individuals. Motility, general: Receptors and signals Motility, general: Innervation Nutrition: Nutrients and gut function } "Postprandial Gallbladder Kinetic in Normals, Type 1 (IDDM) and Type 2 (NIDDM) Diabetics"

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"P P 31 0737" P 31 0737 **Real Time Ultrasonography for Measurements of Galldbladder Motility in Children with Upper Dyspeptic Syndrom**

\*I.M. Russeva, M.D. Georgieva-Shakola

Dept. of Pediatrics, Medical University, Varna, Bulgaria Motility disorders of galldbladder are a problem in pediatric gastroenterology. Early diagnosis by real-time ultrasonography is applied in measurements of gastrointestinal motility particularly of this of galldbladder. Study's aim was: to establish the disorders of galldbladder motility & their structure according to modern noninvasive diagnostic method; to reveal the role of prokinetic in hypokinesia and spasmolytic in hyperkinesia of galldbladder. In 1996, 25 children (14 girls and 11 boys) aged 9–14 years with upper dyspeptic syndrome were investigated. They were examined clinically and by real-time ultrasonography. The ellipsoid method was applied in measurement of galldbladder motility. After 30 min. & 50 g. chocolate control investigation was performed. The patients with hypokinesia were treated with Motilium (0.5 mg/kg 2 m), these with hyperkinesia with Spasmalgon (synthetic cholinolytic { - } 20 mg/kg 1 m). After 2 m. the same method of measurement of galldbladder motility was applied. Dyskinesia of galldbladder was established in 16/25 cases (64%): hypokinesia-in 14/25 cases (56%) and hyperkinesia-in 2/25 cases (8%). After 2 m. in 12/14 hypokinetic patients clinical symptoms were not observed. In 10 of them- ultrasonographic measurement of galldbladder was normal. Complete healing (clinical & ultrasonographic) was established in hyperkinetic patients. It was concluded that real-time ultrasonography should be the diagnostic method of choice in childhood galldbladder motility disorders. These disorders are very common in children. Prokinetic or spasmolytic reduce the symptoms & motility changes. Radiology and ultrasound: Diagnosis Motility, general: Functional GI disorders } "Real Time Ultrasonography for Measurements of Galldbladder Motility in Children with Upper Dyspeptic Syndrom"

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"P P 31 0738" P 31 0738 **Spontaneous Bacterial Peritonitis in Brazil: Prevalence, Predictive Factors and Prognosis**

\*F.A.F. Figueiredo, H.S.M. Coelho, J.A. Segadas, A. Queiroga, C.R. Silva

Universidade Federal do Rio de Janeiro (UFRJ/Universidade Estadual do Rio de Janeiro (UERJ), Rio de Janeiro, Brasil *Background/Aims:* Spontaneous Bacterial Peritonitis (SBP) is a common and potentially fatal complication of cirrhosis. Multiple variants of this infection have been described during the past decade. Few studies have investigated SBP in Brazil. In order to investigate prospectively prevalence, predictive factors and prognosis of the episode of SBP, we studied 143 in and outpatients with cirrhosis admitted to UFRJ and UERJ between January, 1995 and January, 1996. *Methods:* All patients were submitted to a questionnaire, physical examination, blood analysis and abdominal paracentesis with ascitic fluid analysis. Seventy-four variables were analysed. The patients were followed for a mean follow-up period of 4 months and survival was determined. *Results:* The prevalence of SBP was 20%. Culture-positive SBP, Culture-negative Neutrocytic Ascites and Bacterascites were identified in 24%, 66% and 10%, respectively. After uni- and multivariate analysis, only anterior gastrointestinal hemorrhage, serum albumin and ascitic fluid C4 reached statistical significance ( $p = 0.05$ ) as predictive factors for the development of the SBP. The in-hospital and follow-up mortality rates were 33.3% and 53.8% for the SBP patients and 8.5% and 31.9% for the non-SBP patients, respectively ( $p = 0.01$  and  $p = 0.04$ ). The cumulative probability of survival in the SBP group was significantly lower than the probability of the non-SBP group ( $p = 0.05$ ). *Conclusions:* We conclude that SBP is a frequent complication, depends of the severity of liver failure and is a marker for poor prognosis in patients with liver cirrhosis. Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy Clinical practice: Epidemiology (non cancer) } "Spontaneous Bacterial Peritonitis in Brazil: Prevalence, Predictive Factors and Prognosis"

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"P P 31 0739" P 31 0739 **The Effect of Erythromycin and Cisapride on Postprandial Gallbladder Emptying in Healthy Humans** J. Tsiaoussis, G. Tzouvaras, E. Chrysos, E. Epanomeritakis, N. Kariotakis, A. Mantides, O. Zoras,

\*E. Xynos, J.S. Vassilakis

Dept of General Surgery, University Hospital of Heraklion *Background:* Cisapride and erythromycin exhibit prokinetic properties and increase the rate of postprandial gastric emptying. The *aim* of the study was to evaluate the potential effects of erythromycin and cisapride on gallbladder postprandial emptying in healthy volunteers. *Subjects-Method:* Ten healthy male subjects (age: 25–33, mean age: 29 years) had their gallbladder emptying assessed by real-time ultrasonography on three different occasions, two days apart each, and in a random order as follows: a) after ingestion of 300 ml of fresh milk (lipids 4%) (postprandial emptying) b) after giving 200 mg erythromycin intravenously followed immediately by the ingestion of 300 ml of milk and c) after giving 10 mg of cisapride per os followed 30 min later by the injection of 300 ml of milk. Gallbladder volume was calculated every 5 min for 60–90 min. From the emptying curves (plotting of volume against time) the pattern of emptying was assessed, and the lag phase duration, the ejection fraction and time by which maximal emptying was achieved were calculated. *Results:* Erythromycin significantly reduced the lag phase duration from 3.6 – 4.2 SDmin (milk alone) to 1.3 – 3.5 SDmin (milk plus erythromycin) ( $p < 0.04$ ) and increased the lag phase of postprandial gallbladder emptying from 60.6 – 8.5 SD% (milk alone) to 78 – 8.5 SD% (milk plus erythromycin) ( $p < 0.0006$ ). Cisapride increased the ejection fraction of postprandial gallbladder emptying from 60.6 – 8.55 SD% (milk only) to 67.1 – 8.8 SD% (cisapride plus milk) ( $p < 0.005$ ). The effect of erythromycin on postprandial gallbladder emptying was significantly more pronounced than that of cisapride (ejection fraction: 78 – 8.5 SD% after erythromycin and milk vs 67.1 – 8.8 SD% after cisapride and milk;  $p < 0.005$ ). *Conclusions:* Erythromycin and cisapride significantly enhance the postprandial gallbladder motor response, by increasing the extent of emptying. Motility, general: Functional GI disorders } "The Effect of Erythromycin and Cisapride on Postprandial Gallbladder Emptying in Healthy Humans"

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"P P 31 0740" P 31 0740 **Interdigestive Gallbladder Contractions in a Real-Time Ultrasonographic Study: Differences between Patients with Gallstones and Controls**

\*B. Brand, S. K. Fehne, E.F. Stange

Department of Internal Medicine I, University of Lüneburg, Germany *Aim:* Spontaneous gallbladder contractions occur in phase II of the migrating motor complex. This study compares these contractions in gallstone patients and controls. *Method:* We evaluated a new technique using a fixed fingertip array (Picker, Hofheim). Gallbladder dimensions of asymptomatic (n = 7) and symptomatic (n = 8) gallstone patients, as well as healthy controls (n = 10) were registered continuously. After a fasting period of at least 6 hours we measured all individuals every 5 minutes over a 6–8 hour period. Gallbladder volumes were estimated by the ellipsoid method. Minor oscillations less than 30% were excluded. To calculate the total amount of bile released per hour (gallbladder-index) we added all contractions and divided them by the total measurement time in hours. Exclusion criteria: cholecystitis, cholestasis, liver cirrhosis, thoracical or abdominal surgery, diabetes mellitus, age > 65 years, relevant medication. *Results:* Spontaneous gallbladder contractions of up to 86% and 35 ml were observed in all individuals except in 4 asymptomatic patients. Compared to the controls we found a significant reduction in frequency and magnitude of the contractions in asymptomatic but not in symptomatic gallstone patients. Controls Asymptomatic Symptomatic x SD x SD x SD Spont. contractions % 47.7 – 8.0<sup>2</sup> 16.7 – 19.5 46.3 – 5.6<sup>2</sup> Spont. contractions ml 16.8 – 6.2<sup>1</sup> 6.1 – 7.6 11.9 – 3.2 Gallbladder-index %/h 26.3 – 12.9<sup>2</sup> 4.1 – 5.0 20.5 – 7.0<sup>2</sup> Gallbladder-index ml/h 8.9 – 4.8<sup>2</sup> 1.4 – 1.6 4.8 – 1.3<sup>2</sup> Number of contract./h 0.5 – 0.2<sup>2</sup> 0.1 – 0.1 0.4 – 0.1<sup>2</sup> 1 p < 0.05, 2 p < 0.01 vs asymptomatics (Mann-Whitney-U-Test) *Conclusion:* Asymptomatic but not symptomatic gallstone disease appears to be associated with a reduced gallbladder motility in the interdigestive state. Gallstone patients with normal spontaneous contractions are likely to be symptomatic. Liver and bile ducts, 2: Gallstones, formation, treatment } "Interdigestive Gallbladder Contractions in a Real-Time Ultrasonographic Study: Differences between Patients with Gallstones and Controls"

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## "P P 31 0741" P 31 0741 **Poor Postprandial Gallbladder Contractility Does Not Predict Impaired Interdigestive Motility**

\*B. Brand, S. K\fhne, E.F. Stange

Department of Internal Medicine I, University of L\fcbeck, Germany *Aim:* Impaired postprandial gallbladder motility is established as an exclusion criterion for nonsurgical treatment of gallstone disease (oral bile salts, shock wave lithotripsy). Little is known about the spontaneous gallbladder motility during phase II of the migrating motor complex, though fragment clearance may also be influenced by this mechanism. We compared the postprandial and the spontaneous gallbladder contractility of gallstone patients and healthy controls. *Method:* By using a fixed fingertip array (Picker, Hofheim), gallbladder diameters of 7 asymptomatic and 8 symptomatic gallstone patients, 2 diabetics as well as 10 healthy controls were registered. After a fasting period of at least 6 hours we measured every 5 minutes over 6–8 hours. The individual volumes were calculated from the corresponding diameters using the ellipsoid method and regression analysis. The postprandial gallbladder contraction was registered with a 3.5 Mhz curved array 45 minutes after a standardized fatty meal (250 ml Nutrodrip). Exclusion criteria: cholecystitis, cholestasis, liver cirrhosis, thoracal or abdominal operations, age > 65 years, relevant medication. *Results:* The means of postprandial versus spontaneous contractions were comparable in the healthy (52.3 vs 47.7%) and the symptomatic (57.6 vs 46.3%) but not in the asymptomatic (51.1 vs 16.7%) and the diabetic group. However, the individual values were correlated poorly in the healthy ( $r: 0.26, p = 0.47$ ) and the symptomatic ( $r: 0.05, p = 0.91$ ) group. Four individuals (one out of each group) showed impaired postprandial contraction (< 30%) but three of them had a normal interdigestive motility. *Conclusion:* Postprandial contractility alone may be an inadequate measure of gallbladder function. Postprandial and interdigestive contractions correlate poorly suggesting different mechanisms of stimulation. Gallstone patients with poor postprandial but sufficient interdigestive contractility should probably not be excluded from non-surgical treatment. Liver and bile ducts, 2: Gallstones, formation, treatment } "Poor Postprandial Gallbladder Contractility Does Not Predict Impaired Interdigestive Motility"

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## "P P 31 0742" P 31 0742 Can Cisapride Overcome the Effects of Octreotide (OT) on Gallbladder Emptying?

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<sup>3</sup> The Radcliffe Infirmary, Oxford, UK *Background:* We and others have shown that OT inhibits meal-stimulated gallbladder (GB) emptying and induces the formation of cholesterol-rich GB stones. The effects of the prokinetic drug, cisapride, on the GB are controversial and it is not known whether cisapride can overcome the inhibition of GB emptying caused by OT and thereby prevent the formation of OT-induced GBS. *Methods:* We, therefore, used a randomised, double-blind, placebo-controlled, cross-over design to study the effects of cisapride (10 mg qds for 2 weeks) on GB emptying, assessed by real-time ultrasound after a fat-rich liquid meal, in 8 acromegalic patients (age range 21–69 yrs; 4 women) receiving long-term (> 3 months) octreotide (100–200 µg tds) and in 8 non-acromegalic patients (age range 28–74 yrs; 5 women) from the Gastroenterology Outpatient Clinic. Fasting (FV) and residual (RV) GB volumes, the extent of GB emptying — as assessed by the ejection fraction (EF) — and the rate of GB emptying (RGE) were calculated. *Results:* Mean values — SEM Acromegalic patients Non-acromegalic patients Cisapride Placebo Cisapride Placebo FV (ml) 56 – 8.5\*\* 37 – 5.6 25 – 4.6\* 15 – 1.3 RV (ml) 38 – 7.2\* 24 – 4.4 8 – 1.3 6 – 0.3 EF (%) 31 – 6.8 36 – 6.9 65 – 2.6 60 – 2.1 RGE (ml/min) 0.48 – 0.19\* 0.28 – 0.13 0.38 – 0.08\* 0.24 – 0.05\* p < 0.05, \*\* p < 0.005 compared to placebo *Summary/Conclusions:* These results show that cisapride increases the FV and, in the acromegalics, the RV, but leaves the EF unchanged, whilst significantly increasing the RGE. Since stasis (large RV) and EF are probably more important than RGE in GBS pathogenesis and if GB dysmotility is rate-limiting, cisapride is unlikely to prevent the formation of OT-induced GBS. Liver and bile ducts, 2: Gallstones, formation, treatment }" "Can Cisapride Overcome the Effects of Octreotide (OT) on Gallbladder Emptying?"

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## "P P 31 0743" P 31 0743 Obesity and Rapid Weight Loss: Effect of Different Very Low Calorie Diets on Gallbladder Motility and Gallstone Formation

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Obesity is considered a risk factor for gallstone formation. Very low calorie diets (VLCD) represent a common treatment for morbid obesity; however an increased risk of gallstone formation has been reported during rapid weight loss induced by VLCD. Impaired gallbladder motility is considered among the pathogenetic factors for gallstone development. Since diet composition, and mainly its fat content, modulates gallbladder contraction and most of the commonly used VLCD are characterized by a low fat content, this study was aimed at evaluating in obese subjects during weight loss the effect of different VLCD on gallbladder motility, biliary lipid composition and gallstone formation. Sixteen gallstone-free obese subjects (4 males, 12 females, age: 35.5 – 2.8 yrs, BMI: 41.3 – 1.4 kg/m<sup>2</sup>, mean – SE) were studied. Gallbladder motility was evaluated by an ultrasonographic (US) technique in response to a standard liquid meal. Subjects were randomly allocated to two weight reduction programs, each lasting 90 days; each program (A and B) was characterized by a different VLCD: -A: 520 kcal, 3.1 g of fats, 39.1 g of proteins, 123.2 g of carbohydrates; -B: 570 kcal, 12.5 g of fats, 51.1 g of proteins, 60.4 g of carbohydrates. At days 45 and 90 of the program the appearance of gallstones was investigated by US and gallbladder motility study repeated as at baseline; in 4 subjects for each group biliary lipid composition was also evaluated. Statistical analyses were performed using Mann-Whitney test (independent samples) and Wilcoxon test (paired samples); results were expressed as mean – SE. BMI significantly ( $p < 0.05$ ) decreased in each group during the program: A, from 40.3 – 1.5 to 33.8 – 1.2 kg/m<sup>2</sup>; B, from 42.3 – 2.0 to 35.4 – 1.6 kg/m<sup>2</sup>. Gallbladder motility, expressed as percent emptying, remained unchanged during the program A (58.8 – 4.2 before, 71.1 – 3.5 at day 45, 68.4 – 4.0 at day 90), while a significant ( $p < 0.04$ ) increase at day 45 but not at day 90, was observed during program B (56.4 – 4.5 before, 72.4 – 3.2 at day 45, 66.4 – 5.2 at day 90). Fasting gallbladder volume decreased during weight reduction but this decrease was significant ( $p < 0.04$ ) in group B (35.7 – 4.6 ml before, 23.4 – 5.3 at day 45, 25.2 – 3.8 at day 90) but not in group A (34.6 – 4.5 ml before, 25.8 – 3.7 at day 45, 26.9 – 4.2 at day 90). One out of the 8 subjects (37.5%) who followed the program A, but none in the program B, developed asymptomatic gallstones. Biliary cholesterol, expressed as percent molar, significantly ( $p < 0.05$ ) increased at day 45, and then decreased, while no differences were found in biliary bile acids and phospholipids. These results suggest that VLCD with high fat content could prevent gallstone formation in obese subjects during weight reduction. Liver and bile ducts, 2: Gallstones, formation, treatment } "Obesity and Rapid Weight Loss: Effect of Different Very Low Calorie Diets on Gallbladder Motility and Gallstone Formation"



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"P P 31 0744" P 31 0744 **Role of 5-Hydroxytryptamine in Gall Bladder Motility**

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*Introduction:* The bovine gall bladder is a useful model to study motility due to its similar morphological structure and bile composition to human gall bladder. Control of contraction by CCK and cholinergic neurones is well documented, but the role of 5-Hydroxytryptamine (5-HT) is not adequately investigated. This study aimed to investigate the role of 5-HT in mediating contraction and the effect of the selective 5-HT<sub>3</sub> antagonist Ondansetron. *Methodology:* Bovine gall bladder muscle strips (0.5–1.0 cm) were placed into 10 ml organ baths and attached to an isometric force transducer (Grass FT03), linked to a computer to record the contraction traces. The organ baths contained Krebs Henseleit solution, continuously perfused with 95% O<sub>2</sub> and 5% CO<sub>2</sub>, at 37°C. Cumulative concentration response curves were produced to KCl (2.5–320 mM) and 5-HT (10<sup>-8</sup>–3 × 10<sup>-4</sup> M). The role of 5-HT<sub>3</sub> receptors was studied by performing concentration-response curves to 5-HT in the presence of Ondansetron (45 minutes, 10<sup>-8</sup> M, 10<sup>-7</sup> M, 10<sup>-6</sup> M) followed by a concentration response curve to 5-HT. *Results:* The optimum resting force was found to be 3 g. A concentration-dependent contraction was elicited to both KCl and 5-HT. The maximum contraction to KCl occurred at 80 mM and to 5-HT at 10<sup>-4</sup> M. Frequent phasic contractions occurred especially at submaximal stimulation and were abolished by addition of 10<sup>-5</sup> M indomethacin in the bathing medium. Ondansetron had no effect in the concentrations used in the maximum response of 5-HT curve. *Conclusion:* 5-HT, an important gut neurotransmitter, has a role as a mediator in gallbladder motility. Ondansetron, a widely used powerful anti-emetic, did not affect contractility, suggesting no role of 5-HT<sub>3</sub> receptors in gallbladder motility in our experimental model. Motility, general: Receptors and signals } "Role of 5-Hydroxytryptamine in Gall Bladder Motility"

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## "P P 31 0745" P 31 0745 Cholescintigraphic Assessment of Bile Flow Delay in Symptomatic Cholecystomized Individuals

\*E. Tankurt, E. Ellidokuz, H. Durak, B. Degirmenci, H. Akbaylar, I. Simsek, \d6. G\`f6nen

Depts. of Gastroenterology and Nuclear Medicine, Dokuz Eyl\`fcl University, Izmir, Turkey Cholescintigraphy is one the proposed methods in the evaluation of sphincter of oddi functions in cholecystomized individuals. *Aim:* We evaluated the scintigraphic hepatic hilum-duodenum transit time (HHDTT) in symptomatic and asymptomatic cholecystomized outpatients in this study. *Methods:* Ten cholecystomized patients with typical biliary type pain were included in the study. These were 2 males and 8 females with a mean age of 51.1 – 10.4. Seven asymptomatic cholecystomized individuals (all female with a mean age of 45.0 – 14.5) were included, as the control group. All of the patients and control subjects were evaluated by ERCP and/or ultrasonography (USG) and had no evidence of choledocholithiasis. Biliary emptying was measured by hepatobiliary scintigraphy using 5 mCi Tc-mebrofenine. *Results:* HHDTT was longer than 8 minutes in 6 patients (60%) while it was 7 minutes or shorter in all of the control subjects. The mean value of HHDTT was 12.7 – 3.3 (3–19) and 6.0 – 0.4 (4–7) minutes in patients and controls respectively ( $p < 0.05$ ). On the other hand, dilatation of common bile duct (more than 8 mm) was present in 6 patients but none of the controls. No correlation was found between the common bile duct diameter and HHDTT. *Conclusion:* Cholescintigraphic HHDTT is delayed in some cholecystomized patients with typical biliary type pain. This group may require further investigations or therapy (e.g. sphincterotomy). Endoscopy, specific: Biliary Radiology and ultrasound: Diagnosis } "Cholescintigraphic Assessment of Bile Flow Delay in Symptomatic Cholecystomized Individuals"

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"P P 32 0747" P 32 0747 **Incidence of Colorectal Adenomas (CRA) in a Cohort without Prior Personal or Family History of CRA or Colorectal Cancer (CRC)**

\*B. Paillot, P. Czernichow, P. Michel, A.M. Queuniet, C. Daubert

Centre H. Becquerel and Hop. Ch. Nicolle F 76031 Rouen, France Although people without history of CRA or CRC constitutes the vast majority of the population, it is difficult to recommend a definite attitude towards prevention for this group which is considered at low risk, according to prevalence studies. The aim of this study was to evaluate the incidence rate which has not been determined until now. The study includes 450 persons enrolled in a colonoscopic cancer prevention program since 1979 to 1992 who had at least 2 flexible sigmoidoscopies. Participants who had at the 1st exam present or past personal or first degree relatives history of CRA or CRC were excluded. The material consist of 298 women (66%); 170 persons were less than 50 yrs old (38%) while 28 were 70 or older (16%). The mean annual incidence rate has been calculated with a 95% confident interval (CI) from the actuarial method. Age and sex influence has been evaluated by mean of the Log-rank test. The median time of follow-up was 46 mths (9–160) and 163 persons (36.2%) underwent more than 2 exams (max. = 6). 32 subjects with CRA have been detected i.e. a mean annual incidence rate of 1.7% (CI: 1.0%–2.3%). It was higher for men than for women ( $p < 0.03$ ), and it increased with age ( $p < 0.01$ ). These rates are much lower than those known for people with prior CRA or CRC which are about 10%/yr, and could be taken into consideration when screening the general population by sigmoidoscopy. Oncology, general: Screening, prevention Oncology, general: Epidemiology Oncology, specific: Colon, rectum } "Incidence of Colorectal Adenomas (CRA) in a Cohort without Prior Personal or Family History of CRA or Colorectal Cancer (CRC)"

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"P P 32 0748" P 32 0748 **Negative Influence of Homologous Blood-Transfusions on the Evolution of Patients with Colorectal Carcinoma. {A Meta-analysis}** R. Meier<sup>1</sup>,

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<sup>2</sup> University Hospital Basle, Switzerland

Janssen-Cilag AG, Baar, Switzerland Several publications mainly based on retrospective data, had shown a Negative influence of homologous blood-transfusions (HBT) on the evolution of patients with colorectal carcinoma. Several prospective studies have tried to clarify the issue and this analysis is an attempt to quantitatively assess the current knowledge. *Material and Methods:* This analysis concerns only prospective studies in colorectal Ca. listed in Medline between 1984 and 1996. Patients were classified as receiving homologous blood (HBT), autologous (ABD) or no blood transfusion (No BT). The time of transfusion considered was from the immediate pre- until the post-operative period. The parameters analyzed were 1\b0) the incidence of post-operative infections and 2\b0) Recurrence rates (both local & distant) at study end-point (usually 5 years). Data were analyzed using the Mantel-Haentzel-Peto method; significance was accepted if  $p < 0.05$ . *Results:* Rate of infections: 5 Studies compared HBT to No BT (N = 1594) and 3 studies compared HBT to ABD (N = 694) Rate of infections were 32% vs. 12% ( $p < 0.001$ ) and 27% vs. 22% (n.s.). Recurrence rates: 3 Studies compared HBT to No BT (N = 1556) and 2 studies compared HBT to ABD (N = 338) Rate of recurrence were 41% vs. 24% ( $p < 0.001$ ) and 41% vs. 31% (n.s.). The combined risk of an infection and/or recurrence is almost significantly higher after HBT than after ABD (Odds Ratio = 1.32;  $p = 0.054$ ). *Conclusions:* Patients requiring a BT appear to be at higher risk of infection or recurrence than No BT, but the comparability of these pts. is questionable. Patients receiving HBT appear to be at a somewhat greater risk of infection or recurrence than those receiving ABD. Larger studies are needed in order to give a final answer to this question. }" "Negative Influence of Homologous Blood-Transfusions on the Evolution of Patients with Colorectal Carcinoma. {A Meta-analysis}"

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**"P P 32 0749" P 32 0749 Human Papillomavirus (HPV) and Colon Cancer: No Viral DNA Sequence Found neither in Tumors nor in Normal Adjacent Mucosae. Jullian, R. Benamouzig, A. Mordrelle, A. Martin, A. Pompidou, J. Rautureau**

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Hospital Avicenne, 93009 Bobigny Cedex, France The presence of human papillomavirus 6, 16, 18 and 33 was previously reported in up to 50% of colorectal carcinomas (Cheng et al, Gut 1995). The E6 protein of these high risk types was shown to bind to the tumor suppressor p53 protein and to promote its degradation. The aim of our study was to further investigate the putative role of these HPV types in colorectal carcinogenesis. Tumoral samples stored in liquid nitrogen from 55 patients were used. Normal adjacent mucosae was also available in all these cases. All clinicopathological data including age, sex, histological differentiation, immunohistochemical p53 status, tumour stage, tumour location, metastatic status and survival years were recorded. Samples were growded in liquid nitrogen. DNA was extracted with phenol-chloroform after lysis in buffer with detergent and proteinase K. Two PCR experiments were performed: (i) multiplex PCR using 3 sets of primers (E6 gene of HPV 16, 18 and internal control target located into the embryonic myosin heavy chain gene (ii) another one using consensus L1 primers. The PCR products were analysed after restriction mapping on 5% polyacrylamide gel stained with ethidium bromide. This multiplex HPV 16/18 PCR shows a sensitivity of 15 viral copies per sample. HPV DNA sequences could not be detected in any of the tumoral sample nor in the normal adjacent mucosa by any of the PCR techniques used. These results suggest that HPV are not involved in colorectal carcinogenesis at least in French patients. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum Immunology and microbiology: GI infections in adults }" "Human Papillomavirus (HPV) and Colon Cancer: No Viral DNA Sequence Found neither in Tumors nor in Normal Adjacent Mucosae"

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"P P 32 0750" P 32 0750 **The Role of Cholecystectomy in the Oncogenesis of the Digestive Tract** Daniel Tuculanu<sup>1</sup>, Ioan Romosan<sup>1</sup>, Iosif A. Szucsik<sup>2</sup>, Constantin Tudor<sup>1</sup>, Lelia Susan<sup>1</sup>, Calin Dascau<sup>1</sup>

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<sup>2</sup> 3-rd Surgical Clinic, University of Medicine and Pharmacy Timisoara, Romania The preset study estimates the oncogenic risk after cholecystectomy, starting from the fact that the duodeno-gastric reflux (commonly noticed in cholecystectomized patients) is one of the major factors involved in the occurrence of gastric epithelium metaplasia. The authors have carried out a retrospective analysis of 462 cases that were consecutively diagnosed in our medical department with cancers of the digestive tract: 67 cases with oesophageal cancer, 223 cases with gastric cancer and 172 cases with colo-rectal cancer. Seventy-nine patients had cholecystectomy in their history (9% of those with oesophageal cancer, 17% of those with gastric cancer, and 20% of those with colo-rectal cancer). In all three localisations the subgroups of cholecystectomized patients presented certain features that differentiated them from the rest of the patients: in the case of the oesophagus we noticed the predominance of the feminine gender, of the localisation in the lower third, and of the adenocarcinoma histological type; in the case of the stomach we noted the prevalence of the fungating endoscopic type and of intestinal histological type; in the case of colo-rectal cancer the localisation in the right half of the large bowel were predominant. A common characteristic for all localisations was the earlier age when the cancer set in and a long period since the surgical intervention. All these data suggest that cholecystectomy plays a role in the oncogenesis of the digestive tract, either through the direct action of the biliary constituents (lysolecithin, biliary acids), or through the sensitivisation of the mucosa to the action of other aggressive factors. Oncology, specific: Oesophagus Oncology, specific: Stomach Oncology, specific: Colon, rectum } "The Role of Cholecystectomy in the Oncogenesis of the Digestive Tract"

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**"P P 32 0751" P 32 0751 Family Study on Colorectal Cancer from the Digestive Cancers Registry of "Calvados": An Intermediate Report**

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<sup>1</sup> Unité INSERM 351, Villejuif, France

<sup>2</sup> Registre des tumeurs digestives du Calvados, Caen- France In France, colorectal cancer (CCR) is the most frequent cancer for both females and males (26000 new cases each year). Although an increased risk has been associated with a family history of CCR in nearly all epidemiological studies, few population-based family studies have been performed. A population-based family study has been carried out in Calvados, France, from September, 1st, 1993. The main aim of this study is to define the role of genetic factors in the disease transmission accounting for environmental factors from a sample of systematically recorded family data. Results of a feasibility study connected with the above study showed a high proportion of contacted people who agreed to participate and a good representativity of the recruited cases compared with the registered cases. A report of the definitive study progress is presented in this paper. During 30 months, 837 new cases of colorectal cancer have been diagnosed in Calvados. Four hundred three families have been included today. A high proportion of included persons (index cases and relatives) accepted being taken a blood sample (about 80%). The mean age for the index cases is 68.1 years for men (age range: 39 to 91 yrs) and 69.8 years for women (age range: 34 to 94 yrs). Twenty two per-cent of the families have at least one colorectal cancer in addition to the index case. For 14 per-cent of them, at least one colorectal cancer occurred in the first degree relatives (i.e: sibship, children or parents). Fifteen per-cent of the families have at least one breast cancer, 13% a stomach cancer. For 7 per-cent of the families, one breast or one stomach cancer occurred in the first degree relatives. The recruitment of new cases will stop in September 1997. About 670 families are expected to be included. Oncology, specific: Colon, rectum Oncology, general: Epidemiology Oncology, general: Molecular biology, genetics } "Family Study on Colorectal Cancer from the Digestive Cancers Registry of "Calvados": An Intermediate Report"

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"P P 32 0752" P 32 0752 **Selenium Status in the Patients with Colorectal Adenoma and Colorectal Carcinoma**

\*R. Krstic, M. Ugljesic, T. Milosavljevic, M. Bulajic, I. Ujic

Institute for Digestive Diseases, University Clinical Center, Belgrade, Yugoslavia Selenium is increasingly recognized as a versatile anticarcinogenic agent. Selenium appears to operate by several mechanisms depending on dosage and chemical form of Selenium (Se) and the nature of the carcinogenic stress. Se prevents the malignant transformation of cells by acting as a "redox switch" in the activation/inactivation of cellular growth factors and other functional proteins through the catalysis of oxidation/reduction reactions. We investigated Se status in the colorectal adenoma (CA) group of patients (pts.) who underwent endoscopic polypectomy, and operated group of pts. with colorectal carcinoma (CC). The control group were healthy volunteers from Public Health Medicine. Concentrations of Se were examined in polyp tissue, carcinoma tissue, plasma, erythrocyte, lymphocytes, hair and 24-h urine samples. Malondialdehyde (MDA) was also investigated as an indicator of oxidation stress. The results showed that CA group and CC group of pts. had significantly lower concentrations of Se in erythrocytes and in plasma, Se concentrations were increased in urine, and it was lower in hair and lymphocytes, but not significantly. Se concentrations in CA tissues was higher, in CC tissue was lower, comparing with healthy volunteers. Concentrations with Se were lower in the examined operative edge of the colonic tissue in the CC group, comparing with healthy volunteers. Values of MDA were 200–1000 times higher in the CC tissue and 6–40 times in the CA tissue, comparing with healthy volunteers. Oncology, specific: Colon, rectum Nutrition: Nutrients and gut function } "Selenium Status in the Patients with Colorectal Adenoma and Colorectal Carcinoma"

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## "P P 32 0753" P 32 0753 **Familial Adenomatous Polyposis in Lithuania**

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*Purpose of the study:* While establishing the polyposis register, to present data on familial adenomatous polyposis patients (FAP) in local population. *Methods used:* From March 1995 to March 1996, possible data on polyposis patients in our republic was collected and information disseminated via professional and public sources about the register and disease itself. Screening of the 1<sup>st</sup> relatives was centralized and attempts to coordinate prophylactic treatment were made. Criteria of registration followed international guidelines. *Results:* 23 polyposis families were registered with known 54 affected persons. 9 of these families have been isolated cases. A detailed information on 17 patients with colorectal cancer revealed 4 (23.5%) to have synchronous cancers. Earliest onset of colorectal cancer was in a 21 year old male. From 16 patients 12 (83%) had duodenal adenomas, from 16 patients 4 (32%) had mandibular osteomas and 13 (93%) of 14 patients had CHRPE (congenital hypertrophy of retinal pigment epithelium). First DNA tests have been performed for our polyposis patients. *Conclusion:* Increasing collaboration with medical professionals and knowledge about FAP should be an important factors influencing further successful registration and treatment of FAP patients. Oncology, general: Screening, prevention Oncology, general: Epidemiology Oncology, specific: Colon, rectum } "Familial Adenomatous Polyposis in Lithuania"

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"P P 32 0754" P 32 0754 **Screening for Hereditary Non-Polyposis Colorectal Cancer within a County Register in Romania**

\*L. Gheorghe, G. Aposteanu, C. Gheorghe, Al. Oproiu

Center of Gastroenterology, Fundeni, Bucharest, Romania One of the most important roles of the hereditary non-polyposis colorectal cancer (HNPCC) Registry is to coordinate the screening programs. It provides the opportunity for colorectal cancer (CRC) prevention in family members who are at 50% lifetime risk. The aim of this prospective controlled longitudinal study was to evaluate the efficacy of the screening within a county HNPCC Registry (established in early 1989) in Bucharest area in Romania.; 21 families fulfilling "the Amsterdam criteria" were extracted from a cohort of 808 CRC between March 1990–March 1996. For the ascertainment of probands, information were collected about all types of malignancies, age at onset, location and histology. The genealogical studies and pedigrees construction were made as accurate as possible. The family members at risk were identified and call-up into the study. The screening group consisted in 54 subjects undergoing periodic examinations (full colonoscopy/sigmoidoscopy and barium enema) at 2–3 yr. interval whereas 87 subjects of the control group had no screening examinations. The adenoma/CRC detection and survival curves were compared by the Kaplan-Meier product limit method between the two groups of asymptomatic at-risk subjects. Adenoma/CRC occurred in 10/6 screened subjects (16.5% positive examinations) vs 2/20 control subjects. The tumor Dukes stage (A + B vs C + D) was more favorable in screened group with one case of death caused by CRC vs 10 in control group at the end of the study. Although the adenoma/CRC occurrence did not differ significantly ( $p = 0.81$ ), survival curves showed a significantly better survival in screened vs non-screened subjects ( $p = 0.04$ ). *Conclusion:* the 2–3 yr. interval screening programs on HNPCC, although detecting a similar rate of neoplastic colorectal changes, demonstrate a significant survival benefit in screened vs non-screened subjects with HNPCC, contributing to a more favorable prognosis. Oncology, specific: Colon, rectum Clinical practice: Management strategy Endoscopy, specific: Colon, rectum } "Screening for Hereditary Non-Polyposis Colorectal Cancer within a County Register in Romania"

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**"P P 32 0755" P 32 0755 Hereditary Non Polyposis Colon Cancer (HNPCC) Prevalence: A Prospective Multicentric Study**

\*G. Riegler, A. Savastano, F. Selvaggi, R. Ciociano, G. Riccio, E. Manzo, R. Iorio, R. Carratu', Gruppo di Studio SIED-Campania, P. Borgheresi, G.B. Rossi, G.D. DePalma, P. Russo, A. Piscitelli, F. Baldi, F. Guardascione, P. DiGiorgio, E. D'Avenia, F. Montanaro, E. Parente, O. Saffiotti, M. Bozzi

Seconda Università di Napoli, Cattedra di Gastroenterologia -Italy Prevalence of HNPCC was reported to be 1–5% depending on the adopted criteria. The aim of this study was to define the prevalence in a South Italy region (Campania), lacking in a Cancer Register. We have studied 501 patients with endoscopic first diagnosis of colorectal cancer, observed in 13 Campania clinics. The Family Pedigrees have been collected and all cases of cancer reported, checking the diagnosis from death certification, case sheet and evidence of the family doctor. The 501 patients included 275 men and 226 women: 61 (12.2%) < 50 years of age. Twenty-four (4.8%) showed vertical transmission - and 38 (7.6%) transversal aggregation - of colorectal cancer. Right colon localization (upper splenic flexure) was shown by 125 (25%) pts with 7 cases (1.4%) of synchronous tumours. We have identified 5 (1.0%) HNPCC families that corresponded to Amsterdam criteria (a = at least three colorectal cancer, b = two first-degree relatives with cancer in different generation, c = one of them less of 50 years old). Amsterdam criteria seemed to be too restrictive, so we have weighted the prevalence with the "three less one criteria method": a + b conditions were shown by 6 pts (1.2%), a + c by none, b + c by 3 pts. (0.6%). In conclusion, with expanded criteria, fourteen HNPCC patients were recorded with a prevalence of 2.79%.  
Oncology, general: Epidemiology  
Oncology, specific: Colon, rectum  
Oncology, general: Molecular biology, genetics } "Hereditary Non Polyposis Colon Cancer (HNPCC) Prevalence: A Prospective Multicentric Study"

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## "P P 32 0756" P 32 0756 **Increased Prevalence of Adenomas in Colorectal Cancer Patients from HNPCC Kindreds**

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Portugal *Background:* Hereditary non-polyposis colorectal cancer (HNPCC) is an autosomal dominantly inherited syndrome characterized by propensity to develop colorectal cancer (CRC) at a young age. There is increasing evidence that aggressive adenomas are the precursor lesions in HNPCC. Whether there is an increased prevalence of adenomas is still unclear. The assessment of the nature of precancerous lesions in HNPCC will have a major impact on the design of preventive strategies. *Aims:* To compare the prevalence and histopathology of adenomas in CRC-bearing members of HNPCC kindreds with sporadic CRC patients. *Patients and Methods:* We included 11 patients with CRC retrospectively classified as belonging to HNPCC kindreds (Group A) and 59 consecutive patients with sporadic CRC (Group B). HNPCC was diagnosed according to Amsterdam criteria. Absence of information regarding the entire colon was an exclusion criteria for both groups. We registered all adenomas found in the perioperative colonoscopy, operative specimen and endoscopic examinations of the remaining large bowel during routine surveillance. Adenomas and cancers were classified according to WHO criteria. Staging was by the Dukes classification. Differences between groups were calculated using the chi-square test. *Results:* Group A – 11 patients, 1 male and 10 females, mean age 54.2 (b1 13.9); Group B – 59 patients, 31 males and 28 females, mean age 59 (b1 10.3). CRC location: Group A – rectum 18% (2/11), left colon 18% (2/11), right colon 64% (7/11); Group B – rectum 45% (26/59), left colon 25% (15/59), right colon 30% (18/59). CRC histopathology and Dukes stage were similar in both groups (except for the greater frequency of mucinous tumors in Group A – 54% vs 17%). We found synchronous adenomas in 54% of patients in Group A (6/11) and in 25% of patients (15/59) in Group B –  $p < 0.05$ . There was a trend towards greater adenoma size in Group A (19.8 mm vs 13.9 mm) compared to Group B. We found no differences in the frequency of villous features or high grade dysplasia. Mean time of follow up was similar in both groups (58.2 months, 4–495). Metachronous adenomas were detected in 66.6% of Group A patients and 15.7% of Group B patients –  $p < 0.01$ . *Conclusions:* CRC in HNPCC patients is associated with an increased prevalence of adenomas, both synchronous and metachronous. This strongly supports the idea that adenomas are the precursor of cancer in HNPCC, further supporting the profilactic value of colonoscopic surveillance. Oncology, specific: Colon, rectum Oncology, general: Proliferation, carcinogenesis } "Increased Prevalence of Adenomas in Colorectal Cancer Patients from HNPCC Kindreds"

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"P P 32 0757" P 32 0757 **Mutational Analysis of the hMLH1 Gene Using an Automated Two-Dimensional DNA Typing System**

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<sup>2</sup> Laboratory of Molecular Medicine, Institute of Medical Science, Tokyo, Japan *Purpose:* At present, single-strand conformation polymorphism (SSCP) is the most widely used method of mutational analysis because of its simplicity and relatively high sensitivity. However, SSCP is not economical when the number of samples is small. Moreover, regarding sensitivity, the method called denaturant gradient gel electrophoresis (DGGE) is more excellent. Hence, we tried to set up optimal conditions of an automated two-dimensional DNA typing system based on the principle of DGGE for mutational analysis of hMLH1 and to examine its usefulness as a mutational analysis method. *Methods:* To determine optimal conditions, we used five different kinds of germline mutation among six HNPCC pedigrees and two somatic mutations in a single RER+ sporadic endometrial cancer, which had been already revealed by other means. Furthermore, by this method we screened the entire coding regions of hMLH1 in DNAs isolated from affected individuals belonging to two HNPCC kindreds and four HNPCC-like kindreds, and from four patients with multiple primary cancers as well as eight RER+ sporadic colorectal cancers. *Results:* All mutations used as positive controls were detectable by the 2-D DNA methods. Twenty-one spots covering all 19 coding exons were visualized on a single gel, and we could envisage whether and where any mutations existed. We also detected novel germline mutations in one HNPCC proband and one RER+ sporadic colorectal cancer, and one polymorphism in two HNPCC-like kindreds. *Conclusion:* This new diagnostic method is very useful and offers a major improvement over current approaches. Oncology, general: Molecular biology, genetics Oncology, general: Screening, prevention Oncology, specific: Colon, rectum } "Mutational Analysis of the hMLH1 Gene Using an Automated Two-Dimensional DNA Typing System"

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## "P P 33 0758" P 33 0758 The Influence of Intestinal Transit Rate on Colonic Luminal pH and Stool Short Chain Fatty Acid Concentration

\*S.J. Lewis, K.W. Heaton

Department of Medicine, Bristol Royal Infirmary, Bristol BS2 8HW Populations at low risk of colonic cancer consume large amounts of fibre and starch (fermented by bacteria to short chain fatty acids (SCFA)) and pass acid bulky stools. Traversing the colon SCFA are absorbed and luminal pH increases to neutral. One SCFA, butyrate, is the colon's main energy source and inhibits malignant transformation *in vitro*. Low colonic pH should be associated with high levels of butyrate and thus decreased predisposition to cancer. We set out to test two hypotheses: 1. Altering colonic transit rate alters colonic pH. 2. Distal colonic luminal pH is correlated with the SCFA (especially butyrate) content of the stools. 13 healthy volunteers took in turn supplements of wheat bran (mean 28.3 g/day), senna laxative and loperamide, each for nine days with a 2 week washout period. Before and in the last 4 days of each intervention period dietary intake, whole gut transit time (WGTT), stool pH, stool SCFA concentrations (by GLC) and intracolonic pH (using a radiotelemetry capsule for continuous monitoring) were assessed. There was no difference between dietary intakes specifically total fibre, NSP or fat at the start and end of each interventional period. pH measurements were similar in the distal colon and stool. WGTT decreased and stool output increased with wheat bran and senna, *vice versa* with loperamide. Changes in WGTT were least impressive for wheat bran. Baseline stool SCFA concentration correlated with distal colonic pH ( $r = -0.417$ ,  $p = 0.01$ ) and WGTT ( $r = -0.623$ ,  $p < 0.001$ ), similar correlations were seen for baseline stool butyrate (distal pH  $r = 0.434$ ,  $p = 0.007$  & WGTT  $r = 0.610$ ,  $p < 0.001$ ). Colonic pH and stool SCFA concentration: effect of transit-altering agents Mean Colonic pH Stool SCFA ( $\mu\text{mol/g}$ ) \* $p < 0.05$  Middle Distal Butyrate Total start end start end start end start end Wheat bran 6.8 6.6 7.1 6.9\* 69 79 443 451 Senna 6.9 6.4\* 7.1 6.7\* 63 193\* 376 836\* Loperamide 6.9 7.0 7.1 7.2 69 23\* 531 345\* There is a relationship between bowel transit rate (diet being constant) and stool pH, stool SCFA concentration and distal colonic pH. This may explain the associations between colonic cancer and dietary fibre, stool output and stool pH, in that stool pH is a marker for SCFA levels including butyrate. Nutrition: Nutrients and gut function Motility, specific: Colon, anorectum } "The Influence of Intestinal Transit Rate on Colonic Luminal pH and Stool Short Chain Fatty Acid Concentration"

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**"P P 33 0759" P 33 0759 Non-Invasive Recording of Colonic Electrical Activity Based on Experimental Investigations A. Noeva,**

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The study was aimed at non-invasive recording of the electrical activity of the human colon, i.e. electrocolography (EColG). Experiments were made on dogs with silver, bipolar, ball-shaped electrodes chronically implanted on the muscle wall of the colon. Skin electrodes were placed on the abdominal wall in the beginning of each experiment. Slow waves were led off in the electrocolomyogram (EColMG), corresponding to low-amplitude waves in the non-invasive electrocologram (EColG). The bursts of spike potentials with the colonic slow waves in the EColMG corresponded to an increase of the amplitude of the EColG waves, manifesting an increased colonic motility. There was a good correlation between the number and frequency of spike potentials in a group and the wave amplitude in the EColG. Thus the functional state of the colon could be judged by the differences in the amplitude of the EColG waves. The electrical activity of the descendent colon of fifteen healthy volunteers was recorded by skin electrodes stuck on the abdominal wall along the descendent colon projection. The electrogastrogram (EGG) was led off too. The electrical activity of the colon and stomach were recorded on an original 2-channel electrogastrograph. A method for complete elimination of the cardiac artifacts was elaborated and successfully implemented. The means – S.E.M. of the frequency of colonic and gastric waves were calculated. Two kinds of EColG waves according to the frequency were identified: i) waves with a frequency in the range of 5.85 – 0.50 cpm and ii) waves with a frequency in the range of 2.37 – 0.31 cpm. The frequency of the EColG waves was compared with that of the EGG waves. There was a significant difference between the frequencies of the EColG waves and the frequency of the EGG waves – 3.26 – 0.26 cpm (n = 7). Thus the proposed electrogastrographic method proved to be suitable for non-invasive registration of the electrical activity of the human colon. It could also provide reliable information on the EColG wave frequencies at visual inspection. Supported by Grant L-539 from the National Fund "Scientific Research", Bulgaria. } "Non-Invasive Recording of Colonic Electrical Activity Based on Experimental Investigations"

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## "P P 33 0760" P 33 0760 Characteristics of Cecal Circular Smooth Muscle Cells from Guinea Pigs with Carrageenan-Induced Colitis

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<sup>1</sup> Harasanshin Hospital, Taihakucho 1–8, Hakata-ku, Fukuoka, Japan

<sup>2</sup> Third Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan Studies on the functional changes in colonic muscle from patients with ulcerative colitis (UC) have yielded conflicting results. This study was designed to evaluate the inflammation-associated changes in colonic muscle motility using isolated cecal circular smooth muscle cells from guinea pigs with carrageenan-induced colitis (UC-like colitis). The smooth muscle cell length in the basal state of animals with colitis was compared with that in normal animals. In addition, the effect of contractile agents (cholecystokinin-8 [CCK-8], carbachol), and relaxing agents (N<sup>6</sup>, 2'-O-dibutyryl adenosine 3', 5'-cyclic monophosphate [dBcAMP] and N<sup>2</sup>, 2'-O-dibutyryl guanosine 3', 5'-cyclic monophosphate [dBcGMP]) on isolated muscle cells with or without colitis were assessed. In the basal state, the mean cell length in animals with colitis was significantly ( $p < 0.001$ ) shorter than that in normal animals. CCK-8 and carbachol-induced contraction with colitis was significantly decreased by 72.2% ( $p < 0.05$ ) and 60.3% ( $p < 0.001$ ), respectively, compared with that in normal animals. dBcAMP and dBcGMP had no significant effect on smooth muscles from animals with colitis. The data showed that the weak contractile response in animals with colitis was due to the basal cell length which was significantly shorter than that in normal animals, and suggested that the relaxing mechanism of smooth muscles in animals with colitis was disturbed. Intestinal disorders: IBD, basic Motility, general: Functional GI disorders Motility, specific: Colon, anorectum } "Characteristics of Cecal Circular Smooth Muscle Cells from Guinea Pigs with Carrageenan-Induced Colitis"

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"P P 33 0761" P 33 0761 **Histopathology of Hypoganglionosis in Whole Mount Preparations of the Human Colon**

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Department of Medicine IV, Univ. Hosp. of Heidelberg at Mannheim, Germany

<sup>1</sup> Dept of Pathology, Univ. of Basel, Switzerland Traditional histopathological methods like the acetylcholin-esterase reaction on sections of the colon bowel are normally used to diagnose and to investigate the histopathology of abnormalities of the enteric nervous system including the hypoganglionosis. The hypoganglionosis is only defined as a reduction of nerve cells of about 50%. In contrast to these methods we have investigated the histopathology of the enteric nervous system in whole mount preparations of resected segments of the colon of 10 patients suffering from severe constipation caused by aganglionosis and hypoganglionosis by NADPH-diaphorase reaction. We could recognize that the meshwork of the enteric plexus is very irregular. The density of the ganglia and nerve strands is reduced. The ganglia are very small and contain a small number of nerve cells. The morphology of the nerve cells is very uniform in contrast to normal enteric nerve cells. Functionally the nerve cells are characterised by weak NADPH-staining as expression of low NOS-content, which can cause constipation. We may conclude that NADPH-diaphorase-reaction on whole mount preparations of the human colon is a simple and reproducible method for the histopathological investigation of congenital defects of the ENS. Using this methods we could provide a completion to the previous histopathological image of the hypoganglionosis. sponsored by DFG: Kr 1257/2-1 Motility, general: Innervation Motility, specific: Colon, anorectum } "Histopathology of Hypoganglionosis in Whole Mount Preparations of the Human Colon"

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## "P P 33 0762" P 33 0762 Direct Contractile Effect of CCK on Caecal Circular Smooth Muscle Cells Via Both CCK<sub>A</sub> and CCK<sub>B</sub> Receptors

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Cholecystokinin (CCK) contracts gastrointestinal smooth muscle cells. However there has not been sufficient investigation about receptors for CCK on smooth muscle cells. Receptors for CCK are divided into two subtypes: CCK<sub>A</sub> and CCK<sub>B</sub>. This study was designed to investigate the CCK receptor subtype responsible for caecal circular smooth muscle contraction by CCK. *Methods:* Smooth muscle cells were isolated from caecal circular smooth muscle layer of the guinea pig. Cells were stimulated by test agent. At the end of incubation, acrolein was added. The length of 50 cells in microscopic fields was measured by image splitting micrometry, and the percent decrease in mean cell length was determined by comparison with the control. Kinetic studies were performed. Cells were incubated with a fixed concentration of CCK-8 for various length of time. For subsequent experiments, the optimal incubation time was used. A dose-response curve for CCK-8 ( $10^{-13}$ – $10^{-8}$  M) was determined. We assessed the inhibitory effect of various concentrations of CCK<sub>A</sub> receptor-selective antagonist, FK480 on  $10^{-9}$  M CCK-8-induced contraction; the inhibitory effect of various concentrations of CCK<sub>B</sub> receptor-selective antagonist, YM022 on  $10^{-9}$  M CCK-8-induced contraction; the inhibitory effect of  $10^{-10}$  M FK480 on each concentrations of CCK-8-induced contraction; the inhibitory effect of  $10^{-10}$  M YM022 on each concentrations of CCK-8-induced contraction; and the inhibitory effect of a combination of  $10^{-10}$  M FK480 and  $10^{-10}$  M YM022 on each concentrations of CCK-8-induced contraction. *Results:* Both FK480 and YM022 inhibited  $10^{-9}$  M CCK-8-induced contraction in a concentration-dependent manner. A significant inhibition was obtained at a concentration as low as  $10^{-10}$  M FK480 and  $10^{-10}$  M YM022. At a concentration of  $10^{-10}$  M, both FK480 and YM022 shifted the concentration-response curve for CCK-8 to the right. In addition, a combination of  $10^{-10}$  M FK480 and  $10^{-10}$  M YM022 shifted the concentration-response curve for  $10^{-10}$  M FK480 alone or  $10^{-10}$  M YM022 alone to the right. *Conclusion:* Our results strongly suggest that the guinea-pig caecal circular smooth muscle cell contains both CCK<sub>A</sub> and CCK<sub>B</sub> receptors and the contractile effect of CCK-8 is mediated via both of these receptors. Motility, general: Receptors and signals Motility, specific: Colon, anorectum } "Direct Contractile Effect of CCK on Caecal Circular Smooth Muscle Cells Via Both CCK<sub>A</sub> and CCK<sub>B</sub> Receptors"

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"P P 33 0763" P 33 0763 **Long-Term Octreotide Treatment Increases Large Bowel Transit Time (LBTT), the Proportion of Deoxycholic Acid (% DCA) in Serum and the Risk of Gallstone Formation**

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<sup>2</sup> Depts of Endocrinology St Bartholomew's Hospital, London

<sup>3</sup> The Radcliffe Infirmary, Oxford, UK *Background:* OT increases the % DCA and the cholesterol saturation of gallbladder bile and together with impaired meal-stimulated gallbladder emptying, this induces the formation of cholesterol-rich gallbladder stones (GBS). Prolongation of intestinal transit has been proposed as the mechanism for the increase in the % DCA, but our earlier unpaired studies failed to show a significant effect of OT on large bowel transit — important since the colon is the site of DCA formation and absorption. *Methods:* We, therefore, used a radio-opaque marker shape technique to measure LBTT in 8 acromegalic patients (age range 22–69; 4 women) before and during long-term (> 3 months) octreotide treatment (100–200 µg tds by sc injection). Moreover since there is an exchange, and ultimately an equilibrium, between bile acids in serum and bile, we also measured the % DCA in fasting serum from 6 of these patients, using gas chromatography-mass spectrometry. *Results:* The mean LBTT increased from 42 – SEM 4.3 h before to 55 – 5.1 h during OT treatment ( $p < 0.0001$ ) and the mean % DCA increased from 15 – 2.5% to 28 – 4.7% ( $p < 0.05$ ). Furthermore, there was a significant linear relationship between LBTT and % DCA ( $r = 0.87$ ,  $p < 0.0005$ ). *Conclusions:* The results of these paired studies show that OT prolongs LBTT and leads to an associated increase in the % DCA in serum, and by implication the % DCA in bile — thereby increasing the risk of gallstone formation. Liver and bile ducts, 2: Gallstones, formation, treatment Liver and bile ducts, 2: Bile acids synthesis Motility, specific: Colon, anorectum }" "Long-Term Octreotide Treatment Increases Large Bowel Transit Time (LBTT), the Proportion of Deoxycholic Acid (% DCA) in Serum and the Risk of Gallstone Formation"

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## "P P 33 0764" P 33 0764 Presence of Functional Receptors for Corticotropin Releasing Hormone in Caecal Circular Smooth Muscle Cells of Guinea Pig

\*Y. Iwakiri, Y. Chijiwa, Y. Motomura, H. Akiho, H. Nawata

Third Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan Smooth muscle cells isolated separately from the caecal circular smooth muscle layer of the guinea pig were used to investigate whether corticotropin releasing hormone (CRH) can inhibit directly the contraction produced by cholecystokinin octapeptide (CCK-8). And the role of adenylate cyclase and guanylate cyclase in the direct inhibitory effect of CRH was examined. In addition,  $^{125}\text{I}$ -CRH binding was examined to demonstrate the presence of specific binding site for CRH on isolated smooth muscle cells. *Methods:* The inhibitory effect of various concentrations of CRH on  $10^{-9}$  M CCK-8-induced contraction was examined. And the effect of 2',5'-dideoxyadenosine (an inhibitor of adenylate cyclase), adenosine-3',5'-cyclic monophosphorothionate (an inhibitor of cAMP-dependent protein kinase), phorbol 12-myristate 13-acetate (an inhibitor of particulate guanylate cyclase), 6-amilino-5, 8-quinolinedione (an inhibitor of soluble guanylate cyclase) on the CRH-induced relaxation of caecal circular smooth muscle cells were examined. In addition, the time course changes in  $^{125}\text{I}$ -CRH binding and the ability of unlabeled peptides to displace  $^{125}\text{I}$ -CRH were examined. *Results:* CRH inhibited the contractile response produced by  $10^{-9}$  M CCK-8 in a concentration-dependent manner. An inhibitor of particulate guanylate cyclase and an inhibitor of soluble guanylate cyclase had no significant effect of the relaxation produced by CRH. In contrast, an inhibitor of adenylate cyclase and an inhibitor of cAMP-dependent protein kinase significantly inhibited the relaxation produced by CRH in a concentration-dependent manner. The specific binding of  $^{125}\text{I}$ -CRH to isolated smooth muscle cells reached maximal binding at 120 min. The specific binding of  $^{125}\text{I}$ -CRH was inhibited by unlabeled CRH in a concentration-dependent manner. *Conclusion:* Our findings show the direct inhibitory effect of CRH on caecal circular smooth muscle cells, and strongly suggest the presence of CRH receptor coupled to adenylate cyclase leading to generation of cAMP and activation of cAMP-dependent protein kinase on these cells. Motility, general: Receptors and signals Motility, specific: Colon, anorectum } "Presence of Functional Receptors for Corticotropin Releasing Hormone in Caecal Circular Smooth Muscle Cells of Guinea Pig"

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## "P P 33 0765" P 33 0765 **Faster Intestinal Transit is Associated with Lower Serum Oestrogens**

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<sup>3</sup> Dept of Obs & Gynae, University College London, WC1E 6HX Any factor limiting reabsorption of oestrogens from the colon should lead to increased faecal excretion of oestrogen and reduced serum oestrogens. High fibre diets and wheat bran supplements reduce serum oestrogens, perhaps explaining associations between a high fibre intake and reduced risk of breast cancer. We hypothesised that fibre reduces serum oestrogen concentrations by speeding colonic transit, reducing the time for bacterial deconjugation (by  $\beta$ -glucuronidase a pH dependent enzyme) and/or reabsorption of oestrogens. To test this we altered whole gut transit times (WGTT) in 3 ways and looked for changes in serum oestrogen and in stool pH and  $\beta$ -glucuronidase activity. 40 healthy premenopausal volunteers were randomised to one of 3 groups. Ten subjects took senna then after a washout period wheat bran, both for 2 menstrual cycles. Another 10 did the reverse. A third group of 20 subjects took loperamide to slow down transit for two cycles. All supplements were taken in the maximum tolerated dose. At the beginning and end of each study period blood was taken for oestrogens (day 6 of the menstrual cycle), a 4 day dietary record was kept, WGTT was measured and stools were analysed for pH and  $\beta$ -glucuronidase activity. Serum oestrone sulphate, the major storage form of oestrogen, fell with wheat bran (average dose 20 g/day) and with senna; both unconjugated and non-protein bound oestrone fell only with senna. No significant changes in serum oestrogens occurred with loperamide. Senna and loperamide caused significant alterations in WGTT; changes in those taking wheat bran supplements tended towards a reduction ( $p = 0.06$ ). No significant changes were seen in faecal  $\beta$ -glucuronidase activity. Stool pH changed only with senna, where it fell. There was no significant change in dietary intakes. Changes in geometric means of serum oestrogens (pmol/l) \* $p < 0.05$

	Oestradiol	Oestrone	Oestrone sulphate	Start	End	Start	End	Start	End
Wheat bran	281	262	240	246	1745	1523	*		
Senna	261	226	252	206	*	1833	1647	*	
Loperamide	233	249	219	240	1641	1820			

Speeding up intestinal transit can lower serum oestrogens. Faster intestinal transit may explain the epidemiological association of low risk of breast cancer with a high fibre intake. Nutrition: Nutrients and gut function Motility, specific: Colon, anorectum } "**Faster Intestinal Transit is Associated with Lower Serum Oestrogens**"

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"P P 33 0766" P 33 0766 **Differential Sensitivity of Isolated Smooth Muscle Cells from Normal and Inflamed Human Colons to Contractile Agents. Effects of Calcium Channel Blockers** J.C. Boyer, C. Guittou, P. Pouderoux, M.O. Christen<sup>1</sup>, J.L. Balmes, J.P. Bali

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Laboratoire de Biochimie des Membranes, INSERM CJF 92-07, Faculté de Pharmacie, Montpellier, France

<sup>1</sup> Solvay Pharma, 42, rue Rouget de Lisle 92151 Suresnes Cedex, France Contractile activity of colonic smooth muscles from patients with IBD yielded conflicting results: some of them showed a decreased activity as compared to normal muscles, others reported no significant changes. We compare contractile response to different agonists of smooth muscle cells (SMC) enzymatically isolated from normal (n = 32) and inflamed (n = 33) human colons. The effects of calcium channel blockers (diltiazem and pinaverium bromide) were also evaluated. Contractile responses to CCK (1 nM), CCh (1 nM) and KCl (20 nM) were evaluated by video-microscopic measurements of the mean length of 100 isolated SMC. The efficacies of agonists were significantly lower to induce contraction of inflamed (CCK: 11.86 – 1.40%, CCh: 10.76 – 1.27%, KCl: 11.12 – 1.40%) than normal (CCK: 16.81 – 1.15%, CCh: 15.72 – 1.14%, KCl: 16.14 – 1.20%) colonic SMC; a significant increase in the level of contractions with age was observed (p < 0.05, Spearman test's). In contrast, no significant correlation with sex, smoking, or with the presence of other diseases was found. Pinaverium induced a significant decrease in cell contraction (about 70%) as well in cells from normal as from inflamed tissues. Diltiazem also induced a decrease in cell contraction, but this effect was lower (55%). In conclusion, this study reveals that contraction of SMC from human colons due to the three main agonists CCK, CCh and KCl (i) increased with age in agreement with a higher sensitivity of the colon with age, (ii) was reduced in patients with inflamed tissues, (iii) calcium channel blockers significantly reduced cell contraction in cells from human colon. } "Differential Sensitivity of Isolated Smooth Muscle Cells from Normal and Inflamed Human Colons to Contractile Agents. Effects of Calcium Channel Blockers"

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## "P P 33 0767" P 33 0767 Relations between Methanogenesis and Sulfate Reduction in the Human Colon

\*H. Kroczyński, P. Pochart, P. Marteau, J. Doré, J.C. Rambaud

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CNAM Paris, France

INRA Jouy en Josas, France Sulfate-reducing bacteria (SRB), which could be important in the pathogenesis of ulcerative colitis and inflammatory bowel diseases, are normal inhabitants of the human colon where they represent the major source of sulfide ( $S^{2-}$ ) from the reduction of dietary and mucinous sulfate. Since they can use  $H_2$  as electron donor, authors hypothesized that SRB outcompete the obligate  $H_2$ -utilizing methanogens for  $H_2$ , leading to a mutual exclusion between methanogenesis and sulfate reduction (*Sred*). *Aim*: To test this hypothesis, we compared fecal SRB,  $S^{2-}$  and *Sred* between methane-excretors ( $CH_4+$ ) and non methane-excretors ( $CH_4-$ ). *Methods*: SRB populations able to use  $H_2$  as electron donor (*Desulfovibrio* and *Desulfobulbus*) were enumerated by the agar shake dilution method,  $S^{2-}$  measured using the methylene blue method and *Sred* by incubation at 37°C under anaerobic conditions in the presence of an excess of sulfate (35 mM). All SRB counts were expressed as  $\log_{10}$  CFU/g wet weight, results are mean – SEM. *Results*: 1) All  $CH_4+$  harboured SRB ranging from 4.9 to 8.0  $\log_{10}$  CFU/g. 2) None of the differences between the two groups were statistically significant. Group SRB  $S^{2-}$  *Sred*  $\log_{10}/g$   $\mu mol/g$   $\mu mol/g/h$   $CH_4+$  (n = 17) 6.6 – 0.3 0.9 – 0.1 3.2 – 0.5  $CH_4-$  (n = 16) 6.5 – 0.3 1.1 – 0.4 2.2 – 0.4. *Discussion*: These results do not support the hypothesis of a mutual exclusion between methanogens and SRB in the human colon. Like in other intestinal methanogenic environments such as the sheep rumen, methanogens and SRB co-exist. The latter may actually behave as  $H_2$ -producer using lactate as electron donor and transferring reducing equivalents to methanogens, as it has been shown in vitro using low sulfate concentrations, conditions usually prevailing in the human colon. Intestinal disorders: IBD, etiology and genetics Nutrition: Metabolism Nutrition: Nutrients and gut function } "Relations between Methanogenesis and Sulfate Reduction in the Human Colon"

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## "P P 33 0768" P 33 0768 **Composition of the Caecal Flora in Healthy Humans and Comparison with the Faecal Flora**

\*P. Marteau, P. Pochart, J. Doré, A. Bernalier, G. Corthier, J.C. Rambaud

INSERM U 290, Saint-Lazare Hospital, Paris

INRA, Joy-en-Josas, France Most studies of the human colonic flora concern the faecal flora. Ecological conditions such as substrate availability, pH, and residence time differ greatly between the caecum and the left colon. The composition of the human caecal flora is poorly known due to the difficulties of sampling. *Aim:* To assess the composition of the caecal flora in man using an intubation technique, and compare the caecal and faecal floras. *Subjects and Methods:* The caecal flora was collected under anaerobic conditions using a 4 mm in diameter intestinal tube with a tractable balloon. Faecal samples were collected on the same day. Serial dilution of the samples were prepared in an anaerobic chamber, and plated on the specific media. Comparisons between the caecal and faecal floras were done using the Wilcoxon test. *Results:* Log cfu/g; means (95% confidence intervals) Total anaerobes Facultative Bifido- *Bacteroides* anaerobes bacteria Caecum 8.0 (7.5–8.5) 7.4 (6.9–7.9) 6.7 (5.6–7.7) 7.4 (6.6–8.3) Faeces 10.4 (10.1–10.7) 7.8 (7.1–8.4) 8.9 (8.4–9.5) 8.9 (7.9–9.9) p 0.02 NS 0.02 0.05 *Conclusion:* 1 – studying the composition of the caecal flora is feasible; 2 – facultative anaerobes represent 25% of the dominant flora of the caecum; 3 – their concentrations are stable throughout the colon while strict anaerobes increase more than 100 times between the caecal and faecal flora; 4 – our method should allow to get information on the regulation of the caecal flora which is more prone than the faecal flora to be influenced by ingested substrates. Oesophageal gastric duodenal disorders: EG Reflux } " "Composition of the Caecal Flora in Healthy Humans and Comparison with the Faecal Flora"

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"P P 33 0769" P 33 0769 **Ursodeoxycholic Acid Treatment in Patients with Primary Constipation and Hypercholesterolemia**

\*L. Zamboni, M. Malavolti, R. Talarico, C. Cicognani, A.M. Morselli Labate, C. Sama, L. Barbara

Dipartimento di Medicina Interna e Gastroenterologia, University of Bologna, Bologna, Italy Ursodeoxycholic acid (UDCA), the 7 beta epimer of Chenodeoxycholic acid (CDCA), is a dihydroxy bile acid widely used in the treatment of chronic liver disease, cholesterol gallstones, hypercholesterolemia and dyspepsia. UDCA is able to stimulate the receptor dependent uptake of LDL and it has a strong choleric effect but, in contrast to CDCA, it does not cause any increase of LDL cholesterol, nor diarrhea, nor abnormal results in liver function tests. *Aim* of our study was to investigate the effect of UDCA treatment in patients with primary constipation and hypercholesterolemia. *Methods*. Eleven subjects (4 males, 7 females; age: 59.7 – 7.4 mean – SD) with primary constipation (basal number of bowel movements BM = 2.55 – 0.52 and report of hard stools in all cases: HS = 100%) and hypercholesterolemia (> 200 mg/dl; mean – SD = 240 – 21 mg/dl) were treated for 4 weeks with 9 mg/Kg/day of UDCA in a cross-over study vs. Placebo (4 wks). Differences between the two treatments and basal values were evaluated by means of the Wilcoxon matched pairs (BM and cholesterol) and the McNemar (HS) tests. *Results*. During the study no patient complained about diarrhea, nor presented hypertransaminasemia. BM was significantly ( $P < 0.01$ ) higher after UDCA (4.57 – 1.79) than Placebo (2.45 – 0.32), while the presence of HS was lower (18.2% vs. 100%;  $P < 0.01$ ). During UDCA treatment a significant ( $P < 0.05$ ) decrease in serum cholesterol (227 – 0.05 mg/dl) was also observed. The relationship between the increase in the number of bowel movement and the decrease in serum cholesterol level showed an r value of 0.571 ( $P = 0.067$ ). *Conclusions*. These data support the findings that a slight malabsorption of bile acids could be involved in the serum cholesterol lowering during UDCA treatment. In summary, since UDCA has been widely used without any side effect, it could be proposed in the management of patients with primary constipation and hypercholesterolemia. Intestinal disorders: Constipation Liver and bile ducts, 2: Bile formation, cholestasis } "Ursodeoxycholic Acid Treatment in Patients with Primary Constipation and Hypercholesterolemia"

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"P P 33 0770" P 33 0770 **Cost-Effective Treatment of Constipation in the Elderly:  
Comparison of Milk of Magnesia and Lactulose**

\*Antonis K. Zacharof, C. Petrogiannopoulos, C. Flevaris, J. Poulidakos

Hellenic Red Cross Hospital, Athens, Greece *Purpose:* To compare lactulose and Milk of Magnesia in the treatment of chronic constipation in elderly patients. *Material and Methods:* 210 hospitalized elderly patients with chronic constipation after a 1-week washout period, were given Milk of Magnesia or lactulose at bedtime for 3 weeks; after another 1-week washout period, 3 weeks of treatment with the alternate agent was given. *Results:* There was no significant difference between the efficacy of the two agents as assessed by a number of criteria, including frequency of stools, the number of days in which bowel movements occurred, the need for alternative laxatives or enemas, and symptoms such as bloating, cramping, excessive flatulence, diarrhea, and fecal incontinence. *Conclusion:* Milk of Magnesia and lactulose do not differ significantly for treating constipation; the use of Milk of Magnesia in the place of lactulose is cost-effective in that comparable results are obtained at greatly reduced costs. Motility, specific: Colon, anorectum Intestinal disorders: Constipation } "Cost-Effective Treatment of Constipation in the Elderly: Comparison of Milk of Magnesia and Lactulose"

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"P P 33 0771" P 33 0771 **Diurnal Motor Change in Canine Colostomized Segment** R. Hada<sup>1</sup>, N. Wajima, H. Kobori, K. Mikami, M. Sugai, Y. Sugiyama, M. Konn

<sup>1</sup> Department of Clinical Physiology, Hirosaki University School of Allied Medical Sciences, Hirosaki, Japan

Department of Clinical Surgery, Hirosaki University School of Allied Medical Sciences, Hirosaki, Japan *Background:* The colonic motor activity in dogs is characterized by recurring groups of contraction burst which are separated by motor quiescence. We reported in UEGW' 94 that increased length of the motor quiescence may be the "interdigestive motor pattern" of the canine colon (Gut 33: A 183, 1994). *Aim:* To assess the diurnal motor profile in colostomized segment and to correlate it to that in the upper GI tract. *Methods:* Four force transducers (FT<sub>1</sub> through FT<sub>4</sub>) were implanted on the colon of 9 dogs at an equidistance with FT<sub>1</sub> on the ascending colon and FT<sub>4</sub> on the level of the caudal mesenteric artery. Another FT was implanted on the terminal ileum to distinguish the digestive from the interdigestive motor phase. The dogs were fed either 20 or 10 g/kg meal to modify the duration of the digestive motor phase and a 24 recording of the colonic motor activity was performed. The duration of each group of contraction burst (contractile state, CS) and the length of each motor quiescent state (QS) were sequentially plotted against postprandial time lapse and their temporal profiles were correlated with the first ileal MMC. Later the colon was transected between FT<sub>2</sub> and FT<sub>3</sub> to establish a double-barrelled colostomy and a 24 h recording was resumed. *Results:* In the intact dogs with either 20 or 10 g meal, CS at each FT except FT<sub>4</sub> did not significantly change throughout the recording session. At FT<sub>1</sub> through FT<sub>3</sub>, shortening of QS occurred at 2–4 h and significant increase of QS occurred at 15.3 – 0.3 h with 20 g meal and at 11.5 – 0.8 h with 10 g meal. The onset of this QS prolongation was closely correlated with the appearance of the first ileal MMC ( $r = 0.95$  { - }  $0.92$ ,  $p < 0.001$ ). In the colostomized dogs, the motor profile in the oral colon (FT<sub>1</sub> and FT<sub>2</sub>) was identical to that before colostomy, while no shortening of QS in the early postprandial period nor prolongation of QS in the interdigestive phase was observed in the distal colon (FT<sub>3</sub> and FT<sub>4</sub>). Instead, CS and QS recurred periodically with a fixed value of 4.7 – 0.1 min for CS and 32.6 – 1.8 min for QS, respectively. *Conclusion:* Prolongation of QS in the colon is temporally locked with the interdigestive motor phase of the upper GI tract. Bowel continuity is essential for this QS prolongation to occur over the length of the colon. Each small segment of the colon has its own contractile rhythm which is, however, entrained by the rhythm in a more proximal adjacent segment so far as the bowel wall is continuous. Motility, specific: Colon, anorectum } "Diurnal Motor Change in Canine Colostomized Segment"

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"P P 33 0772" P 33 0772 **Pseudo-Obstruction of the Colon** G. Kouraklis, St. Rossonis,

\*E. Misiakos, J. Kakisis, A. Papachristodoulou, G. Karatzas, J. Gogas

2nd Department of Propedeutic Surgery, Athens University Medical School, Laiko General Hospital, Athens, Greece Pseudo-obstruction of the colon is an acute derangement of the intestinal motility with no evidence of any other obstruction or pathology. Since many controversies still exist in pathogenesis, diagnosis and therapy, the authors report their experience on the subject. During the period January 1969–January 1996, 29 such cases were treated in our Department. Mean age was 71.5 years and there were 17 female and 12 male patients. Clinical picture was that of ileus, while in 15 patients palpation of the abdomen revealed diffuse tenderness. Radiology showed dilatation of the large bowel and on rectal examination air or feces were found. Diagnosis of pseudo-obstruction was established on these findings. First therapeutic attempt was conservative and consisted in administration of fluids and electrolytes, nasogastric suction and rectal tube insertion. Symptoms resolved in 8 cases, while urgent colonoscopy decompression was successfully performed in 7 out of 29 cases. Fourteen patients required operative treatment. Eight of them were submitted to caecostomy and 6 patients to loop colostomy of the transverse colon. Postoperative morbidity occurred in 4 patients, which included cardiac, pulmonary and renal insufficiency. One patient died from bronchopneumonia and heart failure. In conclusion, pseudo-obstruction of the colon demands prompt diagnosis and correct treatment because of the high incidence of colon rupture and the elevated mortality rate this complication presents. Motility, general: Functional GI disorders Motility, specific: Colon, anorectum } "Pseudo-Obstruction of the Colon"

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"P P 33 0773" P 33 0773 **Cisapride in the Treatment of Functional Constipation Refractory to Previous Therapy**. X. Busquets, V. Toledo-Pimentel, N. Gom'ed, Ll. Cus'ed, C. Martinez<sup>1</sup>

Unitat D'Aparell Digestiu, Gabinet de Diagnosi i Troctament Girona, Spain

<sup>1</sup> Clinical R&D Department, Janssen Research Foundation Chronic functional constipation is a very common reason for consultation. *Objective:* The purpose of this study is to assess the efficacy of cisapride in patients with functional constipation refractory to therapy (diet with fiber and laxatives). *Patients and Methods:* A total of 32 patients aged 18–65 years were included. All of them suffered constipation, defined as less than 3 bowel motions per week and not improving on standard therapy (fiber-rich diet and laxatives). They also had low or no urge to defecate and hard stools. The patients underwent an anorectal manometric study and all of them showed an alteration in the rectal-anal inhibitory reflex (RIR) before starting therapy with cisapride 10 mg t.i.d. for two months. Clinical visits were made at 30 and 60 days to assess symptom response. After 30 days without treatment, efficacy was assessed both clinically and manometrically. The efficacy parameters were the number of weekly motions, the improvement in the urge to defecate, and the consistency of stools. *Results:* 98% of the 32 patients participating in the study were women. The analysis of weight, age and height variables showed no statistically significant differences. Cisapride increased the weekly frequency of spontaneous bowel motions in 84% of the cases. The mean baseline value of weekly motions was 2.1/w at the start of the study. After a 12-week follow-up, the average of weekly motions was 5.0/w ( $p = 0.0001$ ). The urge to defecate and the consistency of stools improved similarly to the frequency of motions. The clinical response was consistent with normalization or improvement in RIR in subsequent manometric controls. *Conclusion:* The results show that cisapride is a useful drug for treating constipation related to an RIR impairment, since it significantly increases the frequency of spontaneous bowel motions, improves the urge to defecate and the consistency of stools, and its therapeutic effect persists 4 weeks after discontinuing therapy. Intestinal disorders: Constipation Motility, specific: Colon, anorectum } "Cisapride in the Treatment of Functional Constipation Refractory to Previous Therapy".

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"P P 33 0774" P 33 0774 **Faecal Incontinence Problem in Diabetic Patients** T. Damci, Z. Ersanli,

\*A.F. Celik, A. Dobrucali, H. Ilkova, M. Ozyazar, U. Gorpe, E. Oktay, N. Bagriacik

University of Istanbul, Cerrahpasa Medical Faculty, Dept of Int Med, Turkey

Faecal incontinence is a troublesome problem in diabetic patients. To unveil the extensiveness of faecal and gas incontinence, 250 diabetic outpatients (159 females, 91 males, mean age 53 – 13 and mean diabetes age 10.6 – 7.6) with good glycaemic control (HbA1c < 8) and 250 age and sex matched non-diabetic (NDM) outpatients (161 females, 89 males, mean age 50 – 13) were compared in terms of the below parameters using a visual scale analogue questionnaire. The people who had had abdominal operations and those with organic gastrointestinal, metabolic and hormonal diseases were excluded. All patients also filled in the neuropathy symptom score questionnaire.

DM	NDM	% Scores	% Scores	p
9.7	9.9	1.2	0.7	p > 0.05
9.0	9.8	2.5	1.1	p < 0.05
0.2	0.1	1.3	0.7	p > 0.05
8.6%	0.34	1.4	1%	0.01 + 0.16 p < 0.05
0.14	0.06	0.9	0.75	p > 0.05
79%	3.2	2.8	54%	2.3 + 2.7 p < 0.05
1.09	0.33	2.2	1.11	p < 0.05
2.67	2.79	0.8	0.8	p > 0.05
15%	8%			p < 0.05
3.33	3.55	2.62	3.05	p < 0.05

(Stool consistency: 1: Pellety, 2: Hard, 3: Normal, 4: Soft, 5: Watery) All comparisons made using independent samples t test, those marked \* with chi-square as well. Only straining and laxative usage correlated with neuropathy symptom score (p < 0.05). We found out that although the rate of stool incontinence is increased in diabetic patients than in non-diabetics, this does not interfere with social life considerably. Despite the presence of stool incontinence, the preserved consistency of stool hinders incontinence be perceived as a major social problem in diabetics. Gas incontinence and its interference with social life seem to be much prominent problems in diabetic patients. Motility, specific: Colon, anorectum Intestinal disorders: Anorectal disorders Motility, general: Functional GI disorders }

"Faecal Incontinence Problem in Diabetic Patients"

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"P P 34 0775" P 34 0775 **Effect of a Selective Calcium Antagonist Pinaverium Bromide on Rectal Distension-Induced Sensitivity during Experimental Inflammation in Rat**

\*J. Fioramonti, M.O. Christen, L. Bueno

Departement of Pharmacology, INRA Toulouse and Solvay Pharma, Suresnes France The major features of functional bowel disorders, such as IBS (Irritable Bowel Syndrome) are hypermotility and hypersensitivity of the gut characterized by a lower threshold perception. Pinaverium bromide (PB) a gastrointestinal selective calcium antagonist is indicated in the treatment of IBS. Recently it has been shown to inhibit intestinal contractions induced by GI hormones and mediators [1] suggesting an effect on visceral sensitivity. The aim of this work was to determine the effect of PB on rectocolonic inhibitor reflex and on visceral pain induced by rectal distension in rat in basal state and in hypersensitive state associated with rectal wall inflammation. A series of 6 Wistar rats (250–300 g) was chronically equipped with 2 groups of 3 nichrome electrodes implanted in the wall of the proximal colon and 3 electrodes on the abdominal striated musculature. Rectal distensions with increasing volumes (0.4; 0.8; 1.2 and 1.6 ml) were performed, using an arterial embolectomy catheter, before and 3 days after TNB/ethanol administration (80 mg/kg in 1 ml/kg volume). Pinaverium bromide (10 mg/kg p.o.) was administered one hour before distension. Rectal distension induced an inhibition of colonic motility and an increase in abdominal contractions in a volume-related manner. Pinaverium did not significantly modify the frequency of colonic nor abdominal contractions in normal conditions whatever the volume of rectal distension. Rectal inflammation reinforced the inhibitory rectocolonic reflex and enhanced the abdominal response. Pinaverium bromide significantly ( $p < 0.05$ ) reduced abdominal contraction frequency induced by distension at 1.2 and 1.6 ml volume in inflammatory conditions; for a distension of 1.6 ml the number of abdominal contractions per 5 min was 16.5 – 4.9 for PB vs 23.9 – 8.0 for control. In conclusion, pinaverium bromide (Dicetel<sup>®</sup>) has a marked effect on rectal distension-induced visceral pain in inflammatory conditions in rats. These findings further support the therapeutic value of pinaverium bromide, a GI selective calcium antagonist, in IBS given its effect on both hypermotility and hypersensitivity of the gut.

Reference: Bobo MH., Magous R., Christen MO. & Bali JP., Life Sciences, 54, 1947–1954, 1994 } "Effect of a Selective Calcium Antagonist Pinaverium Bromide on Rectal Distension-Induced Sensitivity during Experimental Inflammation in Rat"

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"P P 34 0776" P 34 0776 **Influences of Dietary Fiber, Guar Gum, and 1,2-Dimethylhydrazine (MNH) on Prostaglandin (PG) Contents in Rat Colonic Mucosa**

\*H. Goto, S. Hase, Y. Niwa, T. Arisawa, S. Kanamori, K. Tachi, T. Watanabe, Y. Hisanaga, T. Hayakawa, S. Sugiyama<sup>1</sup>, Y. Shimomura<sup>2</sup>

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<sup>2</sup> Dept. of Bioscience, Nagoya Institute of Technology, Nagoya, Japan *Purpose.* It has been reported that populations, who consume foods with much fibrous materials and reduce levels of animal fats, have a decreased risk of colonic cancer. However, its precise mechanism remains unknown. This study was designed to clarify effects of dietary fiber, guar gum and DMH, a well known carcinogen, on rat colonic mucosal PG contents. *Materials and Methods.* Five weeks old male Sprague–Dawley rats were divided into 4 groups; a) the non-fiber group: rats were fed a non-fiber diet, b) the guar gum group: rats were fed a fiber diet containing 15% guar gum, c) the non-fiber + DMH group; rats, which were fed a non-fiber diet, were infected with 60 mg/kg of DMH subcutaneously every 6 days 4 times for one month, d) the guar gum + DMH group; rats, which were fed a fiber diet containing 15% guar gum, were infected with 60 mg/kg of DMH as well as group c). All animals were fed each diet for 30 days and sacrificed. After colon was immediately removed, its length and weight were measured and mucosal PGs were assayed by high performance liquid chromatography. *Results.* In the guar gum group and guar gum + DMH group, the length and weight of colon significantly increased compared with those in the non-fiber group and the non-fiber + DMH group, but DMG did not affect on them. Five kind of PGs, *i.e.*, 6-keto-PGF<sub>1{a}}</sub>, TXB<sub>2</sub>, PGF<sub>2{a}}</sub>, PGE<sub>2</sub> and PGD<sub>2</sub> were detected in rat colonic mucosa. The intake of guar gum resulted in the increase in PGE<sub>2</sub> contents and the decrease in 6-keto-PGF<sub>1{a}}</sub> and PGD<sub>2</sub> contents. Administration of DMH increased significantly 6-keto-PGF<sub>1{a}}</sub>, TXB<sub>2</sub> and PGE<sub>2</sub> contents. Guar gum cancelled DMH-induced increase in 6-keto-PGF<sub>1{a}}</sub>, TXB<sub>2</sub> contents. *Conclusion.* These results suggest that 6-keto-PGF<sub>1{a}}</sub> and TXB<sub>2</sub> is likely to be related to DMH-induced changes in rat colon, and that the cancellation of these changes in PG contents by fiber diet might contribute to the prevention of occurrence of colonic cancer. Oncology, general: Proliferation, carcinogenesis }" "Influences of Dietary Fiber, Guar Gum, and 1,2-Dimethylhydrazine (MNH) on Prostaglandin (PG) Contents in Rat Colonic Mucosa"

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"P P 34 0777" P 34 0777 **The Pattern of Distribution of the Interstitial Cells of Cajal (ICC) in the Human Colon**

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<sup>1</sup> Dept. of Histopathology, St. George's Hospital, London, United Kingdom *Aim:* The interstitial cells of Cajal are a population of cells in the gastrointestinal tract which are attracting increasing attention as their putative role in the control of gut motility is evaluated. The aim of this study was to establish the pattern of distribution of ICC in the wall of the normal human colon. *Methods:* ICC express the proto-oncogene c-kit, a cell surface tyrosine receptor. ICC were identified in the colon by immunohistochemical staining, using a rabbit polyclonal anti-c-kit antibody (Oncogene Science). Normal colonic tissue was defined as non-involved tissue obtained at surgical resection for a non-obstructing carcinoma of the colon. The regions of interest were right, transverse and left colon. Thirty nine cases were studied. *Results:* The pattern of distribution of ICC in the colon was the same for the right, transverse and left colon. In the longitudinal muscle layer ICC were identified in the muscle bulk in parallel orientation with the muscle fibres, and also in association with penetrating blood vessels. In the intermuscular plane, many ICC formed a network surrounding the myenteric nerve plexus. In the circular muscle layer ICC were again found in the bulk of the muscle in parallel orientation with the muscle fibres and in association with blood vessels, ICC were also seen lining the intramuscular septa. ICC were identified lining the inner layer of smooth muscle fibres at the submucosal border of the circular muscle. ICC were not identified in the submucosa, muscularis mucosa or mucosa. *Conclusion:* The pattern of distribution of ICC is constant throughout the colon, showing no regional variation, and is consistent with a role in the control of colonic motility. Motility, specific: Colon, anorectum } "The Pattern of Distribution of the Interstitial Cells of Cajal (ICC) in the Human Colon"

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"P P 34 0778" P 34 0778 **Anti-Endomysium, Anti-Reticulin and Anti-Jejunum Type Antibody Testing on Human Appendix**

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Heim P<sup>1</sup>ell Children's Hospital, Budapest, Hungary Primates tissues seem to be important for the specificity of IgA type anti-endomysium (EmA), anti-reticulin (ARA) and anti-jejunum (JeA) antibody determinations in gluten-sensitive enteropathy (GSE). Substrate availability is, however, a frequent problem. *Methods:* Frozen sections were made from appendices surgically removed because of the suspicion of acute appendicitis, but found to be histologically normal. Sera of 300 non IgA-deficient gluten-sensitive patients (107 coeliac disease verified by challenge, 121 flat mucosa and 72 dermatitis herpetiformis (DH) and sera of 127 disease controls were tested by indirect immunofluorescence (IF) with IgA-staining. Conventional assays for EmA, ARA and JeA were carried out on monkey oesophagus, human liver/kidney and jejunum respectively. *Results:* Positive reaction on appendix (APP+) is composed of stainings of the endomysium, reticulin network and tunica propria fibers, each corresponding to the standard EmA, ARA and JeA pattern. APP+ EmA+ JeA+ ARA+ Gluten-enteropathy: Verified CD (n = 107) 100% 100% 100% 98.8% Flat mucosa (n = 121) 99.2% 99.2% 99.2% 94.9% DH (n = 72) 94.4% 94.4% 94.4% 86.6% Non coeliac disease – controls: Flat mucosa (n = 15) 0% 0% 0% 0% Normal mucosa (n = 112) 0% 0% 0% 0% Absorption studies resulted in fading of all components of APP+, irrespective of the fact whether oesophagus, liver or jejunum had been used. *Conclusions:* human appendix IF assay is a suitable and simple alternative to conventional EmA, JeA, ARA determinations of comparable specificity and sensitivity yielding all the three results in the same procedure. Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption: children } " "Anti-Endomysium, Anti-Reticulin and Anti-Jejunum Type Antibody Testing on Human Appendix"

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## "P P 34 0779" P 34 0779 NK1- and NK2-Receptor Gene Expression during TNB-Induced Colitis in Rats

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GI Unit, Dept. of Clin. Pathophysiology, University of Florence, Italy

<sup>1</sup> Malesci Pharmaceuticals, Florence, Italy Increasing evidence indicates that Substance P (SP) and neurokinin A (NKA) are involved in the regulation of several intestinal functions, including absorption/secretion, motility, and immune function. Due to the multiplicity of effects, they have been implicated in the pathogenesis of inflammatory bowel diseases. SP and NKA effects on target cells are mediated by specific receptors, NK<sub>1</sub> and NK<sub>2</sub>: while SP appears to preferentially activate NK<sub>1</sub> receptors, NKA activates NK<sub>2</sub> receptors. In this study we examined the spatiotemporal pattern of NK<sub>1</sub> and NK<sub>2</sub> receptor gene expression during TNB-induced colitis in rats. *Methods:* colitis was induced by intracolonic administration of 0.25 ml of TNB (120 mg/ml) in 50% ethanol. Groups of 5 rats were sacrificed at each of the following time points: 0, 3, 6, 15, 24, 72 h, 1, 2 and 4 weeks after TNB administration. NK<sub>1</sub> and NK<sub>2</sub> gene expression was analyzed on frozen sections by in situ hybridization with <sup>35</sup>S-labeled anti-sense and sense RNA probes and the autoradiographic signal was quantified by an image analysis system. *Results:* moderate NK<sub>1</sub> and NK<sub>2</sub> receptor gene expression was found in the normal rat colon; however, while NK<sub>2</sub> receptor gene expression was localized to smooth muscle cells of the muscularis mucosae and circular muscle, NK<sub>1</sub> receptors were found to be expressed in the circular muscle and cells of myenteric plexus ganglia. De novo expression of both NK<sub>1</sub> and NK<sub>2</sub> receptor mRNA was observed during the acute phase of TNB colitis in mesenchymal cells around dilated submucosal vessels; in contrast, expression in smooth muscle cells of the muscularis mucosae and propria was clearly down-regulated, starting as early as 3 h after TNB and reaching a nadir at 24–72 h. Tachykinin receptor gene expression gradually returned to normal thereafter. We were not able to identify any specific signal on epithelial cells, probably due to the very low, if any, basal expression and to the extensive necrosis of the mucosa following TNB administration. *Conclusions:* our findings suggest that reduced NK<sub>1</sub> and NK<sub>2</sub> receptor gene expression may play some role in the progressive colonic dilatation commonly observed during the acute phase of TNB-induced colitis. Intestinal disorders: IBD, basic Hormones and receptors: Molecular biology }

"NK1- and NK2-Receptor Gene Expression during TNB-Induced Colitis in Rats"

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"P P 34 0780" P 34 0780 **Rectal Mucosal EGF Receptor Tyrosine Kinase (EGF-R tyr-k) Activity and Tyrosine Protein Phosphorylation are Increased in Patients with Adenomatous Polyps (a.p.), Ulcerative Colitis (u.c.) and Colon Cancer (c.c.)**

\*E. Malecka-Panas, J. Tureaud, P.P. Liberski, A.P.N. Majumdar

Dept. Digest. Tract Dis. & Metab Disord., Med School, Lodz, Poland, Wayne St Univ, USA Tyrosine kinase (tyr-k) and a number of growth factors, like EGF and TGF-alpha are known to stimulate G.I. tract proliferation. In humans increased colonic mucosal proliferative activity has been observed in a.p., u.c. and c.c. The aim of the presented study was to determine the differences of proliferative patterns and their correlation in patients with a.p., u.c., and c.c., as reflected by colonic mucosal EGF-R tyr-k, tyrosine protein phosphorylation and PCNA immunoreactivity. The study population comprised 40 patients, aged 36–76 years (mean 58), in which 10 had a.p., 10 – u.c. in remission phase, 10 c.c. and 10 were healthy controls. 6–8 rectal mucosal biopsy specimen were obtained at 10 cm from anal verge and at least 10 cm from any macroscopical mucosal changes during sigmoidoscopy. EGF-R tyr-k was increased in colonic mucosa by 35.2% – in patients with a.p., by 40.6% – in patients with u.c. and by 123% in patients with c.c. Tyrosine phosphorylation of several mucosal proteins (e.g. Mr of 55, 100, 155 and 170) in patients with a.p. and u.c. was 2–3 fold increased and in patients with c.c. 5–6 fold increased, when compared to corresponding control levels. Expansion of proliferative zone towards crypt surface and significant increase ( $p < 0.01$ ) of PCNA mean labeling indices were observed in patients with a.p., u.c. and c.c. as regards to the control group. Significant correlation between EGF-R tyr-k activity and PCNA LI values ( $p < 0.001$ ) was observed within examined group of patients. Increased values of EGF-R tyr-k activity in overmentioned groups of patients may suggest, that tyrosine phosphorylation is involved in colon carcinogenesis. Hormones and receptors: Receptor characterization Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Rectal Mucosal EGF Receptor Tyrosine Kinase (EGF-R tyr-k) Activity and Tyrosine Protein Phosphorylation are Increased in Patients with Adenomatous Polyps (a.p.), Ulcerative Colitis (u.c.) and Colon Ca"

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"P P 34 0781" P 34 0781 **Human Gallbladder Mucin is also Biosynthesized in the Human Colon, But Not in the Small Intestine**

\*B.J.W. Van Klinken, H.A. B'feller, J. Dekker, A.W.C. Einerhand

Pediatric Gastroenterology & Nutrition, Academic Medical Center, Amsterdam, The Netherlands *Purpose:* Inflammatory bowel disease is thought to be associated with alterations in colonic mucins, which form the most important structural components of mucus. Nine human mucin genes, named *MUC1–4*, *5A/C*, *5B* and *MUC6–8*, have been identified. Besides the mucins of which the genes have been cloned at least one other mucin has been reported: Human Gallbladder Mucin (HGBM), that was originally identified in the human gallbladder [1]. HGBM is also expressed in LS174T cells, a human colon adenocarcinoma cell line [2], suggesting that it may also be expressed in the human colon. Therefore, we studied the biosynthesis of HGBM along the longitudinal axis of the human intestine. *Methods:* To analyze mucin biosynthesis, biopsies of the human gallbladder, duodenum, jejunum, colon ascendens, transverse colon and sigmoid were pulse-labeled with [<sup>35</sup>S]methionine/cysteine or [<sup>35</sup>S]sulfate and chase-incubated with complete medium. The biopsies were obtained from healthy tissues. Biopsies and culture media were homogenized and mucins were immunoprecipitated from the homogenates using antibodies raised HGBM (anti-HGBM), which were shown to recognize the unique termini of HGBM [1]. This was followed by analysis on reducing SDS-PAGE and fluorography. *Results:* HGBM precursors were immunoprecipitated from homogenates of human gallbladder, colon ascendens, transverse colon and sigmoid, but not from the duodenum or jejunum. HGBM precursors were detectable at about 470 kDa on SDS-PAGE similar to the molecular mass of HGBM precursors reported by Klomp and co-workers [1]. In pulse-chase analyses of human colon ascendens and sigmoid, mature HGBM was secreted into the medium and was detected at about 600 kDa on SDS-PAGE. Very similar biosynthesis of mature HGBM in the human gallbladder was previously reported [1]. *Conclusions:* Apart from expression in the human gallbladder, HGBM precursors are detectable specifically in the human colon suggesting that this mucin may have a specific function in the large intestine. In addition, mature HGBM was also detected in the colon and secreted. Based on the respective molecular masses of their precursors, HGBM is not identical to *MUC1–4*, *MUC5A/C*, *MUC6* or *MUC7* [2]. Therefore, HGBM may be identical to *MUC5B* or *MUC8*, or may constitute a novel mucin.

Reference: Klomp et al., *Biochem. J.* 1994;304:737–744

Van Klinken et al. *Glycoconjugate J.* 1996, in press. Intestinal disorders: IBD, basicLiver and bile ducts, 1: Cell biology, collagen, fibrosis } "Human Gallbladder Mucin is also Biosynthesized in the Human Colon, But Not in the Small Intestine"

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"P P 34 0782" P 34 0782 **Sodium Channels are Present in the Upper Crypt but Not the Crypt Base in the Distal Colon of the Glucocorticoid-Treated Rat**

\*G.M. Fraser, Y. Niv, M. Sterlin, D. Ecke, M. Bleich, R. Greger, B. Schwartz

Dept. Gastroenterology, Beilinson Medical Center, Clinical Biochemistry Unit, Soroka Medical Center, Israel

Dept. Physiology, Freiburg University, Germany Sodium channels are induced in the rat distal colon by short-term corticosteroid treatment. It has been proposed that these channels are confined to luminal cells whereas chloride secretion is a property of crypt base cells. We used three methods to map the distribution of Na channels along the crypt-lumen axis. *Methods.* Five colonocyte populations (C1–C5) from lumen to crypt base were prepared by  $\text{Ca}^{2+}$  chelation (EDTA). Whole crypts were prepared using a modification of this method. Amiloride-sensitive  $^{22}\text{Na}^+$  uptake (ie  $\text{Na}^+$  channel activity) was determined in vesicles from each cell population using a  $\text{K}^+$  diffusion gradient. Similarly  $^{22}\text{Na}^+$  uptake by whole cells was performed on pooled luminal and crypt colonocytes. A whole-cell patch clamp technique was used to measure membrane conductance (Gm) and voltage (Vm) in luminal, mid-crypt and crypt-base colonocytes during changes in  $\text{Na}^+$  concentration or with 10 micromolar amiloride. *Results.* Glucocorticoid-naïve rats showed no evidence of electrogenic  $\text{Na}^+$  transport. Amiloride inhibited  $^{22}\text{Na}^+$  uptake in vesicles by 60%, 40%, 17%, 11% and 0% in colonocyte populations C1–C5 respectively. In whole cells, amiloride-sensitive  $^{22}\text{Na}^+$  uptake was 20 pmoles  $\text{Na}^+$ /mg protein in the luminal cell population and absent in crypt-base colonocytes. Whole cell recordings of Vm showed hyperpolarization and decrease in Gm when bath  $\text{Na}^+$  was removed or amiloride was added indicating that  $\text{Na}^+$  channel activity was inhibited. The effect was maximal in luminal cells, absent in crypt-base cells and intermediate in the mid-crypt. *Conclusion.* Using 3 different methods we have shown that glucocorticoid-induced  $\text{Na}^+$  channel activity in rat distal colon exhibits a gradient with absent activity in the crypt and maximal activity at the luminal surface. This distribution may have implications for theories of cellular maturation along the crypt-lumen axis. } "Sodium Channels are Present in the Upper Crypt but Not the Crypt Base in the Distal Colon of the Glucocorticoid-Treated Rat"

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"P P 34 0783" P 34 0783 **Human Colonocytes from Endoscopic Biopsies: Isolation, Biochemical Characterization, and Expression of Human Stress Proteins**

\*G. Pedersen, J. Hendel, B. Giese, T. Saermark, J. Brynskov

Dept. Medical Gastroenterology C, Herlev University Hospital, DK-2730, Denmark *Purpose:* Biochemical and biological characterization of normal human colonic epithelial cells has been difficult due to lack of suitable methods for culture of epithelial cells from biopsy material. Therefore, colonic crypts isolated from surgically removed bowel or cancer cell lines have been widely used to study colonocyte functions in vitro. We present here a simple method for the isolation of human colonic epithelial cells isolated from routine biopsies, and demonstrate that these cells metabolize butyrate and express human stress proteins, HSP 60 and 70. *Methods:* Human biopsies obtained by routine diagnostic colonoscopy were treated with EGTA/EDTA and/or enzymes to separate the epithelial cells from the connective tissue. The cells isolated were grown for 1–3 days and the number of cells surviving was monitored by methyl tetrazoleum (MTT) test and DNA quantitation. Colonocyte metabolism of butyrate and glucose was quantitated by  $^{14}\text{CO}_2$  liberation. The expression of HSP 60 and 70 was measured by PCR and immunoelectrophoresis. *Results:* Electron microscopy showed that cells with the typical features of colonic epithelial cells could be isolated from a small number of biopsies ( $n = 2-4$ , 5–20 mg of tissue). Enzymes and thiols were not necessary and appear harmful to the cells. The cells were viable for at least 3 days as judged from MTT and DNA measurements and were able to incorporate radiolabelled aminoacids and sugars into proteins. The butyrate metabolism had a  $K_m$ -value of 0.6 mM. The cells also metabolized glucose. The cells expressed heat shock proteins, HSP 60 and 70 as judged by PCR as well as electrophoretic immunoblotting. *Conclusion:* The experiments show that these primary cultures allow the study of human colonic epithelial functions in vitro. The possibility to establish primary cultures of colonocytes from patients undergoing routine endoscopy may be most valuable in the study of inflammatory bowel diseases. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Endoscopy, specific: Colon, rectum } "Human Colonocytes from Endoscopic Biopsies: Isolation, Biochemical Characterization, and Expression of Human Stress Proteins"

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"P P 34 0784" P 34 0784 **Butyrate Transport in Rat Colonic Apical Membrane Vesicles**  
**O. Schröder, J. Stein, W.F. Caspary**

Division of Gastroenterology, II. Department of Internal Medicine, Johann Wolfgang Goethe-University, Frankfurt, Germany *Background:* In order to study the specificity of the luminal butyrate-HCO<sub>3</sub>-antiporter, the inhibitory potency of several SCFA, their mercapto- and bromoanalogues and anion-channel blockers on the <sup>14</sup>C-butyrate influx from rat colonic apical membrane vesicles has been determined. *Methods:* Apical membrane vesicles (AMV) of the rat colonocytes were prepared by a discontinuous sucrose gradient after isolation of membrane caps. Quality of the membrane preparations was proven by several functional and structural parameters. <sup>14</sup>C-butyrate uptake was measured by rapid filtration technique. *Results:* Preloading of AMV with HCO<sub>3</sub> or butyrate stimulated <sup>14</sup>C-butyrate uptake and resulted in transient accumulation. HCO<sub>3</sub>-stimulated butyrate uptake showed an apparent K<sub>m</sub> of 44.7 – 5.9 mmol/l and a v<sub>max</sub> of 33.2 – 2.7 nmol {\'b4} mg protein<sup>-1</sup> {\'b4} 3 sec<sup>-1</sup>. Intravesicular butyrate uptake was substantially inhibited by addition of 20 mmol/l of acetate (41.4%), propionate (52.4%), butyrate (39.3%) and 3-mercaptopropionate (43.0%), whereas addition of 20 mmol/l of formate, hexanoate, heptanoate, valerate, isovalerate, 2-bromopropionate, 4-bromobutyrate or 1 mmol/l of DIDS and SITS did not alter uptake. 3-mercaptopropionate had a competitive inhibitory effect on butyrate uptake with a binding constant following inhibition of 6.25 – 0.87 mmol/l and a v<sub>max (i)</sub> of 5.82 – 1.01 nmol {\'b4} mg protein<sup>-1</sup> {\'b4} 3 sec<sup>-1</sup>. *Conclusion:* Rat colonic luminal butyrate-HCO<sub>3</sub>-antiport is mediated by a low affinity transport system, which is specific for unbranched SCFA with a chain length from 2 to 4 carbon atoms and 3-mercaptopropionate. }" "Butyrate Transport in Rat Colonic Apical Membrane Vesicles"

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"P P 34 0785" P 34 0785 **Sulphydryl Blocker Induced Rat Colitis is Ameliorated by Intravenous (IV) Injection of Antibody to Colonic Surfactant-Like Particle (C-SLP)**

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St. Louis, MO, U.S.A. We recently characterized a model of experimental colitis induced by iodoacetamide (IA), a sulphydryl blocker, and accompanied by increased leukotriene (LT), prostaglandin E (PGE) and nitric oxide (NO) generation. We also isolated and characterized rat C-SLP and produced its specific antibody (C-SLPAb). The aim of this study was to evaluate the role of C-SLP in IA colitis. Colitis was induced in male Sprague-Dawley rats by intracolonic administration of 0.1 ml 3% IA. C-SLPAb, SP-A-Ab or control serum (0.3 ml) was injected IV 48 hours prior to, at, or 24 hours after damage induction, colons isolated, rinsed with saline, damage assessed, 10 cm segment weighed and tissue processed for microscopy and colonic mucosal NO synthase (NOS) activity measured. Intracolonic IA resulted in extensive macroscopic and microscopic damage, increased colonic weight and NOS activity. C-SLPAb significantly decreased macroscopic damage by 70% when given prior to, or concomitantly with IA, as well as macroscopic damage and colonic weight, without affecting NOS activity. Antibody to SP-A, a specific SLP protein, had no protective effect on damage, nor did injection of C-SLPAb 24 hours after damage induction. Treatment No. Lesion Weight NOS (mm<sup>2</sup>) (g/10 cm) (nmol/g/min) None 20 None 0.60 – 0.02 2.00 – 0.13 IA 21 460 – 83\* 1.4 – 0.1\* 6.6 – 1.1\* IA + control serum 6 664 – 141\* 1.7 – 0.2\* 5.7 – 0.4\* IA + C-SLPAb (48 h pre) 13 136 – 56\*\* 1.17 – 0.08\*\* N.D. IA + C-SLPAb 11 104 – 37\*\* 1.10 – 0.05\*\* 6.8 – 0.4 IA + SP-A-Ab 6 576 – 196\* 1.57 – 1.87\* N.D.\* < 0.05 vs. control; \*\* < 0.05 vs. IA. IA-induced colitis is ameliorated by IV injection of C-SLPAb by a mechanism yet unknown but probably not via NOS activity. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Intestinal disorders, absorption: Enterocyte biology } "Sulphydryl Blocker Induced Rat Colitis is Ameliorated by Intravenous (IV) Injection of Antibody to Colonic Surfactant-Like Particle (C-SLP)"

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"P P 34 0786" P 34 0786 **Effect of a Sigma Ligand, Igmesine, on Intestinal Hypersecretion Induced by Prostaglandin E2 in Man** G. Shi<sup>1</sup>,

\*S. Bruley des Varannes<sup>1</sup>, J. Genève<sup>2</sup>, C. Rozé<sup>3</sup>, J.P. Galmiche<sup>1</sup>

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<sup>2</sup> Institut de Recherche Jouveinal, Fresnes, Paris, France

<sup>3</sup> INSERM U410, Paris, France Endogenous peptides like PYY and NPY exhibit an antisecretory effect in experimental models probably through neuronal sigma sites. Igmesine is a new sigma ligand that was shown to be active in animal models of diarrhea without affecting intestinal motility. *Aim of the study:* To assess the effect of two doses (25 and 200 mg) of igmesine, a sigma ligand, on intestinal hypersecretion induced by prostaglandin E2 (PGE2) in man. *Methods:* 2 groups of 8 healthy volunteers participated in this placebo-controlled randomized double-blind crossover study: 8 received igmesine 25 mg and placebo, 8 received igmesine 200 mg and placebo during 2 different sessions. At each session, the experimental procedure was as follows: on the first day, a triple lumen tube was placed into the jejunum. On the following two days, 2 intestinal perfusion sessions were performed, 24 hours apart, each according to the following sequence: oral intake of igmesine (8 subjects: 25 mg, 8 subjects: 200 mg) or placebo at t0, intraluminal perfusion (10 ml/min) of an isotonic solution from t0 to t90 min and then perfusion of a solution containing PGE2 (Prostine E<sub>2</sub><sup>R</sup>, 5 μmol/l) from t90 to t270 min. The intestinal fluid was continuously collected at the proximal and distal tips of the catheter to assess the movements of water and electrolytes in the intestinal segment being studied (30 cm), PEG being used as marker. *Results:* Although inactive at 25 mg dose (data not shown), igmesine 200 mg strongly reduced the secretory flow of water and electrolytes during the PGE2 perfusion (Table, m – s.e.m., \* p < 0.05, ANOVA). H<sub>2</sub>O Na<sup>+</sup> K<sup>+</sup> Cl<sup>-</sup> } HCO<sub>3</sub><sup>-</sup> } (ml/h) (mmol/h) (mmol/h) (mmol/h) (mmol/h) Placebo 285 – 63 39 – 8 2.0 – 0.3 32 – 7 7 – 1 Igmesine 200 \*35 – 27 \*5 – 8 \*1.0 – 0.3 \*3 – 7 \*2 – 1 ANOVA for repeated measures over time showed that the effect of igmesine 200 mg was maintained during the PGE2 perfusion. No side effect related to igmesine was reported. *Conclusion:* This study shows for the first time in man the intestinal antisecretory effect of a sigma ligand, suggesting the potential interest of this new pharmacological class as a therapeutic tool. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Epithelial transport } " "Effect of a Sigma Ligand, Igmesine, on Intestinal Hypersecretion Induced by Prostaglandin E2 in Man"

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"P P 34 0787" P 34 0787 **Distribution of CEA/FAS/FAS-Ligand/Tunel in Normal and Ulcerative Colitis Colon**

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The luminal epithelial cells of colon are positive for Fas antigen (Fas) and Fas-ligand (Fas-L) on their baso-lateral surfaces, contain TUNEL positive nucleus and undergo apoptosis. The apical surface of these cells are also positive for carcinoembryonic antigen (CEA), a maker of terminally differentiated colonic epithelial cells. Our finding that the Fas/Fas-L/TUNEL associated epithelial cells were found in the crypt of active ulcerative colitis (UC) prompted us to investigate whether CEA is also associated with these cells. Portions of biopsies of normal colon and that of colon of active UC were fixed in 10% formalin and processed using a routine histology procedure. The breaks in nuclear DNA were detected by TUNEL method. Fas and Fas-L were localized using rabbit antisera against an extra-cellular domain of Fas and an intra-cellular domain of Fas-L as the first antibody, respectively. For the localization of CEA using CEA, mouse monoclonal anti-human CEA as the first antibody. The CEA was limited to the apical surface of the luminal surface epithelial cells of normal colon. Whereas, in the UC colon, CEA was at the apical surface of the luminal and crypt epithelial cells. The distribution of the CEA positive cells coincided with that of cells with apoptotic markers, namely Fas/Fas-L/TUNEL. The coincidental expression of CEA on cells with various apoptosis markers suggest that the cells undergoing apoptosis in the crypts of UC colon are fully differentiated and the hastened differentiation of epithelial cells in UC colon maybe a cause of apoptosis. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation Motility, specific: Colon, anorectum } "Distribution of CEA/FAS/FAS-Ligand/Tunel in Normal and Ulcerative Colitis Colon"

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"P P 35 0788" P 35 0788 **Corrections of Postoperative Incontinence in Children by Penna's Operation** V.N. Grona,

\*A.A. Muzalev

Donetsk State Medical University, Ilichavenue 16, Donetsk, 340003, Ukraine *Introduction.* Unsatisfactory functional results following operative treatment of anorectal defects constitute 30%–50%. *Materials and methods.* Correction of postoperative incontinence was made in 20 patients (8 boys and 12 girls). All the children had been operated on previously by various techniques for anorectal defects and ensuing complications. Out of 20 patients 8 children were operated twice, 4 – trice. A scary deformity of the anorectal area was revealed in all the children, out of them 5 patients showed anterior ectopy of the rectum with empairment of the entrance to the vagina, the posterior wall of the distal third of the vagina was destroyed. Rectal tenesmus in all the patients decreased sharply or was apsend. When choosing a technique of surgical correction of postoperative incontinence we preferred Penna's operation wich allowed to form a locking apparatus from the remaining elements of the pubo-perineal loop and the external sphincter of the rectum. 1 to 1.5 month prior to the operation all the children had been applied suspended two-trunc colostoma. If the patients had previously undergone abdomino-perineal proctoplastics, they were applied transversostoma (8 patients); and sigmostoma after perineal proctoplasty (12 patients). Soft profilactic bougerage of the rectum was begun at 15 days, transrectal electrostimulation of the sphincter apparatus muscles was carried out 3 to 4 weeks later. Temporary colostoma was closed 1.5 to months following Penna's operation. *Results.* 18 patients were followed up from 6 months to 5 years. Good results were received in 10 patients, satisfactory – 7 patients. unsatisfactory – one patient. Underdevelopment of the sacrococcygeal portion of the spine was the major reason of the unsatisfactory result in the study. *Conclusion.* We consider Penna's operation in this category of patients to be the operation of choice. Intestinal disorders: Constipation Intestinal disorders: Anorectal disorders Intestinal disorders: Anorectal disorders: children } "Corrections of Postoperative Incontinence in Children by Penna's Operation"

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## "P P 35 0789" P 35 0789 **Overlapping Sphincteroplasty for Anal Incontinence**

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Department of General Surgery and Organ Transplantation, University of Naples "Federico II", School of Medicine, Naples, Italy

Surgical correction of anal incontinence is best suited to those patients with traumatic disruption of the sphincter ring. Such damage may result from obstetric as well as iatrogenic injuries or, less frequently, road accidents or sexual abuse. Surgical repair by wrap-over technique has been shown to restore satisfactory function in most cases. The present study intended to assess clinical and functional results of overlapping sphincteroplasty. From 1991 to 1995, a total of 40 repairs were performed in 39 severely incontinent patients (17 M, 22 F; mean age 34 – 11 years, range 23–52). Preoperative and postoperative assessment included anal manometry, endosonography and electromyography. Mean follow-up was 23 months (range 5–54). Statistical analysis was performed using the Wilcoxon signed rank test. Aetiology of anal incontinence is shown in the table.

Etiology	N. patients	Percent
Obstetric injury	16	41%
Previous anorectal surgery	21	53.8%
Road accident	2	5.2%
Total	39	100%

\*2 patients with associated recto-vaginal fistula

Endosonography was able to preoperatively reveal 36/39 external anal sphincter defects with a 92% correlation with surgery. Overall, 36 patients were clinically improved by surgery with 30 (78%) regaining normal continence and 6 (14.4%) showing fair function. Only one patient received a temporary colostomy. Septic complications occurred in 7 cases (18%). The procedure failed in three patients (7.6%) who were then submitted either to a re-do sphincteroplasty or to an electrically stimulated graciloplasty. All of them are totally continent after their salvage procedure. Endosonography is useful in mapping the anal sphincters and plan the best type of operation. Overlapping sphincteroplasty is the procedure of choice in case of traumatic anal incontinence. Dynamic graciloplasty can be offered to highly selected patients in whom previously attempted conventional repairs had failed.

Intestinal disorders: Anorectal disorders }

"Overlapping Sphincteroplasty for Anal Incontinence"

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"P P 35 0793" P 35 0793 **Balloon Expulsion Test and Perineometry as a Screening Test in Diagnosing Anismus**

\*C.I. Sohn, P.L. Rhee, J. Kim, K.C. Koh, S.W. Paik, J.C. Rhee

Division of Gastroenterology, Samsung Medical Center, Seoul, Korea *Purpose:* The aim of this study is to investigate the role of balloon expulsion test and perineometry as a screening test in diagnosing defecation disorder. *Method:* The inclusion criteria was defecation disorder patients on Rome criteria, that is excessive straining on more than 25% of occasions and sensation of incomplete evacuation on more than 25% of occasions. All the patients were diagnosed the cause of defecation disorder through balloon expulsion test in left lateral decubitus position and sitting position, perineometry, colon transit time, defecogram including ejection fraction of defecation, anorectal manometry and sigmoidoscopy to rule out organic disease. 10 asymptomatic persons were also examined as a normal control. *Result:* Among 60 defecation disorder patients, anismus was (56%), descending perineum syndrome (7%), rectocele (3%), rectal intussusception (1%), combined disorder (7%) and normal pelvic function (25%). The weight that was needed to expel balloon in left lateral decubitus position in anismus patients was significantly higher than normal control (average 767 gm:330 gm,  $p < 0.05$ ). The time that was needed to expel balloon in sitting position was significantly longer than normal control (average 5.6 min:2 min,  $p < 0.05$ ). Perineal movement in anismus patients was significantly shorter than normal control (average 0.7 cm:1.3 cm,  $p < 0.05$ ). The weight that was needed to expel balloon in left lateral decubitus position in anismus patients was inversely related to ejection fraction on defecogram. *Conclusion:* Balloon expulsion test and perineometry are good screening test in the diagnosis of defecation disorder. Motility, general: Functional GI disorders Motility, specific: Stomach } "Balloon Expulsion Test and Perineometry as a Screening Test in Diagnosing Anismus"

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## "P P 35 0794" P 35 0794 **Visceral Sensitivity and Systemic Autonomous Responses to Rectal Distension in Healthy Volunteers**

\*M.B. Jacobsen, S. Spetalen, S. Blomhoff, M. Vatn

Rikshospitalet, University of Oslo, Norway Visceral sensitivity is claimed to be changed in IBS patients. In 18 healthy, female volunteers (19–57 years) we assessed retest reliability and normal values for rectal visceral perception by a computerised barostat (Synectics, Sweden) and sympathetic, and parasympathetic responses to rectal distension. Unchanged position of the barostat balloon was secured by concomitant anal pressure registrations and the pressure values for feeling of gas, urge to defecate and discomfort were registered by a randomised, double staircase inflation procedure in phasic distension mode with 1 mmHg steps lasting 20 seconds with 30 seconds intervals. The intrarectal pressure reported to cause discomfort was repeated as a singular inflation at the end of the study. Heart rate variability (HRV) and skin conductance (SC) were recorded throughout the study. Influence of posture changes were measured by positioning the subjects towards an adjustable plate which could be tilted in 5 degrees intervals. The whole protocol was repeated after two days. First feeling of gas was at (mean – SD) 11.8 – 5.4 mmHg, urge to defecate at 13.5 – 6.0 and discomfort at 29.3 – 10.1 mmHg. 95% confidence interval for discomfort in healthy females is 20.2–38.8 mm Hg and for compliance 7.5–11.9 ml/mmHg. Correlation coefficients (c.c.) (Pearson) for these parameters were 0.89, 0.91 and 0.79 respectively. Student T-test showed no differences and coefficients of variation were 0.24, 0.20, and 0.24 respectively. Following exposure to the discomfort threshold skin conductance increased 0.4 – 0.5  $\mu$ S compared to baseline at a latency of 4.6 – 2.0 sec. The c.c. (test-retest) was 0.78. Basal HRV was 70 – 92 ms and remained unchanged following induction of rectal discomfort with a c.c. of 0.92. Changes in posture within 30 degree did not influenced volumes in the balloon at high pressure levels, while large differences were noted at lower pressures. In conclusion, measurements of visceral sensitivity and peripheral autonomous responses to rectal discomfort were performed with high reproducibility. Motility, general: Functional GI disorders Motility, specific: Colon, anorectum } "Visceral Sensitivity and Systemic Autonomous Responses to Rectal Distension in Healthy Volunteers"

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## "P P 35 0795" P 35 0795 **Dynamic Graciloplasty for Faecal Incontinence: The One Stage Procedure**

\*J.-L. Faucheron, E. Tarla, P. Leyman, J.-P. Lefaucheur, R. Parc

Centre de Chirurgie Digestive, Hospital Saint-Antoine, Paris, France Dynamic graciloplasty is a new surgical option in the treatment of severe faecal incontinence. If most authors prefer a two-stage procedure (transposition of the gracilis muscle around the anus and implantation of the electrical stimulator and intra-muscular electrodes few weeks later), the construction of the neo-sphincter can be performed by a one stage graciloplasty and implant procedure. To assess this new technique we report the results of a prospective study conducted from June 1994 to May 1996. Eighteen patients (8 women) of mean age 33 years (range 15–62) were operated on for severe faecal incontinence. The aetiology of incontinence was anal atresia (n = 8), surgical or obstetrical trauma (n = 6), non-surgical trauma (n = 3) and spina bifida (n = 1). Four patients had a previous unsuccessful Pickrell operation and were operated on in a two-stage procedure. Three further patients also had a delayed stimulator implantation because of a perineal operative complication. In all other patients a one-stage dynamic graciloplasty was performed. There were no difference between the one-stage procedure (n = 11) and the two stage procedure (n = 7) with regard to: 

- clinical functional result
- manometric results
- surgical complications (sepsis, pain, explant).

 The advantages of the one-stage procedure over the two-stage procedure are: better electrode positioning, less risk to the nerve because it is more readily identifiable and one surgical act instead of two. Clinical practice: Management strategy Intestinal disorders: Anorectal disorders Motility, specific: Colon, anorectum } "Dynamic Graciloplasty for Faecal Incontinence: The One Stage Procedure"

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"P P 35 0796" P 35 0796 **Perianal Bleeding, Pruritus Ani, and the Baboon Syndrome**

\*H. Rohde, H. Heegewaldt, E. Lohmar, J. Brings, R. Eisebitt

Gastroenterologic Unit and Institute for Numeric Statistics, Cologne, Germany *Background:* Pathogenesis and aetiology of perianal bleeding, itching, pain and burning are often obscure. Inadequate cleansing (Smith 1982, Alexander-Williams 1983, Jones 1992) is accused as well as wet wipes (Harrington 1992) and moist toilet paper (Bruynzel 1992). *Methods:* We asked two groups of patients by a 41-item-questionnaire about their daily cleaning habits (shower, bath, moist toilet paper or water after motions etc.). Those who came for gastroscopy (n = 130) without anal complaints (G) and patients with a Baboon syndrome (Bs) defined as perianal lesions caused by overvigorous anal cleansing (n = 182) with bleeding, itching and burning. The latter had proctological investigation and endoscopy of the colon. Patients with a Bs were urged to refrain from use of water to clean their anus. Follow up after four weeks by telephone interview (anal symptoms) and by haemocult test was performed in those 67 patients with a Bs only and no lesions at total colonoscopy. *Findings:* Remarkable differences were found between the Bs- and the G-group: many doctors seen because of anal complaints (53% vs 15%), using a wet face-cloth after motions (40% vs 23%), using water and fingers after motions (22% vs 8%), washing their anus before sleeping (45% vs 25%), being treated because of piles (40% vs 20%). At 4-weeks follow up pruritus ani of Bs-patients had dropped from 45% to 5%, pain from 36% to 3%, haemocult testing became negative in all patients who changed their cleaning habits but symptoms and haemocult test remained nearly unchanged when this regimen was refused (p < 0.001, McNemar). *Conclusion:* To find out the cause of perianal bleeding, itching, pain and burning it is of utmost importance to ask patients about their daily cleaning habits. In contrast to most gastroenterologist we recommend only dry anal cleaning to prevent a Baboon syndrome. Intestinal disorders: Anorectal disorders } "Perianal Bleeding, Pruritus Ani, and the Baboon Syndrome"

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"P P 35 0797" P 35 0797 **Therapeutic Fiber and Bleeding Haemorrhoids**. *J. Mat* 'e9,

\*A. G\ 'f3mez, J.A. Correa, T. Le\ 'f3n, M. P\ 'e9rez, J.M. Pajares

Gastroenterology Department, Hospital de la Princesa, Madrid, Spain *Aim:* To assess prospectively the effect of fiber additions on internal bleeding haemorrhoids and haemorrhoidal prolapse. *Patients and Methods:* 50 patients (mean age = 48.3 – 13 yrs., 29 M/21 F) were referred to our Department for endoscopic study of recurrent rectal bleeding. All the patients underwent anoscopy before and after treatment to evaluate a) haemorrhoids bleeding on contact, b) the number of congested haemorrhoidal cushions and c) the degree of haemorrhoidal prolapse. Exclusion criteria were the presence of coagulation disorders or potentially bleeding colorectal lesion and the concomitant intake of laxative, anticholinergic or prokinetic drugs. Patients were randomized in two groups, 23 in the study group were treated with 35 g/d of *Plantago Ovata* and 27 in the control group with placebo for a 40 day course. Differences in the number of bleeding episodes, congested haemorrhoidal cushions and degree of prolapse were analyzed with the Student's test and the Welch Correction. A significance level of  $p < 0.05$  was accepted. *Results:* 1 patient from the study group and 3 from the control group were excluded. During the first 15 days of treatment, the number of daily bleeding episodes decreased from 5.2 – 2.9 to 4.8 – 3.8 in the study group versus 6.7 – 3 to 6.4 – 3 in the control group (n.s.). The next 15 days it decreased to 3.1 – 2.7 and 5.5 – 3.2 respectively ( $p < 0.05$ ). A further reduction to 1.1 – 1.4 was found after the last 10 days in the study group versus 5.5 – 2.9 in the control group ( $p < 0.001$ ). The number of congested haemorrhoidal cushions decreased from 2.5 – 1 to 1.6 – 1.2 ( $p < 0.01$ ) in the study group, without differences in the control group. No change in the degree of haemorrhoidal prolapse was observed after treatment in the study group nor in the control group. *Conclusions:* 1) Fiber supplements significantly improved bleeding from internal haemorrhoids; 2) Therapeutic fiber effects are not immediate, appearing at least after a month of treatment; 3) Fiber does not reduce haemorrhoidal prolapse but significantly improves congested haemorrhoidal cushions. Intestinal disorders: Anorectal disorders }" "Therapeutic Fiber and Bleeding Haemorrhoids"

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"P P 36 0799" P 36 0799 **Metronidazole Resistance Influences the Efficacy of the Short-Term Triple Therapies, Involving Metronidazole, in the Eradication of Helicobacter Pylori (Hp)**

\*S. Georgopoulos<sup>1</sup>, S. Karatapanis<sup>1</sup>, V. Vretou<sup>2</sup>, S. Katranis<sup>1</sup>, A. Mentis<sup>3</sup>, V. Artiki<sup>1</sup>

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Recent studies have shown that newer, one week, triple therapies, involving Metronidazole (Met), are highly effective and safe in treating Hp infection. *The aim* of our study was to estimate the efficacy of two, one week, triple therapies, involving Met, on Met sensitive (Met<sup>(S)</sup>) and Met resistant (Met<sup>(R)</sup>) Hp strains. *Patients–Methods:* Sixty-one patients (aged 19–83 yrs, mean 44.9) with a positive Hp culture, were randomized in two treatment groups. Group A (n = 32, 22 men, 62.1% smokers) received Omeprazole 20 m bid + Amoxicilline 1 gr bid + Met 500 mg bid for one week. All patients underwent a new endoscopy 4 weeks after the end of treatment to assess eradication of Hp (by CLO-test, histology and culture). Antibiotic test was performed in all isolated Hp strains. *Results:* Eradication of Hp was achieved in 27/32 (84.4%) patients of group A vs 21/29 (72.4%) of group B (p = NS). The incidence of Met<sup>(R)</sup> Hp strains was 12/32 (37.5%) in group A vs 11/29 (27.9%) in group B (p = NS). According to Met resistance of Hp strains the success rate of both therapies was: Group A: 20/20 (100%) in Met<sup>(S)</sup> strains vs 7/12 (58.3%) in Met<sup>(R)</sup> strains (p < 0.01) and Group B: 17/18 (94.4%) in Met<sup>(S)</sup> strains vs 4/11 (36.4%) in Met<sup>(R)</sup> strains (p < 0.05). *Conclusion:* The response to treatment of patients harbouring Met<sup>(R)</sup> Hp strains was significantly lower compared to those with Met(S) strains, in the Met containing newer, one week, triple therapies. Consequently, their efficacy, in the treatment of Hp infection, might be negatively influenced in areas with high (> 35%) incidence of Met Hp resistance. Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Management strategy }" "Metronidazole Resistance Influences the Efficacy of the Short-Term Triple Therapies, Involving Metronidazole, in the Eradication of Helicobacter Pylori (Hp)"

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"P P 36 0800" P 36 0800 **Influence of Metronidazole Resistance on the Efficacy of Two, Short-Term, Triple Therapies Based on Clarithromycin, in the Eradication of Helicobacter Pylori (Hp)**

\*S. Georgopoulos<sup>1</sup>, S. Karatapanis<sup>1</sup>, A. Mentis<sup>3</sup>, A. Mylonakis<sup>1</sup>, V. Vretou<sup>2</sup>, V. Artiki<sup>1</sup>

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Recent studies have shown that newer, one week, triple therapies based on Clarithromycin (CL) are highly effective and safe in treating Hp infection. *The aim* of our study was to estimate the influence of metronidazole (Met) resistance in the Hp eradication rates achieved by two, one week, triple regimens that involve either one (CL) or two (CL plus Met) antibiotic agents. *Patients-Methods:* 78 patients (aged 19–83 yrs, mean 45.6) with a documented Hp infection (by CLO-test, histology and culture) were randomized in two treatment groups: Group A (n = 40, men 27, 62.5% smokers) received Omeprazole (Ome) 20 mg bid +CL500 mg bid +Metronidazole (Met) 500 mg bid, for one week. Group B (n = 38, men 24, 61.3% smokers) received Ome 20 mg bid +CL500 mg bid +TBD (De Nol) 120 mg qid, for one week. All patients underwent a new endoscopy 4 weeks after the end of treatment to assess eradication of Hp. Antibiotic sensitivity test was performed in cultured Hp isolates. *Results:* Eradication of Hp was achieved in 34/40 (85%) patients of group A vs 34/38 (89.5%) of group B (p = NS). Culture and antibiotic sensitivity test revealed 12/32 (37.5%) Met resistant (Met<sup>R</sup>) Hp strains in group A and 13/32 (40.6%) in group B (p = NS). The response to treatment of patients harbouring Met<sup>R</sup> strains was significantly lower compared to those with Met<sup>S</sup> strains, in group A, [7/12 (58.3%) vs 20/20 (100%), p < 0.01]. In contrast, the efficacy of group B regimen was comparable in Met<sup>R</sup> and Met<sup>S</sup> strains [12/13 (92.3%) vs 17/19 (89.5%), p = NS]. *Conclusion:* The efficacy of the newer, short-term, triple therapy involving two antibiotics (CL + Met) is probably depended on the incidence of Met<sup>R</sup> Hp strains. In areas with low CL resistance of Hp, an alternative mono-antibiotic triple regimen may be equally effective and well tolerated.

Oesophageal gastric duodenal disorders: Helicobacter Pylori  
Clinical practice: Management strategy } "Influence of Metronidazole Resistance on the Efficacy of Two, Short-Term, Triple Therapies Based on Clarithromycin, in the Eradication of Helicobacter Pylori (Hp)"

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## "P P 36 0801" P 36 0801 Omeprazole Based Dual and Triple Therapies for Eradication of Helicobacter Pylori

\*Ahmet Aydin, Galip Ersöz, Ahmet Musoglu, Mustafa Tunçer, Hanefi Çavuşoğlu

Depts. of Gastroenterology and Pathology, Ege University, Turkey To investigate the efficacy of various omeprazole (O)/antibiotic combinations in the eradication of Helicobacter pylori (Hp), duodenal ulcer or non ulcer dyspepsia patients with Hp infection were allocated to one of the following treatments: O 20 mg b.i.d. + amoxicillin (A) 1000 mg b.i.d. for 2 weeks (OA), O 20 mg b.i.d. + Clarithromycin (C) 500 mg b.i.d. for 2 weeks (OC<sub>500</sub>), O 20 mg b.i.d. + C 250 mg b.i.d. for 2 weeks (OC<sub>250</sub>), O 20 mg b.i.d. + A 1000 mg b.i.d. + C 500 mg b.i.d. for 1 week (OAC<sub>500</sub>) O 20 mg b.i.d. + A 1000 mg b.i.d. + C 250 mg b.i.d. for 1 week (OAC<sub>250</sub>). Endoscopic examinations were performed and six gastric biopsies (2 for histological examination, and 1 for urease test from both antrum and corpus) taken before and one month after completion of therapy. Before treatment, both of the tests were positive for Hp in all cases. Eradication was defined by negativity of both the diagnostic methods. **Results:** Treatment No. of cases Hp eradication Adverse events OA 34 22 (64.7%) 2 (5.9%) OC<sub>500</sub> 35 20 (57.1%) 12 (34.3%) OC<sub>250</sub> 18 6 (33.3%) 1 (5.6%) OAC<sub>500</sub> 30 28 (93.3%) 10 (33.3%) OAC<sub>250</sub> 29 27 (93.1%) 3 (10.3%) Taste perversion was the most common adverse event in cases treated with OC<sub>500</sub> and OAC<sub>500</sub> (31.4% and 30%, respectively). **Conclusions:** 1. One-week OAC regimens achieved significantly higher eradication rates than two-weeks OA and OC treatments. 2. Eradication rates in one-week OAC regimens were found to be similar with less adverse events in cases treated with OAC<sub>250</sub>. 3. One-week OAC<sub>250</sub> combination may become the treatment of choice for eradication of Hp. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Omeprazole Based Dual and Triple Therapies for Eradication of Helicobacter Pylori"

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"P P 36 0802" P 36 0802 **Intravenous Omeprazole Plus Antibiotics in Helicobacter-Related Peptic Ulcer Patients with Major Stigmata of Recent Hemorrhage — A Preliminary Report of a Randomized Controlled Trial**

\*C.Y. Chen<sup>1</sup>, C.Y. Chen, T.T. Chang, X.Z. Lin

<sup>1</sup> Department of Internal Medicine, Chia-Yi Christian Hospital, Taiwan

National Cheng Kung University Hospital, Taiwan *Aims:* Eradication of H pylori significantly reduces the rate of ulcer rebleeding. Dual therapy with omeprazole and amoxicillin should be considered in all H pylori-positive patients with ulcer bleeding. The aim of the present study was to examine the effect of intravenous route of dual therapy in active ulcer bleeding. *Methods:* In a prospective study, one hundred and thirty two patients with endoscopy documented ulcer bleeding with major stigmata of recent hemorrhage (active bleeding or non-bleeding visible vessel) were entered. Endoscopic injection therapy was performed in all patients with a mean volume of 7.5 mL of 1:10000 epinephrine. One hundred patients (75.5%) with documented H pylori infection (by rapid urease test and histologic findings) were randomly assigned to receive 40 mg omeprazole intravenously every day and ampicillin-sulbactam 750 mg three times daily intravenously for 3 days and 20 mg omeprazole twice daily and 500 mg amoxicillin three times daily for 11 days (Group A) or 20 mg omeprazole twice daily and 500 mg amoxicillin three times daily for 2 weeks (Group B). Subsequently, both group received 20 mg omeprazole daily orally for 4 weeks. Patients underwent a second endoscopy 3 days later and again at the end of 6 weeks. *Results:* Early rebleeding occurred less in Group A. (1/50 or 2% vs 5/50 or 10%,  $P > 0.05$ ). All these 6 patients were excluded. Disappearance of major SRH was significantly higher in Group A (45/49 or 91.8%) than in Group B (32/45 or 71.1%;  $P > 0.05$ ) at the second endoscopy. H pylori eradication rates were 89.7% (44/49) in Group A and 77.7% (35/45) in group B. ( $P > 0.05$ ) Ulcer healing rates were 93.8% (46/49) in Group A and 95.5% (43/45) in Group B. ( $P > 0.05$ ) *Conclusions:* Intravenous form of dual therapy can be started immediately in HP-positive ulcer hemorrhage with major SRH. Rapid disappearance of major SRH and lower early rebleeding rate could be achieved. It can be an alternative choice for H pylori treatment in acute peptic ulcer bleeding. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Intravenous Omeprazole Plus Antibiotics in Helicobacter-Related Peptic Ulcer Patients with Major Stigmata of Recent Hemorrhage / A Preliminary Report of a Randomized Controlled Trial"

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"P P 36 0803" P 36 0803 **Relevance of Metronidazole Resistance in Predicting Failure of Omeprazole, Clarithromycin and Tinidazole to Eradicate *Helicobacter Pylori***

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Centre for Digestive Diseases, Leeds General Infirmary, Leeds, UK

<sup>1</sup> Dept. Public Health Medicine, Leeds, UK *Introduction:* Omeprazole 250 mg od/bd, clarithromycin 250 mg bd and tinidazole 500 mg bd for 7 days (OCT) is an effective regimen against *H pylori* but the effect of metronidazole resistance on this regimen is unclear. *Methods:* *H pylori* positive patients were prescribed OCT and cure of the infection was assessed by <sup>13</sup>C-UBT 5 weeks after therapy. Metronidazole resistance was determined by the disc diffusion method. Samples were stored at { - }70\°C for re-culture and MIC assessment by E test. *Results:* 141 *H pylori* infected patients were enrolled. The organism was successfully cultured in 119/141 (84%) cases and the overall eradication rate was 125/141 (89%). The incidence of metronidazole resistant strains was 121/141 (38%). OCT was successful in 62/69 (90%) patients harbouring fully sensitive strains of *H pylori* compared with 42/45 (93%) of patients with strains that were resistant to metronidazole alone ( $p = 1.0$ ). MIC was assessed in 23 samples. A cut-off point of > 4 mg/L to define metronidazole resistance gave eradication rates of 57% in sensitive and 56% in resistant strains. If the cut-off was re-defined as > 32 mg/L then eradication rates were 70% in sensitive but only 30% in resistant strains. *Conclusion:* The disc diffusion method is not helpful in predicting OCT failure but the E test may be of value. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Relevance of Metronidazole Resistance in Predicting Failure of Omeprazole, Clarithromycin and Tinidazole to Eradicate *Helicobacter Pylori*"

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## "P P 36 0804" P 36 0804 Comparison of the Effect of Omeprazole, Klarithromycin and Metronidazole Combinations in Different Two Doses for One Week Therapy of Helicobacter Pylori Infection

\*A. Doburcali, N. Bagatur, M. Tuncer, F. Hamsioglu, A. \c7elik, S. G\`f6ksel<sup>1</sup>, K. Bal, H. Uzunismail, E. Oktay, I. Din\`e7

<sup>1</sup> Gastroenterology and Pathology, Istanbul, Turkey

Departments of Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey Helicobacter pylori (Hp.) is the principal cause of chronic active gastritis and duodenal ulcer, and has been linked epidemiologically with the development of gastric carcinoma. The aim of this study was to evaluate the efficacy and tolerability of low and high dose short-term triple therapies for cure of Hp infection. 60 patients with Hp infection (16 with duodenal ulcer disease and 44 with antral gastritis) were divided two groups (30/30) for different cures. First group was treated with omeprazole 20 mg o.i.d, klarithromycin 250 mg, b.i.d. and metronidazole 500 mg, b.i.d and second group was treated with omeprazole 20 mg b.i.d, klarithromycin 500 mg b.i.d. and metronidazole 500 mg b.i.d. for a week. Four weeks after the treatment withdrawal, cure of Hp infection was evaluated by urease test and histopathologic examination. The eradication rate of Hp infection was 50% in the first group (18 patients were reported side effects; methallic taste in 17 and pruritus in one) and 80% in the second group (24 patients were reported side effects; methallic taste in 24, epigastric diccomfort and mild nausea in 12 and diarrhea in 3) ( $p < 0.05$ ). In conclusion; eradication rate of one week triple therapy with omeprazole, klarithromycin and metronidazole combination was increased with high doses but also side effects were increased with augmented doses. Therapy Omeprazole 20 mg o.i.d Omeprazole 20 mg b.i.d Klarithromycin 250 mg b.i.d Klarithromycin 500 mg b.i.d Metronidazole 500 mg b.i.d Metronidazole 500 mg b.i.d Mean age 43 (18–70) 47 (18–73)  $> 0.05$  Male/Female (n) 10/20 12/18  $> 0.05$  Antral gastritis (n) 30 30  $> 0.05$  Duodenal ulcer (n) 9 7  $> 0.05$  Hp. eradication rate (%) 50 80  $< 0.05$  Side effects (%) 56 80  $< 0.05$  Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Comparison of the Effect of Omeprazole, Klarithromycin and Metronidazole Combinations in Different Two Doses for One Week Therapy of Helicobacter Pylori Infection"

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"P P 36 0805" P 36 0805 **Comparison of Two One-Week Triple Therapy Regimens in the Eradication Rates of *Helicobacter Pylori* Infection with Associated Duodenal Ulcer. A Randomized Study (Preliminary Results)**

\*M. Forne, J.M. Viver, J.C. Espinos, S. Quintana, A. Salas, J. Garau

Hospital M. de Terrassa, Barcelona, Spain *Aim:* To evaluate the efficacy and tolerability of two one-week triple regimens in *H. pylori* eradication and duodenal ulcer healing. *Methods:* 171 consecutive patients with duodenal ulcer and proved *H. pylori* infection diagnosed by rapid urease test, histology (2 biopsies from antrum and 2 from the corpus) and/or culture (2 biopsies from the antrum), were randomized in two short treatment groups. Group (OCC): patients (84) were given omeprazole 40 mg bd, clarithromycin 500 mg bd and colloidal bismuth subcitrate (CBS) 120 mg qd for 7 days. Group (OCA): patients (87) were treated with the same dosage of omeprazole and clarithromycin plus amoxicillin 1 gr bd for 7 days. No patient received follow-up treatment. Ulcer healing and *H. pylori* eradication were assessed 4 weeks after cessation of therapy. *Results:* Three patients 2/OCA and 1/OCC group were lost to follow-up. *H. pylori* was eradicated in 68/83 patients of the OCC group, (81.9%); 95%-CI: 71%–89% and in 77/85 patients of the OCA group (90.6%); 95%-CI: 81%–96%. (OCC vs OCA:  $p = 0.1$ ). Duodenal ulcer healing was documented in 77/83 (92.8%) patients in the OCC group and in 80/85 (94%) patients in the OCA group ( $p = 0.7$ ). Ulcer healing was more frequently observed in patients cured of *H. pylori* infection than in the group of the patients with persisting infection (96.5% vs 73.9%;  $p < 0.001$ ). Side effects were infrequent and minor, one patient (OCA) suffered from slight dizzinesses during the last two days of treatment that persisted for another 7 days, and one patient (OCC) had skin rash (clarithromycin was stopped on day 5 of therapy). *Conclusions:* 1. Both one-week regimens were effective in the eradication of *H. pylori* and duodenal ulcer healing; 2. They were well tolerated and their cost is similar. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Comparison of Two One-Week Triple Therapy Regimens in the Eradication Rates of Helicobacter Pylori Infection with Associated Duodenal Ulcer. A Randomized Study (Preliminary Results)"

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"P P 36 0806" P 36 0806 **High Eradication Rate of Helicobacter Pylori (HP) in Patients Unsuccessfully Treated Previously** M. Tjivras<sup>1</sup>, V. Balatsos<sup>2</sup>, M. Tsirantonaki<sup>1</sup>, N. Skandalis<sup>2</sup>, A. Archimandritis<sup>1</sup>

<sup>1</sup> Department of Pathophysiology, Medical School, University of Athens, Greece

<sup>2</sup> Gastroenterology Section, Laiko Gen Hospital and Gastroenterology Clinic, Gen State Hospital of Athens, Greece *Aim:* To estimate the effectiveness of a new regimen in eradicating HP in patients with duodenal ulcer (DU) unsuccessfully treated previously by the "classic" triple (tripotassium dicitratobismuthate (TDB) 120 mg qid, metronidazole 500 mg tid, tetracycline 500 mg qid) or dual (omeprazole 20 mg bid, amoxicilline 500 mg qid) therapy. *Patients and methods:* 133 patients (M: 82, F: 51) aged 17–81 years with endoscopically diagnosed DU (diameter  $\{ \backslash b3 \}$  5 mm) in whom "classic" triple or dual therapy failed to eradicate HP. CLO test was done (at least two pieces from the antrum and the gastric body) to confirm the presence and the "eradication" of HP at the entry and at least one month after the end of the treatment respectively; in 31 patients, the presence and the "eradication" of HP was confirmed by histology as well. Patients were given omeprazole 60 mg (20 mg in the morning and 40 mg in the evening) plus amoxicillin 2 gr qid for 10 days and subsequently TDB (De-Nol) 120 mg qid for 6 weeks plus metronidazole 500 mg tid for 10 days. *Results:* 124 patients were followed up. Five of them (4%) withdraw because of side effects (protracted diarrhea, stomatitis, skin rashes). One more patient presented mild diarrhea for 3 days but continued on the treatment. HP eradication was confirmed in 113 of 119 patients examined (95%) and complete ulcer healing was observed in 118 of them. *Conclusion:* This regimen seems to be highly effective in eradicating HP and in healing DU without major side effects. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "High Eradication Rate of Helicobacter Pylori (HP) in Patients Unsuccessfully Treated Previously"

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**"P P 36 0807" P 36 0807 Cost Savings Using the International Gastro Primary Care Group (IGPCG) Management Plan J. Brun, S.A. Brunton, F. Carelli, H. Haslbauer, P. Heyse, H. Maurer, P. O'Connor, W. Peterz, K. R\ fcdy,**

\*M.J. Whitaker

International Gastro Primary Care Group Upper gastrointestinal (GI) disorders are common in many countries world-wide and the costs of treatment represent a significant proportion of primary health care budgets. In the UK, for every 20 patients visiting their GP, one will have upper GI symptoms and therefore, optimal management is important. The IGPCG has devised an upper GI management plan in the form of a treatment algorithm which leads GPs logically through the paths of diagnosis and treatment options. This management plan allocates patients, based on predominant symptoms to one of the following subcategories: motility disorder likely, ulcer disease likely or gastro-oesophageal reflux disease (GORD) likely. A computer model was designed to evaluate whether using the IGPCG management plan can lead to cost savings in practice. Current upper GI treatment costs were obtained from International Marketing Statistics (IMS) Mediplus search of 47,303 patients taken from 728 GPs. Figures for overall cost per patient and for the different disease subcategories were established for current practice and the IGPCG management plan. The overall cost per patient is £398.48 currently, compared to £366 for the IGPCG algorithm which represents a saving of 30%. For the two upper GI disease subcategories, motility and ulcer, the IGPCG cost per patient is considerably lower than currently. The estimated current cost per motility patient is £3130 compared to an IGPCG cost of £354. IGPCG analysis of total costs including GP time and use of hospital services, revealed that of the three disease subcategories motility patients had the lowest cost per patient. In conclusion, using the IGPCG algorithm significantly reduces treatment costs, particularly for those patients with an underlying motility disorder who are treated with prokinetic drugs such as cisapride. Clinical practice: Management strategy } "Cost Savings Using the International Gastro Primary Care Group (IGPCG) Management Plan"

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"P P 36 0808" P 36 0808 **Does Initial Choice of *Helicobacter Pylori* (Hp) Treatment Regimen Influence the Recurrence Rate of Duodenal Ulcer (DU)? A Meta Analysis** J.Q. Huang, Y. Chen, J. Wilkinson,

\*R.H. Hunt

McMaster University Medical Centre, Hamilton, Ontario, Canada DU has a one year recurrence rate over 60% in untreated patients and – 30% in patients on maintenance therapy (APT 1990;4:283). Studies suggest that cure of Hp infection reduces DU recurrence. However, data sets are small and results vary considerably between studies and regimens. We undertook a meta analysis to evaluate any differences in DU recurrence with respect to Hp status and the different drug regimens used for DU healing and eradication. *Methods:* A fully recursive, Medline search identified 126 articles from 1984 to 1995. 41 met inclusion criteria: i) DU healed by antisecretory drug and antimicrobial(s) and documented endoscopically; ii) ulcer recurrence diagnosed by endoscopy; iii) Hp status ascertained by two methods; iv) adult patients and articles in English language. Studies were grouped by different regimens, Hp status and time points following DU healing. *Results:* Groups 6 m (%) arms 12 m (%) arms 18 m (%) arms 24 m (%) arms One 293/476 (68) 9 221/529 (42) 19 19/64 (30) 5 27/100 (27) 5 Two\* 335/435 (77) 8 479/552 (87) 14 33/43 (77) 2 64/90 (71) 3 Three<sup>#</sup> 186/199 (94) 9 767/866 (89) 23 33/38 (87) 2 96/119 (81) 2 Hp<sup>\*\*\*</sup> 345/598 (58) 15 244/606 (40) 21 24/81 (30) 3 37/150 (25) 4 Hp<sup>†</sup> 470/495 (95) 15 957/993 (96) 28 61/64 (95) 3 82/89 (92) 3 No. expressed as No. in remission/No. assessed. m = months; One = CBS/H<sub>2</sub>RA/PPI; Two = two-drug regimen; Three = three-drug regimen. \*vs one p < 0.001; #vs two p < 0.001; \*\* vs Hp<sup>†</sup> p < 0.001 by log rank test, Kaplan-Meier. *Conclusions:* Results confirmed DU recurrence in up to 73% untreated patients after 24 months irrespective of Hp status. Hp eradication significantly changed DU natural history and reduced recurrence rate to 4% at 12 months and 8% at 24 months. Three-drug regimens achieved the highest remission rate over time compared to one and two-drug regimens. DU recurrence depends on initial drug regimen and Hp status. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Does Initial Choice of *Helicobacter Pylori* (Hp) Treatment Regimen Influence the Recurrence Rate of Duodenal Ulcer (DU)? A Meta Analysis"

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## "P P 36 0809" P 36 0809 Effect of Omeprazole, Clarithromycin and Tinidazole on the Eradication of Helicobacter Pylori and Healing of Gastric Ulcer

\*F. Bazzoli, R.M. Zagari, S. Fossi, P. Pozzato, C. Mwangemi, L. Ricciardiello, P. Simoni, A. Roda, E. Roda

Cattedra di Gastroenterologia, Universit\`e0 di Bologna *Background.* Eradication of Helicobacter (H.) pylori is a key factor for the cure of peptic ulcers. Eradication of H. pylori seems to be more difficult to achieve in gastric ulcer (GU) patients than in patients with duodenal ulcer (DU) or gastritis. On the other hand healing rates after conventional treatment with antisecretory drugs were also reported to be lower in GU than in DU patients. Recently, we reported the high efficacy of 1 week low-dose triple therapy with Clarithromycin, Omeprazole and Tinidazole on long-term eradication of H. pylori infection in patients with non-ulcer dyspepsia and DU. *Purpose.* The aim of the present study was to investigate the efficacy of 1 week low-dose treatment with Clarithromycin, Omeprazole and Tinidazole followed by 3 weeks of Omeprazole in eradicating H. pylori infection and ulcer healing in patients with GU. *Methods.* 49 patients (28 males, 21 females; age (yrs) range 32–71, mean 49) with non-NSAID GU and H. pylori infection received Omeprazole 20 mg u.i.d. for 4 weeks and, during the first week, a combination antimicrobial treatment with Clarithromycin 250 mg b.i.d. and Tinidazole 500 mg b.i.d.. H. pylori infection as well as eradication was assessed by histology (Haematoxylin-Eosin, Giemsa), quick urease test and <sup>13</sup>C-Urea Breath Test (<sup>13</sup>C-UBT). Upper GI endoscopy with 3 antral and 2 corpus-fundus biopsies and <sup>13</sup>C-UBT were performed prior to treatment and at 1, 3 and 6 months after the end of treatment. The healing rate in patients treated with antimicrobials was compared to a H. pylori positive, nonNSAID GU historical control group (no. 53; 31 males; age (yrs) range 30–75, mean 50) previously treated with Omeprazole 20 mg u.i.d. for 4 weeks, matched by age, sex, history of smoking and site and size of GU. *Results:* Only 2 patients complained of moderate glossitis and transient taste disturbance which cleared up after completing therapy. At 1 month after the end of treatment, eradication of H. pylori was obtained in 47/49 patients (95.9%, 95% CI: 90.3%–100%). Ulcers healed in 46/49 (93.9%, 95% CI: 87.2%–100%) of the patients treated with antimicrobials and in 38/53 (71.7%, 95% CI: 59.6–83.8; p < 0.003) of the omeprazole patients control group. Follow-up evaluations performed at 3 and 6 months confirmed H. pylori eradication and persistent healing of GU in the patients treated with antibiotics. *Conclusions:* One week low-dose triple therapy with Omeprazole 20 mg u.i.d., Clarithromycin 250 mg b.i.d. and Tinidazole 500 mg b.i.d. is also highly effective in H. pylori eradication in patients with GU. The GU healing rates in patients treated with antibiotics and antisecretory drugs are significantly higher than those reported in patients treated with only antisecretory agents. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Effect of Omeprazole, Clarithromycin and Tinidazole on the Eradication of Helicobacter Pylori and Healing of Gastric Ulcer"

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## "P P 36 0810" P 36 0810 Clarithromycin-Based Therapy Failure: What Comes Next?

\*J.P. Gisbert, D. Boixeda, C. Mart\edn de Argila, F. Bermejo, A. Al-Mostafa, C. De la Serna, A. Garc\eda Plaza

""Ram\fn y Cajal"" Hospital, Madrid, Spain *Purpose:* Recently, eradication therapies containing clarithromycin have been extensively used and are associated with a high *H. pylori* eradication rate. However, it is still to be elucidated how to proceed when these therapies fail. This topic is of an utmost concern because of the ever increasing use of clarithromycin-based therapies. Therefore, we studied the efficiency of omeprazol + amoxicillin + metronidazole (OAM) in this situation, to avoid retreatment with clarithromycin. *Methods:* Eleven patients treated unsuccessfully with one-week twice-daily therapy with omeprazol (20 mg) + clarithromycin (500 mg) + amoxicillin (1 g) (OCA) received a therapy consisting of omeprazole (20 mg b.i.d.), amoxicillin (1 g b.i.d.) and metronidazole (500 mg b.i.d.) (OAM) for one week. This same combination was administered to six patients in whom omeprazol (20 mg b.i.d.) plus clarithromycin (500 mg t.i.d.) (OC) had also failed in eradicating *H. pylori*. Our previous protocols defined eradication failure as the presence of *H. pylori* in biopsies (H & E) or a positive C<sup>13</sup>-urea breath test. A breath test was repeated one month after completing therapy in all patients, but endoscopy (with biopsies) was performed in only ten patients. Compliance was evaluated by tablet count. Eradication was defined as the absence of *H. pylori* by breath test and histology (when available). *Results:* *H. pylori* eradication rates were 36% (4/11) and 83% (5/6) in groups OCA and OC, respectively (Fisher test, p = 0.088). The distribution of demographic variables in both groups was: age (44 – 17/54 – 16 yrs), sex (82/100% males), and smoking (36/17%), respectively. Compliance of therapy was complete in all patients. No relevant adverse effects were reported. *Conclusion:* These preliminary results suggest that a one-week twice-daily OAM therapy has a low efficiency in eradicating *H. pylori* when a previous triple therapy with clarithromycin and amoxicillin (OCA) has failed. However, if the results of this study are confirmed, OAM combination could be an alternative when dual therapy with clarithromycin (OC) has failed. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Clarithromycin-Based Therapy Failure: What Comes Next?"

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"P P 36 0811" P 36 0811 **High Dose of Nizatidine in Double Therapy Eradicates Helicobacter Pylori**

\*L.A. Bancu, S. Bataga, A. Bratu, I. Torok

University County Hospital, Tg. Mures, Romania Eradication of Helicobacter pylori (Hp), prevents duodenal ulcer (DU) relapse. *Aim of study:* evaluation of a double therapy regimen using high dose of Nizatidine (Axid) on Hp eradication and DU healing. *Patients and methods:* 60 consecutive pts with DU and biopsy proven Hp infection were randomised to the following therapy regimens: *A:* Nizatidine 300 mg b.i.d + Amoxicilline 750 mg b.i.d., 14 days. *B:* Colloidal Bismuth Subcitrate (De-Nol) 240 mg b.i.d. one month, + Metronidazole 500 mg t.i.d + Amoxicilline 750 mg b.i.d., 14 days. Endoscopy, Hp status (by rapid urease test and histology) were repeated two month after cessation of therapy, and side-effects were evaluated. *Results:* DU was healed in all pts. Hp was eradicated in 26 pts. (86.66%) in group A and 27 pts. (90%) in group B. Both cohorts A, and B were formed by 30 pts. In group A, side-effects were neglectable and pts. compliance very good. *Conclusion:* Nizatidine in high dose associated to Amoxicilline cures Hp and DU, beside good drug tolerance. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "High Dose of Nizatidine in Double Therapy Eradicates Helicobacter Pylori"

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## "P P 36 0812" P 36 0812 Comparison of Lansoprazole and Omeprazole Against Gastric H/K-ATPase, H<sup>+</sup> Secretion and Growth of H. Pylori

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<sup>1</sup> Department of Molecular & Cell Biology, University of California at Berkeley, U.S.A. *Purpose:* Lansoprazole (L) is a fluorinated derivative of omeprazole (O) and rival PPI for treatment of ulcer disease. This study seeks to identify pharmacological properties which differentiate these two drugs. *Methods:* Inhibition of aminopyrine (AP) accumulation and enzyme recovery were measured in rabbit gastric glands. Acid output was measured in vivo in rat and guinea pig. MIC values against H. pylori were determined for ten fresh isolates. Drugs were incorporated in agar plates, inoculated then incubated in a microaerophylic atmosphere for 5 days. *Results:* There was no significant difference between the IC-50 values for inhibition of AP accumulation by L (0.53 – 0.08 μM) and O (0.47 – 0.08 μM). Recovery of glands, assessed by AP reaccumulation after treating with 20 mM 2-mercaptoethanol, was also identical. Both L and O were more effective inhibitors of stimulated acid output than basal secretion and both drugs displayed a similarly sustained duration of action in the rat with inhibition of acid secretion detectable 24 hr after dosing at 2 mg/kg s.c. However L (IC-50 1.2 μmol/kg) was 2.5-times more potent than O (IC-50 3.0 μmol/kg) measured 2 hr after i.v. injection. This may reflect differences in pharmacokinetic handling in the rat since the two drugs were of similar potency in anaesthetized guinea pigs. MICs for L against H. pylori varied between 32 μg/ml (6 strains) and 64 μg/ml (3 strains) up to 128 μg/ml (one strain). L was marginally more effective than O against H. pylori but there was considerable overlap in activity. *Conclusions:* L is essentially indistinguishable from O as an inhibitor of H<sup>+</sup> transport and acid output. Claimed differences in binding to isolated enzyme would appear to be irrelevant for antisecretory activity and hence clinical efficacy. Potency differences in rat may reflect species specific pharmacokinetic properties resulting from polyfluorination. While both L and O inhibit H. pylori, relevance of this bactericidal action of PPIs is debatable, particularly since they are given as enteric-coated formulations. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Comparison of Lansoprazole and Omeprazole Against Gastric H/K-ATPase, H<sup>+</sup> Secretion and Growth of H. Pylori"

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## "P P 36 0813" P 36 0813 Short-Term Therapy of Helicobacter Pylori Gastritis

\*M.M. Dollinger, M. Kroesen, H.C. Dollinger

Department of Internal Medicine, University of Ulm, Germany *Aim:* The study was designed to compare the efficacy and tolerability of the Al-Mg-antacid hydrotalcite (HT) and the proton pump inhibitor (PPI) pantoprazole given in combination with different antibiotics for the eradication of *H. pylori* in patients with chronic gastritis and non-ulcer dyspepsia (NUD). The study also examined the gastritis variables and the correlation between the *H. pylori* status and the dyspeptic symptoms. *Methods:* Fifty-six patients with positive histology and positive <sup>13</sup>C-urea breath test who were found to have dyspepsia were divided into three groups. Group A: 11 pts were given two tablets of HT q.d.s. (total neutralization capacity 111.2 mval/d) and ampicillin 1000 mg b.d. for 10 days. Group B: 20 pts were treated with pantoprazole 40 mg b.d. and ampicillin 1000 mg b.d. for 10 days. In both groups, metronidazole 500 mg b.d. was given for the last three days (days 8–10). Group C: 25 pts received pantoprazole 40 mg b.d. plus clarithromycin 500 mg b.d. and metronidazole 500 mg b.d. for 7 days. Eradication was determined using <sup>13</sup>C-UBT one month after the end of treatment. Differences in the degree and activity of gastritis between initial and final endoscopies were calculated by Wilcoxon matched pairs test. Symptom severity was scored by patients visual analogue scales (VAS) and by doctors' assessment. *Results:* *H. pylori* eradication was achieved in 45% of group A, 70% of group B, and 96% of group C. Independently of the eradication regimen, cure of the infection brought a marked reduction in the degree of antral gastritis and an even greater improvement in the activity, with a resolution of symptoms in 88% of pts. *Conclusion:* The results support the causal relation between *H. pylori* infection and gastritis. Furthermore, in chronic gastritis, *H. pylori* seems to play an important role in the symptoms of NUD. The success of antimicrobial therapy can be improved by effective control of gastric acid secretion, and the one-week triple therapy with PPI and two antibiotics not only is well tolerated, but also has high and similar efficacy in comparison with the eradication regimens in gastric and duodenal ulcer. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Short-Term Therapy of Helicobacter Pylori Gastritis"

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"P P 36 0814" P 36 0814 **Evaluation of the Combination of Omeprazole and Azithromycin with or without Metronidazole in Eradicating Helicobacter Pylori**

\*A. Vcev, A. Vceva, D. Pezerovic, D. Stimac, M. Rubinic, A. Ivandic, B. Dmitrovic, D. Vukovic, N. Micunovic

Clinical Hospital Osijek Clinical Hospital Centre Rijeka, Croatia *Purpose:* We evaluated the benefit of 7 therapeutic schedules with omeprazole (OME) and azithromycin (AZ) with or without metronidazole (ME) for eradication of Helicobacter pylori. *Methods:* Helicobacter pylori status was determined by rapid urease test and histology before and 4 weeks or more after therapy. 7 groups of H. pylori infected patients with peptic ulcer disease were studied. Group 1 (n = 25) and 2 (n = 25) received OME 20 mg/day for 14 days and AZ 500 mg/day for 5 days. Group 2 received and ME 3 {'b4} 500 mg/day for 5 days. Group 3, 4, 5, 6 and 7 received OME 40 mg/day for 14 days. Group 3 (n = 16) received AZ 500 mg/day for 5 days. Group 4 (n = 20) received AZ 500 mg/day for 9 days. Group 5 (n = 20) received AZ 500 mg/day for 9 days and ME 3 {'b4} 500 mg/day for 7 days. Group 6 (n = 19) received AZ 2 {'b4} 500 mg for 9 days. Group 7 (n = 15) received AZ 2 {'b4} 500 mg/day for 9 days and ME 3 {'b4} 500 mg/day for 7 days. Side effects were recorded in all patients. *Results:* The eradication rate in group 1, 2, 3, 4, 5, 6 and 7 was 64%, 72%, 62.5%, 70%, 75%, 73.7% and 86.6%. 21.4% (30/140) patients experienced minor or mild side effects, none discontinued therapy because of side effects. *Conclusion:* We conclude that omeprazole 40 mg/day for 14 days, azithromycin 2 {'b4} 500 mg/day for 9 days and metronidazole 3 {'b4} 500 mg/day for 7 days is effective treatment for eradication H. pylori infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Evaluation of the Combination of Omeprazole and Azithromycin with or without Metronidazole in Eradicating Helicobacter Pylori"

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"P P 36 0815" P 36 0815 **Eradication of Helicobacter Pylori Decreases the Rate of Duodenal Ulcer Recurrence and Rebleeding** G. Macr\ec, S. Milani, E. Surrenti, M.T. Passaleva, G. Ciancio, S. Faenzi, O. Morelli, M. Romano, A. Calabr\f2, G. Salvadori, C. Surrenti

Gastroenterology Unit, Department of Clinical Pathophysiology, and University of Florence, Italy *Background:* gastrointestinal hemorrhage is the most frequent complication of peptic ulcer disease. It has recently been suggested that HP infection may be a risk factors for the relapse of peptic ulcer and rebleeding. *Aim:* we evaluated the effects of HP eradication on the recurrence of bleeding from duodenal ulcer (DU) in young patients with 46 to 70 months of follow-up. *Methods:* from June 90 to June 92, we analyzed 32 pts (all males, mean age 30.2 yrs, range 22–46) with endoscopically proved HP positive bleeding DU. All pts received Omeprazole (40 mg/day) for 4 wk followed by Colloidal Bismuth (480 mg/day) for 2 wk associated with Amoxicillin (2 g/day) during the first wk, substituted by Metronidazole (750 mg/day) during second wk. After 6 wk all pts underwent upper digestive endoscopy with antral biopsies in order to assess ulcer healing and HP eradication (Giemsa stainign and rapid urease test). Upper digestive endoscopy with antral biopsies was performed once a year for 46–70 months. *Results:* Ulcer healing was found in 32/32 pts (100%). HP eradication was obtained in 23/32 pts (71.9%). After 12 months, 2 previously eradicated pts had been reinfected (8.7%). In the following 24 month, ulcer recurred in 10/11 HP-positive pts (reinfected and eradicated). Rebleeding was noted in 5/11 (45%) HP-positive pts. These pts were treated with omeprazole 40 mg/day for 4 wk with complete healing. In the following 24–48 month ulcer recurred in 10/11 pts HP-positive pts. Rebleeding was noted in 7/10 (70%) of them. Patients who were not reinfected by HP (21/32) did not show any evidence of DU relapse during follow-up. Thus, the rate of rebleeding episodes along the period of the follow-up was significantly lower in pts with long term eradication of HP, in comparison with those who did not. *Conclusion:* long term eradication of HP can decrease the rate of DU recurrence and rebleeding. }" "Eradication of Helicobacter Pylori Decreases the Rate of Duodenal Ulcer Recurrence and Rebleeding"

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"P P 36 0816" P 36 0816 **Triple Therapy (Omeprazol + Amoxicillin + Clarithromycin) for Helicobacter Pylori Eradication in Patients with Peptic Ulcer. No Difference between Six or Twelve Days**

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*Intro:* Modern therapies for eradication of Helicobacter pylori try to be more effective and to achieve better compliance being shorter and cheaper. Some seven-days regimens with omeprazole, amoxicillin and clarithromycin have proved high eradication rates. In Spain available packaging of both antibiotics used carries 12 capsules in. If we use 7 days regimens we need double number of packages and lots of pills are wasted.

*Aim:* To ascertain the efficacy of a triple therapy with omeprazole, amoxicillin and clarithromycin for Helicobacter pylori eradication in regimens of 6 and 12 days.

*Patients and Methods:* We conducted a clinical trial to eradicate Helicobacter pylori infection in patients with peptic ulcer. 132 consecutive patients (80 M/52 F, mean age: 49.7, range: 19–84) submitted to upper digestive tract endoscopy because symptoms of dyspepsia, were included in the study. Diagnosis of Helicobacter pylori infection was achieved when, at least, two of the following tests were positive: histologic examination of antral biopsy specimens in frozen tissue sections on H-E and Giemsa, rapid urease test (Jatrox-test) and C<sup>13</sup> urea breath test. Triple therapy consisting in omeprazole 20 mg/bid, amoxicillin 1 g/bid and clarithromycin 500 mg/bid was given to patients at the time of diagnosis. Duration of treatment was non-randomly assigned for 6 and 12 days. Control of eradication was assessed by C<sup>13</sup> urea breath test after 6 weeks of finishing treatment. Statistical analysis was performed using { ? }<sup>2</sup> test with Yates correction.

*Results:* Eradication rates in the different groups are: 6 days 81.7% (67/82) 12 days 86% (43/50) No statistical difference of eradication was found between both regimens (6 vs 12 days). Costs of the 2 regimens were 85 and 170 \$, respectively for 6 and 12 days.

*Conclusions:* 1. Triple therapy (omeprazol + amoxicillin + clarithromycin) in a short course of 6 days is so effective for eradicating Helicobacter pylori in peptic ulcer than a 12 days therapy. 2. Cost-effectiveness for a 6 days regimen is excellent. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Triple Therapy (Omeprazol + Amoxicillin + Clarithromycin) for Helicobacter Pylori Eradication in Patients with Peptic Ulcer. No Difference between Six or Twelve Days"

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"P P 36 0817" P 36 0817 **Eradication of *H. Pylori* Infection in Peptic Ulcers with Four Different Drug Regimens**

\*M. Katicic, V. Presecki, M. Marusic, M. Prskalo, M. Ticak, B. Sabaric, V. Colic-Cvrlje, B. Papa, S. Naumovski-Mihalic, M. Dominis, S. Kalenic, S. Dzebro

Clinical Hospital Merkur, Medical School, University of Zagreb, Zagreb, Croatia *Aim:* Four different therapeutic regimens for *H. pylori* eradication were compared in patients with gastric (GU) and duodenal ulcer (DU). *Methods:* 70 GU (M/F 36/34, mean age 57) and 153 DU patients (M/F 90/63, mean age 49) who were positive for *H. pylori* underwent endoscopy, urease test, histology and serology at the beginning of the study and 4 weeks after the end of the treatment. They were randomly assigned to four treatments groups: A) Omeprazole 20 mg b.d., Amoxicillin 1 g b.d. for 14 days (n = 57), B) Omeprazole 20 mg b.d., Amoxicillin 1 g b.d. for 14 days, metronidazole 500 b.d. for 10 days (n = 63), C) Omeprazole 20 mg b.d., Amoxicillin 1 g b.d., Clarithromycin 500 mg b.d. for 7 days (n = 48), D) Omeprazole 20 mg b.d., Amoxicillin 1 g b.d., Clarithromycin 500 mg b.d. for 14 days (n = 52). *Results:* Th-groups No. patients Eradicated (%) Healing (%) Tot. GU DU Tot. GU DU Tot. GU DU Group A 57 23 34 42 52 35 81 83 80 Group B 63 17 46 63 71 61 86 82 87 Group C 48 20 28 83\* 80 86 94 95 93 Group D 52 17 35 92\* 91 93 98 95 100\* p < 0.05, C and D in comparison with A and B *Conclusion:* Combination Omeprazole + Amoxicillin had a low efficacy in the eradication of *H. pylori*. Two weeks Omeprazole + Amoxicillin + Clarithromycin therapy is the most effective, but one week of the same regimen is effective enough, simple and relatively well tolerated. Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infections in adults } "Eradication of H. Pylori Infection in Peptic Ulcers with Four Different Drug Regimens"

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"P P 36 0819" P 36 0819 **Helicobacter Pylori Eradication with Dual and Triple Therapy: A Cost-Effectiveness Analysis**

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<sup>2</sup> University of Magdeburg, Germany

<sup>3</sup> Byk Gulden Pharmaceuticals, Konstanz, Germany *Purpose:* *Helicobacter pylori* (*H. pylori*) is broadly accepted as a major prerequisite for the development of peptic ulcer disease and its elimination prevents ulcer relapse in the vast majority of patients. This health economic study compares the cost-effectiveness of two extensively tested treatment schemata: a 14 days dual therapy with a proton pump inhibitor (PPI) and amoxicillin, which produced variable cure rates and a 7 days short term triple therapy (i.e. a PPI and two antibiotics), which resulted in very high cure rates. *Methods:* Possible therapy courses for *H. pylori*-cure were implemented by a decision tree model. The probabilities for the use of a particular course of treatment were determined by a survey of 100 office-based specialists in Germany. The underlying eradication and ulcer relapse rates were analysed by literature research and subsequent meta-analysis. For the analysis, direct costs (medication, diagnostics and consultations with the physicians) were considered. *Results:* Taking only the medication costs into account, the *daily* costs of triple therapy were higher than those of dual therapy. However, the *total* medication costs of triple therapy were 34% lower than those of dual therapy. Carrying out a cost-effectiveness analysis, from the point of the German healthcare system, the total costs per year for a patient with successful *H. pylori* eradication therapy were DEM 1082 with dual and only DEM 657 with triple therapy. The robustness of this result was validated by several sensitivity analyses concerning the medication costs (price range) and the eradication rates (confidence intervals). *Conclusion:* This health economic analysis showed that triple therapy is not only *more effective* but also *more efficient* than dual therapy. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Helicobacter Pylori Eradication with Dual and Triple Therapy: A Cost-Effectiveness Analysis"

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## "P P 36 0820" P 36 0820 What Is the Best Rescue Therapy for Omeprazole Plus Amoxicillin?

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**Introduction:** Helicobacter pylori infection has change the natural course of peptic ulcer disease. Dual therapy with omeprazole and amoxicillin was the most popular therapy in the treatment of Helicobacter infection. Better compliance, few side effect and rapid disappearance of ulcer symptoms made it become the first line anti-HP therapy. However, variable success rate was results.

**Patients and Methods:** 425 patients with endoscopically documented peptic ulcer and positive H pylori infection were included. The definition of positive H pylori infection consisted of both positive CLO test and histological examination. Everyone received Omeprazole 20 mg bid and amoxicillin 500 mg tid for 14 days. Ranitidine 150 mg bid was given for 4 weeks. Repeat endoscopy was done to look for ulcer healing and H pylori eradication. The eradication rate of dual therapy was 76%. There were 102 patients who failed in initial H pylori eradication. We made randomization into three group: group A (36 patients): omeprazole 20 mg bid and amoxicillin 500 mg tid for 14 days, group B (33 patients): De-Nol 300 mg qid, amoxicillin 500 mg qid, metronidazole 500 mg qid for 14 days; group C (33 patients): omeprazole 20 mg bid, clarithromycin 250 mg bid, metronidazole 500 mg bid for 7 days. Repeat endoscopic examination with 4 biopsy (2 antrum and 2 body) for H pylori eradication was done 4 weeks after anti-Hp therapy.

**Results:** Total eradication rate of H pylori in the second line therapy was 81.3% (83/102), including group A: 63.8% (23/36), group B: 90.9% (30/33), and group C: 90.9% (30/33). We further classified the eradication rate into the subgroup according to CLO < 1 hour (I), and CLO > 1 hour (II): CLO < 1 hour CLO > 1 hour

Group	CLO < 1 hour	CLO > 1 hour
Total	12/22 (52.1%)	11/14 (78.5%)
Group A	23/36 (63.8%)	14/15 (93.3%)
Group B	30/33 (90.9%)	30/33 (90.9%)
Group C	15/17 (88.2%)	15/16 (93.7%)
Total	43/57 (75.4%)	40/45 (88.0%)
Total	83/102 (81.3%)	

We found that triple therapy and PPI, clarithromycin, metronidazole got better HP eradication than high dose dual therapy. (P < 0.05) There was no significant difference in the H pylori eradication in subclassification into CLO < 1 hour or CLO > hour in rescue therapy.

**Conclusion:** New and traditional triple therapy both were good regimens for rescue of initial failure of dual therapy. Bacterial urease activity seemed not influence the H pylori eradication in the second line rescue therapy. Oesophageal gastric duodenal disorders: Helicobacter Pylori }

"What Is the Best Rescue Therapy for Omeprazole Plus Amoxicillin?"

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## "P P 36 0821" P 36 0821 **Three-Day Octreotide-Assisted *Helicobacter Pylori* Triple Eradication Therapy. Six Month Follow-Up**

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**Purpose.** Orally administered antibiotics for *H. pylori* eradication therapy exert their effect by local diffusion into the gastric mucosa. However, gastric emptying reduces antibiotic-mucosa contact time. We tested the hypothesis that a three-day *H. Pylori* triple eradication therapy with concurrent octreotide administration may potentiate antibiotic effect by delaying gastric emptying.

**Methods.** 26 symptomatic *H. pylori*-positive patients with active duodenal (n = 20) or gastric (n = 6) ulcer participated in this pilot study. All patients received a three-day course of octreotide (0.1 \b5g subcutaneously t.d.s.), amoxicillin and metronidazole (500 mg orally q.d.s.) and colloid bismuth subsitrate (CBS) (240 mg b.d). CBS treatment was continued for another four days. Endoscopy with antral biopsies for CLO-test, culture and crush tissue smears were performed on admission to the study, at 4, 8 weeks and six months post-treatment.

**Results.** 24/26 (92.3%) ulcers were completely healed at 4 weeks and remained healed at 8 weeks. All 24 patients with a healed ulcer became *H. pylori* negative at 4 weeks. The eradication rate at 8 weeks was 88.5% (23/26). All 24 patients remain asymptomatic at 6 months. In 19/24 patients who accepted to have endoscopy at six months, ulcers remained healed, but the *H. Pylori* eradication rate dropped to 68.4% (13/19).

**Conclusion.** Our results show that a three-day octreotide-assisted *H. pylori* eradication triple therapy is highly effective, to maintain a peptic ulcer in remission at six-month follow-up.

Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: GD disorders, acid peptic } " "Three-Day Octreotide-Assisted *Helicobacter Pylori* Triple Eradication Therapy. Six Month Follow-Up"

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"P P 36 0822" P 36 0822 **What Is the Optimal Method of H. Pylori Eradication in Patients Chronically Treated with Non-steroid Antyinflammatory Drugs?** H. Kordecki, R. Kosik, P. Milkiewicz

Dept. of Gastroenterology M. Curie Hospital, Szczecin, Poland Wide use of non-steroid antyinflammatory drugs (NSAID) markedly increased the frequency of gastric and duodenal mucosal lesions. It is suggested that eradication of H. pylori (H.p.) in persons with some mucosal changes being protractedly treated with NSAID is more optimal and cheaper method in comparison with those continually taking prostaglandins (e.g. misoprostol). *The aim of our study* was to estimate the relapse rate of mucosal lesions 10 months after the end of therapy in persons chronically taking NSAID. Eradication of H.p. was carried out in the majority of patients. The remaining patients were treated with H-2 blockers only. *Material and methods:* Endoscopic examinations were performed (EVIS 100 – Olympus equipment) in 150 patients receiving chronically NSAID. In 107 persons (71%) taking NSAID lesions were found: 87 patients stomach erosions, 61 stomach ulcers, 75 duodenal erosions and 53 duodenal ulcers. Thirty-two were diagnosed to have multiple ulceration and erosions. In 75 (70%) out of this group H.p. infection was disclosed (rapid urease test and microscopical examination). However negative results were detected in 32 patients (34%). Patients who had mucosal lesions in stomach or/and duodenum were treated by one of these four methods: 1. ranitidine only (R) 2. colloidal bismuth with amoxicillin and metronidazole (CB + A + M) 3. omeprazole with amoxicillin and metronidazole (O + A + M) 4. omeprazole with clarithromycin and tinidazole (O + C + T) *Results:* Treatment No of One month after therapy Ten months after therapy pat. healings eradication healings eradication rate rate rate rate R 12 6 (50%) 2 (17%) 2 (17%) 0 (0%) CB + A + M 25 19 (76%) 16 (64%) 9 (36%) 7 (28%) O + A + M 26 24 (92%) 24 (92%) 24 (92%) 3 (88%) O + C + T 12 11 (92%) 12 (100%) 12 (100%) 12 (100%) *Conclusions:* 1. The best method resulting in long-term-healing and eradication of H.p. was the treatment with O + C + T. 2. The therapy with H-2 blockers is ineffective in H.p. positive patients protractedly taking NSAID. *Clinical practice:* Management strategy Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "What Is the Optimal Method of H. Pylori Eradication in Patients Chronically Treated with Non-steroid Antyinflammatory Drugs?"

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## "P P 36 0823" P 36 0823 Triple Therapy with Omeprazole, Clarithromycin and Amoxicillin for Cure of Helicobacter Pylori Infection

\*S.P. Chen, B. Lian, S.H. Wen

Dept. of Gastroenterology, Peking Union Medical College Hospital, Beijing, China The aim of this clinical study is to determine the eradication rate of Helicobacter pylori (Hp) infection using omeprazole 20 mg twice daily, clarithromycin 500 mg twice daily and amoxicillin 1000 mg twice daily for one or two weeks, in comparison with colloidal bismuth subcitrate 240 mg twice daily, amoxicillin 1000 mg twice daily and metronidazole 400 mg twice daily for two weeks. 168 patients with Hp associated chronic gastritis or duodenal ulcer were allocated to three therapeutic groups: Group I (N = 55) and Group II (N = 57) were treated with triple therapy of omeprazole, clarithromycin and amoxicillin for one week and two weeks respectively, and Group III (N = 56) was treated with bismuth triple therapy for two weeks. The Hp status was determined by rapid urease test and histology of Warthin-Starry stain. The eradication rates in group I, Group II and Group III were 89.2%, 94.8% and 71.4% respectively. The eradication rates of both Group I and Group II were significantly higher than that of Group III ( $P < 0.05$ ). There were no statistical significant difference in the eradication rate between Group I and Group II. The incidence of side effects in Group III (49.6%) was significantly higher than that in Group I (19.3%) and Group II (25.8%). There were two patients withdrawn due to side effects during bismuth triple therapy. Our results showed that triple therapy with omeprazole, clarithromycin and amoxicillin is more effective and better tolerated than the bismuth triple therapy in the treatment of H. pylori infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Triple Therapy with Omeprazole, Clarithromycin and Amoxicillin for Cure of Helicobacter Pylori Infection"

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## "P P 36 0824" P 36 0824 Comparison of Different Drug Regimens for Helicobacter Pylori Eradication

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**Background:** Helicobacter pylori (HP) has a world wide distribution, however in Egypt the incidence of infection rises to over 80% in young adults. Eradication of HP from the forgut has been sought using multiple agents in the form of dual or triple therapy regimens. No treatment schedule is yet considered ideal either due to limited access of antimicrobial agents or the organisms resistance especially to imidazoles.

**Aim:** To compare the efficacy and side effects of four alternative triple therapy regimens.

**Patients and Methods:** One hundred patients with endoscopically proven upper gastrointestinal lesions 35% duodenal ulcer and 28% gastric ulcer, 22% antral gastritis, 15% duodenitis, who are also positive to H.P. by histological biopsies stained by Gienisa, CLO test and serology. Histopathological assessment was done to all patients prior initiation of therapy. Patients were randomized into groups according to the following drug combinations: Group (1): (n = 25) Ranitidine 300 mg + Amoxicillin (AMO) 500 mg t.d.s. + Metronidazole 4 250 mg. Group (2): (n = 25) Ranitidine 300 mg + AMO 500 mg t.d.s. + Tinidazole 500 mg B.d. Group (3): (n = 25) Omeprazole (Omp) 40 mg + AMO 500 mg t.d.s. + Met 4 250 mg. Group (4): (n = 25) Omp 40 mg + AMO 500 mg t.d.s. + Tinidazole 500 mg B.d. Antimicrobials were given for 2 weeks and anti secretory drugs were given for 4 weeks. Reassessment was done 4 weeks after the end of antimicrobial therapy and after 6 months by endoscopic examination and biopsy. In patients showing failure of adequate eradication inspite of compliance to treatment, culture of H.P was done using metronidazole and tinidazole amoxycilline impregnated strips or discs.

**Results:** Endoscopic evidence of healing was detected in 80% (20/25) of group 1, 92% (23/25) of group 2, 84% (21/25) of group 3 and 96 (24/25) in group 4. duodenal ulcer responded in 33 (94.3%) of cases, gastric ulcer in 25 (98.3%), antral gastritis in 19 (86.4%) and duodenitis in 13 (86.7%). The percentage of H.P eradication was 80%, 92%, 88% and 96% in groups 1, 2, 3, 4 respectively with an overall H.P eradication in 89% of the patients. The side effects were uncommon (nausea in 5%, diarrhoea in 2% and bitter taste in 2%). Out of the 11 patients who failed to erradicate H.P., 8 (72.7%) were resistant to metronidazole, one to amoxycillin and one to tinidazole and no resistance was detected in the last patients. Relapse rate was 3%.

**Conclusion:** (1) Omeprazole + Amoxycillin + Tinidazole was the most effective regimen for eradication of H.P (96%). (2) Triple therapy with H, antagonist (Rantidine) + Amoxycilline and Tinidazole proved good effectiveness (92%) and was more economic than Omeprazole triple therapy. (3) Tinidazole was more effective than metronidazole and was not accompanied with resistance. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Comparison of Different Drug Regimens for Helicobacter Pylori Eradication"

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"P P 36 0825" P 36 0825 **Helicobacter Pylori Eradication in Gastric Ulcer Disease: One Year Prospective Multicenter Study** F. Di Mario, G.A. Grasso<sup>1</sup>, S. Kusstatscher, M. Ferrana, N. Dal B'f2, M. Bortolon, G. Tafner<sup>2</sup>, R. Marin<sup>3</sup>, A. Caroli<sup>4</sup>, S. Salandin, M. Cassaro, M. Rugge, G. Battaglia<sup>1</sup>

Padova, Italy

<sup>1</sup> Venezia, Italy

<sup>2</sup> Trento, Italy

<sup>3</sup> Dolo, Italy

<sup>4</sup> Montebelluna, Italy Hp infection plays a different role in the pathofisiology of gastric (GU) and duodenal ulcer (DU). Since now, few studies are available on GU follow-up after Hp eradication. Therefore, the aim of this study was to evaluate ulcer relapse rate after Hp eradication in GU patients. *Material and Methods:* we enrolled in a prospective multicenter study 72 consecutive outpatients (mean age 49; range 26–79, M/F 38/34) referred for Hp positive GU. Hp status was evaluated by three different tests (histology, CLO test and serology). Study design: four endoscopies were performed during the follow-up: at baseline, two months after the end of a triple therapy treatment, at six and twelve months. Hp eradication was considered successful when both histology and CLO test resulted negative. *Results:* Over 72 patients 14 subjects remained Hp positive after the treatment. One out of the 58 eradicated pts become positive at six months. Seven GU relapses were observed (5 in Hp{ - } and 2 in Hp+ pts); in 2/5 Hp{ - } pts relapsed, a NSAIDs intake was documented. *Conclusions:* 1) Hp eradication in GU is related with a low relapse rate (5/57); 2) Contrary to the outcome observed in DU pts, only 2/14 Hp+ GU relapsed during a twelve months follow-up; 3) Almost 50% of GU relapses in Hp{ - } pts are related with NSAIDs assumption. }" "Helicobacter Pylori Eradication in Gastric Ulcer Disease: One Year Prospective Multicenter Study"

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"P P 36 0826" P 36 0826 **One Year Follow-Up after Eradication of H. Pylori Infection in Preventing Duodenal Ulcer Bleeding** S. Salandin, N. Dal B'f2, S.A. Grassi<sup>1</sup>, M. Ferrana, S. Kusstatscher, F. Vianello, A. Pilotto, M. Bortolon, F. Farinati, G. Battaglia<sup>2</sup>, F. Di Mario

Padua University, Italy

<sup>1</sup> Marostica, Italy

<sup>2</sup> Venice Hospital, Italy *Aim:* The study was designed to evaluate the role of Hp infection associated with NSAIDs intake in duodenal ulcer bleeding. *Methods:* In an open five years prospective study (12–24 months) 50 consecutive patients Hp positive (37 M, 13 F; mean age 56, range 27–68) showing in the last 12 months at least one episode of bleeding duodenal ulcer, endoscopically documented, were enrolled. Eighteen subjects showed an intake of ulcerogenic drugs (NSAIDs+ve) causally related with bleeding episode. From each patient smoking habit, alcohol intake, blood group and family history of peptic ulcer were also recorded. The Hp status was assessed by means of urease test, hystology and serology. After an informed consent all patients received an eradication therapy (dual or triple regimen for 14 days); eradication rate was assessed 2 months after the end of the treatment as mentioned above. All subjects were followed-up by endoscopy (every 12 month and at any symptomatic recurrence) and clinical evaluation every six months. *Results:* Overall, in 35 out of the 50 patients (70%) Hp infection was eradicated (12 NSAIDs+ve and 23 NSAIDs{ -}ve). Only one patient (Hp+ve/Nsaids{ -}ve group) showed a bleeding episode at the fifth month of follow-up. Seven patients showed ulcer relapse (3 in Hp+ve/NSAIDs+ve and 4 in Hp+ve/NSAIDs{ -}ve group); no Hp{ -}ve patient relapsed. No statistical differences were detected in Hp+ve vs Hp{ -}ve subjects as regards clinical and epidemiological parameters. *Conclusions:* These preliminary data seem to confirm the importance of Hp infection eradication in preventing bleeding duodenal ulcer, both in NSAIDs positive and negative groups. }" "One Year Follow-Up after Eradication of H. Pylori Infection in Preventing Duodenal Ulcer Bleeding"

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"P P 36 0827" P 36 0827 **In vitro Evaluation of Helicobacter Pylori Resistance to Five Antimicrobial Agents in Italy**

\*A. Savio, R. Negrini, S. Di Nocera, A. Paterlini, P. Cesari, G. Franzin, S. Orsola

FBF Hospital, Brescia, Italy We evaluated the "in vitro" sensitivity to metronidazole, amoxicillin, tetracyclin, erythromycin and azithromycin of 66 strains of *Helicobacter pylori* (*H. pylori*) isolated from the gastric mucosa of dyspeptic patients. Susceptibility was determined by disc diffusion on agar plates. 29 patients (group A) had never been treated for *H. pylori* infection while 37 patients had previously received an unsuccessful treatment for the infection: 9 patients (group B) had been treated with omeprazole + amoxicillin and 28 patients (group C) with tinidazole + amoxicillin + colloidal bismuth subcitrate and/or omeprazole. All the isolates from group C were found to be resistant to metronidazole. The natural metronidazole resistance, evaluated in patient without previous anti-*H. pylori* treatments containing nitroimidazoles, was around 21% (17% and 33% in group A and B respectively) and wasn't related to age or sex. No strains resistant to azithromycin were found. Tetracyclin resistant strains accounted for 4.5% (0%, 11% and 7% in group A, B and C respectively). The overall resistance to azithromycin was 15% (9%, 0% and 25% in group A, B and C). Susceptibility to erythromycin, tested in 15 cases only, always matched with azithromycin susceptibility. The occurrence of strains of *H. pylori* resistant to nitroimidazoles as well as to macrolides is rather frequent in our geographic area. In our study a resistance to metronidazole was always found in case of failure of the therapeutic schedule containing a nitroimidazole: this suggests to avoid further alternative therapeutic combinations including nitroimidazoles in these cases. In vitro testing of *H. pylori* sensitivity seems to be important before embarking on treatments aimed at eradicating this bacterium. This holds true particularly in course of therapeutical trials, in case the eradication of this microorganism is of crucial importance as in low-grade gastric MALT lymphoma, and after a previous unsuccessful antibacterial treatment. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "In vitro Evaluation of Helicobacter Pylori Resistance to Five Antimicrobial Agents in Italy"

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"P P 36 0828" P 36 0828 **A Second Regimen of Omeprazole (O) Plus Amoxicillin (A) Increases the Rate of H. Pylori (HP) Eradication in Patients with Duodenal Ulcer**

\*S. Michopoulos, H. Bouzakis, M. Sotiropoulou<sup>1</sup>, I. Vougiadiotis, E. Pardalos, I. Papaspyrou<sup>1</sup>, N. Kralios

<sup>1</sup> Gastroenterology Unit, "Alexandra" Univ. Hospital, Athens, Greece

<sup>1</sup> Pathology Unit, "Alexandra" Univ. Hospital, Athens, Greece The combination of O + A has been proposed as an HP eradication treatment with controversial efficacy. It has been suggested that pre-treatment with O reduces the eradication rate. On the other hand, resistant to A, HP strains have not yet been identified. The *aim of our study* was to examine if a second administration of O + A increases significantly the overall success rate of HP eradication and whether the pre-treatment with O or duration of antibiotic treatment influence these results. *Patients and Methods:* 149 patients with duodenal ulcer were enrolled in our study. They have been randomly allocated in 2 groups and received respectively: *Group I:* (80 patients) Pre-treatment with O 20 mg for 10 days, followed by O 40 mg + A 2 gr for 10 days and O 10 mg for 20 days and *Group II* [controls]: (69 patients) who received both O 40 mg + A 2 gr from the beginning, subdivided in *Ia:* (29 patients): O + A for 10 days plus O 20 mg for 30 days and *Ib:* (40 patients): O + A for 15 days plus O 20 mg for 25 days. The patients of group I who failed to eradicate HP were randomly subdivided into *Ia:* 22 patients who received the same regimen and *Ib:* 28 patients who received both O + A from the beginning (O 40 mg + A 2 gr for 10 days plus O 20 mg for 30 days). The HP eradication has been estimated by histology (2 antral + 2 fundic biopsies) 4–6 weeks after the end of each treatment. *Stat:* Chi-square *Results:* 20% (CI: 11–29) of group I (75 patients) and 37% (CI: 24–49%) of group II (63 patients) eradicated HP after the first treatment  $p < 0.05$  (11 drop out). Additionally 12/22 patients of group Ia and 12/28 of group Ib eradicated HP after the second attempt of O + A (NS) [10 drop out]. There was no difference between Ia and Ib. The subgroup Ib was significantly different from group I ( $p < 0.05$ ). *Conclusions:* 1) The simultaneous administration of OM + A for 15 days has the best eradication rate, but remains low (37%). 2) The readministration of O + A has a substantial additional success rate, irrespectively of pre-treatment with O. *Clinical practice: Management strategy* Oesophageal gastric duodenal disorders: Helicobacter Pylori } "A Second Regimen of Omeprazole (O) Plus Amoxicillin (A) Increases the Rate of H. Pylori (HP) Eradication in Patients with Duodenal Ulcer"

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"P P 36 0829" P 36 0829 **Cimetidine and Amoxicillin — Clavulanic Acid for Ulcer Disease with Helicobacter and Herpes Simplex Virus**

\*N.A. Vinogradov, M.A. Vinogradova, R.R. Gazizova

Hospital No 3, Moscow, Bashkir Medical University, Ufa, Russia *Purpose:* To evaluate the cimetidine and amoxicillin-clavulanic acid made by Smith Kline Beecham (Tagamet and Augmentin respectively) for cases of peptic ulcer. To assess the influence of infection with Herpes Simplex virus (HSV) on ulcer disease. *Patients and methods:* 55 patients aged 18–80, illness duration 1–20 years: 26 stomach ulcer (SU), 26 duodenal ulcer (DU), 3 with SU and DU at once. Concomitant reflux-esophagitis — 22, chronic pancreatitis — 18. Bleeding (Forrest I–II) — 8 cases, when cimetidine was used i.v. 200 mg every 6 hours till hemostasis and then orally 800 mg per day alike the peptic ulcer exacerbation dose. Three comparable randomized groups: the 1st (n = 20) received cimetidine as monotherapy, the 2nd (n = 20) — cimetidine with Augmentin 375 mg 3 times a day for 10 days, the 3rd (n = 15) cimetidine with the triple therapy (bismut subcitrate, metronidazole, ampicillin). Helicobacter pylori (HP) was isolated by histological or cytological methods. The presence of HSV in the mucosa biopsy specimens was verified by fluorescein-iso-thio-cyanate-linked HSV-antibodies. *Results:* Ulcer healing was sooner in the 2nd versus the 3rd group, and was the latest in the 1st. HP elimination occurred in 18 of the 2nd and in 12 patients of the 3rd group. Cimetidine caused esophagitis and pancreatitis remission. The most resistant to therapy ulcers were characterized by laboratory evidence of HP and HSV simultaneous presence in the mucosa. *Conclusion:* Cimetidine and amoxicillin-clavulanic acid combined therapy is an advisable regimen for peptic ulcer with HP. HSV must cause immunosuppression with subsequent mucosa restitution depression and HP-infection aggravation. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: GI infections in adults } "Cimetidine and Amoxicillin / Clavulanic Acid for Ulcer Disease with Helicobacter and Herpes Simplex Virus"

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"P P 37 0830" P 37 0830 **Local Immune Response on Helicobacter Pylori Associated Gastric Ulcer before and after Eradication Treatment** R. G. Gr'eivalos, A. Terr'e9s,

\*M. F. Bermejo, J.A. Moreno, J.M. Mateos, J.M. Pajares

Gastroenterology Department, Hospital de la Princesa, Madrid, Spain The development of peptic ulcer is associated with the presence of Helicobacter pylori (HP). The *Aim* of this study was to determinate the phenotype, distribution, and expression of immunological phenotype markers and antigenic recognition molecules (HLA class I and II) in the gastric mucosa of gastric ulcer patients before and after the eradication treatment. *Methods*: Immunoperoxidase staining was performed in frozen cryostat sections from antrum gastric biopsies of 15 patients with HP associated gastric ulcer before and after eradication of the bacteria. Controls included mucosa from no infected healthy donors. Gastric biopsies were obtained through upper endoscopy, and status HP was determined by rapid ureasa test, <sup>13</sup>C-urea breath test and histological examination. Sections were stained with the following monoclonal antibodies: anti-CD2, anti-CD4, anti-CD8, anti-CD11b, anti HLA-DR and W6/32. *Results*: Before treatment intraepithelial lymphocytes (IEL) and lamina propria T cells were CD8+ while CD4+ cells were predominant in follicles. Most of them, CD8+ and CD4+ cells expressed the activation marker CD2+. CD11b expression was high and numerous cells expressing this marker infiltrate the lamina propria. HLA-DR expression by epithelial cells was noticeable. After treatment the infiltration of mononuclear cells remain very similar to pretreatment status but expression by the epithelium was also noticed. *Conclusion*: Helicobacter pylori eradication in patients affected of gastric ulcer does not affect the mononuclear infiltration in the mucosal lamina propria. However, a noticeable decrease of neutrophilic-macrophagic infiltration can be observed in that location after eradication. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Local Immune Response on Helicobacter Pylori Associated Gastric Ulcer before and after Eradication Treatment"

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"P P 37 0831" P 37 0831 **Decrease of Mucosal Interleukin 8 Contents in Patients with *Helicobacter Pylori*-Gastritis after Successful Eradication**

\*T. Fujino, H. Kuwayama, M. Tachibana, M. Fukuyo, Y. Shijo, K. Chishima, N. Shimoyama, Y. Katayama, K. Kitazawa, K. Kawauchi, T. Saito, H. Mori

Department of Medicine, Dai-Ni University Hospital, Tokyo Women's Medical College, Tokyo

Although the precise pathogenesis is not known, infection of *Helicobacter pylori* (*H. pylori*) causes mucosal inflammation of the stomach, leading to persistent chronic active gastritis. Gastric mucosal inflammation is characterized by neutrophil accumulation with abundant release of a number of cytokines including interleukin 8. In the present study we assessed mucosal interleukin 8 content before and after *H. pylori* eradication with special reference to histologic gastritis. Sixty gastritis patients with *H. pylori* infection was enrolled in this study. Four biopsies were taken each from antrum and gastric body. Three biopsies were processed for histology, culture, and rapid urease test respectively. Remaining one was homogenized and stored at  $-80^{\circ}\text{C}$  for later measurement of mucosal interleukin 8 (IL-8) content. IL-8 and protein were measured by EIA and Bio-Rad respectively. Endoscopy with biopsy sampling was made at least 4 weeks after dual *H. pylori* eradication therapy, consisting metronidazole 250 mg and amoxicillin 250 mg t.i.d. for 14 days. When any of the above 3 tests positive it was considered *H. pylori*-positive. Only when all 3 tests were negative, it was considered as being *H. pylori*-negative. Results of IL-8 were summarized in the following table (pg/mg). Eradication outcome IL8 Before Tx IL8 After Tx Success 397.190 – 51.804 49.547 – 12.094 \*Failure 470.643 – 60.483 395.618 – 80.239 \*Significant difference from Tx failure group. **Conclusion:** Gastric mucosal content of IL8 was significantly decreased after successful eradication of *H. pylori* which was well correlated with improvement of histologic gastritis. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Decrease of Mucosal Interleukin 8 Contents in Patients with *Helicobacter Pylori*-Gastritis after Successful Eradication"

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"P P 37 0832" P 37 0832 **Usefulness of Symptomatological Pattern in Predicting the Outcome of Dyspeptic Patients after Hp Eradication: A Prospective Six Months Study** A. Buda, M. Bortolon, S. Salandin, N. Dal Bo<sup>2</sup>, S. Kusstatscher, G. Laino, G. Leandro<sup>1</sup>, G. Battaglia<sup>2</sup>, F. Vianello, M. Cassaro, M. Rugge, F. Di Mario

Padua, (BA) Italy

<sup>2</sup> Venice, (BA) Italy

<sup>1</sup> Castellana Grotte (BA) Italy The usefulness of H.p. eradication in NUD is still controversial. For a better evaluation of dyspeptic patients which could have an improvement of their symptoms after eradication, they were subdivided in three groups: A: ulcer-like; B: dismotility-like; C: reflux-like. *Methods:* 119 H.p. positive subjects (61 M; mean age 51.5; range 25–76) entered an open, prospective controlled study. All underwent different treatment schedules with either Amoxicillin or Clarithromycin plus Metronidazole and Omeprazole for one week. Endoscopy: at baseline and two months after the end of therapy (T2); 7 gastric biopsies were taken from gastric antrum and body to assess Hp status by histology (Giemsa, Warthin Starry, immunohistochemistry) and rapid urease test (CLO test). All pts remained untreated for a six months follow-up period (T6). *Results:* Overall, 86/119 (74.5%) pts were cured and 96% showed a disappearance of gastritis activity at T2. Eradication rate in the 3 groups was 79.3% group A; 68.3% group B; 75.8% group C). Overall, 45% of eradicated subjects and 22% of not-eradicated were asymptomatic at T2, 31% and 6.2% at T6, respectively. Subdividing the pts according with their symptomatological pattern, the percentages were as follows: Group A: T2 = 60.9%; T6 = 65.2% Group B: T2 = 36.5%; T6 = 7.4% Group C T2 = 43.5%; T6 = 39.2% (p = 0.001). *Conclusions:* 1) Overall, 44.8% and 31% of dyspeptic pts were symptom-free 2 and 6 months after a successful H.p eradication therapy, respectively. 2) Higher asymptomatic rate was obtained in the ulcer-like group (60.9% at T2, unchanged at T6); 3) The disappearance of gastritis activity was confirmed in 96% of cured patients. }" "Usefulness of Symptomatological Pattern in Predicting the Outcome of Dyspeptic Patients after Hp Eradication: A Prospective Six Months Study"

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"P P 37 0833" P 37 0833 **Effect of Eradication of Helicobacter Pylori on Gastric Histology and Gastric Function Parameters in Gastric Ulcer**

\*G. Maconi, P. Parente, M. Lazzaroni, O. Sangaletti, M. Minguzzi, S. Bargiggia, L. Vago<sup>1</sup>, G. Bianchi Porro

Department of Gastroenterology, L. Sacco Hospital, Milan, Italy

<sup>1</sup> Department of Pathology, L. Sacco Hospital, Milan, Italy *Aim.* The evolution of gastritis and the behaviour of serum gastrin and pepsinogen (Pgl) levels and gastric emptying of solids were studied in 16 consecutive patients (11 males; mean age: 54.5 – 9.1 yrs) with H. pylori (Hp) positive, uncomplicated, non-NSAIDS related gastric ulcer (GU) over a follow-up of three months after eradicating therapy. *Patients and methods.* Gastritis score was assessed according to the Sydney System on antral and corpal biopsies before the treatment consisting of omeprazole 40 mg a day for 1 month and amoxicillin 1 g three times daily for 14 days, and 3 months after ulcer healing. In addition a series of functional tests including basal and meal-stimulated serum gastrin concentration, serum Pgl levels and an evaluation of gastric emptying of solids by means of serial ultrasonographic measurement of gastric antrum area were performed at the same intervals. *Results.* Double therapy for Hp resulted in successful eradication in 8 of 16 patients. In Hp-eradicated pts mean activity and inflammatory scores of gastritis in antrum and corpus significantly fell after 3 months. No significant changes of mean gastritis scores were observed in the case and control group concerning intestinal metaplasia and atrophy both in the antrum and corpus. In contrast, pts with persistent Hp infection showed a significant worsening of gastritis activity in the corpus after treatment. In Hp eradicated patients the means of integrated gastrin response to meal [(AUC pg/ml/h): 23428 – 5727 vs 17623 – 3993], but not fasting gastrin concentration [(pg/ml) 67.7 – 14.4 vs 59.6 – 11.9], fell significantly during the follow-up and also serum Pgl levels significantly decreased as compared to baseline [(ng/l) 95.0 – 27.8 vs 79.7 – 32.3]. In contrast fasting and maximal antral area and gastric emptying remained unchanged over time. In the control group, no significant modifications of any of the above mentioned parameters were observed during the follow-up. *Conclusion.* Our findings suggest that, as already shown in duodenal ulcer pts, Hp eradication significantly reduces gastric activity, but not atrophy and intestinal metaplasia, in GU pts as well. In addition, gastrin and Pgl release, but not gastric emptying are significantly modified in the short-run by Hp eradication. Oesophageal gastric duodenal disorders: Helicobacter Pylori. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Effect of Eradication of Helicobacter Pylori on Gastric Histology and Gastric Function Parameters in Gastric Ulcer"

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## "P P 37 0834" P 37 0834 Gastric Mucosa Nucleolar Organiser Regions (AgNORs) and Helicobacter Pylori Infection: Impact of Eradication

\*T. Rokkas, C. Liatsos, A. Lazaris, D. Tabakopoulos, E. Panagou, A. Karameris

Gastroenterology Unit and Histopathology Laboratory 401 Army General Hospital, Athens, Greece Despite the fact that the association of Helicobacter pylori (H. pylori) with an increased risk of gastric cancer has been well-documented, the exact mechanisms of this association, have not been elucidated. *Aim:* The aim of the present prospective study was to contribute to the exploration of these mechanisms by studying the relationship between H. pylori infection and the silverstaining nucleolar organiser regions (AgNORs) in endoscopic biopsies in gastric antrum as it is known that the number of AgNORs per nucleus has been positively correlated with proliferative rate and ploidy. To do that we studied a total of 28 H. pylori (+) patients and the results were compared with 22 endoscopically and histologically normal H. pylori ({-}) patients (control group), who were comparable to the H. pylori (+) group for age and sex. In addition a group of 10 H. pylori (+) patients were examined before and after successful eradication of H. pylori and normalisation of gastric histology. *Results:* In the H. pylori (+) patients the mean number of AgNORs per nucleus was 5.43 – 0.18 (SEM) and was significantly higher than the respective number in the control group (3.27 – 0.13, p = 0.001). In patients studied before and after H. pylori successful eradication the corresponding numbers were 5.50 – 0.31 and 3.20 – 0.20 (p = 0.003) and the latter did not differ significantly from the control group of H. pylori ({-}) patients. *Conclusions:* H. pylori infection alters the replication cycle of gastric mucosa inducing hyperproliferation and possible ploidy abnormalities. However, it remains unclear whether these alterations are induced directly by the bacterium or by the gastric inflammation. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Proliferation, carcinogenesis }" "Gastric Mucosa Nucleolar Organiser Regions (AgNORs) and Helicobacter Pylori Infection: Impact of Eradication"

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"P P 37 0835" P 37 0835 **Evolution of Histologic Lesions of Gastric Mucosa after Eradication of *H. pylori* in Duodenal Ulcer Patients. A Six-Month Follow-Up Study**

\*J.P. Gisbert, D. Boixeda, C. Redondo, Ranz F. Hernandez, Mart\edn C. de Argila, C. De la Serna, L. De Rafael

"Ram\fn y Cajal" Hospital, Madrid, Spain *Purpose:* To study changes in histologic gastritis at gastric antrum and body after *H. pylori* eradication in duodenal ulcer patients, at an early stage and after six months. *Methods:* Seventy-six patients with duodenal ulcer disease were prospectively studied. At endoscopy biopsy specimens were taken from duodenal bulb, gastric antrum, body and fundus (H&E, Gram stain and culture). A patient was considered to be *H. pylori*+ when microbiology or histology demonstrated colonization in any location. An endoscopy with biopsy samples taken from antrum and body was performed one month after therapy completion and four months later. Different therapy regimens were used: amoxicillin/clavulanate plus omeprazole or ranitidin; classic triple therapy; and omeprazole or ranitidin alone. *Results:* All patients were *H. pylori*+. Eradication was achieved in 47% (n = 36) of patients. In *H. pylori* eradicated patients, rates of chronic gastritis/chronic active gastritis prior to treatment and two and six months later were, respectively: 100/96%; 38/23%; 16/5.6% in gastric antrum. The corresponding values for gastric body were: 54/38%; 12/12%; 12/5.6%. An histologic improvement, overall and in the acute inflammatory component, was observed one month after therapy completion (p < 0.001). Four months later, although histologic improvement was more marked, differences were not significant compared with results in the first month. No changes in histologic pattern was observed when eradication failed. *Conclusion:* An improvement in gastric antral and body gastritis was associated with *H. pylori* eradication in duodenal ulcer patients. This successful evolution was observed immediately after eradication and confirmed six months after diagnosis. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Evolution of Histologic Lesions of Gastric Mucosa after Eradication of *H. pylori* in Duodenal Ulcer Patients. A Six-Month Follow-Up Study"

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"P P 37 0836" P 37 0836 **Severity of Antral Gastritis in a Group of Duodenal Ulcer Patients with Cured H. Pylori Infection — One Year Follow-Up Study**

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<sup>2</sup> Provincial Hospital, Dept of Pathology, Warsaw, Poland  
The aim of the study was to evaluate the changes of severity of antral gastritis during one year observation after *H. pylori* eradication in the group of patients with duodenal ulcer. *Material and methods:* 40 patients (22 F + 18 M) with duodenal ulcer and with *H. pylori* infection were followed up with respect to the evolution of antral gastritis during one year after healing an ulcer and *H. pylori* eradication achieved by 14 days treatment by 40 mg/d omeprazole and 2 g/d amoxicillin. Endoscopy was done before treatment and repeated at the end of treatment, 4 weeks, 4 months, 8 months and 12 months after treatment. At least two antral bioptic samples had been taken during every endoscopy. Activity of gastritis was described according to Sydney classification. Statistical analysis was performed by Chi-square method. *Results:* Severity of antral gastritis during one year observation is presented on the table. Results are expressed as the percentage of patients. Degree Start End 4 4 8 12 of of the of the weeks months months monthsgastritis treatment treatment Mild 5% 32.5% 60% 55% 57.5% 60% Moderate 25% 40% 30% 37.5% 35% 32.5% Severe 70% 27.5% 10% 7.5% 7.5% 7.5% No one of patients showed the relapse of the ulcer or *H. pylori* infection. *Conclusions:* 1). Patients with cured *H. pylori* infection showed significant regression of antral gastritis. 2). The regression of antral gastritis was observed in the time of treatment and first 4 weeks after the treatment of *H. pylori* infection. During later observation the severity of antral gastritis remained stable. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Severity of Antral Gastritis in a Group of Duodenal Ulcer Patients with Cured H. Pylori Infection / One Year Follow-Up Study"

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"P P 37 0837" P 37 0837 **Erosive Duodenitis and *Helicobacter Pylori* Infection: Response to Eradication Therapy with Omeprazole, Amoxicillin and Clarithromycin**

\*J.P. Gisbert, D. Boixeda, Mart\edn C. de argila, F. Bermejo, C. Redondo, A. San Rom\e1n, Plaza A. Garc\eda

""Ram\fn y Cajal"" Hospital, Madrid, Spain *Purpose:* To study the prevalence of *H. pylori* infection in patients with erosive duodenitis, the associated gastric histologic lesions, and the response to an eradication therapy with omeprazole and two antibiotics. *Methods:* Fifty-five patients with erosive duodenitis were prospectively studied (mean age 48 – 16 yrs, 70% males). At endoscopy, biopsies from both gastric antrum and body were obtained for histologic study (H&E). A C<sup>13</sup>-urea breath test was also performed. Omeprazole (O) 20 mg b.i.d. plus two of the following antibiotics were administered for one week: amoxicillin (A) 1 g b.i.d., clarithromycin (C) 500 mg b.i.d., metronidazole (M) 500 mg b.i.d. Endoscopy (with biopsies) and breath test were repeated 1 month after completing therapy. *Results:* All patients were *H. pylori*-positive (n = 55). Overall, eradication was obtained in 85% (95% CI = 74–92%). Eradication rates for different therapies were: OAC: 94% (29/31); OCM: 85% (11/13); OAM: 64% (7/11) (p < 0.05 when comparing OAC and OAM). Overall, duodenal erosion healing was obtained in 80% (74–88%). Healing rates for different therapies were: OAC: 87% (27/31); OCM: 92% (12/13); OAM: 45% (5/11). Both OAC and OCM achieved better healing rates than OAM (p < 0.05). Duodenal erosion healing was achieved in 87% (75–94%) of cases with eradication therapy success, while only in 38% (n = 3) when eradication was not achieved (p < 0.01). An histologic improvement, both in the gastric antrum and body, was demonstrated in *H. pylori*-negative patients (p < 0.01). Compliance of therapy was complete in all patients and no relevant adverse effects were reported. *Conclusion:* A high prevalence (100%) of *H. pylori* infection in patients with erosive duodenitis was observed. A one-week twice-daily therapy with omeprazole plus two antibiotics (OAC or ACM) was very effective in *H. pylori* eradication, duodenal erosion healing, and resolving associated histologic gastritis. These observations suggest that erosive duodenitis should be considered a variant form of duodenal ulcer disease and be treated accordingly, that is, with *H. pylori* eradication therapy. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Erosive Duodenitis and Helicobacter Pylori Infection: Response to Eradication Therapy with Omeprazole, Amoxicillin and Clarithromycin"

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"P P 37 0838" P 37 0838 **Eradication of H. Pylori Infection in Patients with Corporal Atrophic Gastritis (CAG): A Consecutive Open Study** B. Annibale, M. Marignani, M. Paoletti, S. Angeletti, M.R. Aprile<sup>1</sup>, G. D'Ambra, C. Bordi<sup>1</sup>, G. Delle Fave

Dept Gastroenterology, University "La Sapienza" Roma, Italy

<sup>1</sup> Dept Pathology, University "La Sapienza" Parma, Italy CAG is a condition characterized by atrophy of oxyntic mucosa hypo/achlorhydria and fasting hypergastrinemia. It has recently been observed that a significant proportion of CAG patients are Hp infected and that Hp infection is significantly associated with the development of corporal atrophy in patients treated long-term with proton pump inhibitors. No studies until now have been specifically addressed to prospectively investigate in CAG patients, if it is possible to treat the infection since the lack of acid secretion could determine less favourable condition to its eradication. *Materials and Methods* 19 consecutive patients (15 F, 4 M aged 34–72) with Hp positive CAG (histology, culture, Ig G; at least two of these tests positive) were treated for 4 wks with bismuth subsalicylate 240 b.i.d.; amoxicilline 1 g. tid post-prandially and metronidazole 250 mg tid post-prandially were given during the first 2 wks of therapy. Endoscopy was again performed after 6 mos, to evaluate Hp status by histology and culture in antral (n = 5) and body biopsies (n = 8). The gastritis status was graded according to the Sydney system. Fasting gastrin levels (pg/ml; specific RIA) and title of IgG Hp (U/l; Elisa GAP test, Biorad) were also determined. Results are expressed as median (range), non-parametric test for paired data was used for statistical evaluation. *Results:* Overall eradication rate was 78.9% (15/19 pts). Minor side effects were recorded in about half of patients, but none determined therapy withdrawn. Gastrin levels decreased dramatically in eradicated patients [220 (49–1400) vs 42 (10–285); p < 0.001] as IgG Hp [80 (10–100) vs 31 (0–65); p < 0.005] Corporal chronic inflammation and atrophy were significantly reduced after eradication [respectively: 2 (1–3) vs 1 (0–2); p = 0.001 and 2 (1–3) vs 1 (0–3); p = 0.031]. Inflammation activity completely regressed [1 (0–3) vs 0 (0–0)]. *Conclusions:* These data show that is possible to efficaciously treat Hp infection in corporal atrophic gastritis, obtaining a pronounced reduction of fasting gastrin levels and a significative reduction in the score of chronic gastritis. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Eradication of H. Pylori Infection in Patients with Corporal Atrophic Gastritis (CAG): A Consecutive Open Study"

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"P P 37 0839" P 37 0839 **Cure of *Helicobacter Pylori* Infection Does Not Affect Acidity in the Spontaneously Secreting Stomach of Duodenal Ulcer Patients**

\*B. Tillenburg, U. Peitz, G. B\`f6rsch, M. Stolte, J. Labenz

Elisabeth Hospital Essen and Klinikum Bayreuth, Germany *Purpose:* The present study was designed to evaluate the long-term effect of curing *H. pylori* infection on the intragastric acidity in duodenal ulcer patients. *Methods:* Eleven duodenal ulcer patients infected by *H. pylori* were studied. 24-hour pH recordings were performed before treatment of the infection as well as 4 weeks and 1 year after the cure. Glass electrodes were placed 5 cm below the cardia. *Results:* Cure of *H. pylori* infection was associated with a marked improvement of antrum and corpus gastritis and a decrease of the fasting gastrin levels. The acidity in the spontaneously secreting stomach, however, remained unchanged: median gastric pH during 24 hours (before cure vs 4 weeks after cure vs 1 year after cure): 1.1 vs 1.2 vs 1.2,  $p > 0.3$ , daytime: 1.0 vs 1.1 vs 1.1,  $p > 0.4$ , postprandial: 1.4 vs 1.3 vs 1.3,  $p = 0.5$ , night-time: 1.6 vs 1.0 vs 1.1,  $p > 0.1$ ; mean  $[H^+]$  activity (24 hours): 88.4 vs 70.4 vs 79.0 h  $\{b\}$  mmol/l,  $p > 0.45$ ). *Conclusions:* Despite a decrease of the gastrin release and a decrease of the acid output (El Omar et al, Gastroenterology 1995; 109: 681–91), the intragastric acidity remains unchanged after the cure of a *H. pylori* infection in duodenal ulcer patients, suggesting that the net effect of the decreased acid output on the gastric pH is compensated by other mechanisms, e.g. the loss of neutralizing substances like ammonia generated by *H. pylori*. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Cure of Helicobacter Pylori Infection Does Not Affect Acidity in the Spontaneously Secreting Stomach of Duodenal Ulcer Patients"

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"P P 37 0840" P 37 0840 **Role of *H. Pylori* Eradication in the Prophylaxis of Ulcer Bleeding Recurrence**

\*J.P. Gisbert, D. Boixeda, C. Mart'edn de Argila, R. Aller, V. Defarges, J. Urmann, A. Garc'eda Plaza

""Ram\ 'f3n y Cajal"" Hospital, Madrid, Spain *Purpose:* Several studies have demonstrated that eradication of *H. pylori* (HP) is associated with a low rate of ulcer recurrence. Our purpose was to verify the effect of HP eradication on ulcer bleeding recurrence. *Methods:* Patients with acute hemorrhage secondary to duodenal ulcer were included in this prospective study. Exclusion criteria were the administration of antibiotics, bismuth, or non-steroidal anti-inflammatory drugs within 30 days prior to endoscopy. During hospitalization a therapy with H<sub>2</sub> antagonist at standard doses was administered. Biopsies were obtained (H&E) at diagnostic endoscopy, and a C<sup>13</sup>-urea breath test was also performed in the following days. At discharge, HP+ patients were randomised to receive different eradication therapies (proton pump inhibitor (PPI) plus 1 or 2 antibiotics, for 2 and 1 week, respectively), followed by the PPI up to 1 month. Endoscopy with biopsies was repeated 1 month after completing therapy, and a breath test was performed again. Eradication was defined as the absence of HP by both diagnostic methods. Patients with therapy failure received a second course of therapy. Patients with therapy success did not receive maintenance anti-ulcer therapy and were controlled at 6 and 12 months with a C<sup>13</sup>-urea breath test. *Results:* At present, thirty-three patients (mean age: 49 – 12 years, 89% males) have achieved eradication (two of them required a second course of therapy). Ulcer healing was achieved in 88% (CI 95%: 73–95%) of patients. In the four cases with ulcer persistence, healing was reported in an ultimately endoscopy performed 1 month later. Follow-up of patients was: 2 mths (n = 4), 6 mths (n = 23), and 1 yr (n = 6). Reinfection was not demonstrated in any patient at 6 or 12 mths. No bleeding episodes were observed in the follow-up period (mean: 6 mths, range: 2–12 mths). *Conclusion:* This preliminary study suggests that rebleeding does not occur in patients with complicated ulcers with HP infection eradicated. Therefore, this data recommend HP eradication as the treatment of choice after hemorrhage from a duodenal ulcer, and suggest that maintenance anti-ulcer therapy is not necessary if eradication is achieved. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding }" "Role of *H. Pylori* Eradication in the Prophylaxis of Ulcer Bleeding Recurrence"

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"P P 38 0841" P 38 0841 **Effects of Nonsteroidal Anti-Inflammatory Drugs on Glutathione S-Transferases of the Rat Digestive Tract**

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Dept. of Gastroenterology St. Radboud University Hospital, Nijmegen, the Netherlands Nonsteroidal anti-inflammatory drugs (NSAIDs) have been demonstrated to reduce cancer rates in oesophagus, stomach and colon of both humans and animals. Earlier, we showed that high human gastrointestinal tissue levels of glutathione S-transferase (GST), a family of detoxification enzymes consisting of class Alpha, Mu, Pi and Theta isoforms, were inversely correlated with cancer risk. We investigated whether the NSAIDs indomethacin, ibuprofen, piroxicam, acetyl salicylic acid (ASA) and sulindac, incorporated in the diet at 25, 400, 400, 400, and 320 ppm, respectively, influenced rat gastrointestinal GSTs. Male Wistar rats were fed normal or supplemented lab chow for two weeks. Oesophagus, stomach, intestines and liver were isolated and cytosolic fractions were prepared. Herein, GST activity towards 1-chloro-2,4-dinitrobenzene was measured and levels of GST isozymes were determined by densitometrical analyses of Western blots after immunodetection with monoclonal antibodies. Wilcoxon rank sum test was used to assess statistical significance of differences between treated and control groups. Indomethacin, ibuprofen, piroxicam and sulindac induced GST enzyme activity and class Mu levels in oesophagus and small intestine, and GST Alpha levels in small intestine. Piroxicam enhanced gastric and hepatic GST Alpha levels as well. GST Pi levels were raised in stomach by ibuprofen, ASA and sulindac, in small intestine by indomethacin, piroxicam, ASA and sulindac. In conclusion, enhancement of glutathione S-transferases, resulting in a more efficient detoxification of carcinogens, may explain in part the anticarcinogenic properties of nonsteroidal anti-inflammatory drugs. Oncology, general: Screening, prevention Nutrition: Metabolism } "Effects of Nonsteroidal Anti-Inflammatory Drugs on Glutathione S-Transferases of the Rat Digestive Tract"

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"P P 38 0842" P 38 0842 **Site Specific Ulcer Relapse in Non Steroidal Anti Inflammatory Drug (NSAID) Users: Improved Prognosis with *H. Pylori* and with Omeprazole Compared to Misoprostol**

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<sup>4</sup> Astra Hassle AB, Molndal, Sweden *Introduction* NSAIDs cause gastric and duodenal ulcers and retard healing. We therefore compared healing and prophylactic efficacy of omeprazole and misoprostol in NSAID users and investigated whether *H. pylori* or the initial ulcer site predicted relapse. *Methods* 935 patients with gastric ulcer (GU) or duodenal ulcer (DU), or > 10 gastric or > 10 duodenal erosions were randomised to receive omeprazole (OME) 20 mg mane, OME 40 mg mane, or misoprostol 200 µg qid under blinded conditions for 4 or 8 weeks until healed and open OME 40 mg for up to 16 weeks if unhealed. 732 evaluable patients with treatment success (no ulcer, and < 5 erosions at each site and no more than mild dyspepsia) were re-randomised to OME 20 mg mane, misoprostol 200 µg bid or placebo and followed for 6 months or to treatment failure (ulcer or > 10 erosions at either site or moderate/severe dyspepsia or discontinuation due to adverse events). *Results* Overall treatment success was similar for healing with each active treatment but omeprazole was significantly better tolerated. Overall, omeprazole was significantly more effective than misoprostol for maintenance (p = 0.001, log rank test). *Treatment success* (%) for patients with GU or DU at entry was: Initial GU Initial DU Healing Ome 20 Ome 40 Miso Ome 20 Ome 40 Mison 131 140 141 73 73 76 Hp { - } 71% 61% 67% 80% 74% 74% Hp + 82% 80% 63% 82% 84% 69% Maintenance Placebo Ome 20 Miso Placebo Ome 20 Miso Hp { - } 32% 44% 61% 30% 65% 35% Hp + 26% 75% 46% 14% 85% 41% Of patients with GU at relapse, 73% had had GU initially compared with 72% of DU relapses who had DU initially. *Conclusions* In NSAID users: (1) Initial ulcer site predicts relapse site. (2) Omeprazole 20 mg mane is similar to misoprostol for healing and maintenance of *Hp* negative ulcer patients, and for GU healing and maintenance in NSAID users. (3) Omeprazole is superior to misoprostol for healing and prevention of DUs associated with NSAID use and for all ulcer patients who are *Hp* positive. (4) Omeprazole appears to be more effective for the healing and prevention of NSAID associated ulcers in *Hp* positive patients than *Hp* negative patients. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Site Specific Ulcer Relapse in Non Steroidal Anti Inflammatory Drug (NSAID) Users: Improved Prognosis with *H. Pylori* and with Omeprazole Compared to Misoprostol"

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"P P 38 0843" P 38 0843 **Quality of Life (QoL) in Patients with Non-Steroidal Anti-Inflammatory Drug (NSAID) Associated Gastroduodenal Lesions During Healing and Maintenance. A Randomised Comparison of Omeprazole and Misoprostol**

\*I. Wiklund<sup>4</sup>, A.J. Swannell<sup>2</sup>, N.D. Yeomans<sup>3</sup>, G. Langstrom<sup>4</sup>, J. Naesdal<sup>4</sup>, C.J. Hawkey<sup>1</sup>

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<sup>2</sup> Dept of Rheum/Rehab, City Hospital, Nottingham, UK

<sup>3</sup> Dept of Medicine, Western Hospital, Melbourne, Australia

<sup>4</sup> Astra Hassle AB, Molndal, Sweden *Background* Gastric and duodenal ulcers and erosions are commonly associated with NSAIDs, but there are few comparative QoL data that can be used to assist in identifying optimal treatment of such lesions. *Aim* To compare the effect on QoL of omeprazole (ome) 20 or 40 mg om or misoprostol (miso) 200 \b5g qid during healing. In the maintenance study ome 20 mg om was compared with miso 200 \b5g bid or placebo. *Methods* QoL was assessed in an international double-blind parallel-group study. In the healing phase 618 male (40%) and female (60%) arthritic patients, mean age 59 years, with ulcers or erosions, completed the Nottingham Health Profile (NHP) and the Gastrointestinal Symptom Rating Scale (GSRS) at baseline and after 4/8 weeks. In the maintenance phase, 513 patients were re-randomised and treated for 6 months. The NHP is a general health profile and measures the burden of illness, while GSRS, which uses a seven-graded Likert scale, evaluates 15 gastrointestinal symptoms which combine into clusters describing Diarrhoea, Indigestion, Constipation, Abdominal pain, and Reflux. *Results* Patients with arthritis generally have a poor health-related QoL, in particular regarding fatigue, sleep disturbances, mobility and pain. During healing, ome 20 mg om showed a significant advantage in relieving reflux symptoms ( $p < 0.0005$ ), abdominal pain ( $p < 0.0005$ ), indigestion ( $p = 0.04$ ) and total GSRS score ( $p < 0.0005$ ) compared with miso, while miso induced diarrhoea ( $p < 0.0005$ ). During maintenance, ome was similarly more effective in relieving reflux symptoms ( $p = 0.0005$ ), abdominal pain ( $p = 0.003$ ), indigestion ( $p = 0.008$ ), and overall symptoms ( $p = 0.0003$ ) than miso. Also the lower dose of miso induced diarrhoea compared to placebo ( $p = 0.04$ ). *Conclusion* In arthritic patients, who are severely incapacitated in terms of QoL, omeprazole 20 mg om provided more effective control of dyspeptic symptoms and was better tolerated than misoprostol. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Quality of Life (QoL) in Patients with Non-Steroidal Anti-Inflammatory Drug (NSAID) Associated Gastroduodenal Lesions During Healing and Maintenance. A Randomised Comparison of Omeprazole and Misopros"

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"P P 38 0844" P 38 0844 **Increased Effectiveness of Omeprazole Compared to Ranitidine in Non Steroidal Anti Inflammatory Drug (NSAID) Users with Reference to *H. Pylori* Status**

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<sup>3</sup> Dept of Medicine, Western Hospital, Melbourne, Australia

<sup>4</sup> Astra Hassle AB, Molndal, Sweden *Introduction* Ranitidine is known to be inferior to both omeprazole and misoprostol in both healing and prophylaxis of NSAID-associated gastric ulcers. We investigated whether the site of initial lesion predicted relapse site and whether differences between ranitidine and omeprazole were attributable to ulcer site or *Hp* status. *Methods* 541 patients with gastric or duodenal ulcer *or* more than 10 gastric erosions *or* more than 10 duodenal erosions were randomised to receive treatment with omeprazole (OME) 20 mg mane, OME 40 mg mane *or* ranitidine (RAN) 150 mg bid and cumulative treatment success (no ulcer, < 5 erosions at each site, no more than mild dyspepsia) was recorded over 8 weeks. 432 patients were re-randomised to blinded maintenance treatment with OME 20 mg mane *or* RAN 150 mg bid and followed for 6 months *or* to treatment failure (ulcer *or* > 10 erosions at *either* site *or* moderate/severe dyspepsia *or* discontinuation due to adverse events). *Results* Overall treatment success (defined as above) was significantly better for omeprazole than ranitidine during both the healing (p {\'a3} 0.001, Mantel Haenszel test) and maintenance phase (p = 0.004, log rank test). *Treatment success* (%) is shown in the table, by initial lesion. Initial GU Initial DU Healing Ome 20 Ome 40 Ran Ome 20 Ome 40 Rann 77 72 75 43 47 47 *Hp* { - } 63% 59% 37% 74% 73% 59% *Hp* + 80% 80% 67% 80% 82% 72% Maintenance *Hp* { - } 47% - 32% 70% - 61% *Hp* + 75% - 63% 90% - 62% 68% of all patients with GU relapse had GU initially; 90% with DU relapse had DU initially. *Conclusions* NSAID ulcers tend to relapse at their initial site. Acid suppressing drugs are *more* effective for healing and prevention of NSAID associated ulcers in *H. pylori* positive than negative patients. Omeprazole is superior to ranitidine overall, and particularly for healing of NSAID-associated ulcers in *H. pylori* negative patients. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "Increased Effectiveness of Omeprazole Compared to Ranitidine in Non Steroidal Anti Inflammatory Drug (NSAID) Users with Reference to *H. Pylori* Status"

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## "P P 38 0845" P 38 0845 Short-Term Corticosterone Treatment: Different Effects in the Gastrointestinal Tract

\*P. Gama, E.P. Alvares

Institute of Biomedical Sciences, São Paulo, Brasil The feeding pattern and hormones are associated with tissue maturation in different systems, and the GI tract has been widely studied. Although glucocorticoids are thought to have a major importance in growth, a clear response is not yet established for the cell proliferation of the developing gastric and intestinal epithelia. The aim of this study was to evidence the effect of short-term corticosterone administration on the proliferative process of the gastric and intestinal epithelia of 18-d-old suckling rats. For that purpose, we divided the animals into 3 groups: fasted and fed controls (i.p. injection of NaCl); fed hormone-treated (i.p. injection of corticosterone 50 mg/g b.wt.). We examined: a) cell kinetics parameters as metaphasic index (MI) (in both organs) and cell production rate (CPR) (in the stomach), which were achieved by vincristine blockade; b) gastric mucosal and gland thickness; c) possible morphological alterations. All these parameters were analysed in histological slides. Cell proliferation and thickness were subject of Mann-Whitney statistical test. The MI was greatly inhibited in the gastric mucosa ( $P < 0.01$ ), in opposition to the lack of effect observed in the jejunum. The CPR was also inhibited by corticosterone ( $P < 0.05$ ), but no significant effect was detected in thickness. We did not observe any ulcer formation in either organs. These results suggest that the short-term corticosterone administration leads to a potent inhibition of the cell proliferation only in the gastric mucosa. These experiments light up the different responsiveness of the GI tract to corticosterone during suckling period. Supported by FAPESP 92/5086-2 and 92/3970-2 Oncology, general: Proliferation, carcinogenesis Nutrition: Nutrients and gut function } "Short-Term Corticosterone Treatment: Different Effects in the Gastrointestinal Tract"

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"P P 38 0846" P 38 0846 **Gastric Parietal Cell Canallicular Index after NSAID Treatment in Osteoarthritic Patients**

\*M. Valenzuela, J.L. Martin-Ruiz, A. Caballero-Plasencia, I. Alvarez-Cienfuegos, F.F. Nogales

Department of Medicine, University of Granada, Spain Parietal cell canallicular index is related with the acid secretory activity of parietal cells. The *aim* of this study was to assess canallicular index before and after a 7 days treatment with indomethacin or droxicam. *Patients*: 32 osteoarthritic patients, randomly allocated to one of the two treatment groups, underwent endoscopy and biopsies of the gastric corpus mucosa. *Methods*: Biopsies were processed for transmission electronic microscopy. Images at 2500x of 20 parietal cells per patient were analyzed by computerized densitometric morphometry. The size of the secretory canallicular system was automatically measured. The rate of the size of the canalliculum to the size of the cytoplasm was considered as the canallicular index (CI). *Results*: CI was (mean – SEM) 17% – 1.3 before treatment and reached 26% – 1.6 after treatment ( $p < 0.001$ ). CI in superficial parietal cells reached 27 – 2 ( $p < 0.005$ ), and 23% – 2 in the profound parietal cells ( $p = n.s$ ). There were no differences between both therapeutics groups. *Conclusions*: Parietal cell canallicular index, an estimation of the secretory canallicular size, increased after 7 days treatment with NSAID mainly in the most superficial parietal cells. This finding express a hyperstimulation state of the parietal cells which might be an important pathogenic factor in NSAID-induced gastropathy, supporting the indication for preventive co-treatments with proton pump inhibitors. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Gastric Parietal Cell Canallicular Index after NSAID Treatment in Osteoarthritic Patients"

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"P P 38 0847" P 38 0847 **Alteration of the Gastric Mucus and the Gastric Resistance Induced by Aspirin**

\*M. Kagoshima, H. Kodaira, H. Shimada

Department of Clinical Pharmacology, School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan It is well known that the gastric mucus plays an important role in protecting the stomach from noxious agents such as ethanol. However, we reported that oral administration of aspirin reduced the gastric mucosal lesions induced by absolute ethanol or 0.6 N HCl, although aspirin removed the gastric surface mucus (*Gastroenterology* 104 (4): A 121, 1993). In this study, we attempted to examine the effects of aspirin on the mucus in gastric juice, mucous gel layer, surface layer and deep layer, and examined causality between the mucus movement and the gastric resistance. *Method.* Male Wistar rats (180–200 g) were used. The gastric mucus was examined histochemically and biochemically till 24 hr. after oral administration of aspirin (100–300 mg/kg, p.o.). Histochemical studies: Removed stomachs were opened along the greater curvature and fixed in absolute ethanol (–80°C). The paraffin tissue sections of both corpus and antrum were stained with AB-PAS, HID-AB, UEA-I (Ulex europaeus Agglutinin I) and PNA (Peanut Agglutinin) stainings, and then observed histochemically. Each positive area was measured by our computer image processing system. Biochemical studies: Gastric mucin were prepared from gastric juice, mucous gel, surface and deep mucosa. Each sample was used for analysis of hexose and sialic acid. *Results.* Surface mucus (PAS or UEA-I positive mucus) in both corpus and antrum significantly decreased at 0.25 to 12 h. after oral administration of aspirin. Hexose contents also decreased in corpus mucosa. However, the deep corpus mucus (PNA positive mucus) significantly increased at 0.25 to 1 h. after administration of aspirin. Sialomucin was scarcely detected in normal mucosa but increased in the mucosa at 1 to 12 h. after oral administration of aspirin. Sialic acid increased in gastric juice, mucous gel, and surface mucosa at 1 h. after administration of aspirin. Moreover, acidic mucin (HID-AB positive mucus) increased in surface mucosa at 6 to 12 hr. and recovered to normal range at 24 hr. after administration of aspirin. *Conclusion.* We concluded that the aspirin-treated stomach enhanced the resistance to injury caused by strong irritants and this function is probably mediated by gastric mucus such as PNA positive mucus in deep mucosa and sialomucin in juice, gel layer and surface layer. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Alteration of the Gastric Mucus and the Gastric Resistance Induced by Aspirin"

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## "P P 38 0848" P 38 0848 **Low Dose Misoprostol as Prophylaxis Against Low Dose Aspirin-Induced Gastroduodenal Mucosal Injury**

\*M.T. Donnelly<sup>1</sup>, A.F. Goddard<sup>1</sup>, B. Filipowicz<sup>1</sup>, S.V. Morant<sup>2</sup>, M.J. Shield<sup>2</sup>, C.J. Hawkey<sup>1</sup>

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**Introduction:** Misoprostol, a prostaglandin analogue, given in conventional doses (200 \b5g bd – qds) prevents aspirin-induced gastroduodenal mucosal damage, but is associated with side-effects. In view of the increasing use of low dose aspirin for secondary prevention of vascular disease, we wished to study whether low dose misoprostol (100 \b5g) could prevent gastroduodenal damage due to low dose aspirin (300 mg) whilst avoiding side-effects.

**Methods:** 32 age and sex-matched healthy volunteers aged 18–45 were enrolled in this double blind, placebo controlled, parallel group study. Endoscopy was performed on days 0, 5, 14 and 28. Paired antral and corpus biopsies were taken for prostaglandin estimation and plasma samples for thromboxane estimation. Mucosal abnormalities and adverse events were noted. Volunteers were randomised to one of two drug regimens: 100 \b5g placebo misoprostol and aspirin 300 mg daily or 100 \b5g misoprostol and aspirin 300 mg daily for 28 days. Compliance was assessed by tablet counting, prostaglandin and thromboxane measurements. The primary endpoint was the total number of gastroduodenal erosions assessed endoscopically. Anatomical site and nature of erosions were secondary endpoints.

**Results:** Data were analysed using a generalised linear model. 28 day results

Parameter	Placebo	Misoprostol	p value
No. of haemorrhagic erosions/subject	12.5	5.0	< 0.05
No. of non-haemorrhagic erosions/subject	18.8	18.8	NS
No. of petechiae/subject	6.3	43.8	< 0.001

Subjects with haemorrhagic erosions 12.5 5.0 < 0.05  
Subjects with non-haemorrhagic erosions 18.8 18.8 NS  
Subjects with petechiae 6.3 43.8 < 0.001

There was no significant difference in the side-effect profile between the placebo and misoprostol treated groups.

**Conclusions:** We conclude that low dose misoprostol provides effective prophylaxis against endoscopically assessed gastroduodenal mucosal damage caused by low dose aspirin and is free of significant side-effects. Clinical practice: Management strategy }

"Low Dose Misoprostol as Prophylaxis Against Low Dose Aspirin-Induced Gastroduodenal Mucosal Injury"

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"P P 38 0849" P 38 0849 **Prostaglandin Enhances the Recovery of Mucin Content in the Surface Layer of Rat Gastric Mucosa at the Restititional State after NSAID (HCl-Aspirin) Induced Mucosal Damage**

\*T. Sakai, K. Ishihara, K. Saigenji, K. Hotta

Departments of Internal Medicine and Biochemistry, School of Medicine, Kitasato University, Sagamihara, Japan Applying the newly developed mucus-scraping method, the mucin content was measured in the different layers of rat gastric mucosa which had been injured by topical application of HCl-Aspirin, and the effect of a prostaglandin (PG) E<sub>2</sub> derivative was estimated after its administration at 3 hrs following the injury. *Material and Methods:* Male Wistar rats weighing 160–170 g were orally administered 0.15 N HCl-Aspirin (20–200 mg/kg) and killed at 1, 3, 5, and 7 hrs following the drug administration. Gastric lesions were macroscopically observed, and then the surface mucosa, deep corpus and antrum mucosa were separately collected. The mucin in each layer was extracted, and the content was determined as previously described (*Gastroenterol Jpn* 1992; 27: 466–472). 16, 16-Dimethyl PGE<sub>2</sub> (30 μg/kg) was administered 3 hrs after the HCl-Aspirin administration, and the effect of this agent on the gastric mucosal restitution was estimated by determining the mucin content in each layer of the mucosa at 7 hrs. *Results:* 1) Gastric macroscopic injury was observed in all cases of HCl-Aspirin treated rats at 3 hrs. 2) At 7 hrs after the administration, the macroscopic and light microscopically observable injury induced by the 50 mg/kg HCl-Aspirin was significantly recovered. 3) A considerable decrease and a notable recovery in the surface mucin was noted at 3 and 7 hrs, respectively, after the administration, but the mucin content of the deep corpus was not significantly changed during the experimental period by this HCl-Aspirin dose. 4) The PG treatment after 100 mg/kg HCl-Aspirin administration significantly recovered the surface mucin content. (126% vs. control, 200% vs. single HCl-Aspirin dosing) However, no significant change in the deep corpus mucin content could be achieved. *Conclusion:* Changes in gastric mucin content induced by low dose (50 mg/kg) HCl-Aspirin were mainly limited to the surface mucosal layer. PG might participate in the restitution of the gastric mucosa by the accumulation of mucin mainly in the surface mucous cells. The estimation of mucin content in the different layers of the gastric mucosa could be a useful tool to study the restitution from gastric mucosal injury. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Prostaglandin Enhances the Recovery of Mucin Content in the Surface Layer of Rat Gastric Mucosa at the Restititional State after NSAID (HCl-Aspirin) Induced Mucosal Damage"

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"P P 38 0850" P 38 0850 **Alendronate Causes Gastric Mucosal Damage Similar to Aspirin**  
D.Y. Graham, H.M. Malaty,

\*R.W. Goodgame

VAMC, and Baylor College of Medicine, Houston, TX USA Alendronate and pamidronate are primary amino-bisphosphonates used in the treatment of metabolic bone disease. Both drugs have been associated with erosive esophagitis and pamidronate is approved in the US only for parenteral use. In rats, alendronate causes gastric mucosal damage similar to aspirin or NSAIDs. *Methods:* We performed a blinded, crossover, randomized, single-center, placebo controlled comparison of alendronate (40 mg/day), aspirin (1,300 mg/day), and placebo using endoscopy to evaluate the presence and degree of mucosal damage to the esophagus, stomach, and duodenal bulb. *Results:* 12 normal volunteers were studied both before and after 4 days of drug therapy. Placebo caused no visible endoscopic damage. In contrast, both aspirin and alendronate were associated with visible gastric mucosal injury in the majority of those studied (75% and 58%, respectively) and both were significantly greater than placebo ( $p < 0.001$ ). The gastric mucosal injury was deemed severe in 50% of those receiving either alendronate or aspirin. One alendronate-associated gastric ulcer was also seen. Esophageal and duodenal bulb injury was seen once each and both were associated with alendronate. *Conclusion:* The primary amino-bisphosphonate alendronate causes mucosal injury to the upper gastrointestinal tract similar to aspirin. Even when used according to manufacturer's dosing instructions alendronate should be used with caution. Oesophageal gastric duodenal disorders: GD disorders, acid peptic }  
"Alendronate Causes Gastric Mucosal Damage Similar to Aspirin"

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## "P P 38 0851" P 38 0851 Production of Inflammatory Mediators in Patients with NSAID-Induced Gastropathy

\*V.D. Pasechnikov, D.V. Bobryshev, S.G. Mnatsakanian, I.G. Khripunova

Stavropol Medical Academy, Stavropol, Russia Arthritis patients (AP) have an increased risk of the upper gastrointestinal tract mucosal damage because of their need of long-term non-steroidal anti-inflammatory drugs (NSAID) therapy. The aim of this study was to investigate whether cytokines and arachidonic acid metabolites are involved in the inflammatory reaction of NSAID-induced injury of gastric mucosa (GM) and to determine the effect of cytoprotective therapy on GM in AP. In 10 AP receiving Diclofenac (100 mg, daily, orally; 3 weeks) and 10 AP patients receiving Arthrotec (0.2 mg Misoprostol-PGE<sub>1</sub> + 50 mg Diclofenac, orally, bid; 3 weeks), the GM production of IL-1, TNF, 6-keto-PGF<sub>1α</sub>, TxB<sub>2</sub> and LTB<sub>4</sub> was measured in biopsy specimens after incubation in special conditions. The levels of IL-1, TNF, TxB<sub>2</sub> and LTB<sub>4</sub> were markedly increased ( $p_{1-5} < 0.05$ ), whereas 6-keto-PGF<sub>1α</sub> production was significantly ( $p_{1-2} < 0.05$ ) decreased in the GM in AP, before and 3 wks after start of Diclofenac therapy. No significant differences were found between the production of IL-1, TNF, 6-keto-PGF<sub>1α</sub>, TxB<sub>2</sub> and LTB<sub>4</sub> in the GM in AP before and after Arthrotec therapy. The results of this study show that the GM injury mediators production in AP treated by Diclofenac differed from those receiving Arthrotec. NSAID may cause adherence of neutrophils to the vascular endothelium, probably through the release of cytokines and arachidonic acid metabolites. It may play a role in ischemic cell injury, and impaired repair of mucosa. Misoprostol, as a part of Arthrotec, effectively prevented Diclofenac-induced GM injury mediators production. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: GD disorders, acid peptic Immunology and microbiology: Host defense mechanisms } "Production of Inflammatory Mediators in Patients with NSAID-Induced Gastropathy"

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"P P 38 0852" P 38 0852 **Selective COX-2 Inhibition: Its Relevance for NSAID-Gastrointestinal Toxicity**

\*H.G. Dammann, F. Burkhardt, Th.A. Walter

Institute for Clinical Research, Hamburg, Germany *Purpose:* The main limitation in the use of NSAIDs is their gastrointestinal (GI) toxicity. The recent discovery of cyclooxygenase isoforms has resulted in further elucidation of the mechanisms of action of NSAIDs. An inducible cyclooxygenase COX-2 produces mediators of inflammation, and a constitutive cyclooxygenase COX-1 has a cytoprotective effect on the gastric mucosa. Consequently NSAIDs that have a higher activity against COX-2 than COX-1 may produce fewer GI-side effects. Meloxicam is a new NSAID derived from enolic acid with a preferential COX-2 inhibitory capacity. *Methods:* Meloxicam has been tested in controlled short- and long-term clinical trials in over 5000 patients, mainly in osteoarthritis (OA) and rheumatic arthritis (RA) to determine its clinical efficacy and GI-safety profile. *Results:* In the treatment of OA and RA meloxicam 7.5 and 15 mg daily was as effective as standard doses of naproxen, piroxicam and diclofenac. Meloxicam, however, produced fewer GI-side effects. Compared to the other drugs significantly less upper GI perforation, ulceration and bleeding occurred with meloxicam ( $p < 0.05$ ). Overall, there were significantly ( $p < 0.05$ ) fewer discontinuations due to GI-side effects with meloxicam (meloxicam 7.5 mg and 15 mg: 3.5 and 4.8% respectively, piroxicam: 6.7%, diclofenac: 10.5%, naproxen: 10.7%) as well as less dyspepsia and abdominal pain. *Conclusions:* Meloxicam shows a favourable GI-tolerability profile. This seems to be directly related to its preferential inhibitory effect on COX-2 over COX-1. Thus, the main advantage of selective COX-2 inhibition will be in producing an improved risk/benefit profile for the NSAIDs by maintaining efficacy, but improving GI-safety. Oesophageal gastric duodenal disorders: GD disorders, acid peptic }  
"Selective COX-2 Inhibition: Its Relevance for NSAID-Gastrointestinal Toxicity"

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"P P 38 0853" P 38 0853 **Combination Therapy of Rebamipide, a Novel Antiulcer Agent, with Low Dose Metronidazole and Amoxicillin Decreases Gastric Mucosal IL-8 and Heals Gastritis**

\*M. Tachibana, T. Fujino, H. Kuwayama, M. Fukuyo, Y. Shijo, K. Chishima, N. Shimoyama, K. Kitazawa, Y. Katayama, M.K. Kawauchi, T. Saito, H. Mori

Department of Medicine, Daini University Hospital, Women's Medical College, Tokyo, Japan

**Objective** Rebamipide is a novel antiulcer agent used in Japan. The exact mode of rebamipide action is not known, but proposed mechanisms of this compound include anti-radical formation. Because gastric *Helicobacter pylori* infection is characterized by active persistent mucosal inflammation, we assessed the effect of rebamipide on H pylori-gastritis. **Methods** *H. pylori* status was confirmed by culture, histology, and rapid urease test at the time of endoscopy. A total of 56 *H. pylori* positive gastritis patients were enrolled in this clinical trial. Patients were randomly assigned into 2 groups and received either rebamipide 100 mg + amoxicillin 250 mg + metronidazole 250 mg t.i.d. or rebamipide 100 mg alone. Rebamipide was continued for 6 weeks whereas 2 antibiotics were for the first 2 weeks only. Four biopsies were taken each from antrum and gastric body. Three biopsies were processed for histology, culture, and rapid urease test respectively. Remaining one was homogenized and stored at  $-80^{\circ}\text{C}$  for later measurement of mucosal interleukin 8 (IL-8) content. IL-8 and protein were measured by EIA and Bio-Rad respectively. Reendoscopy was performed at least 4 weeks after completion of all medication. **Results** *H. pylori* eradication was achieved in 21 among 26 patients treated with rebamipide + amoxicillin + metronidazole. None of the patient treated with rebamipide alone showed eradication of *H. pylori*. Gastric mucosal IL-8 contents were significantly decreased after successful eradication, which was well correlated to the improvement of histologic gastritis, in rebamipide + amoxicillin + metronidazole group. **Conclusion** Rebamipide with low dose metronidazole and amoxicillin normalizes gastric mucosal IL-8 and heals gastritis. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Combination Therapy of Rebamipide, a Novel Antiulcer Agent, with Low Dose Metronidazole and Amoxicillin Decreases Gastric Mucosal IL-8 and Heals Gastritis"

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"P P 38 0854" P 38 0854 **Decreased Levels of cGMP in Gastric Mucosa after Acute NSAID Administration. Relationship with Gastric Injury and Its Prevention by Phosphodiesterase Inhibition**

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*Purpose:* NSAID-induced gastric injury is related with the decrease of mucosal protective mechanisms. As opposed to this, cGMP increases mucus production and endothelial cells proliferation. Therefore, the decrease of synthesis of prostaglandins produces a fall in gastric mucosal levels of cGMP. Then, it is possible that NSAID-induced gastric damage can be related with decreased levels of cGMP in gastric mucosa. In this sense, we have investigated the levels of cGMP in gastric mucosa after NSAID administration, their relationship with NSAID-induced gastric damage and its prevention by phosphodiesterase inhibition by 3-isobutyl-1-methyl-xantine (IBMX). *Methods:* We have used Wistar male rats (200–250 g). The NSAID tested have been: piroxicam (PIR) (5, 10 and 20 mg/Kg), sodium diclofenac (DIC) (10, 25, 50 and 100 mg/Kg) and acetylsalicylic acid (ASA) (100, 300 and 500 mg/Kg), in all cases the way of administration was p.o. Three hours after NSAID administration the animals were anesthetized with pentobarbital, the stomach removed, the gastric injury (UI) measured in mm<sup>2</sup> and the mucosa scraped and frozen until cGMP determination by immunoassay. IBMX (10 mg/Kg) was administered s.c., when necessary, 10 minutes before NSAID. *Results:* NSAID-induced gastric injury has been related with the fall of cGMP levels in gastric mucosa ( $p < 0.01$ ). Similarly, both gastric injury and decreased levels of cGMP were dose related. On the contrary, IBMX administration prevents both, NSAID-induced gastric damage and cGMP fall in gastric mucosa. Levels of cGMP after ASA 100, 300 and 500 mg/Kg and after IBMX (50 and 100 mg/Kg of AAS) (153.8 – 77.5; 58.9 – 12.7; 51.8 – 15.2; 149.3 – 81.9; 144.8 – 61.6), PIR 5, 10, 20 mg/Kg and after IBMX (10 and 20 mg/Kg) (112.8 – 34.8; 68.3 – 11.1; 51.7 – 16.9; 154.8 – 55.8; 148.3 – 49.4) and DIC 10, 25, 50 and 100 mg/Kg and after IBMX (25, 50 and 100) (171.3 – 73.8; 68.9 – 20.5; 59.4 – 9.8; 48.3 – 8.1; 146.3 – 31.6; 151.6 – 44.1; 87.3 – 21.6). UI after ASA 100, 300 and 500 mg/Kg and after IBMX (0.45, 2.31; 5.15; 0.35; 0.48), PIR 5, 10 and 20 mg/Kg and after IBMX (0.93; 1.87; 3.21; 0.33; 0.39) and DIC 10, 25, 50 and 100 mg/Kg and after IBMX (0.67; 2.45; 4.59; 7.66; 0.41; 0.50; 0.62; 2.21). *Conclusions.* cGMP plays an important role in NSAID-induced gastric injury and the maintenance of its levels at normal concentrations prevents the production of gastric mucosal damage. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Decreased Levels of cGMP in Gastric Mucosa after Acute NSAID Administration. Relationship with Gastric Injury and Its Prevention by Phosphodiesterase Inhibition"

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"P P 38 0855" P 38 0855 **Effects of Ammonia Solution and Teprenone on Growth Factors, Gastric Mucus and Serum Gastrin in Acetic Acid-Induced Gastric Ulcers in Rats**

\*Y. Tahashi, S. Asada, E. Umegaki, H. Takiuchi, K. Katsu

2nd Dept, of Internal Medicine, Osaka Medical College, Osaka, Japan *Objective:* Ammonia produced by *H. Pylori* is considered to be responsible, in part, for the prolongation and recurrence of gastric ulcer in man. We induced prolonged acetic acid-induced gastric ulcer in rats by administering ammonia solution to the animals, and its effect was evaluated by assaying growth factors, gastric mucus quantity and serum gastrin level. In addition, anti-ulcer activity of teprenone, a mucosal protective agent, was evaluated after the coadministration with ammonia solution. *Materials and Methods:* An acetic acid gastric ulcer was induced in male Wistar strain rats by the method of Okabe et al. and a prolonged gastric ulcer model was obtained by administering 0.1% ammonia solution to the animals. Rats given tap water instead of ammonia solution served as controls. Teprenone was administered orally in a dose of 200 mg/kg/day admixed with ration. Animals were sacrificed at various time intervals after ulcer induction and the ulcer size was measured. The ulcer lesion was punched out as a tissue specimen for determination of b-FGF, TGF- $\beta$  1, PDGF by ELISA. The quantity of surface cell mucus was calculated in computerized image of microscopic section after PAS staining. The serum gastrin level was determined by RIA system. These results were compared among the control, ammonia and ammonia + teprenone group. *Results:* The healing of ulcer was delayed in the ammonia group, compared to the control group, while coadministration with teprenone tended to inhibit the delay of ulcer healing. The tissue level of b-FGF was increased with time, but was lower at all times in the ammonia group than in the control group. In the ammonia + teprenone group, on the other hand, there was an improvement in the tissue level of b-FGF. The tissue level of TGF- $\beta$  1 was lower in the ammonia group than in the control group at one time during the experiment, but was again improved with the administration of teprenone. There was no difference in tissue level of PDGF between the ammonia and the control groups, while its level was increased in the ammonia + teprenone group. The quantity of surface cell mucus and the serum gastrin level were lower in the ammonia group than in the control group, and were higher in the ammonia + teprenone group than in the ammonia group. *Conclusion:* The results of this study suggest that the presence of ammonia in the stomach causes the delay of gastric ulcer healing and effects the tissue levels of growth factors, gastric mucus quantity, serum gastrin level and even the quality of ulcer healing. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Hormones and receptors: Growth factors } "Effects of Ammonia Solution and Teprenone on Growth Factors, Gastric Mucus and Serum Gastrin in Acetic Acid-Induced Gastric Ulcers in Rats"

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## "P P 38 0856" P 38 0856 Changes of Gastric Endocrine Cell Numbers in Rats by Long-Term Treatment with Ammonia

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<sup>1</sup> Department of Surgery, The Kohno Clinical Medicine Research Institute *Aim.* This study investigated the changes of gastrin-immunoreactive cell (G-cell), somatostatin-immunoreactive cell (D-cell), and enterochromaffin-like cell (ECL-cell) numbers in stomachs of rats by 4 or 8 week treatment with ammonia. *Method.* Wistar male rats (8 week old) were treated with distilled water (control), 0.001%, 0.01% or 0.1% ammonia solution (p.o.) for 4 weeks (A4<sub>0.001%</sub>, A4<sub>0.01%</sub>, A4<sub>0.1%</sub>) or 8 weeks (A8<sub>0.001%</sub>, A8<sub>0.01%</sub>, A8<sub>0.1%</sub>). G-cells, D-cells and ECL-cells were immuno-stained with labeled streptavidin–biotin–peroxidase complex method using antibodies to synthetic human gastrin-17, a commercially available somatostatin or histamine antibody. And the cell with visible nuclei was only counted. *Results.* The G-cell numbers in A4<sub>0.001%</sub> and A8<sub>0.001%</sub> group were not significantly different from those of the control group. The G-cell numbers were significantly increased in A4<sub>0.01%</sub>, A8<sub>0.01%</sub> and A4<sub>0.1%</sub> group. However, the G-cell numbers in A8<sub>0.1%</sub> group was significantly decreased compared with those of the control group. The D-cell numbers in A4<sub>0.001%</sub>, A4<sub>0.01%</sub>, A8<sub>0.001%</sub> and A8<sub>0.01%</sub> group were not significantly different from those of the control group. The D-cell numbers in A4<sub>0.1%</sub> showed a tendency to decrease, and it was significantly decreased in A8<sub>0.1%</sub> group. The ECL-cell numbers in A4<sub>0.001%</sub> group was not significantly changed compared with the control group, but they were significantly increased in A8<sub>0.001%</sub>, A4<sub>0.01%</sub>, A8<sub>0.01%</sub> and A4<sub>0.1%</sub> group. However, the ECL-cell numbers in A8<sub>0.1%</sub> group was significantly decreased compared with those of the control group. *Conclusion.* In this study, the G-cell and ECL-cell numbers were changed depending on ammonia concentration and its administrated period. The low dose of ammonia increased the G-cell and ECL-cell numbers, but the high dose decreased. It may be explanation for changes in gastric endocrine induced by H. pylori infection. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Changes of Gastric Endocrine Cell Numbers in Rats by Long-Term Treatment with Ammonia"

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"P P 38 0857" P 38 0857 **Role of Free Radicals in Rat Experimental Model of Chronic Gastritis with Ammonia**

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Japan *Helicobacter pylori* (Hp) is known to be closely related to gastroduodenal mucosal lesions. The etiologic mechanisms in Hp induced gastric mucosal injury are presumed to be associated with ammonia produced by urease activity of Hp, monochloramine, and immunological cross reactions. In this study, we assessed the effects of ammonia water on the gastric mucosa and whether free radicals and glutathione (GSH) are involved in the induction of gastric mucosal lesions. In addition, we evaluated the effect of novel anti-ulcer agent tetraprenylacetone (teprenone) in the experimental model with ammonia. *Materials and methods:* Male SD rats were used and sacrificed 6 weeks after the beginning of the study. Gastric mucosal injury was induced by giving 0.1% ammonia water ad libitum for 6 weeks. *Group A;* Water was offered ad libitum. *Group B;* 0.1% ammonia water was offered ad libitum for 6 weeks. *Group C;* 0.1% ammonia water was offered ad libitum and 200 mg/kg/day of teprenone was administered orally for 6 weeks. The tissue sections of removed stomach were prepared to measure the thickness of gastric mucosa in the body and antrum. Serum gastrin levels and tissue levels of myeloperoxidase (MPO), GSH and LPO (which is the index of lipid peroxidation) in the frozen gastric mucosa were determined. *Results:* (mean – SD, \*\*\* p < 0.005 vs. Group A.) Gastrin (pg/ml) mucosal thickness (µm) body antrum Group A. 106 – 13.9 766 – 19.1 551 – 21.0 Group B. 122 – 11.4 744 – 22.2 457 – 12.7 \*\*\* Group C. 99.6 – 6.3 768 – 24.0 536 – 16.8 MPO LPO GSH Group A. 0.52 – 0.27 6.6 – 1.2 1012 – 208 Group B. 1.09 – 0.09 \*\*\* 10.5 – 1.2 \*\*\* 1164 – 198 Group C. 0.67 – 0.09 6.4 – 1.3 1217 – 226 *Conclusion:* It was suggested that a significant elevation in MPO and LPO activity is associated with gastric mucosal atrophy induced by long-term administration of ammonia water, and that the anti-ulcer agent teprenone inhibits the gastric mucosal atrophy without the elevation in MPO and LPO activity. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Role of Free Radicals in Rat Experimental Model of Chronic Gastritis with Ammonia"

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"P P 38 0858" P 38 0858 **Importance of Sensory Nerves and Nitric Oxide (NO) in Gastric Cytoprotection Induced by Epidermal Growth Factor (EGF)**

\*S.J. Konturek, T. Brzozowski, Z. Sliwowski

Inst. Physiol. Univ. Sch. Med., Krakow, Poland *Purpose:* Capsaicin and NO have been shown to protect the gastric mucosa against various irritants but their relative importance in the cytoprotection afforded by EGF has not been determined. *Methods:* In this study we examined the effects of intragastric (ig) capsaicin in small dose (0.5 mg/kg), to excite the sensory nerves or in a large systemic (sc) dose (125 mg/kg), to deactivate these nerves, as well as EGF or capsaicin plus EGF on ethanol-induced gastric damage. In addition, the influence of total salivectomy to remove endogenous source of EGF or suppression of endogenous NO synthase with N<sup>G</sup>-nitro-L-arginine (L-NNA 40 mg/kg iv) on ethanol-induced gastric lesions was tested. Gastric lesions were measured planimetrically and gastric blood flow (GBF) was examined by laser Doppler technique. *Summary of results:* Topical application of 100% ethanol produced widespread hemorrhagic mucosal lesions (area – 80 mm<sup>2</sup>) accompanied by about 60% reduction in GBF. Pretreatment with capsaicin (0.5 mg/kg ig), EGF (50 μg/kg sc) or their combination significantly reduced the area of ethanol lesions while restoring the GBF. These protective and hyperemic effects of capsaicin, EGF and their combination were almost completely eliminated by earlier deactivation of sensory nerves by pretreatment with large dose of capsaicin. Salivectomy, which by itself aggravated ethanol-induced lesions, failed to affect the protection and hyperemia afforded by EGF and capsaicin. The suppression of NO synthase with L-NNA reduced significantly the protection and hyperemia caused by EGF and capsaicin. The addition to L-NNA of L-arginine (300 mg/kg iv), the substrate of NO synthase, restored almost completely the protective and hyperemic effects of EGF and capsaicin. Application of CGRP<sub>8–37</sub>, an antagonist of calcitonin gene-related peptide (CGRP), decreased the hyperemia induced by topical capsaicin, EGF or both. *Conclusion:* Cytoprotective and hyperemic effects of EGF involve the excitation of capsaicin-sensitive nerves and endogenous formation of NO and CGRP. Hormones and receptors: Growth factors Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Importance of Sensory Nerves and Nitric Oxide (NO) in Gastric Cytoprotection Induced by Epidermal Growth Factor (EGF)"

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"P P 38 0859" P 38 0859 **Interaction of Capsaicin-Sensitive Nerves with Epidermal Growth Factor (EGF) on Healing of Acute and Chronic Gastric Ulcerations in Rats**

\*T. Brzozowski, P.Ch. Konturek, E.G. Hahn, S.J. Konturek

Inst. Physiol., Univ. Sch. Med., Krakow, Poland

Dept. Med. I, Univ. Erlangen, Germany *Purpose:* Capsaicin (CAP) applied in a small dose protects gastric mucosa by stimulation of sensory nerves but administered in large neurotoxic dose aggravates the mucosal injury due to deactivation of these nerves. EGF accelerates healing of gastric ulcers but its interaction with sensory nerves on this healing has not been assessed. *Methods:* We examined the effects of small (0.5 mg/kg po) and large dose (125 mg/kg sc) of CAP on healing of acute stress-induced lesions and chronic acetic acid-induced gastric ulcers. The rats were sacrificed at 0, 6, 12 and 24 h after restraint stress and 7 days after induction of chronic ulcers. The area of gastric ulcers was measured by planimetry, the gastric blood flow (GBF) by laser Doppler flowmetry, the DNA synthesis by incorporation of <sup>3</sup>H-thymidine to DNA and the EGF in the oxyntic mucosa by RIA and RT-PCR. *Summary of results:* Stress produced acute lesions with a marked fall of GBF (by – 35%) and DNA synthesis (by – 50%). After 24 h these lesions were reduced by 75%, the GBF and DNA synthesis were restored and mucosal EGF was markedly increased. Salivectomy delayed significantly the healing of stress lesions and reduced further the synthesis of DNA and GBF. Stimulation of sensory nerves with CAP (0.5 mg/kg) significantly enhanced the healing of these lesions and raised GBF and DNA synthesis. In contrast, CAP-induced sensory denervation significantly delayed healing and caused a fall in GBF and DNA synthesis at all time intervals after stress. These effects were further aggravated by salivectomy, which resulted in about 80% reduction in mucosal EGF content. CAP at a small dose also accelerated the healing of chronic gastric ulcers and raised markedly GBF and expression of EGF in ulcer area, whereas CAP-denervation and salivectomy delayed healing and reduced the GBF and EGF expression in the ulcer area. *Conclusion:* Sensory neurons interact with endogenous EGF in healing of both acute and chronic gastric ulcers. Hormones and receptors: Growth factors Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Interaction of Capsaicin-Sensitive Nerves with Epidermal Growth Factor (EGF) on Healing of Acute and Chronic Gastric Ulcerations in Rats"

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## "P P 38 0860" P 38 0860 Synchronized Induction in Cyclin-Dependent Kinase Cdk2 and FGF Receptor during Gastric Ulcer Healing

\*B.L. Slomiany, J. Piotrowski, A. Slomiany

Res, Ctr., UMDNJ, Newark, NJ USA The processes of gastric mucosal repair, characterized by massive cell migration, proliferation, differentiation and remodeling, are regulated by growth factors and the extent of cellular expression of their receptors. Cellular responses to growth factors and the cell passage through G1 phase of cell cycle are mediated by D-type cyclins and their specific cyclin-dependent kinases. In the study presented herein, we assessed the gastric mucosal expression of basic fibroblast growth factor receptor (bFGF-R) and cyclin-dependent kinase (Cdk2 p34) with ulcer healing. The chronic gastric ulcers were induced in rats with acetic acid. Following recovery, the animals were treated twice daily for 14 consecutive days either with a 100 mg/kg of ebrotidine or vehicle, sacrificed at different healing intervals, their stomachs dissected and subjected to bFGF-R and Cdk2p32 quantization. The ulcer area was measured by planimetry. In the FGF-R assays mucosal membrane bound <sup>125</sup>IbFGF was quantitated in a gamma counter, while ELISA was employed for Cdk2 p34, measurements. In the absence of ebrotidine the ulcer healing time was 14 days, while treatment with ebrotidine produced a 71% decrease in ulcer area by the 5th day and a complete healing by the 7th day. The results of parallel assays of bFGF-R and Cdk2 p34 revealed that the expression of FGF-R reached a maximum of 2.2-fold increase by the 4th day of healing and remained elevated (1.4-fold) for up to 10 days. Accelerated ulcer healing with ebrotidine was also reflected in Cdk2, the expression of which showed the highest (2.1-fold) increase by the 4th day of healing. The results suggest that the cell cycle regulatory kinase Cdk2 p34 during cellular proliferation associated with ulcer healing is controlled differentially by FGF-R, the induction of which determines the cell cycle progression through G1 and into S phase. Hormones and receptors: Receptor characterization Hormones and receptors: Growth factors Hormones and receptors: Molecular biology } "Synchronized Induction in Cyclin-Dependent Kinase Cdk2 and FGF Receptor during Gastric Ulcer Healing"

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## "P P 38 0861" P 38 0861 Cell Cycle Progression with Ulcer Healing by Sulglycotide

\*A. Slomiany, J. Piotrowski, D. Skrodzka, B.L. Slomiany

Res. Ctr., UMDNJ, Newark, NJ USA The progression of the events associated with gastric mucosal repair following injury is controlled in an orderly manner by a plethora of extracellular bioactive factors exerting their effect on the cell cycle. The transitions between different cycle states are regulated by a family of nuclear proteins, cyclins and cyclin-dependent kinases, the expression of which vary through the cycle stages. The purpose of this investigation was to evaluate the expression of cyclin dependent kinase (CDK) and proliferating cell nuclear antigen (PCNA) with chronic ulcer healing by sulglycotide. The study was carried out on rats with acetic acid induced chronic gastric ulceration. Following postoperative recovery, the animals were given twice daily for 14 consecutive days either a 200 mg/kg dose of sulglycotide or vehicle. At different time interval of healing the animals were sacrificed, their stomachs dissected and the mucosa subjected to PCNA and CDK quantization. The results of assays established that ulcer healing was accompanied by an increase in mucosal expression of PCNA and CDK, In the absence of sulglycotide treatment, the maximum expression of PCNA (4.7 fmol/ml) occurred by the second day of healing and remained elevated for up to six days, while CDK showed the highest activity (17.4–19.7 fmol/ml) at 4–6 days. Sulglycotide caused acceleration in the rate of ulcer healing and this process was reflected in a 2.2-fold enhancement in PCNA expression over that of controls on the second day of treatment and a 2.5-fold enhancement on the sixth day, whereas the CDK expression reached a maximum 2-fold enhancement (33.7 fmol/ml) by the sixth day of treatment and remained elevated (32 fmol/ml) for up to 10 days. The findings indicate that cytoprotective agent, sulglycotide, has the ability to modulate the processes associated with cell cycle progression. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Hormones and receptors: Molecular biology Oncology, general: Proliferation, carcinogenesis } "Cell Cycle Progression with Ulcer Healing by Sulglycotide"

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## "P P 38 0862" P 38 0862 **Role of Hepatocyte Growth Factor (HGF) and Trefoil Peptides in Experimental Gastric Ulcer Healing**

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<sup>3</sup> National Cancer Institut, Frederick, USA

<sup>4</sup> Univ. School of Medicine Osaka, Japan *Introduction:* HGF and trefoil peptides are potent growth factors which are locally secreted during gastric ulcer healing. We assessed the role of HGF, its receptor c-met and trefoil peptides in an experimental gastric ulcer model. *Methods:* Wistar rats with a fundic cryoulcer were treated subcutaneously for 3 and 15 days with either placebo, 1 {\'b4} 40 \\'b5mol omeprazole or 2 {\'b4} 100 \\'b5g/kg HGF. Ulcer healing was assessed by repeated videoendoscopy, immunohistochemistry and in situ hybridization. *Results:* HGF treated rats showed identical healing curves as placebo in contrast to omeprazole which accelerated ulcer healing. HGF treated rats showed a 80% increase of epithelial cell proliferation compared with placebo on day 15, but not in the early healing phase. HGF-receptor protein was decreased on days 3 and 8, but overexpressed in the regenerative glands on day 15. HGF mRNA was detected in mesenchymal cells of the ulcer bed on day 15. Both trefoil peptides rSP (rat spasmodic polypeptide) and pS2 (mouse one p-domain) mRNAs were significant increased in the regenerative epithelium on days 3 and 15. HGF did not influence the expression of trefoil peptides. *Conclusion:* The expression of HGF in mesenchymal cells of the ulcer base and of HGF-receptor in regenerative glands on day 15, suggest a significant role of HGF in the glandular reconstruction in the late phase of ulcer healing. The strong expression of trefoil peptides in the early and late ulcer healing phases supports their relevant role in gastric ulcer healing. Hormones and receptors: Growth factors }" "Role of Hepatocyte Growth Factor (HGF) and Trefoil Peptides in Experimental Gastric Ulcer Healing"

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"P P 38 0863" P 38 0863 **Chronological Changes of G-Cell and ECL-Cell Numbers After Long-Term Acid Suppression in Rats**

\*Chen Gang, Kashiwagi Hideyuki, Omura Nobuo, Moriya Usuke, Hagiwara Eiitirou, Aoki Teruaki

Department of Surgery (II), The Jikei University School of Medicine, Tokyo, Japan *Aim.* This study investigated the chronological changes of gastrin-immunoreactive cell (G-cell) and enterochromaffine-like cell (ECL-cell) numbers in stomachs of rats after 4-week treatment with histamine H<sub>2</sub> receptor antagonist. *Method.* Wistar male rats were treated with famotidine (15 mg/kg/day p.o.) for 4 weeks. After withdrawal of the drug, rats were divided into 8 groups: F<sub>0</sub> (on the day of cessation of famotidine administration), F<sub>3</sub> (3 days after cessation of famotidine), F<sub>5</sub> (5 days), F<sub>7</sub> (7 days), F<sub>10</sub> (10 days), F<sub>14</sub> (14 days), F<sub>28</sub> (28 days) and F<sub>56</sub> (56 days) group and control group (n = 6). G-cells and ECL-cells were immuno-stained with labeled streptavidin–biotin–peroxidase complex method using antibodies to synthetic human gastrin-17, and a commercially available histamine antibody. And the cell with visible nuclei was only counted. *Results.* The G-cell number significantly increased in F<sub>0</sub>, F<sub>3</sub>, F<sub>5</sub>, F<sub>7</sub> and F<sub>10</sub> group compared with control group, but the numbers in F<sub>14</sub>, F<sub>28</sub> and F<sub>56</sub> returned to the control level. The ECL-cell number significantly increased in all famotidine-treated groups and they had not returned to the control level by 56 days after cessation of famotidine. *Conclusion.* The long-term high-dose famotidine administration produced the increase of the G-cell number and ECL-cell number in the rats. The G-cell number seemed to return to the control level in 14 days after cessation of the drug. However, the ECL-number did not return to the control level in this study. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Chronological Changes of G-Cell and ECL-Cell Numbers After Long-Term Acid Suppression in Rats"

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## "P P 38 0864" P 38 0864 Nitric Oxide in the Regulation of Gastrin Release and Gastric Emptying in Humans

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Institute of Physiology, Jagiellonian University, Kraków, Poland Nitric oxide (NO) has been shown to be formed from L-arginine (L-Arg) by constitutive NO synthase in epithelial cells, endothelial cells and nitrinergic nerves of the digestive tract. NO has been implicated in gastric hyperemia associated with gastric secretory stimulation by pentagastrin in anesthetized rats as noncholinergic and nonadrenergic mediator. Recently, it has been shown that NO is involved in the control of gastric acid secretion and gastrin release under physiological conditions in dogs and that those effects are partially mediated by the release of somatostatin. The aim of this study in 10 healthy volunteers was to evaluate the role of NO in the control of gastrin and somatostatin release in response to ordinary feeding. Gastric acid secretion was determined by means of continuous intragastric pH-metry (Digitrapper, Synectics, Stockholm, Sweden) after feeding with 500 ml of caloric, semiliquid meal (Fresubin, Fresenius, Bad Homburg, Germany). Plasma levels of gastrin, somatostatin and insulin were measured using specific radioimmunoassays. The gastric emptying rate after feeding was determined using <sup>13</sup>C-acetate breath test. In this double blind study gastric secretory activity and gastric emptying rate were determined in random order on three different days after pretreatment with 0.9% NaCl (control), N<sup>G</sup>-monomethyl-L-arginine (L-NMMA 60 nmol/kg-min i.v.) or combination of L-NMMA and L-Arg (30 μmol/kg-min i.v.). Pretreatment with L-NMMA suppressed the postprandial increase in gastrin release and caused a small but significantly higher rise of plasma somatostatin when compared to control values. The gastric emptying half-time was reduced by about two fold and during the median two hours, postprandial intragastric pH showed tendency to increase above control values (L-NMMA: 3.6 – 0.4 vs. control: 3.3 – 0.5) but this rise was not statistically significant. Plasma insulin level reached significantly higher postprandial values in tests with L-NMMA compared to control tests probably due to enhanced gastric emptying of meal. Those effects of L-NMMA on the gastric secretory and motor activity as well as plasma hormone release were not observed in tests after pretreatment with the combination of L-NMMA and L-Arg. We conclude that: 1) endogenous NO is involved in the regulation of postprandial gastrin release and these effects appear to be mediated, at least in part, by the release of somatostatin; 2) endogenous NO appears also to be involved in the regulation of gastric emptying presumably mainly through its excitatory action on the proximal stomach, and 3) inhibition of NO synthase enhances plasma insulin release probably due to increased gastric emptying of carbohydrate containing caloric meal. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Motility, general: Receptors and signals Motility, specific: Stomach } "Nitric Oxide in the Regulation of Gastrin Release and Gastric Emptying in Humans"

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"P P 38 0865" P 38 0865 **Effect of Capsaicin and Epidermal Growth Factor on Gastroprotection in the Rat: Influence of Sensory Ablation, Sialoadenectomy, and Close Arterial Infusion with a Calcitonin Gene-Related Peptide Antagonist**

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<sup>2</sup> Department of Physiology, National University of Singapore, Singapore

<sup>3</sup> Department of Pathology, National University of Singapore, Singapore

<sup>1</sup> James Paget Hospital, Norfolk, UK We and others have shown that capsaicin and epidermal growth factor (EGF) protect against gastric mucosal injury in several experimental models. Both chilli, which contains capsaicin, and saliva, which contains EGF, have been proposed as possible protective factors in the pathogenesis of human peptic ulcer disease. The present study aims to understand the mechanisms of gastroprotection afforded by capsaicin and EGF. We investigated the effect of capsaicin, EGF, and a combination of capsaicin plus EGF on ethanol-induced gastric mucosal injury in intact rats, and in rats subjected to sensory ablation, sialoadenectomy, or both operations (n = 8 per group). The effect of sensory ablation and close arterial infusion of hCGRP<sub>8-37</sub>, an antagonist of calcitonin gene-related peptide (CGRP), on the gastric hyperaemic effect of capsaicin and EGF was evaluated in a gastric chamber preparation. Gastric mucosal damage was assessed by planimetry and light microscopy. Capsaicin, EGF and their combination reduced ethanol-induced gastric mucosal damage in rats with intact innervation. In contrast, they did not afford any protection in capsaicin desensitised rats. Sialoadenectomy had no effect. Administration of capsaicin, EGF or their combination increased gastric mucosal blood flow in rats with intact innervation but not after capsaicin desensitisation. Close arterial infusion of hCGRP<sub>8-37</sub>, an antagonist of calcitonin gene-related peptide (CGRP), abolished the hyperaemic effect of both capsaicin and EGF. Our results suggest that capsaicin and EGF may exert their gastroprotective effects via stimulation of capsaicin sensitive afferent neurones with release of CGRP. Hormones and receptors: Growth factors } "Effect of Capsaicin and Epidermal Growth Factor on Gastroprotection in the Rat: Influence of Sensory Ablation, Sialoadenectomy, and Close Arterial Infusion with a Calcitonin Gene-Related Peptide Antag"

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"P P 38 0866" P 38 0866 **Central Effect of Pacap on Gastric Secretion and Gastric Mucosal Blood Flow in Anesthetized Rats**

\*M. Ozawa, M. Aono, K. Mizuta, M. Moriga, M. Okuma

The First Department of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto, Japan PACAP is a neuropeptide originally isolated from ovine hypothalamic tissues and has two amidated forms, PACAP38 and PACAP27. We examined the effects of centrally administered PACAP38 on gastric secretion and gastric mucosal blood flow (GMBF) in anesthetized rats. Male Wistar rats were anesthetized with a urethane injection after 24 hr fast. A stainless steel cannula was implanted in the right lateral ventricle. The gastric secretion study was performed using Ghosh-Lai's rat preparation. PACAP38 or PACAP27 (2, 4, 8 nmol/rat) was administered ICV. Acute cervical vagotomy or atropine injection (10 ug/kg i.v.) was performed 15 min before ICV PACAP38 to examine the vagal pathway. PACAP antagonist PACAP6-38 (4 nmol/rat) was injected ICV to examine the role of PACAP receptor. The effect of ICV or IV bolus injection of PACAP38 on GMBF was examined by a laser doppler flowmeter. ICV PACAP stimulated gastric secretion dose-dependently. PACAP38 was 1.5–2 times more potent than PACAP27 on gastric secretion. By contrast, IV bolus injection of PACAP38 had no effect on basal gastric secretion. PACAP6-38 by itself at higher doses (8, 16 nmol/rat) stimulated gastric secretion. ICV PACAP6-38 at a dose (4 nmol/rat) that had no effect on gastric secretion, atropine or vagotomy pretreatment suppressed the stimulatory effect of PACAP38. ICV PACAP38 increased GMBF continuously, whereas IV bolus injection of PACAP38 increased GMBF transiently. These results suggested that centrally administered PACAP may have a regulatory role in gastric secretion through PACAP receptors and the vagal pathway and modulate GMBF. Hormones and receptors: Brain gut axis } "Central Effect of Pacap on Gastric Secretion and Gastric Mucosal Blood Flow in Anesthetized Rats"

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"P P 38 0867" P 38 0867 **Effect of Glicentin and Oxyntomodulin on Isolated Smooth Muscle Cells from Antrum**

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Glicentin (GLIC) and oxyntomodulin (OXM), two peptides coreleased from ileum and large intestine during digestion which are related to the enteroglucagon concept and represent the main circulating oxyntomodulin-like immunoreactants. Both hormones contain the whole glucagon sequence and a C-terminal octapeptide. Moreover, GLIC has a 32 amino-acids N-terminal extension. GLIC and OXM activities differ from that of glucagon. They are directed towards the digestive tract: inhibition of gastric acid secretion in vivo in rat and man, inhibition of gastric emptying and duodenal motility for OXM in man and inhibition of the antral motor activity at high doses for GLIC in dog. The effect of GLIC and OXM on gut motility prompted us to analyse their activity on the model of smooth muscle cells isolated from rabbit antrum after enzymatic digestion and mechanical stirring. The preparation contained 95% circular muscle cells. Human GLIC and OXM were obtained by chemical synthesis. GLIC or OXM induced a clear shortening of the cells, their maximal contraction corresponding to 13.9 – 0.8% and 15.5 – 0.9% of decrease in mean length. The contraction induced by GLIC and OXM was dose related, the observed EC<sub>50</sub> were 5 and 83 pM respectively. The effect of two C-terminal fragments, OXM (19–37) and OXM (30–37), known to inhibit acid secretion, was also studied. The extent of maximal contraction was maintained (13.7 – 0.5% and 14.9 – 1.1% respectively) but OXM (30–37) was 1800 less potent (EC<sub>50</sub> = 10420 pM) than GLIC whereas OXM (19–37) was as potent as OXM (EC<sub>50</sub> = 72 pM). By contrast, glucagon or tGLP exhibited no contractile effect. In conclusion, it is the first time that a target cell is described for glicentin or oxyntomodulin. These results pointed out the effect of these two coreleased hormones on digestive motility in addition to their well established role on gastric acid secretion. Motility, general: Receptors and signals Motility, specific: Stomach Hormones and receptors: Receptor characterization } "Effect of Glicentin and Oxyntomodulin on Isolated Smooth Muscle Cells from Antrum"

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"P P 38 0868" P 38 0868 **Effect of Epidermal Growth Factor, Capsaicin and Chilli Ingestion on Haemorrhagic Shock-Induced Gastric Mucosal Injury**

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<sup>1</sup> James Paget Hospital, Norfolk, UK We, and others, have shown that epidermal growth factor (EGF), chilli, and its pungent ingredient, capsaicin, are protective against ethanol- and aspirin-induced gastric mucosal injury in animals. In the present study, we further investigated the effect of EGF, capsaicin, and long term ingestion of chilli, on haemorrhagic shock-induced gastric mucosal injury. Fasted, anaesthetised rats (n = 8 per group) were subjected to 60 minutes of haemorrhagic shock by withdrawing the blood, 1.7 ml/100 g body weight, followed by 45 minutes of reinfusion of shed blood. Using an ex-vivo gastric chamber preparation, superficial, white abnormal areas were observed on the gastric mucosa during haemorrhagic shock, and upon reinfusion of shed blood, bleeding occurred at these areas resulting in lesion formation. Gastric mucosal damage was assessed by planimetry and light microscopy. Topical application of EGF (25 µg) to the gastric mucosa prior to haemorrhagic shock significantly reduced the gastric mucosal injury from 30% to 10% (p < 0.05). Similarly, administration of capsaicin (5 mg) prior to haemorrhagic shock reduced the damage to 7% (p < 0.05). The use of EGF and capsaicin after haemorrhagic shock, however, did not produce any beneficial effect. Chilli intake for four weeks (360 mg daily) reduced gastric mucosal injury from 21% to 11% (p < 0.05). Pre-treatment of rats with subcutaneous high dose capsaicin (125 mg/kg body weight) to achieve desensitisation of capsaicin-sensitive afferent neurones abolished the gastroprotection afforded by EGF, capsaicin and four-week chilli intake. Epidermal growth factor, capsaicin and long term chilli intake protect against haemorrhagic shock-induced gastric mucosal injury and that this protection may be mediated by capsaicin-sensitive afferent neurones. Hormones and receptors: Growth factors } "Effect of Epidermal Growth Factor, Capsaicin and Chilli Ingestion on Haemorrhagic Shock-Induced Gastric Mucosal Injury"

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"P P 38 0870" P 38 0870 **Short-Term Sucralfate Administration Alters Potassium Diclofenac Absorption in Healthy Human Volunteers**

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The production of peptic ulcers is a clinically important side-effect of non-steroidal anti-inflammatory drugs (NSAIDs). Sucralfate is a basic aluminum salt of sucrose sulfate that polymerizes in an acid medium to form a viscous substance capable of binding to the gastric and duodenal mucosa. This is thought to accelerate ulcer healing; however, the healing mechanism(s) remains to be fully defined. The objectives of the present work were to study the influence of sucralfate on the pharmacokinetics of diclofenac in eighteen healthy male volunteers. *Methods:* Potassium diclofenac suspension (Cataflam, Ciba-Geigy, 105 mg) was administered orally with or without a five-day pre-treatment with Sucralfate (2000 mg *bid*; phases SUC+ and SUC{-}, respectively), and blood samples were collected before and 0.5, 1.0, 1.5, 2, 3, 4, 6, 8, 12, and 24 h after diclofenac administration. The serum concentrations of diclofenac were quantified by reverse-phase HPLC with U.V. detection. The maximum plasma concentration ( $C_{max}$ ), the time taken to reach this ( $T_{max}$ ), a first-order terminal elimination rate constant ( $K_e$ ), the half-life ( $T_{1/2}$ ), the area under the time-concentration curves from 0–24 h ( $AUC_{0-24}$ ) and the value  $AUC_{0-24}/T_{1/2}$  as an index of diclofenac clearance, were determined. *Results:* Pre-treatment with sucralfate significantly decreased the amount of diclofenac absorbed (75% of the AUC during the SUC- phase) and the  $C_{max}$  (62%) with no significant effect on diclofenac elimination. *Conclusion:* Pre-treatment with sucralfate leads to decreased bioavailability of potassium diclofenac. *Financial support:* CNPq, FAPESP Clinical practice: Management strategy } "Short-Term Sucralfate Administration Alters Potassium Diclofenac Absorption in Healthy Human Volunteers"

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"P P 38 0871" P 38 0871 **Bacterial Endotoxin Lipopolysaccharide (LPS) Protects Gastric Mucosa Via Endogenous Prostaglandins (PG), Nitric Oxide (NO) and Sensory Nerves**

\*T. Brzozowski, P.Ch. Konturek, Z. Sliwowski, S.J. Konturek

Inst. Physiol., Univ Sch Med, Krakow, Poland

Dept Med I, University Erlangen, FRG *Purpose:* LPS induces endotoxemia by releasing various cytokines and NO synthesis but its effects on gastric secretion and mucosal protection have not been tested. *Methods:* We determined the effects of bacterial (*E. coli*) LPS on gastric secretion, acute gastric lesions induced by 100% ethanol, gastric blood flow (GBF) using laser Doppler flowmetry and expression of constitutive (cNOS) and inducible NO synthase (iNOS) messenger RNA in gastric mucosa using RT-PCR. Four series (A–D) of tests were performed on rats; A – with suppressed PG generation by indomethacin (5 mg/kg ip), B – with inhibited NO synthase by N<sup>G</sup>-nitro-L-arginine methyl ester (20 mg/kg iv), C – with deactivated sensory nerves with capsaicin (125 mg/kg sc) and D – with vehicle treatment (control). *Summary of results:* LPS (0.01–1.0 mg/kg) applied intragastrically was ineffective but when given intraperitoneally (ip) it reduced dose-dependently both gastric acid secretion and ethanol-induced mucosal lesions. The dose inhibiting by 50% (ID<sub>50</sub>) these lesions was 0.8 mg/kg and it was accompanied by a significant rise in the GBF. The protective effect of LPS persisted over 6 h, similarly as after exogenous dimethyl PGE<sub>2</sub> (10 μg/kg ip). Pretreatment with indomethacin significantly reduced the gastroprotection and hyperemia afforded by LPS. Intense signals for expression of cNOS and iNOS were detected by RT-PCR in the gastric mucosa of LPS-treated rats. Suppression of NO synthase by L-NAME also significantly reduced the protective and hyperemic effects of LPS against ethanol damage. Addition of L-arginine (300 mg/kg iv), a substrate of NO synthase, restored the protective and hyperemic action of LPS. Deactivation by capsaicin of sensory nerves reduced significantly the protection and hyperemia caused by LPS. *Conclusion:* LPS protects gastric mucosa from acute ethanol-induced damage via the mechanism involving endogenous PG, arginine-NO pathway and sensory nerves. Immunology and microbiology: Host defense mechanisms Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Bacterial Endotoxin Lipopolysaccharide (LPS) Protects Gastric Mucosa Via Endogenous Prostaglandins (PG), Nitric Oxide (NO) and Sensory Nerves"

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"P P 38 0872" P 38 0872 **Effects of Pyloramine on Secretions of Gastric Acid and Gastrin in Rats After Long-Term Acid Suppression**

\*Takaoka Toru, Chen Gang, Kashiwagi Kideyuki, Omura Nobuo, Aoki Teruaki

Department of Surgery (II), The Jikei University School of Medicine, Tokyo, Japan *Aim.* Long-term acid suppression is known to induce hypergastrinemia, but the underlying reasons why there is no increase in acid secretion, so-called acid rebound, after the treatment is widely debated. Acid secretion is known to be regulated by many factors, and long-term acid suppression may produce the change of other regulatory factors. Histamine H<sub>1</sub> and H<sub>2</sub> receptor subtypes are reported to locate on gastrin-immunoreactive cell (G-cell). This study investigates the effects of pyloramine (an H<sub>1</sub> receptor antagonist) on gastric acid and gastrin secretions in rats after 4-week acid suppression. *Method.* Famotidine (H<sub>2</sub> receptor antagonist 15 mg/kg/day p.o.) was administered in drinking water for four weeks. On the 3rd, 5th and 7th day after cessation of famotidine treatment, the gastric juice pH, acid output, and serum gastrin level were measured in rats 5 hours after pylorus-ligation with or without pretreatment of pyloramine (50 mg/kg, i.p.). If administered, pyloramine was given prior to 30 minutes before pylorus-ligation. *Result.* After the cessation of famotidine, the gastric juice pH, acid output and serum gastrin level were not significantly different from those of the control group. However, pretreatment of pyloramine significantly increased the acid output and the serum gastrin level in the famotidine-treated group, but not in the control group. *Conclusion.* These results suggest that gastric acid and gastrin secretions don't increase after long-term treatment with H<sub>2</sub> receptor antagonist because they become inhibited via the H<sub>1</sub> receptor. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation } "Effects of Pyloramine on Secretions of Gastric Acid and Gastrin in Rats After Long-Term Acid Suppression"

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"P P 38 0873" P 38 0873 **Gastric Blood Flow Changes May Differ in the Mucosa and the Extramural Arteries in Response to Different Stimuli**. Casadevall, A. M. 'e9ndez, C.H. Watcher, A. Heinemann, J.I. Elizalde, M. del Rivero, P. Holzer, E. Quintero, J.M. Piqu' e9

University of Barcelona, Spain

University of La Laguna, Spain

University of Graz, Austria Although flow to the mucosal layer mainly depends on the supply from extramural arteries of the stomach, a certain degree of autoregulation may probably takes place with changes on flow resistance in the submucosal arterioles. *Aim:* To compare the gastric mucosal blood flow (GMBF) and the left gastric artery blood flow (LGABF) responses to pharmacological, physiological and pathological stimuli. *Methods:* In urethane anesthetized rats, GMBF and LGABF were measured by hydrogen gas clearance and perivascular ultrasonic transit time respectively. In separate groups of rats measurements were conducted in baseline conditions and after vehicle administration (n = 5), vasopressin infusion (1 mU/min, n = 9), isovolemic hemodilution by exchanging 3 ml of blood by a plasma expander (n = 6), pentagastrin infusion (40 \b5g/kg/h, n = 8) or HCl-taurocholate gastric perfusion (n = 7). In additional groups of rats submitted to hemodilution, pentagastrin infusion or HCl-taurocholate gastric perfusion pretreatment with L-NAME (10 mg/kg) was administered. *Results:* Vasopressin induced a significant reduction in both GMBF and LGABF, but the percent decrement was greater (p = 0.05) in LGABF (47 – 7%) than in GMBF (30 – 4%). Isovolemic hemodilution was followed by an increase in both GMBF and LGABF, the percent increment being significantly (p < 0.05) higher in LGABF (105 – 14%) than in GMBF (60 – 8%). This increment in blood flow was significantly (p < 0.05) attenuated by L-NAME in both the GMBF (78% attenuation) and the LGABF (89% attenuation). In rats infused with pentagastrin, a significantly (p < 0.05) greater increment was observed in GMBF (80 – 9%) than in LGABF (29 – 7%), both increments being attenuated by L-NAME. A similar gastric hyperemic response was seen in the GMBF and the LGABF when gastric mucosa was challenged by HCl-taurocholate perfusion, an effect that was significantly attenuated by L-NAME. *Conclusions:* Gastric mucosal and left gastric artery blood flows changes may differ under certain pharmacological, pathological or physiological stimuli. This illustrates the autoregulatory capability of the vascular tone at the mucosal-submucosal level. In addition, hyperemic responses induced by pentagastrin, hemodilution, and HCl-taurocholate injury are modulated by nitric oxide inhibition in a similar manner in the left gastric artery and in the mucosal microcirculation. } "Gastric Blood Flow Changes May Differ in the Mucosa and the Extramural Arteries in Response to Different Stimuli"

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## "P P 38 0874" P 38 0874 Expression of Epidermal Growth Factor (EGF) and Transforming Growth Factor Alpha (TGF{ a}) during Recovery from Stress Damage

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Inst. Physiol, Jagiell. Univ. Med. Sch. Krakow, Poland *Background:* Stress is known to produce gastric mucosal damage but the mechanism of the recovery of gastric mucosa after stress exposure has not been fully explained. EGF and TGF{ a} are potent mitogenic and growth promoting factors involved in the protection of gastric mucosa against stress-induced damage but expression of these growth factors during mucosal healing after stress exposure has been little evaluated. This study was designed to determine the rate of cell proliferation, changes in the gastric blood flow (GBF) and the expression of EGF and TGF{ a} during mucosal repair after stress. *Material and Methods:* Rats were exposed to 3.5 h of water immersion and restraint stress and sacrificed at 0, 2, 4, 6, 8 and 12 h after stress. The number and area of gastric lesions was determined by planimetry and the GBF was measured by laser Doppler flowmetry. The gastric content was collected for the measurement of luminal release of EGF by radioimmunoassay. The mucosal sections were stained immunocytochemically for proliferating cell nuclear antigen (PCNA) – an index of cell proliferation and for EGF and TGF{ a} with monoclonal antibodies. Expression of EGF and TGF{ a} mRNA in fundic mucosa was determined by reverse-transcriptase polymerase chain reaction (RT-PCR). The first-strand cDNA was synthesised from total RNA and then amplified with specific primers by PCR method. PCR products were separated on 1.5% agarose gel by electrophoresis and then visualised under UV. *Results:* The number of gastric lesions induced by stress averaged 18 – 4 and declined at 2, 4, 6, 8 and 12 h by 9%, 15%, 33% 62% and 85%, respectively. This was accompanied by a significant rise in GBF by 8%, 15%, 26%, 32% and 35%, respectively and a marked increase of the luminal EGF immunoreactivity. PCNA labelling index increased gradually after stress and reached the maximum at 6 h. The immunohistochemical expression of EGF rised time-dependently and reached a peak at 4 h, whereas expression for TGF-{ a} increased gradually from 0 h to 12 h after stress. EGF mRNA was not detectable in intact mucosa but expressed at 0, 2, 4, 6 and 8 h with the maximal signal at 4 h after stress. Expression of TGF{ a} mRNA was present in intact mucosa and during all intervals after stress exposure. *Conclusion:* gastric hyperemia and an increase in cell proliferation are involved in mucosal repair after stress damage and this appears to be mediated by luminal release of EGF and an overexpression of EGF and TGF{ a}.  
Hormones and receptors: Growth factors  
Hormones and receptors: Molecular biology }"  
"Expression of Epidermal Growth Factor (EGF) and Transforming Growth Factor Alpha (TGFalpha) during Recovery from Stress Damage"

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"P P 38 0875" P 38 0875 **Role of Endogenous Nitric Oxide on Water Immersion Stress-Induced Gastric Lesions in Rats**

\*K. Tachi, H. Goto, S. Hase, T. Arisawa, Y. Niwa, N. Ohmiya, M. Hisatomi, T. Watanabe, N. Okada, M. Tsukamura, Y. Hisanaga, T. Hayakawa<sup>1</sup>, S. Sugiyama<sup>2</sup>

<sup>1</sup> Second Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan

<sup>2</sup> Department of Clinical Biochemistry, Institute of Applied Biochemistry, Mitake, Kani-gun, Gifu, Japan *Background.* Gastric mucosal microcirculation is an important factor in the genesis of gastric lesions and nitric oxide (NO) plays a crucial role in the regulation of regional blood flow. This study was designed to evaluate the effect of cetraxate, an anti-ulcer drug, on water immersion stress-induced gastric lesions in relation to the changes in NO synthase activity. *Methods.* Gastric lesions were induced in rats by water immersion stress. The effects of cetraxate on NO synthase activity with or without stress was determined enzymatically. Changes in gastric mucosal prostaglandin (PG) contents with or without stress were also determined using high performance liquid chromatography. Gastric mucosal blood flow was measured by hydrogen gas clearance technique. *Results.* Water immersion stress induced gastric lesions. Cetraxate mitigated significantly the lesions but N<sup>G</sup>-monomethyl-L-arginine (L-NMMA), a specific inhibitor of NO synthase, exacerbated the lesions. The favorable effect of cetraxate was remarkably diminished by administration of L-NMMA. NO synthase activity increased significantly 30 min. after stress and decreased significantly 6 hr. after stress. Cetraxate treatment increased NO synthase activity throughout the experiment in rats with or without stress treatment. Water immersion stress decreased all PGs detected, *i.e.*, 6-keto-PGF<sub>1a</sub>, PGF<sub>2a</sub>, PGE<sub>2</sub> and PGD<sub>2</sub>. Cetraxate prevented stress-induced decreases in PG contents. L-NMMA showed no significant effect on PG contents. Cetraxate increased gastric mucosal blood flow significantly and L-NMMA cancelled out cetraxate-induced increase in blood flow. *Conclusions.* The pharmacological efficacy of anti-ulcer drugs such as cetraxate might be attributable to the enhancement of NO synthase activity resulting in an increase in gastric mucosal blood flow. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Role of Endogenous Nitric Oxide on Water Immersion Stress-Induced Gastric Lesions in Rats"

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"P P 38 0876" P 38 0876 **Novel Evaluation Method for Drug Induced Gastropathy Using Endoscopic Sprayed Powder Drug Delivery System (IV) T. Hoshino,**

\*T. Kishi, K. Abiko, K. Nakazawa, H. Nabana, M. Nunamo, K. Kusakari, M. Ishida

St. Marianna University School of Medicine, Kawasaki, Japan *Aim:* Previously, we have reported that administration of powdered drugs using an endoscopic compressed air drug delivery system technique was useful for the investigation of direct effects of drugs on the gastric mucosa, and demonstrated the direct irritant action of anti-inflammatory drugs. In this study, the direct irritant actions of antibiotics powder studied in canine gastric mucosa using this technique. *Methods:* 2.5 mg/kg of powder drugs were administered at target sites (about 10 mm { f }) on the gastric mucosa of five dogs by endoscopically, followed by observation of changes in the character of the gastric mucosa after 24 hours. *Results:* Minocycline hydrochloride induced mucosal lesions were limited to the target site of gastric mucosa in all dogs. However, no lesions was observed at any other site. Amoxicillin 2/5 dogs (40%) induced superficial gastritis at the antrum, but did not appear to spray sites. Erythromycin did not induced mucosal lesions. The control study of powdered NaCl produced gastric mucosal lesion at the site of administration in all dogs. No lesions were induced by lactose. *Conclusions:* We could observe the experimental gastric mucosal lesion at the target site of the gastric mucosa by an administration of a small amount of powdered drugs via an endoscope. Minocycline hydrochloride induced direct irritant action on the gastric mucosa. Amoxicillin and erythromycin did not induce direct mucosal lesions. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, specific: Stomach, duodenum } "Novel Evaluation Method for Drug Induced Gastropathy Using Endoscopic Sprayed Powder Drug Delivery System (IV)"

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## "P P 38 0877" P 38 0877 **Gastroprotective Properties of Aminosugar Glucosamine and its Derivates**

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Department of Clinical Pharmacy, Department of Organic Chemistry, Ukrainian Academy of Pharmacy, Kharkov, Ukraine

During the last 5–7 years aminosugar glucosamine has been attracting the research workers close attention, as it is an integral element of biological membranes and, included in composition of mixed biopolymers and, being a natural metabolite of human organism, is absolutely harmless. In the field of gastroenterology there's an opportunity of appliment for glucosamine, conditioned by existence of target-organs — stomach in the mucus of which its own glucosamine of neutral glycoproteides is contained, according the data of the literature. In the course of experiments and clinical testing we proved the sudden lowering of endogenous glucosamine in target-organs in pathology of gastrointestinal tract. In the connection of above mentioned material the suggestion about the efficiency of glucosamine in gastric ulcer desease was brought up. The experiments were held on white rats of Wistar line. Gastric ulcer desease was induced by combined intragastric putting of prednyzolon and 80% aethylic spiritus. This model gives the 100% development of gastric ulcer affections of stomach in control animals. The antiulcer activity of the substances was valued at the following features: the ulcer area, the percentage of animals with ulcer, ulceral index. Besides that the contents of endogenous glucosamine was studied in blood serum and gastric tissue. During the experiment, the following substances were studied: glucosamine hydrochloride, N-acetylglucosamine, glucosamine acid, glucosamine pentaacetat, glucosamine disulfatis ("SIGMA", USA), and the original substances, that are the oxalic acid derivates: oxagluccamine with one molecula of glucosamine and dioxagluccamine with two moleculas of glucosamine. The studied substances were putting on before 1 hour of ulcer modeling and 3 hours after of ulcer modeling per os. Experiments that were made shows the gastroprotective properties of all studied substances. The highest antiulcer activity had glucosamine hydrochloride and its synthetic derivates, that lowered the ulcer index in 10, 5 and 30 times, respectively, in comparison with the control group. The contents of endogenous glucosamine in blood serum and gastric mucosa restored to the level of intact rats under the influence of above mentioned substances. Received data makes it possible to propose glucosamine hydrochloride, oxagluccamine, dioxagluccamine for the further investigation on antiulcer activity in order to clinical using. }

"Gastroprotective Properties of Aminosugar Glucosamine and its Derivates"

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"P P 38 0878" P 38 0878 **Involvement of Endogenous Nitric Oxide in the Gastroprotective Activity of Ebrotidine in Rats**

\*D. Palop, L. Conejo, A. Sacristán, J.A. Ortiz

Department of Pharmacology, Centro de Investigación Grupo Ferrer, Barcelona, Spain Ebrotidine is a novel H<sub>2</sub>-receptor antagonist with marked antisecretory potency which affords a remarkable gastroprotective activity against ethanol. In a previous study, we demonstrated that the administration of N-nitro-L-arginine methyl ester (L-NAME), inhibitor of nitric-oxide synthase (NOS), antagonized significantly the gastroprotective activity of ebrotidine. The aim of this study was to investigate the influence of L-arginine and D-arginine on the antagonism exerted by L-NAME in the gastroprotective action of ebrotidine. Two groups of male SD rats received saline (i.v.) 10 min prior to ebrotidine (100 mg/kg i.g.) or the vehicle, while two other groups were given L-NAME (10 mg/kg i.v.) instead of saline under the same conditions. Then, other two groups of rats received L-arginine (200 mg/kg i.v.) or D-arginine (200 mg/kg i.v.) immediately prior to L-NAME and 10 min before ebrotidine. Thirty minutes after ebrotidine or the vehicle all the groups were administered with 100% ethanol (1 ml/rat i.g.) and after 60 min they were sacrificed. Results showed that mucosal damage in the control group in the absence and in the presence of L-NAME was 78.06 – 4.28 mm and 143.71 – 8.61 mm respectively. The lesion inhibition rate was 85% for ebrotidine in the absence of L-NAME. Pretreatment with L-NAME reduced the inhibition rate of ebrotidine to 24%. Finally, L-arginine, natural substrate for NOS, counteracted the reduction in the gastroprotective action of ebrotidine caused by L-NAME, the lesion inhibition rate being 69%, while D-arginine was ineffective and the inhibition afforded by ebrotidine was only 14%. Our findings indicate that nitric oxide plays a crucial role in the gastroprotective activity of ebrotidine. Hormones and receptors: Molecular biology }"  
"Involvement of Endogenous Nitric Oxide in the Gastroprotective Activity of Ebrotidine in Rats"

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"P P 38 0879" P 38 0879 **Neural Mechanisms and Gastroduodenal Resistances to Saline Flow Activated by Acute Blood Volume Expansion in Anaesthetized Rats** J.R.V. Graça, D.I.M. Cavalcante, F. de A.A. Gondim, G.R. Oliveira, M.C.V. Rêgo, H.M.P. Alencar,

\*F.H. Rola

Department of Physiology and Pharmacology, Federal University of Ceará, Brazil. Acute blood volume expansion increases the gastroduodenal resistance to the flow of saline in rats (Xavier-Neto, J. *et al Gut*, 34, 235, 1990). In this study, we searched out the possible gastroduodenal site(s) of resistance and neural mechanisms involved on the phenomenon. Four gut circuits were prepared (gastroduodenal, gastric, pyloric and duodenal) and perfused under barostatically controlled pressure (4 cm H<sub>2</sub>O) on male Wistar rats (n = 64, 200–300 g). Perfusion flow rates did not change in time control euvoletic animals. Blood volume expansion (i.v. Ringer-bicarbonate infusion, 1 ml/min up to a 5% of body weight) reduced perfusion rate in gastroduodenal (10.3 – 0.5 to 7.6 – 0.6 ml/min – p < 0.05), pyloric (9.0 – 0.6 to 5.6 – 1.2 ml/min – p < 0.05), duodenal (10.8 – 0.4 to 8.0 – 0.6 ml/min – p < 0.05), but not in gastric circuit (11.9 – 0.4 to 10.4 – 0.6 ml/min – p > 0.05). The threshold for blood volume expansion effect for gastroduodenal flow was 4% of b.w., 2% for duodenal and 3% for pyloric flow reduction. Mean arterial pressure was not modified, but central venous pressure levels increased (p < 0.05). Yohimbine (3 mg/kg) and prazosin (1 mg/kg) blocked expansion effect on duodenal but not in the pyloric circuit. Atropine (0.5 mg/kg), was ineffective. The results show that blood volume expansion increases gastroduodenal resistance(s) to the flow of liquid in rat; pylorus and duodenum are two important sites of resistance and yohimbine and prazosin (alpha blockade) abolished the phenomenon, but not atropine. Coupled to decreased intestinal absorption and increased secretion rates (Duffy, *et al Gastroenterology*, 75: 413–8, 1979), these modifications on gastroduodenal flow may work as a mechanism to warrant liquid volume homeostasis. *Financial support:* CNPq, CAPES-PET, UFC e UNIMED-Ce. *Motility, specific: Stomach Motility, specific: Small bowel }* "Neural Mechanisms and Gastroduodenal Resistances to Saline Flow Activated by Acute Blood Volume Expansion in Anaesthetized Rats"

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"P P 38 0880" P 38 0880 **Diet-Induced Changes of Rat Gastric Muscle Responses to Acetylcholine, Caerulein and Cholecystokinin. An In Vitro Study**

\*V. Leray, G. Shi, S. Bruley des Varannes, C. Cherbut, J.P. Galmiche

Human Nutrition Research Center, INSERM and INRA, Nantes, France The influence of long-term modifications (i.e. adaptation) of diet on gastrointestinal motility is not well known. In rats, preliminary studies from our laboratory indicated that gastric emptying is delayed after 3 weeks of feeding with low protein diet. We hypothesized that this adaptation could result from changes in the smooth muscle responses to neuromediators. Consequently, we tested the effects of acetylcholine (Ach), caerulein and cholecystokinin (CCK) on fundic and antral contractility of rats chronically adapted to high and low protein diets. *Methods.* Wistar rats (n = 36, final weight: 330–350 g) were adapted during 21 days to two isocaloric diets. A group was fed with a high protein diet (56%), and the other one with a low protein diet (9%). All the rats were compared with control rats fed with standard diet containing 18% of protein (n = 12). Contraction of antrum and fundus longitudinal muscle segments, bathed in Krebs solution, was recorded by a force transducer in response to different doses of Ach ( $10^{-9}$  to  $10^{-3}$  mol/L), caerulein ( $10^{-11}$  to  $3.7 \times 10^{-8}$  mol/L) and CCK ( $10^{-12}$  to  $10^{-6}$  mol/L). Results were expressed as means – SEM and compared to control by unpaired Student's t test. *Results.* High protein diet did not affect responses to Ach, caerulein or CCK. In contrast, after low protein diet fundic response to Ach ( $10^{-3}$  mol/L) significantly decreased: 85.6 – 6.9 g/g of fresh tissue vs 111.1 – 5.5 g/g of fresh tissue (control rats),  $p < 0.02$ . By contrast, the low protein diet resulted in increased antral response to caerulein ( $3.7 \times 10^{-8}$  mol/L): 26.1 – 3.6 mg/mm<sup>2</sup> vs 8.9 – 4.2 mg/mm<sup>2</sup> (control rats),  $p < 0.02$ , and CCK ( $10^{-6}$  mol/L): 7.6 – 1.5 mg/mm<sup>2</sup> vs 3.2 – 0.8 mg/mm<sup>2</sup>,  $p = 0.01$ . *Conclusion.* Adaptation to a low protein diet is associated with significant changes in the motor responses of gastric motility to several mediators. These results are consistent with the delayed gastric emptying previously reported in *in vivo* conditions. The mechanisms whereby this adaptation occurs should be further investigated (up- or down-regulation of receptors?). Nutrition: Nutrients and gut function Motility, specific: Stomach } "Diet-Induced Changes of Rat Gastric Muscle Responses to Acetylcholine, Caerulein and Cholecystokinin. An In Vitro Study"

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## "P P 38 0881" P 38 0881 Adaptive Cytoprotection and Adaptation to Topical Ammonia in Rat Stomach

\*P.C. Konturek<sup>1</sup>, T. Brzozowski<sup>2</sup>, S.J. Konturek<sup>2</sup>, K. Sliwowski<sup>2</sup>, J. Majka<sup>2</sup>, R. Pajdo<sup>2</sup>, H. Ernst<sup>1</sup>, E.G. Hahn<sup>1</sup>

<sup>1</sup> Dept. Med. I Univ. Erlangen, Germany

<sup>2</sup> Inst. Physiol. Jagiell. Univ. Med. Sch. Krakow, Poland Ammonia (NH<sub>4</sub>OH) has been proposed to play a major role in the pathogenesis of the *Helicobacter pylori* (Hp)-associated gastric damage but the mechanism of this damage has not been fully explained. This study was designed to examine possible adaptive cytoprotection and the adaptation of rat gastric mucosa to the irritant action of ammonia (NH<sub>4</sub>OH). Single application of NH<sub>4</sub>OH alone in various concentrations (15–500 mM) caused a concentration-dependent mucosal damage starting at 30 mM and reaching a maximum at 250 mM, similar to that obtained with 100% ethanol and that was accompanied by the fall in the gastric blood flow (GBF) to about 30% of the normal value. When the mucosa was exposed first to the low, non-damaging concentration (15 mM) of NH<sub>4</sub>OH and then insulted with 100% ethanol, the extent of ethanol damage was greatly attenuated as compared to that caused by ethanol alone. This "adaptive" cytoprotection was accompanied by the rise in the GBF and reversed, in part, by the pretreatment with indomethacin, an inhibitor of PG-cyclooxygenase, with L-NAME, a blocker of NO-synthase or with capsaicin deactivating the sensory nerves. Damaging concentration of NH<sub>4</sub>OH (125 mM) caused a widespread mucosal damage after first application but with repeated insults of 125 mM NH<sub>4</sub>OH, a gradual reduction in the mucosal lesions accompanied by an enhanced mucosal cell proliferation and overexpression of epidermal growth factor (EGF) (using immunohistochemistry) and EGF mRNA (using RT-PCR) were noticed. *We conclude that:* 1) NH<sub>4</sub>OH alone damages gastric mucosa only at concentrations exceeding that found in Hp-infected stomach, while at lower concentration acts as "mild" irritant to induce adaptive cytoprotection, 2) this adaptive cytoprotection appears to be mediated, in part, by endogenous PG, sensory nerves and arginine-NO dependent pathway, and 3) repeated applications of NH<sub>4</sub>OH induce gastric adaptation probably mediated by enhanced expression of EGF and its receptors and by an increased mucosal cell proliferation. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Hormones and receptors: Growth factors } "Adaptive Cytoprotection and Adaptation to Topical Ammonia in Rat Stomach"

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"P P 38 0882" P 38 0882 **Tumour Necrosis Factor (TNF) Induces Expression of the Transcription Factor Nuclear Factor  $\kappa$ B (NF $\kappa$ B) in a Human Gastric Epithelial Cell Line**

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The transcription factor, NF $\kappa$ B, plays a major role in the regulation of inflammatory events such as secretion of cytokines, expression of adhesion molecules and potentially cell proliferation. Regulation of expression of this transcription factor appears to occur through tissue-specific mechanisms. In these experiments, we have examined regulation of NF $\kappa$ B by tumour necrosis factor in the human gastric epithelial cell line, AGS, using an electrophoretic mobility shift assay. TNF produced detectable induction of NF $\kappa$ B in AGS cells at a dose of 10 ng/ml. This effect was maximal at 100 ng/ml. Time-course experiments revealed that the effect was maximal at 4 hrs with subsequent reduction at 24 hrs. The protein kinase C activation PMA produced low-level induction of NF $\kappa$ B. Lastly, hydrogen peroxide, a product of the acute inflammatory response did not induce NF $\kappa$ B induction. These findings indicate that TNF can regulate induction of the transcription factor, NF $\kappa$ B, in gastric epithelial cells. As high levels of TNF are produced by gastric mononuclear cells in response to *H pylori*, this may represent a mechanism whereby the gastric immune response to *H pylori* may modulate epithelial cell function.

Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Inflammation }

"Tumour Necrosis Factor (TNF) Induces Expression of the Transcription Factor Nuclear Factor  $\kappa$ B (NF $\kappa$ B) in a Human Gastric Epithelial Cell Line"

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## "P P 38 0883" P 38 0883 Overproduction of NO Retards Wound Healing by Inhibiting Cell Proliferation in a Cultured Rabbit Gastric Epithelial Cell Model

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<sup>1</sup> Dept. of Surgery, University of Helsinki, Finland

Dept. of Gastroenterology, Juntendo Univ. Sch. of Med., Tokyo, Japan Despite the wide knowledge of different physiological effects of NO in gastrointestinal tract, there are no reports on its direct effects in gastric epithelial cells. This study investigates the role of NO in wound repair on a gastric epithelial cell monolayer culture. *Methods:* Isolated rabbit gastric epithelial cells (92% surface mucous cells) were cultured in F-12 round-shaped medium, forming a complete polarized nonolayer cell sheet in 48 h. A round-shaped wound was created by mechanical denudation using rotating silicon tip. The restoration process was monitored by measuring and photographing the wound size every 12 h up to 72 h. The proliferative cells were detected by serial staining for BrdU. NO donor, sodium nitroprusside (SNP) ( $10^{-4}$ ,  $3 \times 10^{-5}$ ,  $10^{-5}$  M), and NO-synthase inhibitor, N-nitro-L-arginine methyl ester (L-NAME) ( $10^{-3}$ ,  $10^{-4}$ ,  $10^{-4}$ ) were added to the serum-free media at the time of wounding. 0 h 12 h 24 h 36 h 48 h Control 3.3 – 0.17 1.6 – 0.12 1.1 – 0.16 0.4 – 0.10 0.2 – 0.12 SNP  $10^{-4}$  3.3 – 0.09 1.7 – 0.04 1.1 – 0.09 1.0 – 0.08\* 0.9 – 0.13\* SNP  $10^{-5}$  3.5 – 0.23 1.7 – 0.15 1.1 – 0.07 0.4 – 0.04 0.2 – 0.02 L-NAME  $10^{-3}$  3.2 – 0.11 1.7 – 0.11 1.1 – 0.17 0.3 – 0.25 0.1 – 0.07 L-NAME  $10^{-4}$  3.4 – 0.12 1.9 – 0.13 1.1 – 0.14 0.6 – 0.21 0.3 – 0.21 *Results.* Quantitative analysis of wound repair is shown in the table (mm<sup>2</sup>, mean – SD, n = 5, \* p < 0.01 compared to controls): SNP inhibited wound repair in a dose dependent manner. In controls, BrdU positive cells were detected mainly at 36 h after wounding. SNP inhibited this proliferation almost totally (BrdU-labelling index 1.5 vs. 0.02%, respectively, p < 0.01). This inhibition was partially reversible, if SN was removed from the culture 24 h after wounding. Inhibition of endogenous NO synthesis by L-NAME had no significant effect. *Conclusion:* The data indicate that NO has no influence on the primary cell migration during wound restoration, but excess of NO retards wound healing by inhibiting cell proliferation. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Management strategy } "Overproduction of NO Retards Wound Healing by Inhibiting Cell Proliferation in a Cultured Rabbit Gastric Epithelial Cell Model"

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"P P 38 0884" P 38 0884 **The Behaviour of BCL-2 Protein during Progression of Gastric Carcinoma**

\*T. Starzynska, K. Marlicz, L.S. Jones, M. Bromley, P.L. Stern

Department of Gastroenterology Pomeranian Medical Academy Szczecin, Poland

Paterson Institute for Cancer Research, Manchester, UK The bcl-2 protooncogene, located on chromosome 18, codes for a 26 Kd protein involved in inhibiting programmed cell death (apoptosis). The role of this protein in human cancer progression remains to be defined. The objective of the present study was to investigate the behaviour of bcl-2 protein during progression of gastric cancer. Immunohistochemical staining for bcl-2 protein was performed in primary gastric carcinomas of different tumour stage, from early to advanced disease (n = 62), coexisting metastases (n = 57) and in a series obtained from recurrent tumours that had progressed to more advanced stages in the following 48–60 months (n = 5). The monoclonal bcl-2 antibody and paraffin material were used. 21% of gastric tumours showed positive bcl-2 staining with protein occurred already in early cancer. In most patients there was coordinate expression of bcl-2 in primary carcinomas, coexisting metastases and recurrent tumours. However, in 2 patients bcl-2 protein was subsequently detected in regional lymph node metastases. The results suggest that the bcl-2 expression is an additional factor in the cascade of molecular alterations seen in gastric cancer and might contribute in some cases to the tumour promotion and in others to tumour progression. Oncology, general: Molecular biology, genetics Oncology, specific: Stomach } "The Behaviour of BCL-2 Protein during Progression of Gastric Carcinoma"

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## "P P 38 0885" P 38 0885 Inhibition of Migration and Proliferation by 5-Fu, CDDP and Cepharanthin Using Cultured Human Gastric Cancer Cell Line

\*R. Iwazaki, S. Watanabe, H. Misawa, K. Ohtaka, K. Ohta, Y. Ohno, M. Hirose, N. Sato

Dept. of Gastroenterology, Juntendo Univ. School of Med. Tokyo, Japan The mechanism of cancer cell metastasis involves cell migration which might be modulated by cytoskeleton, extracellular matrix and growth factors. However, the detail mechanism of metastasis is still unclear. We recently established a new, simple and convenient model to investigate the mechanism of metastasis in vitro using cultured human gastric cancer cell line, and also analyzed directly the role of cytoskeleton. Using this model, we assessed the migration capacity of gastric cancer cell line (undifferentiated adenocarcinoma AGS, differentiated adenocarcinoma MKN28) and also assessed the inhibition of migration and proliferation by 5-FU, CDDP and cepharanthin (CE). *Methods:* Human gastric cancer cell strain, AGS, MKN28 cells ( $3.5 \times 10^5$  cells) were inoculated into the round enclosed area (diameter, 15 mm) by silicon fence in a plastic culture dish and cultured in each F12, RPMI 1640 medium with 10% FBS. Inoculated cells formed round shaped cell sheet in 3 h and subsequently silicon fence was removed and the cancer cell migration was monitored under phase contrast microscope. The number of migrated cells in a unit area of free space was counted after 48 hr. Antineoplastic agents 5-FU, CDDP, and cepharanthin as alkaloids, were added to the medium (1 to  $10^{-5}$  M) to investigate functional and morphological changes of the cells. The cell proliferation were detected by BrdU staining.

*Result:* The number of cancer cells from the edge of the cell sheet at 48 hr after the start of experiment were presented in a table.

Cell Line	Distance (mm)	Control	5-FU $10^{-5}$ M	CDDP $10^{-5}$ M	CE $10^{-5}$ M
AGS	5-10	497	310	267	267
	10-15	36.2	31.0	26.7	26.7
	15-20	40.3	35.0	22.0	22.0
	20-25	47	1.4	40	5.6
	25-30	33	3.5	16	0
MKN28	5-10	424	59	3.5	47
	10-15	55.1	12.0	4.2	38
	15-20	306	1.4	47	0.7
	20-25	47.3	203	24.7	185
	25-30	23.5	178	28.3	5

Data: mean – SD, n = 4, \* p < 0.05, \*\* p < 0.01, mm: distance from the edge of cell sheet

Cancer cells (AGS, MKN28) were inoculated to round-shaped sheet spread concentrically over time due to migration. In controls, the number of cells in the nearest area from the edge of the round cell sheet was each 2.26, 2.38 time higher than that taken at the region 20 to 25 mm from the edge of the cell sheet. There were no differences in migrated cell number between AGS and MKN28. Spontaneous cell migration and proliferation were significantly inhibited by 5-FU, CDDP and cepharanthin in both cell lines in a dose-dependent manner. The inhibited cell proliferation which was assessed by BrdU staining.

*Conclusion:* Present results demonstrated that 5-FU, CDDP and cepharanthin suppressed the capacity of cancer cells to metastasize. Motility, specific: Stomach Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach }

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"P P 38 0886" P 38 0886 **Expression of Autocrine Motility Factor Receptor and Its Relationship to Progression and Prognosis in Human Gastric Cancer**

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<sup>2</sup> Tumor progression and Metastasis, Karmanos Cancer Institute, Detroit, MI, USA  
Autocrine motility factor (AMF) is a cytokine which is produced and secreted by cancer cells and which stimulates both random and directed cell migration through binding to its receptor, a 78 kD cell surface glycoprotein (gp78-AMF receptor). Recent studies have demonstrated that increased expression of gp78 is correlated with a high incidence of recurrence and decreased survival of patients with colorectal cancer and bladder cancer. We retrospectively examined the expression of gp78 in tumor specimens from patients with primary gastric cancer and its relationship to clinicopathological factors. *Materials and Methods:* Using a monoclonal antibody against gp78 (3F3A), an immunohistochemical study of expression of AMF receptor was performed in formalin-fixed paraffin-embedded tissue sections from 221 primary gastric cancers, who were diagnosed and treated at the Department of Surgery II, Kanazawa University, during 1986 to 1991. Immunohistochemical study was performed with the labelled streptavidin biotin method. *Results:* One hundred twenty five out of 221 tumors (56.6%) expressed the AMF receptor gp78. There was not a significant association between gp78 expression and histological type or liver metastasis. Expression of gp78 was associated with macroscopic type, lymphatic invasion, venous invasion, lymph node metastasis, and peritoneal metastasis. In addition, positive rate of gp78 expression significantly raised according to increased grade of tumor penetration or histopathological stage. Patients with gp78 expression had a significantly poor prognosis than those without gp78 expression in primary gastric cancer ( $p < 0.001$ ). To be confined to stage II and III, only gp78 expression had a significant relationship to survival ( $p < 0.05$ ). *Conclusions:* Increased gp78 expression is correlated with tumor invasion, metastasis, and poor prognosis in primary gastric cancer. This result indicates that AMF receptor plays an important role in progression of human gastric cancer. Oncology, general: Molecular biology, genetics  
Oncology, specific: Stomach } "Expression of Autocrine Motility Factor Receptor and Its Relationship to Progression and Prognosis in Human Gastric Cancer"

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"P P 38 0887" P 38 0887 **Expression of bcl-2 Protein in Gastric Cancer and Its Relationship to Prognosis**

\*S. Fushida, E. Bando, Y. Yonemura, K. Taniguchi, T. Fujimura, Y. Hirono, K. Miwa, I. Miyazaki

Second Department of Surgery, Kanazawa University School of Medicine, Kanazawa, Japan *Introduction:* The function of bcl-2 is known to prolong cell survival by preventing the onset of programmed cell death or apoptosis. Overexpression of bcl-2 gene has been found in variety of human malignancies. Here we examined the association between bcl-2 status and prognostic parameters in gastric cancer. *Materials and Methods:* A total of 118 primary gastric cancer specimens embedded in paraffin were used in the present study. Using an anti bcl-2 monoclonal antibody we analyzed immunohistochemically its expression. *Results:* bcl-2 immunoreactivity was detected in 21 cases (18%) and its tissue status was closely associated with tumor size and peritoneal dissemination. In addition, a positive bcl-2 immunoreaction was found to be significantly associated with shorter overall survival. Especially, in the group of patients without stage Ia and IVb, the prognosis of patients with bcl-2 positive tumors was significantly poorer than that of patients with bcl-2 negative tumors ( $p < 0.001$ ). *Conclusion:* These results suggest that immunohistochemical staining for bcl-2 may be useful in evaluating metastatic potential and prognosis in gastric cancer. Oncology, general: Molecular biology, genetics Oncology, specific: Stomach } "Expression of bcl-2 Protein in Gastric Cancer and Its Relationship to Prognosis"

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"P P 39 0901" P 39 0901 **Palliativ Treatment of Malignant Duodenal Obstruction by Self Expanding Metal Stents Inserted through a Percutaneous Endoscopic Gastrostomy**

\*U. Rosenstock, A. Schulte-Bockholt, S. Clemens, B. Pleger, A. Hofmann, M. Keymling

II. Med. Klinik, Klinikum Meiningen, Germany Metal stents as palliativ therapy for esophageal and biliary malignant stenosis are well established. For malignant duodenal outlet obstruction bypass surgery is often performed, but results are poor. Metall stents in these patients are difficult to insert, because the delivery systems available, designed for stent placement in the esophagus, are often too short to insert the stent safely into the pylorus. We here report three patients with advanced antral carcinoma invading the duodenum, in whom surgery was thought to be inappropriate and a wall stent was inserted into duodenum through a PEG. *Material and Methods:* 3 patients with with gastric adenocarcinoma invading the duodenum (2 male, 1 female; 86, 80 and 75 years) who had gastric retention due to the outlet obstruction where treated as follows: After Midazolam sedation or in general anesthesia a 15 Fr. standard gastric pull through percutaneous endoscopic gastrostomy (PEG standard gastral; Fresenius, Germany) was inserted into the stomach. Under fluoroscopic and gastroscopic control a guide wire (Terumo, Japan) was passed into the duodenum and a 7 Fr. ERCP catheter was placed over it. The guide wire was removed and a stiffer guide was placed into the duodenum through the catheter, which was then removed. The wall stent assembly (Wall stent A-V Shunt, uncovered stainless steel, 10 cm usable length, 12 Fr. introducer, 16 mm diameter expanded, 100 mm length; Schneider, Switzerland) was then introduced over the guide wire into the duodenum and released. The expansion of the wall stent was then observed radiologically and endoscopically and it was possible to pass an endoscope through the stent. *Results:* In all three patients stent placement was possible within 30 minutes without complications, the patient was able to be fed a liquid diet or via PEG and the patients were satisfied with the achieved improvement of their quality of life. Survival was 32 and 40 weeks, and the third patient is alive 10 weeks after the stent placement. In one patient cholestasis developed due to liver metastasis and an ERCP was performed through the metall mesh in the duodenum. *Discussion:* Metall stents inserted into the duodenum for malignant outlet obstruction provide effective palliation of patients symptoms and are an alternative to surgery in elderly and high risk patients with incurable GI malignancies. Because the delivery systems of the available metall stents are not suitable for placement into the pylorus due to their length, placement via a PEG makes it possible to insert these stents and furthermore also allows the delivery of nutrients in these patients who's food intake is often reduced by insufficient oral intake. Oncology, specific: Stomach Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Stomach, duodenum } "Palliativ Treatment of Malignant Duodenal Obstruction by Self Expanding Metal Stents Inserted through a Percutaneous Endoscopic Gastrostomy"

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"P P 39 0904" P 39 0904 **Gastric Polyps after Stomach Surgery** C. Spiliadis, V. Vamvakousis, V. Ntelis, A. Konstantinidis, V. Balatsos,

\*K. Paraskeva, Z. Manika, C. Spiliades, N. Skandalis

Gastroenterology Department, General Hospital of Athens *Aim:* To study the incidence of gastric polyps in patients who have undergone stomach surgery. *Patients-Methods:* We retrospectively studied the records of 504 patients with a history of gastric surgery who underwent esophagogastroduodenoscopy (EGD) during the nine year period 1986–1994. These were 296 female and 208 male. The type of surgery was as follows: Billroth II 292 patients, Billroth I 78 patients, gastroenterostomy 134 patients. The indication for EGD were atypical epigastric disturbances in 243 patients, epigastric pain in 192 patients and anemia in 69 patients. The presence, histologic nature and location of gastric polyps at the time of EGD was assessed. These were compared to 16307 patients who underwent EGD during the same time period but had no history of prior surgery of the stomach. *Results:* A total of 46 gastric polyps were found in 30 out of 504 patients with history of gastric surgery, an incidence of 5.9%. By contrast only 474 polyps were found in 253 out of 16307 patients without history of surgery, an incidence of 1.5%. This difference was statistically significant ( $p < 0.001$ ). On histological examination 42 of the polyps from operated patients were hyperplastic (91.3%) and 4 were inflammatory (8.7%). With regard to location 38 out of the 46 polyps (82.6%) were at the anastomotic margin. *Conclusion:* Gastric polyps appear with increased frequency in patients after gastric surgery, the majority are hyperplastic by histology and the most common site is the anastomotic margin. Endoscopy, specific: Stomach, duodenum Endoscopy, general: Instrumentation, diagnosis } "Gastric Polyps after Stomach Surgery"

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"P P 39 0906" P 39 0906 **Open Access <sup>13</sup>C-Urea Breath Tests (OA<sup>13</sup>C-UBT): Comparisons with and Impact on Open Access Endoscopy**

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**Introduction:** We have recently introduced an OA<sup>13</sup>C-UBT service to GPs. Patients < 40 years with dyspepsia were eligible and were given a <sup>13</sup>C-UBT at the LGI. *H pylori* positive patients are given eradication therapy and a repeat <sup>13</sup>C-UBT 2 months later. *H pylori* negative patients are referred back to their GP. We assessed patient satisfaction with this service and its impact on referral to open access endoscopy (OAE). **Methods:** Patients completed an anonymous questionnaire grading their satisfaction with the service on a 5 point Likert scale. Referral patterns to the OA<sup>13</sup>C-UBT and OAE services in patients < 40 years were evaluated retrospectively. **Results:** 251 patients < 40 years have attended the OA<sup>13</sup>C-UBT service. 88/251 (35%) were *H pylori* positive. Patients attending the OA<sup>13</sup>C-UBT service were similar to those attending for OAE in terms of gender, smoking history and alcohol intake but had more severe dyspepsia scores (15.8 7.6 vs. 12.6 6.7 p < 0.001). 145 patients completed a satisfaction questionnaire. 86% stated the service was very good, 10% good and 3% found the service satisfactory. In Aug-94 to Apr-95 321/926 OAE were performed in patients < 40 years old. In Aug-95 to Apr-96 (after the introduction of the OA<sup>13</sup>C-UBT) this fell to 237/924 OAE – a 35% reduction (95% CI = 30–39% reduction: p < 0.001) in endoscopies in patients < 40 years old. Only 6 patients referred for an OA<sup>13</sup>C-UBT have subsequently been referred for endoscopy (all *H pylori* negative). **Conclusions:** Patients are satisfied with the OA<sup>13</sup>C-UBT service and it has reduced endoscopy referral. Oesophageal gastric duodenal disorders: Helicobacter Pylori

Clinical practice: Management strategy }" "Open Access 13C-Urea Breath Tests (OA13C-UBT): Comparisons with and Impact on Open Access Endoscopy"

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"P P 40 0909" P 40 0909 **Overexpression of Mutant P53 and c-erbB-2 Proteins and Mutations of P15 and P16 Genes in Human Gastric Carcinoma: With Respect to Histologic Subtypes and Stages**

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We investigate whether the genetic alterations of several oncogenes and tumor suppressor genes could be correlated with the two histologic subtype, the diffuse and intestinal types of gastric carcinoma (GC). In 60 patients with GC, the overexpression of mutant p53 and c-erbB-2 oncoproteins was studied using immunohistochemical stains. Mutations of p15 and p16 tumor suppressor genes were assessed by polymerase chain reaction, Southern blotting, and direct DNA sequencing. Overexpression of c-erbB-2 and p53 was found in 21 (35.0%) and 27 (45.0%) patients, respectively. Overexpression of the c-erbB-2 oncoprotein was more common in the intestinal type (15/32) and the advanced stage (19/45) of GC. Similarly, p53 overexpression was more frequently found in the intestinal type (19/32) and the advanced stage (24/45) of GC. Homozygous deletions of p16 in exon 1 were found in 6 patients. Neither point mutations of p16 nor alterations of p15 were detected. The frequency of alterations of p53, c-erbB-2, and p16 was not related to sex and *H. pylori* infection. No correlation of genetic changes between any two genes was observed. Alterations of p15 and p16 genes play a limited role in GC. Overexpression of c-erbB-2 and p53 is frequently encountered in the intestinal type advanced GC. The association between genetic alterations and histologic subtypes supports the notion that a distinct pathogenesis exists in different histologic subtypes. Oncology, general: Molecular biology, genetics Oncology, specific: Stomach }" "Overexpression of Mutant P53 and c-erbB-2 Proteins and Mutations of P15 and P16 Genes in Human Gastric Carcinoma: With Respect to Histologic Subtypes and Stages"

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"P P 40 0910" P 40 0910 **Simultaneous Expression of Hepatocyte Growth Factor Receptor (C-MET), Autocrine Motility Factor Receptor (AMFR) and Urokinase-Type Plasminogen Activator Receptor (UPAR) in Gastric Carcinoma. -Especially in Borrmann 4 Type Carcinoma-**

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*Background:* The hepatocyte growth factor receptor (c-MET), autocrine motility factor receptor (AMFR) and urokinase-type plasminogen activator receptor (UPAR) are known to play an important role in tumor cell migration, invasion and metastasis. We have studied simultaneous overexpression of these genes in human gastric carcinoma. *Methods:* we examined immunohistochemically the relationship between tissue status of c-MET, AMFR and UPAR and clinicopathological parameters of 103 gastric carcinomas using resected primary tumor embedded in paraffin. *Results:* Among 103 cases, 44 (46%) cases showed overexpression of c-MET. AMFR and UPAR immunoreactivity was observed in 38 (37%) and 46 (47%) cases. Carcinomas were classified according to Borrmann classification. The all three genes were expressed in 1 case (3%) of early tumors, in no (0%) of localized tumors (Borrmann 1, 2), in 16 cases (39%) of infiltrating tumors (Borrmann 3, 4). Especially, in 13 cases (68%) of Borrmann 4 tumors, this occurrence was significantly higher compared with other macroscopic type ( $p < 0.01$ ). The incidence of overexpression of three genes was also closely associated with lymph node metastasis and peritoneal dissemination. In addition, the overexpression of three or two genes were relevant to lymphatic invasion and microscopic type. *Conclusion:* These results suggest that simultaneous overexpression of c-MET, AMFR and UPAR may be correlated with the progression and invasion of gastric carcinoma, especially biological nature of Borrmann 4 type carcinoma. Oncology, general: Molecular biology, genetics Oncology, specific: Stomach }"  
"Simultaneous Expression of Hepatocyte Growth Factor Receptor (C-MET), Autocrine Motility Factor Receptor (AMFR) and Urokinase-Type Plasminogen Activator Receptor (UPAR) in Gastric Carcinoma. -Espécial"

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"P P 40 0911" P 40 0911 **Immunohistochemical Investigation of Staining Development and Staining Intensity of Immunoreactivity of Sialyl-Tn Antigen in Human Gastric Cancer**

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Third Department of Surgery, School of Medicine, Toho University, Tokyo, Japan A cell surface sugar chain antigen, sialyl Tn (STN), in gastric cancer lesions was immunohistochemically stained for measurement of staining development (positive area) and staining intensity (positive stain), to investigate its relationships to clinicopathological factors and assess its clinical significance as a tumor-related antigen. *Materials and methods* We studied 200 gastric cancer lesions, resected surgically in our department with preoperative STN data available. Thin sections of paraffin-embedded lesions fixed in 10% buffered formalin were immunohistochemically stained according to the streptavidin-biotin (SAB) method. The biological examination was measured in Otsuka Assay Laboratory by RIA. Positive areas and positive stains developed after immunological staining of STN were analyzed with a BECTON-DICKINSON CAS-200 image cytometer. *Results* Intestinal metaplasia in the non-carcinomatous gastric mucosa was positive in immunological staining for STN, while normal gastric mucosa was not stained at all. STN staining was predominantly apical or intraluminal, with the cell surface facing the gland cavity and the extracellularly secreted substance stained. We also observed staining development of cytoplasmic type with additional staining in the cytoplasm. The incidence of STN-staining-positive regions was significantly higher in well differentiated tumors, which was also the case with positive area and positive stain. Both positive area and positive stain increased significantly with increased degree of the depth of invasion and stage progression. These values increased in cases with liver, peritoneal and lymph node metastasis. They also correlated well with serum STN. *Conclusion* We conclude that the positive area and positive stain for STN antigen in the gastric cancer tissue are closely correlated with clinicopathological factors and reflect the degree of clinical progression, suggestive of its clinical significance as a tumor-related antigen. Oncology, specific: Stomach } "Immunohistochemical Investigation of Staining Development and Staining Intensity of Immunoreactivity of Sialyl-Tn Antigen in Human Gastric Cancer"

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"P P 40 0912" P 40 0912 **Cell Proliferation, Oncoprotein Expression (p53, c-erb B-2, bcl-2) and c-ki-ras Mutation in Juvenile Polyposis with Adenoma and Carcinoma of the Stomach**

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<sup>2</sup> Department of Surgery, School of Medicine, Kitasato University, Sagamihara, Kanagawa, Japan

<sup>3</sup> Department of Internal Medicine, School of Medicine, Kitasato University, Sagamihara, Kanagawa, Japan *Aims:* Juvenile polyposis has recently been associated with malignancies. To clarify its neoplastic potential, we analyzed cell proliferation and oncogenetic abnormalities in three cases of juvenile polyposis limited to the stomach (JPs) including coexisting adenoma and adenocarcinoma. *Methods:* A total of 155 slides of polyps, papillary adenoma (Pap-ad), papillary adenocarcinoma (Pap-ca) and signet ring cell carcinoma (Sig) in JPs were selected for Ki67 staining. For control study, the cases of gastritis (Gs), hyperplastic polyp (HP), tubular adenoma (TA), well differentiated adenocarcinoma (W-ca) and Sig were also analyzed. Immunohistochemistry for oncoproteins and DNA direct sequencing for c-Ki-ras were examined for tumors in JPs. *Results:* The Ki67 labeling indices (KLI) for all JPs were lower than that for both HP and Gs cases. The KLI for Pap-ad, Pap-ca and Sig in JPs were lower than that for conventional TA, W-ca and Sig, respectively. P53 was focally expressed in both Pap-ad and Pap-ca in JPs. *Bcl-2* and *c-erb B-2* expression, and *c-Ki-ras* mutation were not detected in all tumors in JPs. *Conclusions:* Cell proliferation of polyps and tumors in JPs were lower than that of non-neoplastic diseases and conventional tumors, respectively. Oncogenetic alterations were not clearly demonstrated. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach } "Cell Proliferation, Oncoprotein Expression (p53, c-erb B-2, bcl-2) and c-ki-ras Mutation in Juvenile Polyposis with Adenoma and Carcinoma of the Stomach"

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"P P 40 0913" P 40 0913 **Flow Cytometric DNA Analysis, Clinicopathological Study and Prognostic Factors of MP Gastric Cancer (Multivariate Regression Analysis by Cox's Proportional Hazards Model)**

\*M. Morise, Y. Sakakibara, Y. Hiki, A. Kakita

Department of Surgery, Kitasato University, Sagamihara, Japan *Objective:* To study the relation between DNA ploidy patterns and prognosis as well as the involvement of other clinicopathological factors in patients undergoing resection of mp gastric carcinomas, analyzed by flow cytometry (FCM). *Subjects and methods:* Seventy-two patients with mp gastric carcinomas who underwent resection at the Department of Surgery, Kitasato University between April 1980 and August 1988 were studied. Tumor specimens obtained at the time of surgery were embedded in paraffin, and DNA ploidy patterns were studied by FCM. In addition, clinicopathological factors were studied by a multivariate analysis to identify predictors of prognosis. *Results:* In univariate analysis (log rank and generalized Wilcoxon test) significant differences ( $p < 0.05$ ) were obtained for four factors: ploidy pattern, tumor location, macroscopic type, and number of lymph nodes with metastasis. A multivariate analysis using a Cox's proportional hazards model identified only two factors, ploidy pattern and tumor location (in this order), as significant predictors of prognosis ( $p < 0.05$ ). *Conclusion:* We concluded that DNA ploidy pattern may be a very useful predictor of prognosis. Oncology, specific: Stomach }"  
"Flow Cytometric DNA Analysis, Clinicopathological Study and Prognostic Factors of MP Gastric Cancer (Multivariate Regression Analysis by Cox's Proportional Hazards Model)"

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"P P 40 0914" P 40 0914 **Blood Flow and Blood Flow Pattern Alteration in Adenocarcinomas of the Gastroesophageal Junction**

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Dept. Visceral and Transplantation Surgery, Univ. Bern.

Inselhospital, 3010 Bern, Switzerland Most fast growing malignant tumors maintain a sufficient nutrient supply by vascular proliferation. We recently demonstrated that blood flow in tumor bearing areas of gastric tumors coincides with an increased expression of CD31, a marker for neoangiogenic endothelial cells. In this study we analyze blood flow (BF) and the blood flow pattern in the gastric wall of patients with proximal gastric adenocarcinomas by laser Doppler flowmetry (LDF). *Methods:* In 6 subsequent patients undergoing gastric and/or esophageal resection for adenocarcinoma of the gastroesophageal junction tumor blood flow was assessed by LDF in normal as well as tumor bearing areas of the gastric wall. Blood flow was recorded for at least 30 seconds after a stable signal was obtained. Post sampling data processing included calculation of systolic and mean blood flow and pulse curve analysis with integral under the curve calculations. *Results:* Blood flow in perfusion units Normal Adenocarcinoma Mean 163.2 (70.4) 368.6 (88.7) \*Systolic 220 (66.0) 514 (102.8) \*\*\*Integral 101 (19.0) 236.6 (113.7) \*Pulsatile index 1.35 1.39 PU – SE, \*p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001 vs normal *Discussion:* Adenocarcinomas of the gastroesophageal junction have an over twofold increase of tumor BF as indicated by an increase in mean and systolic blood flow on laser Doppler sonography. Not only was the total blood flow increased but also the flow curve pattern altered indicating an altered vascular reactivity of tumor microvessels as compared to normal gastric vessels. Oncology, specific: Oesophagus Oncology, specific: Stomach Oncology, general: Proliferation, carcinogenesis } "Blood Flow and Blood Flow Pattern Alteration in Adenocarcinomas of the Gastroesophageal Junction"

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## "P P 40 0915" P 40 0915 Molecular Mechanisms of the Formation of Peritoneal Dissemination from Gastric Cancer

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Surgery II, School of Medicine, Kanazawa University, Kanazawa, Japan *Purpose* A new animal model by the i.p inoculation of highly metastatic gastric cancer cell line MKN-45-P was developed, and the specific genes having a great role in the formation of peritoneal dissemination was identified. *Methods* MKN-45-P was established from a gastric cancer cell line of MKN-45 by the progressive growing of the intraperitoneal passages. By a specific detection method of metastasized human tumor cells in nude mice using PCR, a human  $\beta$ -globin-related sequence in the DNA from various parts of the peritoneum was specifically amplified and detected by gel electrophoresis and by a specific nucleotide probe. A novel *ex vivo* co-culture system using human greater omentum was developed. The differences of the expressions of metastasis related genes (MMP 2/9, uPA, uPAR, AMFR, met, erbB-2, CD-44, Integrin subunits) between MKN-45 and MKN-45-P were examined by RT-PCR. *Results* Greater omentum showed a strong signal of human  $\beta$ -globin gene from the 1st day and the signals gradually increased. The signals in the gonadal fat, mesentery and ovarium could be weakly detected on the 1st day, transiently decreased on the 3rd day, and then increased from 7th day. In the diaphragm, and abdominal wall, signals could be detected from the 7th day. In contrast, small intestine and colon did not show any human  $\beta$ -globin signals. MKN-45-P cells were found to adhere on the naked areas of the submesothelial connective tissue. In *ex vivo* culture system, cancer cells adhered only to the naked area of the submesothelial basement membrane. The expressions of integrin  $\alpha$ 2 and  $\alpha$ 3 subunits in MKN-45-P were extremely elevated than those in MKN-45. Integrin  $\beta$ 1 subunit expression did not change during the intraperitoneal passages. Anti- $\beta$ 1 integrin subunit antibody significantly inhibited the adherent number of MKN-45-P on the omentum. Other metastasis associated genes were not overexpressed in MKN-45-P. From these results, we conclude that the major metastatic rout of the peritoneum may be through milky spots and by the adhesion to the naked connective tissue exposed after shrinkage of the mesothelial cells. In this process, VLA 2 and VLA 3 have a great role in the formation of the peritoneal dissemination from gastric cancer. Oncology, general: Molecular biology, genetics Oncology, specific: Stomach } "Molecular Mechanisms of the Formation of Peritoneal Dissemination from Gastric Cancer"

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## "P P 40 0916" P 40 0916 The Change and Reflection of Curative Operation for Gastric Cancer Patients in every Decade

\*Y. Mikami, M. Mikami, H. Kawasima, R. Hada, H. Suzuki, Y. Sugiyama, Y. Ebina, M. Konn

Department of Surgery II Hirosaki University School of Medicine, Hirosaki, 036, Japan  
*Aim:* The operative curative cases for gastric cancer patients past 34 years were divided into three groups by every decade. The clinical characteristics and the results of each group was retrospectively analyzed. We also examined whether extension of gastric cancer surgery could improve its prognosis.  
*Patients and method:* The 1238 patients with primary gastric cancer except residual or multiple cancer were divided into the following three groups: the former era: 367 patients from April, 1961 to December, 1974 (the former); the mid era: 377 patients from January, 1975 to December, 1984 (the mid); the late era: 494 patients from January, 1985 to December, 1994 (the late). In the general rules of gastric cancer study in Japan, the curative operation included \quoterelative non-curative, relative curative or absolute curative resection\quote. The Kaplan-Meyer method was used for calculation of the postoperative survival rate, and the Chi-square test and generalized Wilcoxon test were used to determine the statistical significance of difference.  
*Result:* The change of each era in stage and curability was that the rate of stage I and absolute curative resection increased, however, that of stage III or IV and relative non-curative resection was decrement. Ten (or five) year survival rate of curative resection in \quotethe late\quote was 79.8 (83.3)%. There was no significant difference between \quotethe late\quote and \quotethe mid\quote in 76.5 (78.8)% although that of \quotethe former\quote was significantly low in 44.2 (56.5)%. When 10 (5) year survival rate by grade or number of lymph node metastasis was examined, there was a significant better prognosis in patients with n0 lymph node metastasis (n0) and the n2 group positive between in \quotethe former\quote and in \quotethe mid\quote or \quotethe late\quote (p = 0.02). It means that in stage III there was a significant difference between them. There was no difference in survival time by the number of lymph node metastasis between in \quotethe mid\quote and in \quotethe late\quote. In the group of n0 lymphnode metastasis and of 4 to 9 lymph node metastasis positive, the survival rate in \quotethe former\quote was significantly worse than that in \quotethe mid\quote (p < 0.001) or that in \quotethe late\quote (p = 0.03). In the group of metastasis positive more than 10, there was no significant difference between both eras.  
*Conclusion:* There was a marked prolongation of the survival time in the curative surgery with R2-dissection after \quotethe mid\quote in comparison with R1 lymphnode dissection in \quotethe former\quote although the ratio of the gastric cancer patients in early stage has been relatively increasing. R3-dissection for the advanced gastric cancer patients was introduced into the operation after 1985 aiming at better prognosis in the curative surgery, however, there was no significant improvement of prognosis. Lymphnode dissection up to R2 level as the standard curative surgery for the gastric cancer patients prolonged the survival time rather than R1 level. Furthermore the curative operation for lymph node metastasis with n0 or at most 4 to 9 was in good prognosis. Oncology, general: TherapyOncology, specific: Stomach }" "The Change and Reflection of Curative Operation for Gastric Cancer Patients in every Decade"

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## "P P 40 0917" P 40 0917 **Re-Evaluation of Surgical Therapy for the Primary Gastric Malignant Lymphoma Patients**

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*Introduction and aim* Gastric malignant lymphoma (ML) is different from the lesion of lymph nodes origin and generally localized close to the primary lesion. Recently there are increasing more reports that even chemotherapy could cure gastric ML patients in early stage. The surgical treatment was retrospectively evaluated on the basis of prognosis and clinicopathologic findings of gastric ML removed surgically. The clinicopathological findings of ML depends on the Japanese general rules for the gastric cancer study.

*Patients and results* The 48 primary gastric ML patients by the end of 1995 from 1975 were analyzed. The ratio occupied in gastric malignancy of primary malignant lymphomas was 1.5%. Ten cases were histologically diagnosed as MALT lymphomas, however, two cases as only benign RLH (Reactive lymphoid hyperplasia). The ratio of sex was almost equal with 25 (M) to 23 (F). Mean age is 59-year-old. The survival time of giant rugae type, superficial type and protruded type were 100%, however, that of Borrmann 2 type 82.5% and Borrmann 3 type 44.4%. Significant difference was recognized in survival rate by macroscopic type. The correlation between lymph node metastases and prognosis was examined. Twenty one cases were alive in 24 cases with n0, and, three cases were dead and 8 alive in 11 cases with lymphnode metastases more than n2-group. But 3 cases were dead in 7 cases with n1-group positive. The 5 year survival rate was 90.9% in n0 group, 76.9% in the cases more than n2-group positive, however 64.3% in n1 group positive. The prognosis of resected ML was better than that of operated gastric cancer patients, but there was no correlation in the grade of lymphnode metastasis. Histopathology of 29 cases was diffuse type and that of 5 follicular type. The six cases with diffuse large cell type were dead in 16. All of MALT lymphoma patients was alive, so this disease was in good prognosis and may present macroscopical superficial type. The 5 year survival rate of follicular type and MALT lymphoma was 100%, and that of diffuse type was 74.7. There were no dead cases with stage I and III. There were five patients dead in 9 cases with stage II, 4 dead in 5 with stage IV. Five year survival rate in stage I and III was 100%, 66.7% in stage II and 33.3% in stage IV, but wasn't correlated. When 5 year survival rate in surgical curability according to the general rules of the gastric cancer study was examined, the ratio in curability C was 42.5%, 81.5% in B and 95.8% in A. Each survival curve by the curability was significantly graded.

*Conclusion* The overall 5 year survival rate of resected gastric ML was 76%. Operative curability A and shallow invasion of ML up to proper muscle (mp) were decisive factors to regulate the prognosis. Histological classification is important factors predicting prognosis. The patients in low grade ML such as follicular type or MALT lymphoma after operation was all alive in extremely good prognosis. As for MALT lymphoma and ML in early stage such as I or II of Japanese classification for gastric cancer, surgical treatment should be first performed.

Oncology, general: Therapy  
Oncology, specific: Stomach  
Oncology, specific: Lymphoma }

"Re-Evaluation of Surgical Therapy for the Primary Gastric Malignant Lymphoma Patients"

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## "P P 40 0918" P 40 0918 High-Dose 5-FU/FA in Advanced Gastric Cancer

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<sup>1</sup> Klinik und Poliklinik für Allgemeine Chirurgie der Westfälischen Wilhelms-Universität Münster

<sup>2</sup> Tumorzentrum Essen The palliative treatment of advanced gastric cancer has been proven before in 5 studies. Palliative chemotherapy has a better effect in comparison to best supportive care according to survival and quality of life. 5-FU, folinic acid (FA) and Cisplatin (C) are active drugs in advanced gastric cancer with a different mode of action. The continuous infusion of 5-FU with folinic acid for 24 h once weekly determines a higher dose intensity and less toxicity as 5-FU bolus therapy. Patients with advanced gastric cancer were treated in a disease orientated phase II study. *Treatment:* FA 500 mg/m<sup>2</sup>, 2 h inf. d 1, 8, 15, 22, 29, 36, 5-FU 2000 mg/m<sup>2</sup>, 24 h inf. d 1, 8, 15, 22, 29, 36, C 50 mg/m<sup>2</sup>, 1 h inf. d 1, 15, 29, Repetition at d 50. Depending on response and toxicity up to 6 cycles were planned. *Pts.-characteristics:* male/female 29/21, age (years) 51 (24–72), measurable/evaluable dis. 33/17, locally advanced disease (LAD) 8, M1 42, 1–2 TU-sites 32, > 2 TU-sites 18, malignant ascites 14 *Results:* CR 4 (8%), PR 21 (42%), maR 8 (16%), CR + PR + maR 33 (66%), stable disease 14 (28%), progression 2 (4%), toxicity related death 1 (2%) CR + PR + maR in: LAD 63%, M1 67%, 1–2 TU-sites 69%, > 2 TU-sites 61%, malignant ascites 63% Median remission duration 8 mts, median survival time all pts. 14 mts, M1 13 mts. *Toxicity:* (grade): leucocytopenia 2 26%, 3 9%, nausea/vomiting 2 35%, 3 4%, mucositis/stomatitis 2 7%, 3 0%, alopecia 2 10%, 3 2% *Conclusions:* HD-FU/FA/C with cont. inf. is an active regimen for advanced gastric cancer with lower toxicities as regimen with FU-bolus-infusion. Other regimens with cont. inf. proven are ECF and ELFI with comparable results. Because of these good results these forms of therapy with 5-FU in continuous infusion seem to be good alternatives for future trials. Therefore this regimen is one arm in a new randomised phase II study of the EORTC and AIO. Oncology, general: Therapy Oncology, specific: Stomach } "High-Dose 5-FU/FA in Advanced Gastric Cancer"

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## "P P 40 0919" P 40 0919 **Development of a Neuroendocrine Carcinoma and Multifocal Carcinoidosis in the Stomach of a Patient with Chronic Atrophic Gastritis**

\*R. Eissele, E. Weihe, R. Arnold

Depts. of Gastroenterology and Anatomy, Philipps University, Marburg, Germany Multifocal carcinoids (MC) are benign neoplasias of the stomach and frequently occur in patients with chronic atrophic gastritis (CAG). Hitherto, no association has been reported between CAG and neuroendocrine carcinomas (NC). We present a case report of a patient with the coincidence of MC and NC in the oxyntic stomach. Furthermore, the cellular origin of both types of tumors were investigated histologically. *Case report:* A 63 year old female patient was admitted to the hospital with upper GI bleeding. An ulcerous tumor in the oxyntic mucosa was found by endoscopy and histologically a NC (G3) was diagnosed. In addition, biopsies of several small polyps in the oxyntic mucosa revealed multiple carcinoids with infiltration of the submucosal layer. In the remaining oxyntic mucosa argyrophil cell hyperplasia (diffuse, linear, micronodular) and severe CAG (type-A) were present. H. pylori infection was absent. Numerous metastasis of the NC could be found in the liver and the net. Serum gastrin levels exceeded 2000 pg/ml. Antibodies against parietal cells and H<sup>+</sup>/K<sup>+</sup>-ATPase were detectable. *Treatment:* Local removal of the NC was necessary because of recurrent tumor bleeding. Serum gastrin levels could be suppressed to near normal values with octreotide (SMS 3 {\b4} 200 \b5g). Since liver metastasis progressed rapidly, chemo-embolization was performed, which resulted in a partial response. *Histological investigations:* Global endocrine markers (NSE, chromogranin-A, Grimelius silver stain) were positive in both types of tumors (NC and MC). Recently, the vesicular monoamine transporter 2 (VMAT2) was found be a selective marker of ECL-cells in the stomach (J Mol Neurosci 1994; 5: 150). Immunohistology with a polyclonal VMAT2 antibody showed a positive immunoreaction in the MC and the argyrophil cell hyperplasia but not in the NC and the metastasis. *Conclusion:* Neuroendocrine carcinomas and multiple carcinoids can occur simultaneously in patients with chronic atrophic gastritis and hypergastrinemia. It seems unlikely that both tumor types derive from the same cell population. Oncology, specific: StomachOncology, general: Proliferation, carcinogenesis }" "Development of a Neuroendocrine Carcinoma and Multifocal Carcinoidosis in the Stomach of a Patient with Chronic Atrophic Gastritis"

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"P P 40 0920" P 40 0920 **Immunohistochemical Study of Laminin, Vitronectin and Tetranectin in Gastric Cancer**

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The purpose of this study is to clarify the localization of laminin (LN), vitronectin (VN) and tetranectin (TN) in gastric cancer by means of immunohistochemistry and to make a comparison with pathological findings to determine their significance in gastric cancer invasion and metastasis.

*Methods:* Sixty-two cases of gastric cancer patients were examined. Tissue specimens were obtained from both normal and cancer tissue of resected stomach. These specimens were examined by immunohistochemical staining. *Results:* Positive staining of LN was observed in basement membrane. It was observed in 24 cases of 29 (82.8%) in differentiated type of adenocarcinomas and in 8 of 33 (24.2%) cases in undifferentiated type of adenocarcinomas. Positive staining ratio for LN was significantly higher in differentiated type than undifferentiated type. Immunoreactivity for VN was observed in internal elastic membrane of blood vessel. The relationship between venous invasion and positive rate of VN staining was examined. Positive staining for VN was observed in 1 of 11 (9.1%) in invasive ( { - } ) group and 22 of 51 (43.1%) cases in invasive ( + ) group. VN positivity was significantly high in the cases with venous invasion. TN staining was observed in the cytoplasm of cancer cells. In differentiated type, the cytoplasmic positive staining was observed in 23 of 29 (79.3%) cases, while in undifferentiated type, positive staining was observed in only 12 of 33 (38.4%) cases. TN positivity was significantly high in the cases of differentiated type. *Conclusion:* The results suggested that positivity of LN and TN were related with histological differentiation of gastric cancer and VN staining was related with venous invasion. Oncology, specific: Stomach }

"Immunohistochemical Study of Laminin, Vitronectin and Tetranectin in Gastric Cancer"

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"P P 40 0921" P 40 0921 **Adenosine Deaminase Activity in Patients with the Intestinal Type of Gastric Carcinoma**

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Department of Gastroenterology, J. Sniadecki's Regional Hospital and Departments of Physiology and Pathomorphology, Medical Academy, Białystok, Poland Our previous study has shown that adenosine deaminase activity is lower in the intestinal than diffuse type of gastric carcinoma (Cancer Lett., 1994). The proposed explanation for that was the rate of tumor growth. The aim of the present study was to analyse only those patients who had recognized the intestinal type of gastric carcinoma either in the non-operated or partially resected stomach. 40 subjects were included in the study; 26 partially gastrectomized and 14 non-operated. Adenosine deaminase activity was determined in the gastric cancer and surrounding unchanged gastric mucosa by means of ammonia liberated from the substrate during 10-min. incubation. We have found that the enzyme activity in the advanced gastric cancer (ascites, metastases) of non-operated stomach as well as that developed in partially resected stomach due to duodenal ulcer was significantly lower than in recurrent cancer of the gastric remnant (no ascites and metastases) (36 – 18.0 and 20.9 – 17.5 vs. 75.8 – 46.8 nmol NH<sub>3</sub>/mg of protein/min, p < 0.05). We have also noticed a significantly lower enzyme activity in the unchanged gastric mucosa surrounding the neoplastic lesion of non-operated stomach than in the unchanged gastric mucosa of partially resected stomach due to malignancy (57.8 – 30.2 vs. 86.5 – 30.2 nmol NH<sub>3</sub>/mg of protein/min, p < 0.05). The other factors than histological type of the tumor are also involved in the regulation of adenosine deaminase activity in the gastric cancer and surrounding cancer unchanged gastric mucosa; one of them may be cancer progression. Oncology, specific: Stomach } "Adenosine Deaminase Activity in Patients with the Intestinal Type of Gastric Carcinoma"

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## "P P 40 0922" P 40 0922 Early Gastric Cancer: Relapse and Prognostic Outcome

\*I. Claro, J. Mendes Correia, P. Lage, A. Suspiro, C. Chagas, R. Pinto, P. Chaves, L. Glória, A. Dias Pereira, C. Nobre Leitão, F. Costa Mira

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Portugal *Background:* Patients with Early Gastric Cancer (EGC) are known to have a good prognosis with a low rate of relapse at five years. *Aims:* To prospectively evaluate prognostic variables in a group of patients in whom curative surgery was performed for EGC between 1983–1995. *Patients and methods:* 90 patients, 48 male and 42 female with a mean age of 58.9 – 13.1 years (22–82) were included in the present study. We have analysed clinical and histopathologic features of the tumor as well as survival curves and percentage of relapses. *Results:* From a histopathologic point of view, 58 patients (64.4%) had an adenocarcinoma and 32 of them (35.6%) presented as signet ring cell carcinoma. TNM staging (UICC) in the surgical specimens was the following: T1N0M0 { - } 78 (86.7%), T1N1M0 { - } 10 (11.1%), T1N2M0 { - } 2 (2.2%). According to the Japanese classification 13 (14.4%) tumors were type I, 8 (8.9%) type IIa, 27 (30%) type IIb, 28 (31.1%) type IIc and 14 (15.6%) type III. During a follow-up period of 52.6 – 42.9 months (1–154), 5 patients relapsed, two of them earlier than 6 months and the remaining three at 30, 43 and 59 months after surgery, respectively. Only one of these patients was re-operated. There were 18 deaths – 5 relapses, 4 peri-operative deaths and 9 patients for others causes. Rate of relapse (5.5%) was not related to histologic features although they were all N0 (TNM). Nonetheless, all these relapses occurred in patients who were operated before 1988 when an extended lymphadenectomy was not routinely performed. In all these patients the number of resected lymph nodes was lower than 5. No metachronous tumors were observed. *Conclusions:* It is possible that limited lymph node resection performed in the eighties was the main responsible for relapses observed in the present series. Therapeutic possibilities of the relapses are limited and therefore, intensive surveillance is probably not advised. Oncology, specific: Stomach Oncology, general: Therapy } " Early Gastric Cancer: Relapse and Prognostic Outcome "

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## "P P 40 0923" P 40 0923 Cag A Protein Seropositivity in Random Population and in Gastric Cancer Patients

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<sup>1</sup> University of Tartu, Estonia

<sup>2</sup> University of Lund, Sweden

<sup>3</sup> IRIS, Siena, Italy *Purpose.* To evaluate the presence of antibodies to CagA protein associated with the risk of developing gastric cancer (GC) in Estonian adult population with high prevalence (87%) of *H. pylori* (HP) infection and to compare it with presence of antibodies to CagA in GC patients. *Subjects and Method.* 199 subjects (86 M, 113 F, median age 41) as a representative sample of adult population (1461 persons) from the South Estonian town of Karksi-Nuia and 45 patients (22 M, 23 F, median age 67) with gastric adenocarcinoma (14 in antrum, 17 in corpus or cardia, 14 in antrum & corpus; types: 17 intestinal, 8 diffuse, 20 indeterminate) operated at the Oncological Clinic in Tartu were studied. HP status was determined using serological evaluation of IgG antibodies to glycine extracted proteins of HP (NCTC11637) as reported previously (Eur. J. Gastroenterol & Hepatol. 1994, 6, 529–533). Anti-CagA IgG were determined by ELISA using a recombinant fragment of CagA antigen of HP CCUG strain (1.25 µg/ml). The absorbance value 0.300 OD was taken as a cut-off level based on a study in 25 HP negative sera (histology, serology). *Results.* IgG antibodies to HP strain NCTC 11637 were revealed in 169/199 (85%) of the population, and in 41/45 (91%) of GC patients ( $p > 0.05$ ). Anti-CagA IgG were seen in 126/199 (63%) of the population sample (in 120/169 of HP positive persons). In GC patients the prevalence of anti-CagA IgG was significantly higher, 39/45 (87%), than in the whole population ( $p = 0.002$ ) in all age groups except 20–29-year old (76%;  $p = 0.25$ ). *Conclusions.* Seropositivity to HP strain NCTC 11637 was similarly high in Estonian adult population and in GC patients. The prevalence of anti-CagA IgG was significantly higher in GC patients than in the population studied. In population, persons aged 20–29 with the highest prevalence of anti-CagA IgG should be given further attention with respect to cancer development. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, specific: Stomach } "Cag A Protein Seropositivity in Random Population and in Gastric Cancer Patients"

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"P P 40 0924" P 40 0924 **Cimetidine Might Affect Gastric Carcinogenesis in Rats Subjected to Gastrojejunostomy**

\*G.S. Hortemo, H. Maartmann-Moe, O. R\ 'f8kke, A. Viste

Department of Surgery, the Gade Institute of pathology, University of Bergen, Haukeland Hospital, Norway *Introduction:* There is some evidence that cimetidine by immunomodulation increases survival in cancer patients. This study was performed to investigate if cimetidine reduced occurrence of gastric cancer following gastrojejunostomy. *Material and methods:* Duodenogastric reflux was established by gastrojejunostomy in 132 male rats (PGV/Mol rats). Half of the animals were postoperatively for a minimum of 38 weeks given cimetidine (100 mg/kg/day) in their drinking water. The animals were killed after 52 weeks of observation and the stomach macroscopically and microscopically investigated. Blood was drawn for analysis of TNF and IL-6. *Results:* In the cimetidine fed group 39.6% (19/48) of the animals developed cancer versus 27.9% (12/43) ( $p = n.s.$ ) in the control group. We found no correlation between TNF and IL-6 versus cancer and cimetidine. *Discussion:* Although not statistically significant, we found a tendency towards an increased rate of cancers in the cimetidine treated group. This effect might be caused by a reduced hydrochloric acid production superimposed on a duodenogastric reflux. Evaluated by TNF and IL-6 we found no immunomodulative effect of cimetidine. Oncology, specific: Stomach } "Cimetidine Might Affect Gastric Carcinogenesis in Rats Subjected to Gastrojejunostomy"

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"P P 40 0925" P 40 0925 **Gastro-Intestinal Sarcomas: Prognostic Significance of the F.N.L.C.C. Histological Grading** C. Genestie<sup>1</sup>,

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<sup>3</sup> Gastro-Intestinal Oncological Department, Institut Gustave Roussy, Villejuif, France  
The FNCLCC (Fédération Nationale des centres de Lutte contre le Cancer) histological grading system has a well established prognostic significance when it is used on smooth tissue sarcomas. Gastro-intestinal (GI) sarcomas are rare and of uncertain behaviour. Mitosis count is the only method for pathologists to evaluate the prognosis of such tumours. The purpose of this work was to evaluate the FNCLCC grading system on a retrospective series of 19 GI sarcomas treated at the IGR Institute. There were 10 women and 9 men (mean age 51 years). The tumour was located in the stomach in 10 cases, in the small intestine in 8 cases and in the anal canal in 1 case. The treatment consisted of surgical removal of the tumour followed in 5 cases by radio or chemotherapy. Histologically, all cases were leiomyosarcomas. The average survival rate was 23 months, with a 5 year survival rate for 22%. All cases were reviewed by two pathologists and the 3 items of the FNCLCC grading system (differentiation, mitosis count, necrosis) were noted in each case. The results show: the FNCLCC grading system has a significant prognostic value ( $p = 0.03$ ) as well as the differentiation item and as the mitosis count item. The necrosis item has no significant value. In conclusion, this preliminary study seems to demonstrate that: (1) the FNCLCC grading system is applicable to GI sarcomas, and (2) a new grading system with only two items (differentiation & mitosis count) could be used on such tumours. Oncology, general: Proliferation, carcinogenesis Oncology, general: Epidemiology Oncology, specific: Stomach }  
"Gastro-Intestinal Sarcomas: Prognostic Significance of the F.N.L.C.C. Histological Grading"

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"P P 41 0926" P 41 0926 **Gastric Smooth Muscle Tumours (SMT): Long Term Results of Surgery in 52 Patients** D. Quinaux,

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<sup>1</sup> Centre Hospitalier Princesse Gr<sup>\</sup>e2ce, Monaco SMT of the digestive tract are of 3 types: leiomyoma (LM), leiomyosarcoma (LMS) and leiomyoblastoma (LMB). They are characterized by their rarity, a difficult diagnosis of malignancy, and therapeutic controversies concerning the extent of resection and the efficacy of chemo- and radiotherapy. We report here about the features and the results of surgery in a series of 52 gastric SMT. From 1981 to 1995, among 105 mesenchymal tumours of the digestive tract operated on in two institutions, 83 (79%) were SMT. Of those, 52 (63%) were gastric and were divided in 14 LM, 26 LMS and 12 LMB. There were 32 males and 20 females, 26 to 85 yr old (mean: 55). The mean delay between the first symptom and the diagnosis was 8 mos (0–60). The most frequent symptoms were: bleeding (41%), palpable mass (41%) and pain (38%), whereas 6 patients (pts) (12%) had no symptoms. The most frequent endoscopic findings were ulcerated (45%) and submucosal tumour (33%). The tumour could be demonstrated by ultrasound and CAT-scan of the abdomen in 27/30 and 22/22 cases, respectively. Its gastric origin was shown in 5 and 8 cases, respectively. Preoperative biopsies (n = 26) were contributive in 11 cases (42%). The mean size of the tumour was 11 cm (1–30) and was larger for LMS. The site of the tumour compared to the angulus did not differ between 3 types. In LMS, contiguous tumour spread of LMS was present in 12 pts (46%), and liver metastases and peritoneal carcinomatosis in 5 pts each. Lymph node metastases were not observed. Complete resection (elective: 45, urgent: 7) with curative intent was achieved in 44 pts (including 18 LMS). Sixteen of 17 total gastrectomies were done for LMS. Extended resections for contiguous spread were done in 14 LMS pts. One patient had only exploration. After pathologic examination of surgical specimens, there were: 16LM, 12LMB, and 24LMS divided in 24 malignant, 24 benign, and 4 intermediate prognosis SMT. Operative mortality was nil and the morbidity rate was 6%. One patient (LMS) was lost to follow-up. During a median follow-up of 6.2 yrs (n = 51), 11 cancer deaths and 4 unrelated deaths (2LM, 1LMS, 1LMB) were observed. After curative resection, 8 pts are alive free of disease (mean follow-up: 5 yrs), and 9 had relapse (mean delay: 28 mos) among whom 4 had liver resection. The mean survival after palliative resection was 1 yr. For LMS, the overall 2-, and 5-yr survival after resection of LMS were 55%, and 43% with a mean survival time of 38 mos. In 3 pts, despite an initial diagnosis of benign SMT, the appearance of distant metastases after 22, 24, and 101 mos switched the diagnosis to malignancy. A prolonged follow-up is needed after resection of so-called benign SMT since the outcome may contradict the initial diagnosis. The type of gastrectomy has to be adapted to the size and the site of the lesion. Extensive lymphadenectomy is not mandatory due to scarcity of nodal invasion. Resections extended to adjacent organs or of metastases with curative intent are worthwhile since no other efficient treatment is available. Oncology, specific: Stomach } "Gastric Smooth Muscle Tumours (SMT): Long Term Results of Surgery in 52 Patients"

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"P P 41 0927" P 41 0927 **Surgical Treatment of Duodenal Adenomas in Familial Adenomatous Polyposis**

\*C. Penna, N. Bataille, R. Parc

Service de Chirurgie Digestive, Hopital Saint-Antoine, Paris, France In familial adenomatous polyposis (FAP) duodenal adenomas are found in 80% of patients and duodenal cancer accounts for the majority of cancer-related death after colectomy. Duodenal adenomas are not amenable to drug or conventional endoscopic treatment. In case of multiple, large, villous and severely dysplastic adenomas (stage IV disease), prophylactic measures to prevent malignant change may become necessary. The aim of this work was to assess the results of surgical treatment of stage IV duodenal polyposis in FAP. Duodenotomy and clearance of duodenal adenomatous polyps was performed 6 times in 5 patients. In no case was the polyp histology more severe than that found at endoscopy. There was 2 duodenal leaks, one which necessitate reoperation. After a mean follow-up of 53 months (36–72) duodenal adenomas recurred in all patients and 4 had stage IV disease. Pancreatoduodenectomy with pylorus preservation and pancreatico-gastric anastomosis was performed in 7 patients. Histology of the specimens revealed 2 unsuspected duodenal carcinoma at an early stage. There was 1 pancreatic leak that was treated medically. After a mean follow-up of 33 months (9–108), 1 patient died of rectal cancer, there was no case of jejunal polyposis and the operation did not affect the bowel function. In FAP, stage IV duodenal polyposis seems to carry a high risk of malignant change. Surgical polypectomy failed to guarantee a polyp-free duodenum and carried a risk of post-operative complications. Duodenopancreatectomy had a low morbidity, revealed cancers at early stages and did not affect bowel function. In colectomized FAP patients, duodenopancreatectomy should be offered in some selected cases of stage IV duodenal polyposis. Oncology, general: Screening, prevention Oncology, specific: Small bowel } "Surgical Treatment of Duodenal Adenomas in Familial Adenomatous Polyposis"

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"P P 41 0928" P 41 0928 **Role of Surgery in Localized Primary Gastric Lymphoma (PGL): Long Term Results of a Prospective Multicenter Study of 45 Patients**

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Groupe d'Etude des Lymphomes Digestifs, Fondation Française de Cancérologie Digestive, France

**Aim:** The role of surgery in the treatment of PGL is still controversial and must be discussed according to the grade of malignancy and the chemosensitivity. Most series are retrospective and mix both high-grade (HG) and low-grade (LG) lymphomas. We aimed to study prospectively a therapeutic strategy based on surgical tumour reduction followed by chemotherapy (CT) adapted to the histological subtype and the radicality of the resection in localized PGL.

**Patients and Methods:** As part of the multicenter study of the French cooperative group collecting gastrointestinal tract lymphomas, localized PGL, either HG (large cells) or LG (small cells), were studied. Primary surgical resection was recommended whenever possible for HG and when reasonable for LG. At this time, total gastrectomy was not systematically mandatory. Surgery was followed, or, when not performed replaced by CT: COP regimen in LG and AVmCP after radical (R) resection or M-BACOP after non radical (NR) resection in HG.

**Results:** From 1984 to 1990, among 54 PGL, we enrolled 45 localized PGL: M/F = 27/18; median age 54.2 yrs; 18 LG and 27 HG; stages I<sub>E</sub>, (n = 30) and II<sub>E</sub>, (n = 15). The median interval between the first symptom and diagnosis was 4.6 mos. Endoscopic biopsies permitted final diagnosis in 78% of cases. Diagnosis was made at emergency laparotomy in 2 patients (pts). There were no differences between the 2 grades of malignancy concerning: site, size, depth of wall invasion, and nodal involvement. Primary laparotomy was undertaken in 40 pts (13LG, 27HG). Thirty five had tumour resection (11LG, 24 HG) either R (4LG, 19HG) or NR (7LG, 5HG). Exclusive CT was given to 10 pts (7LG, 3HG). One anastomotic leak and one jejunal perforation were observed during M-BACOP after NR surgery. The median follow-up was 7 yrs. Among 18 LG, 6 pts did not achieve complete remission (CR) after initial treatment (5 exclusive COP, 1 NR resection). For these pts, CR was achieved after secondary R resection (3), or radiotherapy (2), and second-line CT (1). Among the 12 LG who achieved CR after initial treatment, we observed 1 locoregional relapse (initially NR) after 9.7 yrs and 1 unrelated death. Thus, 16 pts (89%) with LG are alive free of disease (of whom 2 exclusive COP, 6 R, 2 radiotherapy). In HG, 24 pts (89%) achieved CR after initial treatment and 3 pts undergoing laparotomy without resection died within 10 mos despite CT. The overall 5-yr survival (product-limit method) was 91.1% for all pts, 94.1% for LG, and 89% for HG. R resection was associated with better survival rate either in the whole population (p = 0.04) or in HG (100% when R, p = 0.01).

**Conclusion:** In localized PGL, initial CR and long term disease-free survival were obtained each time primary or secondary radical surgery were performed in association with CT. Compared to surgery, the roles of radiotherapy in LG or exclusive CT in HG should be evaluated in larger randomized trials.

Oncology, specific: Stomach  
Oncology, specific: Lymphoma }

"Role of Surgery in Localized Primary Gastric Lymphoma (PGL): Long Term Results of a Prospective Multicenter Study of 45 Patients"

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"P P 41 0929" P 41 0929 **Blood Gastrin Level, Stomach Stump Acid-Forming and Evacuatory Functions in Patients with Postgastroresectional Disease (PGRD): Aspects of Pathogenesis**

\*O.O. Abrahamovych, M.P. Pavlovsky, E.S. Abrahamovych, M.O. Abrahamovych

Medical Institute, Lviv, Ukraine The aim of the investigation was to study blood gastrin level, stomach stump acid-forming function (SSAFF) and evacuatory function (EF) of esophagogastrointestinal system (EGIS) and their role in PGRD pathogenesis in long terms (5–33 years) after gastric resection. The study included 241 patients (pts) with PGRD: 91.2% men, 8.8% women; age from 28 to 73 years; 29.4% after Billroth-I, 70.6% – Billroth-II; 17.6% – resection of 1/2, 73.5% – 2/3, 8.8% – 3/4 stomach. Radioimmunologic study of basal blood gastrin concentration, intragastral pH-metry of stomach stump, radiographic and radionuclide evacuatory esophagogastrointestinalography (RNEGIG) were performed to all the pts. The results show that in 77.3% pts basal free HCL was absent; normochlorhydric – in 9.7%. The acid-forming function after submaximal histamine stimulation was characterized by absence of free HCL in 33% pts and hyperchlorhydric in 16.4% pts. The correlation between SSAFF and gastrin level was weak ( $r = 0.27$ ). Before stimulation achlorhydric was evident in the majority of cases and didn't depend on basal gastrin level; after stimulation the pts with normal HCL-diminished. 55.0% pts with hypergastrinemia were with hyper – (15%) or normochlorhydric (40%), only 10% – with achlorhydric. Hyperchlorhydric was established in 14.3% pts with normal gastrin level, achlorhydric – in 38.1%. 16.2% pts with low gastrin had high HCL concentration. Complicated mechanisms of SSAFF disorders can be connected with disorders of parietal cells function, second-rate messengers, especially  $Ca^{2+}$  and Ca-poliphosphoinosid system, ensuring gastrin action through alfa-adrenoreceptors. Evacuatory function of EGIS was significantly accelerated ( $p < 0.001$ ): the time of evacuation beginning 1.9 – 0.5 min, the duration of half-evacuation 27.4 – 4.3 min, overall evacuation 62.0 – 6.3 min. Gastroesophageal reflux was diagnosed in 79.4% pts, duodeno (jejuno) gastral reflux – in 97.1%, duodenostasis – in 76.5% pts. The results showed also that RNEGIG hasn't advantages in comparison with radiographic method in study of evacuation from stomach stump. Nevertheless, it was much more useful to reveal refluxes and duodenostasis. *Conclusions:* The established changes indicate the importance of gastrin metabolism, stomach stump acid-formation and evacuatory function disorders in the pathogenesis of postgastroresectional disease, which must be taken into account in diagnostics, evaluation treatment results by secretory and evacuatory regulating drugs, and prognosis. Hormones and receptors: Clinical disorders Oesophageal gastric duodenal disorders: GD disorders, acid peptic Motility, specific: Stomach } "Blood Gastrin Level, Stomach Stump Acid-Forming and Evacuatory Functions in Patients with Postgastroresectional Disease (PGRD): Aspects of Pathogenesis"

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"P P 41 0930" P 41 0930 **Prevalence of H. Pylori Infection in Subtotal Gastrectomy and Vagotomy**

\*M. Tuncer, C. Uras, A. Dobrucali, I. Yurdakul, F. Hamsioglu, A. \c7elik, S. Tuncer, N. Bagatur, E. Oktay

Gastroenterology Department of Cerrahpasa Medical Faculty of Istanbul University, Istanbul, Turkey *Purpose:* We investigated the prevalence of H. pylori infection in patients with gastrectomy plus piloroplasty, for the treatment of peptic ulcer disease. *Methods:* Fifty-five patients age: 48–72, mean: 60 yrs; 90% male) with subtotal gastrectomy and vagotomy were investigated: Billroth I (n = 32), Billroth II (n = 12) and vagotomy plus piloroplasty (n = 11). At endoscopy biopsy specimens were taken from fundus and both sides of anastomosis (H&E stain, Gram stain and culture). *Results:* The percentage of H. pylori infection was 48% in patients with Billroth I; Billroth II: 42%; and vagotomy + piloroplasty: 92%, No differences were found between both reconstruction procedures. However, differences ( $p < 0.01$ ) were obtained when comparing percentages of H. pylori infection between subtotal gastrectomy and vagotomy. In gastrectomized infected patients, H. pylori was detected in 76% of cases at gastric fundus, and in 96% of biopsies from the anastomotic region ( $p < 0.05$ ). *In Conclusion:* The prevalence of H. pylori infection was low (44%) in patients with subtotal gastrectomy and no differences were observed between both reconstruction procedures. H. pylori infection after vagotomy plus piloroplasty was significantly higher (92%). In gastrectomized infected patients, H. pylori was detected with a higher frequency at anastomotic region, than in biopsies obtained from the gastric fundus. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Prevalence of H. Pylori Infection in Subtotal Gastrectomy and Vagotomy"

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"P P 41 0931" P 41 0931 **Catecholamines in Gastric Juice and Tissues before and after Vagotomy**

\*A.V. Shaposhnikov, K.M. Islam, Y.S. Sidorenko

Rostov Research Oncology Institute, Rostov-on-Don, Russia The purpose of the study was to reveal influence of vagotomy on local concentration of catecholamines in gastric tissues and in nonstimulated basal juice. *Methods.* The levels of epinephrine (E), norepinephrine (NE) dopa (DO) and dopamine (DE) were investigated in gastric juice of 10 patients with duodenal ulcer disease before and at 2nd, 14th and 30th days after combined posterior truncal with anterior seromuscular vagotomy by Taylor. The same substances were also investigated in gastric tissues of 50 white rats at 1st, 2nd, 7th and 14th days after the same operations. For identification of catecholamines were used spectrofluorometry method. The results of the study of patients gastric juice are given below (in ng/ml). Before After operation (days) 2 14 30 Epinephrine 0.39 +{ - } 0.1 +{ - } 0.2 +{ - } 0.3 +{ - } 0.03 0.03 0.02 0.09 Norepinephrine 2.5 +{ - } 1.5 +{ - } 1.8 +{ - } 1.9 +{ - } 0.05 0.02 0.02 0.02 Dopa 1.3 +{ - } 2.4 +{ - } 2.7 +{ - } 2.1 +{ - } 0.02 0.03 0.03 0.01 Dopamine 4.5 +{ - } 6.0 +{ - } 9.1 +{ - } 7.5 +{ - } 0.03 0.03 0.04 0.05 Concentrations of E and NE decreased by 0.8–3.9 times, especially at 2nd and 14th day after operation. On the contrary, levels of DO and DE were increased. The same pic-pure was revealed in gastric tissues of experimental rats. *Conclusion:* Vagotomy leads to activation of sympathetic nerve system with local liberation of catecholamines in gastric tissues and then into gastric juice. Low levels of E and NE may be explained by negative feedback mechanism of their production. These changes may influence at gastric motility and regional hemodynamics after vagotomy. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Hormones and receptors: Clinical disorders }" "Catecholamines in Gastric Juice and Tissues before and after Vagotomy"

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"P P 41 0932" P 41 0932 **Systemic Vascular Changes in Early Dumping Syndrome**

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<sup>2</sup> Dept. of Nephrology, University Hospital Leiden, The Netherlands Early dumping after gastric surgery has been attributed to systemic hypovolemia caused by redistribution of blood into the splanchnic vascular bed. The somatostatin analogue octreotide effectively prevents the occurrence of dumping symptoms. We have explored the systemic hemodynamic changes in early dumping that occur after provocation with glucose. Six patients with proven early dumping (partial gastrectomy n = 6, age 31–75 yr) 6 patients after gastric surgery (partial gastrectomy n = 6, age 35–70 yr) without dumping (disease-controls) and 6 healthy volunteers (n = 6, age 25–64 yr) were studied on two separate occasions. After an overnight fast 50 g glucose was given orally 15 min after s.c. administration of 25 µg octreotide or placebo in random order. Heart rate (HR) was measured and mean arterial blood pressure (MAP) was monitored by Dynamap; forearm blood flow (FBF) and forearm vascular resistance (FVR) were measured with plethysmography. Results are presented as peak increments after glucose provocation relative to basal values (\* p < 0.05). Dumping Disease controls Healthy controls { D } HR (bpm) 17 – 4\* 1 – 2 { - } 3 – 2 FBF (%) 141 – 19\* 107 – 14 90 – 14 FVR (%) 75 – 8\* 85 – 11 107 – 17 Baseline MAP was 92 – 7, 91 – 4 and 82 – 2 mmHg resp.; MAP after glucose provocation was 89 – 5, 86 – 2 and 79 – 2 mmHg resp. Octreotide prevented the increases in HR and FBF and decrease in FVR after dumping provocation. After glucose provocation patients with early dumping showed increases in HR and FBF, however without a drop in blood pressure, indicating acute peripheral vasodilatation. *Conclusions:* In patients with early dumping a glucose challenge does not induce a hypovolemic state as assumed previously but causes a peripheral vasodilatation and hyperdynamic state. Octreotide completely prevents these changes. Intestinal disorders: Splanchnic circulation, ischemia Nutrition: Nutrients and gut function Intestinal disorders, absorption: Pathophysiology of diarrhea } "Systemic Vascular Changes in Early Dumping Syndrome"

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"P P 42 0933" P 42 0933 **Lactulose/Mannitol (L/M) Test: Clinical Usefulness in Crohn's Disease (CD) Patients**

\*V. Di Leo, R. D'Inc\`e0, C. Venturi, M. Minotto, A. Ferronato, G.C. Sturniolo

Division of Gastroenterology, University of Padua, Italy We studied intestinal permeability in 181 CD patients (78 female, mean age 42 years, range 15–72), 52 with ileal disease and 54 with colonic disease, in order to determine its clinical significance. In each patient L/M test, CDAI and acute phase reactive proteins (APRP: ESR, RCP and acid-alpha1 glycoprotein) were evaluated. L/M test was considered positive when  $> 0.030$ , clinical remission when CDAI  $< 150$  and inflammatory activity (IA) present when 2 of the 3 APRP were above the normal value. CD patients underwent 450 evaluations: clinical remission was found in 340 occasions, while CDAI  $> 150$  was found in 110. IA was present in 73% of the occasions of clinical activity. L/M test was positive in 72% of active ileal or ileocolonic disease and in 37% of active colonic CD, with a 63% overall concordance of positive L/M test and CDAI  $> 150$ . Sensitivity, specificity, PPV and NPV of L/M test and IA with respect to CDAI are as follows: L/M test IA Sensitivity 62% 72% Specificity 78% 87% PPV 49% 64% NPV 87% 87% No statistical significant difference was found between the two parameters. L/M test together with IA increased sensitivity to 85% and NPV to 94%. In our study, L/M test performed as IA in defining clinical activity. It may improve the evaluation of the clinical status of CD patients and could be proposed as an useful adjunctive and/or alternative to biochemical parameters, being less invasive and expensive. Intestinal disorders: IBD diagnosis, monitoring } "Lactulose/Mannitol (L/M) Test: Clinical Usefulness in Crohn's Disease (CD) Patients"

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"P P 42 0934" P 42 0934 **Assessment of Clinical Disease Activity in Crohn's Disease Patients with Ileostomy** S. Acciuffi,

\*S. Ghosh, A. Ferguson

Gastrointestinal Unit, Department of Medicine, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU, Scotland *Purpose:* Assessment of clinical disease activity is difficult in patients with Crohn's disease (CD) and ileostomy. The CDAI has not been validated in such patients and generally these patients are excluded from therapeutic trials of new drugs. In CD patients without ileostomy, whole gut lavage fluid (WGLF) IgG concentration correlates very well with CDAI. Other markers of gut protein loss such as WGLF albumin and  $\alpha_1$ -antitrypsin also correlate with CDAI. We therefore aimed to perform a prospective study in CD patients with ileostomy, comparing a modified CDAI with WGLF IgG, albumin and  $\alpha_1$ -antitrypsin concentrations. *Methods:* 10 patients with Crohn's disease and ileostomy were recruited. Their symptoms comprised of a combination of increased stomal output, abdominal pain, and tiredness. They prospectively filled in a CDAI diary card for 7 days prior to having a whole gut lavage with a polyethylene-glycol electrolyte solution (Klean-Prep, Norgine UK). In their CDAI diary, the patients recorded the number of times they emptied their bags, instead of the number of loose motions. The clear fluid obtained after complete gut cleansing was collected, filtered, processed by the addition of protease inhibitors and stored at  $-70^{\circ}\text{C}$ . IgG was assayed by an ELISA, and albumin and  $\alpha_1$ -antitrypsin by immunoturbidimetric assay. *Results:* The CDAI in the 10 patients ranged from 67 to 468. Seven patients had CDAI  $> 150$ . WGLF IgG ranged from 0 to 40  $\mu\text{g/mL}$ . There was no correlation between the modified CDAI and WGLF IgG concentrations ( $r = 0.06$ ;  $p = \text{NS}$ ). Similarly, WGLF albumin ( $r = -0.15$ ;  $p = \text{NS}$ ) and  $\alpha_1$ -antitrypsin ( $r = 0.37$ ;  $p = \text{NS}$ ) did not correlate with the modified CDAI. An experienced physician's global assessment and decision as to active or inactive disease corresponded to WGLF IgG concentration (and generally to albumin and  $\alpha_1$ -antitrypsin concentrations) but not to modified CDAI. *Conclusion:* A modified CDAI is not a valid instrument in assessing clinical disease activity in patients with CD and ileostomy. Objective markers of mucosal inflammation using the technique of WGLF may be useful in these patients. Intestinal disorders: IBD diagnosis, monitoring } "Assessment of Clinical Disease Activity in Crohn's Disease Patients with Ileostomy"

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"P P 42 0935" P 42 0935 **Cyclosporine Therapy and Fistula Closure in Crohns Disease**

\*J. O'Neill, S. Pathmakanthan, J. Goh, S. Costello, P. MacMathuna, R. O'Connell, J. Crowe, J. Lennon

Gastrointestinal Unit, Mater Hospital, Dublin, Ireland Use of Cyclosporine A (CyA) has been proposed in Fistulous Crohns disease but its efficacy is unclear. We report use of CyA in 8 patients with active fistulous Crohns disease who had failed standard therapy. The 8 patients (1 M 7 F) with a mean age of 29 (range 24–45) had a total of 10 fistulas (5 perianal, 2 rectovaginal, 1 enterocutaneous, 1 enterovaginal and 1 enterocolic). All patients continued maintenance medical therapy of salicylates, azathioprine and oral steroids which were not altered during treatment period. Intravenous CyA was commenced at a dose of 4 mg/kg/day for up to 10 days. 7 patients were subsequently maintained on oral CyA commencing at a dose of 8 mg/kg/day with doses adjusted to reach trough levels of 150 ng/ml. Oral therapy was continued for a mean 12 weeks (range 4–32) with serum CyA and renal indices monitored weekly. Of the 8 patients, 7 showed an initial response after a mean of 4 days as defined by improvement of Crohns Disease Activity Index (median decrease 48, 7/7 < 150); symptomatic improvement evidenced by decreased discharge from fistula, decrease in perifistular inflammation and improvement in patient comfort. One patient required immediate fistulotomy after no response to intravenous CyA was observed. Two patients (25%) had a sustained response while on oral CyA, one of whom has maintained a partial response after discontinuing CyA for 6 months. Fistulotomy was delayed in 5/8 patients and performed electively after a mean 5.2 months (range 2–24). Follow up (mean 8 months) in these patients has shown no recurrence. Mild side effects were observed in 4 patients including diarrhoea (1), nausea and vomiting (1) and hirsutism (2). No renal impairment was noted and no patient was withdrawn from therapy due to side effects. Temporary remission of fistula activity through CyA therapy allows for subsequent elective fistulotomy in more favourable conditions. Clinical practice: Management strategy Intestinal disorders: IBD, therapy } "Cyclosporine Therapy and Fistula Closure in Crohns Disease"

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"P P 42 0936" P 42 0936 **CDAI is Inadequate for Diagnosis of Post-Operative Recurrence of Crohn's Disease**. R. Caprilli, A. Viscido,

\*G. Taddei, G. Corrao, P. Torchio

University of L'Aquila, L'Aquila, Italy

Gruppo Italiano per lo Studio del Colon e del Retto (GISC)\*It is commonly accepted that the most accurate diagnosis of post-operative recurrence is obtained by endoscopy or barium meal. The availability of laboratory parameters or clinical indexes would be of great value for this purpose. Aim of this study was therefore to assess the ability of CDAI score and some laboratory parameters to detect recurrence. The study was performed in 110 pts who entered the Italian multicentre randomised controlled trial on the effectiveness of 5-ASA in the prevention of post-operative endoscopic recurrence (R. Caprilli and GISC. *Aliment Pharmacol Ther* 1994; 8: 35–43). ESR, Hb, Ht, RBC, WBC, iron, proteins, albumin, and CDAI score were assessed at 6, 12, 24, and 36 months after surgery. At the same intervals colon-ileoscopy was performed in all pts. The association between these variables and the presence of recurrence, diagnosed by colon-ileoscopy was analysed. The mean value of each laboratory variable and CDAI was compared in the two groups of pts, those with and those without recurrence. *Results:* None of the laboratory parameters was significantly different between the two groups. The mean value of CDAI score tended to be higher in pts with endoscopic recurrence compared to those without recurrence, but the difference was significant only at six months of follow-up: 119 – 98 (SD) and 75 – 62 respectively ( $t = 2.66$ ;  $p < 0.05$ ) although remaining in the normal range. In order to achieve a better evaluation of CDAI ability to discriminate between the two groups of pts, it was performed the ROC (Receiver Operating Characteristic) analysis, that plots the conjunctive behaviour of sensibility and specificity for each possible cut-off of CDAI score. The area under ROC curve is considered as the best index of discriminant capacity of the test (area under curve = 1.00 indicates a perfect discriminatory capacity of the test). The area under ROC curve was 0.65, indicating that CDAI is capable to discriminate pts with and without recurrence only in 65% of the cases. Considering a cut-off value of the CDAI as 150, this figure corresponds to 89% specificity and 30% sensitivity. *In conclusion* the results of this study indicate that CDAI and routine laboratory features are not of practical value in predicting recurrence. The low sensitivity of CDAI is due to the fact that about 50% of the recurrences are asymptomatic in the first years following surgery. Colonoscopy remains the best method to diagnose post-operative recurrence of CD. Results of clinical trials based on CDAI to assess post-operative recurrence should be reconsidered.\* G. Latella, G. Frieri, P. Vernia, (L'Aquila); A. Tragnone (Bologna); G. D'Albasio G. Salvadori, I. Paladini, F. Ficari, G. Vannozzi (Firenze); D. Valpiani (Forlì); G.P. Rigo, M. Mastronardi, P.L. Codeluppi (Modena); G.C. Sturniolo, R. D'Incà (Padova); F. Pallone, L. Capurso, A. Andreoli, A. Gioieni, R. Lorenzetti, A. Ciaco, C. Papi, M. Luminari (Roma); F.P. Rossini, V. Ponti, A. Bertone (Torino). Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy } "CDAI is Inadequate for Diagnosis of Post-Operative Recurrence of Crohn's Disease"

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"P P 42 0937" P 42 0937 **Role of Ultrasound in the Detection of Post-Operative Recurrence of Crohn's Disease (CD)** S. Greco, R. Sostegni,

\*G. Rocca, R. Pellicano, A. Musso, M. Astegiano, M.T. Fiorentini<sup>1</sup>, M. Rizzetto, T. Cammarota<sup>2</sup>, A. Pera<sup>1</sup>

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<sup>1</sup> Divisione di Gastroenterologia, Ospedale Mauriziano, Torino, Italia

<sup>2</sup> Servizio di Radiologia, Ospedale S Lazzaro, Torino, Italia *Purpose* Ultrasound scanning (US) is a non-invasive method for the diagnosis and for monitoring the effects of therapy in CD. Aim of the study is to evaluate the overall accuracy of US versus clinical data, laboratory, radiology, endoscopy and surgical specimen in the detection of post-operative recurrence. *Patients and Methods* Starting from 1986, 208 US were performed in the follow-up of 92 patients operated because of Crohn's disease complications. US was made at six months and then once a year after surgery or when clinically indicated. Clinical recurrence was defined following commonly accepted criteria. Surgical recurrence was confirmed by the specimen available for patients re-operated during the follow-up. Ultrasound recurrence was defined by the presence of 1) bowel thickening (more than 5 mm) with or without 2) bowel stenosis 3) bowel dilatation. *Results* Accuracy of ultrasound Examinations Accuracy % US+ only % US{ - } % versus Laboratory recurrence 206 46 67 3.4 Clinical recurrence 208 63 69 4.3 Colonoscopy 62 81 14.5 4.8 Radiology 54 93 3.7 3.7 Re-operation 22 100 0 *Accuracy*: agreement between US and any of the other methods. *US + only*: percentage of recurrence detected by US and not by the compared method. *US { - }*: percentage of recurrence seen by one of the other methods but not by US. *Discussion* US scanning is more sensitive than any other method in detecting post-operative recurrence in operated Crohn's disease. Given the low sensitivity of laboratory and clinical data US is a promising non-invasive and convenient method for detecting recurrence in the post-operative follow-up of these patients. Intestinal disorders: IBD diagnosis, monitoring } "Role of Ultrasound in the Detection of Post-Operative Recurrence of Crohn's Disease (CD)"

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## P P 42 0938" P 42 0938 Association Studies in Crohns Disease: Approaches in Choosing the Right Design

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<sup>2</sup> Institute of Medical Genetics, Charit'e9 Medical School, 10098 Berlin/Germany *Purpose:* As the genetic basis of IBD is being uncovered, association studies are playing an important role in the fine mapping especially of minor risk loci. Accurate predictions of sensitivity and specificity of specific designs are of pivotal importance for the later interpretation of data. However, the theoretical basis of these studies in polygenic disorders is still incompletely understood. In order to provide guidelines for a robust and sensitive design, the properties of different strategies were evaluated using a computer simulation. *Methods:* We developed a computer program "popsim" (C programming language), which allows for the simulation of genetic transmission in populations up to 3 million individuals under a polygenic model (prevalence: 0.05%,  $\{1\}_s = 20$ ). Non-overlapping generations and random mating were assumed. The population is propagated according to Mendelian laws, no further theoretical assumptions are made. *Results:* Estimates on the persistence of initial associations originating from founder populations were obtained as a function of the recombination fraction  $\{Q\}$ . Only tightly linked markers were found to become fixed on rare disease alleles and thus could persist over several hundred generations. In the presence of population heterogeneity, case-control studies were found to be susceptible to false positive results, whereas parental control designs performed well under these conditions, although at a slightly lower sensitivity. *Conclusion: Choice of markers:* Only markers tightly linked to suspected risk genes, e. g. intragenic polymorphisms, should be considered for association studies ( $\{Q\} \ll 0.5$  cM). *Choice of study design:* Unless the sample can be shown to be homogenous, only a parental control design should be chosen and evaluated by one of the appropriate tests (TDT: "transmission-disequilibrium-test", or HRR: "haplotype relative risk") Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } " Association Studies in Crohns Disease: Approaches in Choosing the Right Design"

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## "P P 42 0940" P 42 0940 Impressive Histologic Improvement after TNF Antibody (cA2) Therapy in Active Crohn's Disease

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Dep of Gastroenterology, University of Leuven, Belgium

<sup>1</sup> Dep of Pathology, University of Leuven, Belgium TNF- $\alpha$  is an important mediator of inflammation in Crohn's disease (CD). We studied the histologic effects of cA2 therapy in a detailed and systematic way. Biopsies of 13 patients with active CD before and 4 weeks after a single placebo or cA2 infusion (5, 10 or 20 mg/kg) were reviewed by one blinded pathologist. A minimum of six biopsies were taken per patient at every occasion in the most inflamed areas. If ulcers were present, biopsies were taken in the vicinity. Seven pts had colitis, four ileocolitis and two ileitis only. Assessment of the severity of inflammation was based on epithelial alterations (architecture and cytology), inflammatory changes (granulocyte, lymphocyte and plasma cell infiltration), the presence of ulcerations and/or granulomas and the number of biopsies affected. A score from 0–3 was given for each item according to severity. The minimal score was 0, the maximum score 16. In addition to classical H&E, immunohistochemical stainings for HLA-Dr, CD68 (activated macrophages), ICAM-1 and LFA-1 were performed using an indirect immunoperoxidase method. *Results:* The mean total activity score in the cA2 treated group dropped from 6.7 (2–12) to 3.0 (0–7) in ileitis and from 7.6 (2–12) to 3.0 (0–8) in colitis compared to 11 (10–12) before and 9 (6–12) after in placebo pts. The changes in the inflammatory components of the score were most pronounced. The enhanced epithelial HLA-Dr and endothelial ICAM-1 and numbers of CD68+ monocytes and LFA-1+ lymphocytes observed at week 0 markedly decreased along with the classic components of inflammation in CD pts treated with cA2 but not in the placebo group. *Conclusion:* Monoclonal TNF- $\alpha$  antibody therapy markedly improves histologic disease activity in active Crohn's ileitis and colitis. The improvement is mainly due to a dramatic decrease of the inflammatory infiltrate parallel to a reduction of HLA-Dr expression and the number of CD68+ and LFA1+ cells, whereas the architectural changes grossly remain unchanged 4 weeks after treatment. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Impressive Histologic Improvement after TNF Antibody (cA2) Therapy in Active Crohn's Disease"

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"P P 42 0941" P 42 0941 **Suppression of Bone Formation by Methylprednisolone But Not by Budesonide CIR in Active Ileocolonic Crohn's Disease**

\*G. D'Haens, A. Verstraete, F. Baert, M. Peeters, R. Bouillon, P. Rutgeerts

Depts of Gastroenterology and Endocrinology, University of Leuven, Belgium One of the most severe long-term side effects from prolonged corticosteroid use is osteopenia with an increased fracture risk. Bone formation can be assessed by *osteocalcin*, a noncollagenous protein synthesized by osteoblasts, while bone resorption can be measured with urinary (deoxy)pyridinolines (collagen cross-links). *Aim:* to compare the effect of conventional oral glucocorticosteroids and oral Budesonide CIR (Entocort<sup>®</sup>, Astra) on bone metabolism in active ileocolonic Crohn's disease (CD). *Methods:* 29 pts with active CD (CDAI > 200) were randomly treated with either methylprednisolone (MP) 32 mg/day PO for 3 weeks and then tapered by 4 mg/week (total 10 weeks) (13/29 pts), or budesonide CIR (BU) 9 mg/day PO for 10 weeks (16/29). Six pts with quiescent CD on 5-ASA were used as controls. We measured serum calcium (Ca), phosphorus (P), alkaline phosphatase (AP), osteocalcin (OC) levels and urinary (deoxy)pyridinolines before the start and at week 4 and 10 of therapy. *Results:* Neither in the MP group (n = 13, 5 M/8 F, age 39.5 – 3.3 yrs), nor in the BU group (n = 16, 4 M/12 F, age 39.3 – 3.4 yrs), any changes in serum Ca, P or AP were observed. OC, however, decreased from 50.8 – 22.1 ng/ml at w0 to 20.0 – 1.8 ng/ml at w4 (p = 0.05) and 18.1 – 1.9 ng/ml at w10 (p = 0.05) in the MP group versus from 32.0 – 23.9 ng/ml at w0 to 29.6 – 4.9 ng/ml at w4 and 37.0 – 5.4 ng/ml at w10 (NS) in the BU group. OC in the control group (n = 6, 1 M/5 F, age 36.2 – 4.5 yrs) was comparable to w0 in the MP group and w0, w4 and w10 in the BU group. Urinary (deoxy)pyridinolines remained unchanged in all groups throughout the trial. *Conclusions:* Osteoblast function is suppressed with conventional steroids but not with budesonide CIR, while bone resorption appears unaffected. Topical steroids are probably safer for long-term use with regard to bone metabolism. Intestinal disorders: IBD, therapy Clinical practice: Management strategy Nutrition: Metabolism } "Suppression of Bone Formation by Methylprednisolone But Not by Budesonide CIR in Active Ileocolonic Crohn's Disease"

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"P P 42 0942" P 42 0942 **Colorectal Cancer in Colonic Crohn's Disease — High Frequency of DNA-Aneuploidy**

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University Hospital, Leuven, Belgium *Aim:* The risk for colorectal cancer (CRC) in colonic Crohn's disease (CD) seems to be of the same magnitude as in extensive, longstanding ulcerative colitis (UC) and colonoscopic surveillance has been advocated. Mucosal dysplasia and DNA-aneuploidy are early warning markers of malignant transformation in UC. Data are scarce concerning the occurrence of such premalignant lesions in colonic CD. This study aimed at investigating the DNA ploidy pattern in CD-patients with manifest CRC. *Methods:* Biopsies and surgical specimens from patients with colonic or ileocolonic CD who presented with CRC between 1988 and 1995, were scrutinized histologically and analysed by flow cytometry (FCM) for assessment of DNA-ploidy pattern. CRC type, site and presence of distant mucosal dysplasia/DNA-aneuploidy was determined as were patient characteristics. *Results:* 17 CRC:s in 14 patients (7 men) were analysed. Median age at diagnosis of CRC was 55 years (range 21–70) and median duration of CD was 11 years (1–45). 11 (65%) of the cancers were found proximal to the splenic flexure. DNA-aneuploidy was found in 13/17 (76%) of the cancers. Concomitant dysplasia/DNA-aneuploidy was found in 5/14 patients and preceded the finding of CRC in 3/3 patients having been subjected to prior colonoscopic surveillance. *Conclusion:* A right-side predominance of CRC in longstanding ileocolonic/colonic CD was found, and DNA-aneuploidy was a common feature. Since the findings of DNA-aneuploidy may precede the development of invasive carcinoma, inclusion of FCM analyses of colorectal biopsies may therefore be a valuable complement to assessment of dysplasia in trying to identify high-risk CD-patients prone to develop CRC within the frame of colonoscopic surveillance programs. Intestinal disorders: IBD diagnosis, monitoring Oncology, specific: Colon, rectum Oncology, general: Screening, prevention } "Colorectal Cancer in Colonic Crohn's Disease / High Frequency of DNA-Aneuploidy"

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## "P P 42 0943" P 42 0943 Use of Heparin in the Treatment of Chronically Active Crohn's Disease

\*J.L. Dupas, F. Brazier, T. Yzet, J.C. Duchmann, B. Roussel, F. Iglicki

Department of Gastroenterology, University Hospital, Amiens, France It has been suggested that the combination of hypercoagulable state and vasculitis may contribute to the pathogenesis of Crohn's disease (CD). Heparin, acting by its anticoagulant and immunodulatory properties, may be effective in the treatment of active inflammatory bowel diseases. *Aim:* To evaluate effects of heparin in the treatment of patients with chronically active CD who failed to respond to corticosteroid and azathioprine. *Methods:* 10 patients (6 F, 4 M; mean age 30 yrs; range 16–66) with chronically active Crohn's disease (CDAI > 200) were included in this open label study. Disease was confined to the colon in 4 patients and extended to colon and ileum in 6 patients. All patients were treated with either prednisolone 20–50 mg/d (n = 7), or prednisolone 25–35 mg/d plus azathioprine 1–2 mg/kg/d (n = 3). Doses of previous treatments were unchanged in the 3-weeks period before and during heparin therapy. Patients were administered heparin, either intravenously 3000 UI/4 hrs for 1 week then subcutaneously 2500 UI/10 kg bid for the following 1 to 3 weeks (n = 4), or subcutaneously 2500 UI/10 kg bid for 1 to 4 weeks (n = 6). All patients were clinically and biologically evaluated every week during the study then every 2 weeks after the end of heparin treatment. *Results:* Mean duration of heparin treatment was 21 days (7–28). 6/10 (60%) patients fulfilled remission criteria (CDAI < 150) and 1 patient reported significant clinical improvement (CDAI > 100) within 2 to 4 weeks; 3 patients failed to respond. The mean CDAI decreased from 304 (95% CI 239–369) before to 161 (95% CI 89–234) (p < 0.05) after heparin treatment. The mean C-reactive protein decreased from 82 mg/l (95% CI 38–125) before to 43 mg/l (95% CI 14–73) (p < 0.05) at the end of heparin treatment. After discontinuation of heparin, prednisolone tapering was resumed in 5/7 responders. All of these patients were still in remission after 3 months follow up. *Conclusions:* These results suggest that heparin may be useful in the treatment of patients with chronically active Crohn's disease who failed to respond to conventional treatments. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Use of Heparin in the Treatment of Chronically Active Crohn's Disease"

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"P P 42 0944" P 42 0944 **Crohn's Colitis in Stockholm County**

\*A. Lapidus, O. Bernell, G. Hellers, G. L'f6fberg

Department of Medical and Surgical Gastroenterology and Hepatology, Huddinge University Hospital, Sweden *Background:* The annual incidence of Crohn's disease (CD) in Stockholm County increased from  $1.4/10^5$  in 1955–59 to  $4.6/10^5$  as mean 1970–89. The proportion of colonic disease doubled during the study period from 14% to 32% as mean 1980–89. *Aims:* To describe the natural history of Crohn's colitis over time with regard to incidence, extent at diagnosis, initial treatment, age and gender. *Material and Methods:* Retrospectively, registers for in- and outpatients were investigated for possible cases of CD according to Lennard-Jones' criteria. All patients who got the diagnosis of Crohn's colitis in 1955–89 and were residents in Stockholm County at time for diagnosis were included into the study. Data for extent of colitis at diagnosis, initial treatment, clinical course within the first year of diagnosis and time for surgery were registered. *Results:* 512 cases of Crohn's colitis were included into the study. The annual incidence of colitis increased from 0.2 in 1955–59 to 1.6 in 1985–89 with an increasing proportion of distal colonic disease during the latter study period (23% vs. 33%  $p < 0.05$ ). Clinical remission was achieved within one year after diagnosis in 75% of the cases. 78% had at least one relapse. The risk for surgery within the first year of diagnosis decreased from 25% to 14% during the study period. The overall risk for surgery was 52%. The cumulative risk for surgery was higher among the patients with chronic continuous disease compared to those who achieved remission within the first year. Patients with distal colonic disease run a lower risk for surgery compared to the other patients. Except for a higher propensity for distal disease among those aged  $> 60$  years at diagnosis, there were no differences according to age or gender. *Conclusion:* While the incidence of Crohn's disease remained stable during the last 20 years, the incidence of Crohn's colitis (particularly distal disease) increased. Half of the patients with colitis required surgery with highest risk for those with chronic continuous disease and lowest risk for those with distal disease. *Clinical practice:* Epidemiology (non cancer) Intestinal disorders: IBD, basic } "Crohn's Colitis in Stockholm County"

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"P P 42 0945" P 42 0945 **Therapy of Refractory Crohn's Disease by 7S-Immunoglobulins** Ch. Schmidt

Medizinische Poliklinik, Bonn, Germany About 10 to 20% of patients with inflammatory bowel disease are resistant to usual drug therapy. As immunoregulatory disturbances play an important role in pathophysiology we tried to improve the situation in therapy-resistant cases of Crohn's Disease by additional intravenous application of 7S-immunoglobulins. In an open controlled trial 20 patients with therapy-resistant Crohn's Disease received 10 g 7S-immunoglobulin (Venimmun<sup>®</sup>) per day for 10 days. Mean duration of illness was 10.3 ± 1.4 years and 9 patients had one or more operations in the past. Mean CDAI was for more than 6 months higher than 200. Patients received prednisolone (16.4 ± 4.0 mg/die) and 5-ASA (2.2 ± 0.3 g/die). Before and after therapy CDAI, laboratory data and immunoglobulins were checked. Activity index (CDAI) decreased during therapy from 20.1 ± 17.7 to 9.9 ± 8.6 ( $p < 0.0001$ ). Frequency of diarrhoea was reduced from 4.5 ± 0.8 to 1.8 ± 0.3 ( $p < 0.001$ ). At the end of therapy CDAI was in all patients lower than 150. In 9 patients CDAI decreased by more than 100 points. Follow up was done in 11 patients up to 6 months. 73% of patients were in remission even after a period of 6 months. BSR increased during therapy from 27.9 ± 5.2 to 37.6 ± 7.8 mm/h ( $p < 0.03$ ). Leucocytes decreased and lymphocytes increased (13.3 ± 3.0 vs. 23.3 ± 2.8;  $p < 0.008$ ). Alpha-2-globulin decreased by 1.8% ( $p < 0.01$ ). IgG, IgG1, IgG2, IgG3, IgG4 and even IgA increased significantly during therapy ( $p < 0.001$ ). Flow cytometry of peripheral lymphocytes showed different results with increasing B-lymphocytes and decreasing CD4-cells. Additional therapy of refractory Crohn's Disease by 7S-immunoglobulins was effective in our study. Immunoregulatory effects seem to be responsible for successful immunoglobulin therapy in Crohn's Disease. However mechanisms of acting of immunoglobulins are not identified. Further investigations are necessary. Immunology and microbiology: Inflammation } "Therapy of Refractory Crohn's Disease by 7S-Immunoglobulins"

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"P P 42 0946" P 42 0946 **A Prospective Randomized Trial in Active Crohn's Disease Comparing Prednisolone, a Polymeric Diet and a Polymeric Diet Plus Prednisolone**

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Polymeric diets may be useful in active Crohn's disease but their effects in conjunction with steroids have not been adequately studied. In this prospective trial, 35 patients were randomized to receive intravenous prednisolone (0.75 mg/kg of body weight) (group I, N = 11), a polymeric diet [Nutrison High Energy, 1.5 l/day delivered via a nasoduodenal tube (group II, N = 11), or the previously described polymeric diet plus prednisolone (group III, N = 13). All patients received mesalazine (Salofalk 500 mg three times a day). The three treatment groups were similar with respect to sex, age, age at disease onset, anatomic site of disease, disease activity (Crohn's Disease Activity Index, CDAI), nutritional status, and previous medical or surgical treatments. Seven patients (two in groups II, III and three in group I) were undergoing the first attack of disease. Three patients had complicated disease (one in group I, two in group III). A satisfactory response to treatment was defined by a fall of CDAI by 100 points or below 150. After 4 weeks of treatment, there were 8 responders in group I (72.7%), 5 responders in group II (45.5%) and 10 responders (77%) in group III; differences were not significant. However, patients who received prednisolone (groups I and III) showed a better response than did patients who received only a polymeric diet whereas the combination therapy increased only marginally the effect of prednisolone. In addition, the time to response was significantly higher in patients receiving polymeric diet alone (18.9 – 3.5 days *versus* 5.9 – 2.1 days in group I and 5.2 – 1.5 days in group III,  $p < 0.01$ ). Polymeric diet did not increase body weight or other indices of nutritional status. Irrespective of treatment, all patients undergoing the first attack of disease were responders. Of the six failures in group II, 4 patients responded to prednisolone. Thus, polymeric diets should not be considered as a substitute for steroids at least in patients presenting with a relapse of Crohn's disease.

Intestinal disorders: IBD, therapy } "A Prospective Randomized Trial in Active Crohn's Disease Comparing Prednisolone, a Polymeric Diet and a Polymeric Diet Plus Prednisolone"

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"P P 42 0947" P 42 0947 **Restricted T Cell Receptor V $\beta$  Regions in Crohn's Disease Patients Suffering from Joint Complications**

\*N. Löffler, T. Kucharzik, W. Domschke, R. Stoll

Department of Medicine B, University of Münster, Münster, Germany Little is known about the mechanisms triggering both the development and perpetuation of extraintestinal complications in Crohn's disease (CD). The aim of the present study was to test the hypothesis that the T-cell immune response in CD patients with joint complications may be altered when comparing with patients without extraintestinal manifestations. We used a semiquantitative polymerase chain reaction assay to analyse the T-cell antigen receptor repertoire in peripheral blood T cells from eight CD patients suffering from peripheral arthritis and ankylosing spondylitis, twelve CD patients without extraintestinal manifestations, and from seven non-CD patients with ankylosing spondylitis showing typical changes on joint radiographs. Being concerned that different patterns may be seen in different phases of the inflammatory disease process, we have also taken care to analyse sequential samples at various time points of the disease. Expression of all 22 V $\beta$  genes was found in each healthy control and in each CD patient without extraintestinal manifestations and showed no major variation over time. Southern hybridization analysis of amplified products revealed a highly restricted V $\beta$  repertoire in all CD patients suffering from peripheral arthritis and ankylosing spondylitis. In contrast, non-CD-patients with ankylosing spondylitis without signs or symptoms of gastrointestinal problems demonstrated the presence of the entire V $\beta$ -repertoire. Our longitudinal studies confirmed variable V $\beta$  usage over time, as certain transcripts were found only in distinct temporal phases of disease. Our data are not directly suggestive of a common super-antigen model of CD, but instead emphasize a specific decrease in signals throughout the TCR V $\beta$  repertoire in CD patients suffering from joint complications. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Restricted T Cell Receptor V $\beta$  Regions in Crohn's Disease Patients Suffering from Joint Complications"

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"P P 42 0948" P 42 0948 **Effect of Mild Exercise on Ileal Crohn's Disease (CD) in Remission**

\*R. D'Inc'e0, C. Mestriner, M. Varnier, D. Martines, A. D'Odorico, M. Bortolami, M. Minotto, S. Pigozzo, G.C. Sturniolo

Division of Gastroenterology, University of Padua, Italy We investigate the possible noxious effects of mild exercise in CD patients in remission by examining gastrointestinal transit time and permeability, lipid peroxidation and inflammatory cells function. Six male CD pts were evaluated before and after exercise (1 hr at 60% VO<sub>2</sub> max), with lactulose breath test and lactulose/mannitol (L/M) test, malondialdehyde (MDA) levels, neutrophyl activity and IL-6 production. Seven healthy volunteers served as controls. Sugars were measured by spectrophotometry, MDA by fluorimetry and neutrophyl activity by chemiluminescence after PMA, fMLP and zymosan stimulations. Oro-caecal transit time and urinary L/M recovery were unchanged after exercise both in CD pts and in controls. MDA levels significantly increased in CD pts after exercise (1.77 – 0.4) with respect to baseline (1.62 – 0.4) ( $p < 0.05$ ). Respiratory burst activity of isolated neutrophyls was significantly increased after exercise in CD pts with fMLP (65 – 20.2) and zymosan (238.9 – 35.6) stimulations compared to controls (22.7 – 4.3 and 133.88 – 37.15 respectively,  $p < 0.05$ ) while PMA did not affect neutrophyl function in both groups. Exercise significantly decreased basal IL-6 production of isolated lymphocytes both in CD pts (2.7 – 3.5 vs 0.7 – 0.5) and controls (8.1 – 7.1 vs 2.7 – 4.2) while LPS response was similar in both groups. In conclusion, mild exercise may have detrimental effects in CD since it increases lipid peroxidation and turns on inflammatory cells while it does not seem to affect gastrointestinal transit time and permeability. Intestinal disorders: IBD diagnosis, monitoring }  
"Effect of Mild Exercise on Ileal Crohn's Disease (CD) in Remission"

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"P P 42 0949" P 42 0949 **Change from Ulcerative Colitis to Crohn's Disease: Two Features of the Same Disease?** M. Dinca, W. Fries, A. Cecchetto<sup>1</sup>, A. Martin

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<sup>1</sup> Istituto di Anatomia Patologica, Universit\`e0 di Padova, Italy Anecdotal reports have raised the possibility that a change from Ulcerative Colitis (UC) to Crohn's Disease (CD) or vice versa may occur during the course of IBD. Aim of this study was to assess the frequency of this change and the role of associated factors. *Methods:* we reviewed the files of 1114 patients with IBD who attended the outpatients clinics of our Institution from 1979 to 1995. We defined the clinical, endoscopic and histological criteria for an "unequivocal" diagnosis, in order to exclude cases in which the diagnosis was indeterminate at the time of first assessment. For a diagnosis of CD we used as endoscopic criteria the presence of aphthae, skip lesions and/or stenosis and histological criteria were the presence of follicles, granulomas and/or full thickness inflammation. *Results:* we found only 5 cases where a "real" (i.e. endoscopy and histology confirmed) change in diagnosis occurred, all of whom had an initial diagnosis of UC. All were young males and the change took place within two to five years from the onset of disease in four of the patients and in three months in the fifth. Four were smokers or ex-smokers and 3 had been treated with several courses of high doses of steroids. None had familiar cases of IBD. We conclude that a change in diagnosis, always from UC to CD is rare (7.9/thousand cases of UC). It affects young males and takes place within few years after the initial diagnosis of disease. We could not demonstrate any causal relation with steroid intake. Intestinal disorders: IBD diagnosis, monitoring } "Change from Ulcerative Colitis to Crohn's Disease: Two Features of the Same Disease?"

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"P P 42 0950" P 42 0950 **Bone Mineral Density and Its Evolution in Patients with Crohn's Disease** M. Dinca, W. Fries, L. Leone, G. Luisetto<sup>1</sup>, F. Bottega<sup>1</sup>, F. Peccolo<sup>1</sup>, A. Martin

Divisione di Gastroenterologia, Universit\`e0 di Padova, Italy

<sup>1</sup> Istituto di Semeiotica Medica, Universit\`e0 di Padova, Italy Low bone mineral density has been demonstrated in patients with Inflammatory Bowel Disease. Aim of our study was to assess the prevalence of osteopenia and the rate of bone loss in patients with Crohn's Disease (CD). *Methods:* We studied 32 patients (19 men and 13 women), mean age 37 years (range 18–69), 14 of whom had CD limited to the colon and 18 with ileocolonic involvement. Bone mineral density was measured by dual-energy x-ray absorptiometry of the lumbar spine. In 21 patients (65.6%) the measurement was repeated after a mean of 23 months (range 9–48). During the follow-up period 8 patients (25%) received steroid therapy and 6 (18.7%) calcium and vitamin D supplements. Osteopenia was defined as z-score below { - }1.5. The fracture threshold was considered bone mineral density (BMD) of 0.8 g/cm<sup>2</sup>. Results were related to site and extent of disease and type of medication. *Results:* Osteopenia was present in 18 patients (56.2%) with values below the fracture threshold in 5 (15.6%). In the 21 patients in whom we measured BMD twice, no significant changes were observed, not even in those treated with steroids. We conclude that osteopenia is frequent in patients with Crohn's disease but is a slow-evolving process and, at least in the short interval of our observation, independent of disease localization and of steroids intake. Intestinal disorders: IBD diagnosis, monitoring }" "Bone Mineral Density and Its Evolution in Patients with Crohn's Disease"

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## "P P 42 0951" P 42 0951 Low Skinfold Thickness Predicts Osteoporosis in Crohn's Disease

\*R. Robinson, F. Al-Azzawi, S.J. Iqbal, K. Abrams, J. Mayberry

Gastrointestinal Research Unit, Leicester General Hospital, Gwendolen Road, Leicester, U.K. The aims of this study were to investigate the relation of skinfold thickness (SFT) to bone mineral density in Crohn's disease (CD), and to evaluate SFT as a screening test for osteoporosis in CD. *Methods:* 117 patients with confirmed Crohn's disease were studied (Male = 49). Pregnancy, ankylosing spondylitis, medical conditions or medication affecting bone density were exclusion criteria. Bone mineral density was measured at lumbar spine (L2–L4) and left hip (femoral neck, trochanter, Ward's triangle) by dual energy X ray absorptiometry (DEXA). SFT was measured over the dorsal aspect of the right hand using Holtain Tanner Whitehouse callipers. The thickness of a longitudinal skinfold over the 4th metacarpal was measured 3 times by a single observer and the mean calculated. *Results:* Osteoporosis was present in 14 (12%) of the patients. Mean SFT was significantly lower in patients with osteoporosis than patients with normal bone density (Difference in means = 0.74 mm, 95% CI 0.33 to 1.15,  $p < 0.001$ ). There was a strong correlation between SFT and bone mineral density at all measured sites: Lumbar spine ( $r = 0.41$ ,  $p < 0.0001$ , 95% CI 0.25 to 0.55), femoral neck ( $r = 0.38$ ,  $p < 0.0001$ , 95% CI 0.21 to 0.53), Ward's triangle ( $r = 0.38$ ,  $p < 0.0001$ , 95% CI 0.21 to 0.53) and trochanter ( $r = 0.33$ , 0.16 to 0.48,  $p < 0.0001$ ). SFT was associated with bone mineral density independent of age, BMI and lifetime steroid use ( $p < 0.05$ ). If a significantly low SFT is taken as  $> 1$  SD below the mean normal value (2.64 (0.71) mm), then subjects with an SFT less than 1.9 mm were at significantly greater risk of osteoporosis ( $p < 0.05$ , odds ratio 5.48, 95% C.I. 1.36 to 22.0). As a diagnostic test for osteoporosis, an SFT of 1.9 mm has 93% specificity and 29% sensitivity. Using 2.5 mm as the 'cut off', specificity falls to 54% and sensitivity increases to 93%. *Conclusions:* In patients with CD there is a strong correlation between SFT and bone mineral density at the hip and lumbar spine. Measurement of hand skinfold thickness is a simple clinical marker of bone mineral density in CD, and will be a useful screening test to determine which patients need DEXA. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, basic }

"Low Skinfold Thickness Predicts Osteoporosis in Crohn's Disease"

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## "P P 42 0952" P 42 0952 Crohn's Disease — A Hyperreactivity of the Tight Junctions?

\*J.D. Söderholm, G. Olaison, L. Hedman, L. Franzén, C. Tagesson, R. Sjödahl

Dept's of Surgery, Pathology and Occupational Medicine, University Hospital, Linköping, Sweden Patients with Crohn's disease (CD) have a disturbed intestinal permeability. The epithelial tight junctions (TJ) regulate the mucosal barrier to hydrophilic molecules. The dynamics of TJ permeability during exposure of the mucosa to modulating substances has not been studied previously in CD. *Purpose:* To study paracellular permeability and electrical parameters in inflamed and non-inflamed ileal mucosa from patients with CD and controls patients during exposure to sodium caprate (C10), a fatty acid found in dairy products with effects on TJs in cell lines, and cytochalasin B (CytB), a well established TJ modulator. *Methods:* Five cm of the ileum was taken from 7 patients with CD and 8 patients operated for colonic cancer. The mucosa was dissected from the muscular layer and the specimens were mounted in Ussing chambers. Transepithelial potential difference (PD), electrical resistance (ER), short circuit current ( $I_{SC}$ ) and permeation of  $^{51}\text{Cr}$ -EDTA and  $^{14}\text{C}$ -mannitol was studied for 90 min in control segments and in segments modulated with C10 or CytB with washout at 10 min and 45 min, respectively. *Results:* Both CytB and C10 induced a partly reversible increase in tight junction permeability. Non-inflamed mucosa from CD patients showed a more pronounced decrease in PD, ER,  $I_{SC}$  and a larger increase in  $^{51}\text{Cr}$ -EDTA permeability during modulation with C10 than did control mucosa. In inflamed CD mucosa permeability in unmodulated specimens was increased compared to controls, whereas the effect of modulators was less pronounced. *Conclusions:* The results indicate a hyper-reactivity of the tight junctions in non-inflamed ileal mucosa in CD. This may be of importance for the pathogenesis in Crohn's disease. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders, absorption: Epithelial transport } "Crohn's Disease / A Hyperreactivity of the Tight Junctions?"

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"P P 42 0953" P 42 0953 **Is ANCA Positivity in Crohn's Disease (CD) Associated with Particular Clinical Features?**

\*E. Louis, V. Mommens, D. Franchimont, J. Salmon, P. Mahieu, J. Belaiche

Departments of Gastroenterology and Immunology, CHU Sart Tilman, 4000 Liège, Belgium According to different studies, 10 to 20% of CD patients are ANCA +. The significance of that positivity is still unknown. The aim of our study was to compare ANCA + and ANCA { - } CD populations on the basis of several clinical features. *Patients and methods:* ANCA were searched, using an immunohistochemical method, in a sample of 180 CD patients. Twenty one of them (11.6%) were ANCA +. They were compared to a group of 41 ANCA { - } CD patients, matched for gender, smoking and duration of the disease. Comparisons on certainty of the diagnosis, type and location of the disease, systemic manifestations, age at onset, family history of IBD, need for surgery or immuno-suppressive treatment, were made using, either Fisher's exact test, or t test. *Results:* the frequency of gastro-duodenal location of CD was significantly higher in ANCA + CD patients (33.3% vs 4%;  $p < 0.01$ ). There was also a trend to an increased frequency of inflammatory disease and to a decreased frequency of stenosing disease among ANCA + CD. The need for surgery tended to be less frequent in ANCA + CD, but the need for immuno-suppressive drug tended to be more frequent in the same population. Finally, the age at onset tended to be higher in ANCA + patients (37.4 vs 28.5 years;  $p = 0.053$ ). *In conclusion,* a minority of CD patients are ANCA +. This may represent a particular subset of CD, characterized by an increased frequency of gastro-duodenal location, and perhaps later onset, more inflammatory and less stenosing disease. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Is ANCA Positivity in Crohn's Disease (CD) Associated with Particular Clinical Features?"

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## "P P 42 0954" P 42 0954 **Familial Crohn's Disease: Study of 18 Families**

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Société Liégeoise de Gastroentérologie, CHU Sart Tilman, 4000 Liège

The most recent data from epidemiology and molecular biology in Crohn's disease are consistent with a multifactorial, polygenic inheritance with a possible genetic heterogeneity. The aim of our study was, first to evaluate among families, the concordance rate for the type and location of the disease, and second, to compare familial and sporadic CD on the basis of the type and location of the disease, and age at diagnosis. *Patients and methods:* 16 families with 2 affected first degree relatives (n = 32), 2 families with 3 affected first degree relatives (n = 6), and 155 sporadic CD were studied. The expected numbers of concordant cases among families were calculated using the binomial law and compared to the observed numbers by a Chi<sup>2</sup> test. Comparison between familial and sporadic CD was done by a Chi<sup>2</sup> or a Kruskal-wallis test. *Results:* 1) There was a significant increase in concordance rate for stenosing disease and a decrease for inflammatory disease, among the families. 2) Age at diagnosis was the same in sporadic and familial CD. There was an increased frequency of ileal (p = 0.022), and stenosing (p = 0.005) CD and a decreased frequency of colonic (p = 0.006) and inflammatory (p = 0.028) CD, in familial CD. *In conclusion,* 1) Among families, the concordance rate for stenosing CD was higher than expected, which may reveal the genetic inheritance of that feature. 2) Ileal and stenosing diseases were more frequent in familial than in sporadic CD, which may suggest some heterogeneity in CD. Clinical practice: Epidemiology (non cancer) Intestinal disorders: IBD, etiology and genetics }

"Familial Crohn's Disease: Study of 18 Families"

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## "P P 42 0955" P 42 0955 **Low Symptomatic Load in Crohn's Disease with Surgery and Medicine as Complementary Treatments**

\*P. Andersson, G. Olaison, G. Bodemar, S. Almer, J. Dabrosin-Söderholm, R. Gotthard, P.O. Nyström, K. Smedh, M. Ström, R. Sjödahl

Dept of Medico-Surgical Gastroenterology, University Hospital, Linköping,

Sweden *Background:* The treatment of Crohn's disease has changed due to the recognition of its chronicity. Maintenance medical treatment and limited resections has evolved as major concepts of management. Medicine and surgery are complementary, their indications being related, and both aim to reduce symptoms. The study aimed at to investigate how these treatment concepts influenced the symptomatic load in Crohn's disease. *Patients and methods:* An unselected population-based cohort of 202 patients from our primary catchment area and 119 referred patients were investigated. Symptoms were evaluated by a symptom-index, the physician's global assessment and the patient's perception of health by means of visual analogue scale. *Results:* Of catchment area patients 53% were on medication and the annual rate of abdominal surgery was 5.7%. Corresponding figures for the referred patients were 63% and 8.2% respectively. According to the symptom-index 75% were in clinical remission, 16% had mild, 8% moderate and 1% severe symptoms. Corresponding figures according to the physician's assessment were 63, 26, 10 and 1 percent. Patient's perception of health was 82% in normal health. Symptoms and perceived health were similar in referred patients. *Conclusion:* The large majority of patients with Crohn's disease can live in remission or have only mild symptoms. Intestinal disorders: IBD, therapy } "Low Symptomatic Load in Crohn's Disease with Surgery and Medicine as Complementary Treatments"

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"P P 42 0956" P 42 0956 **Osteoporosis in Crohn's Disease in a Danish Out-Patient Clinic: Bone Mineral Measurements and Biochemical Markers**

\*H. Andreassen, M. Rix, E. Hylander

Departments of Internal Medicine and Gastroenterology, Roskilde County Hospital K\8ge, Denmark *Methods:* BMD was measured at the lumbar spine (L2–L4), the hip and of the forearm, using the Hologic 2000 DEXA-scanner. Biochemical markers of bone formation (osteocalcin) and bone resorption (urinary pyridinoline) were analyzed. *Patients:* 56 unselected patients (33 females, 23 men) with Crohn's disease, mean age 41 years (SD 14.6), mean BMI 23.6 kg/squaremeter (SD 4.0 kg/squaremeter), half of whom had a bowel resection, were studied. *Results:* Osteopenia (defined as a T-score (mean BMD value for the young adult) less than { - }1 SD)) was found in the lumbar spine, the hip (neck-region) or the forearm in 52%, 64% and 46% of patients, respectively. Osteoporosis (defined as a T-score less than { - }2.5 SD) was observed in 14%, 16% and 16% of patients, measured in the same areas. In 25% of cases osteoporosis occurred at any of those sites. Increased urinary pyridinoline was found in 16% of the patients (mean value for the whole group: 46.6 nmol/mmol creatinine, SD 28.0, normal values 38.8 – 10.8), elevated urinary deoxy-pyridinoline in 4% (mean: 11.1 nmol/mmol creatinine, SD 7.2, normal values 13.0 – 4.6). Nine % of the patients had serum-osteocalcin above normal range (mean value for the group 9.0 – 4.4). *Conclusion:* In a Danish cross-sectional study of unselected patients with Crohn's disease, attending an out-patient clinic, osteoporosis is found in 25% (WHO-criteria). Biochemical markers of bone turnover indicates increased bone resorption. Nutrition: Metabolism } "Osteoporosis in Crohn's Disease in a Danish Out-Patient Clinic: Bone Mineral Measurements and Biochemical Markers"

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"P P 42 0957" P 42 0957 **Bone Metabolism and Remodelling in Crohn's Disease**

\*J. Bures, V. Palicka, L. Pl'edskov'e1, J. V'e1vrov'e1, P. Zivn'fd, S. Rejchrt, M. Sirok'fd, P. &Rbreve;ehorkov'e1

Charles University Teaching Hospital, Hradec Kr'e1lov'e9, Czech Republic *Purpose of the study* was to evaluate bone metabolism and remodelling in Crohn's disease. *Methods.* Thirty-five patients with Crohn's disease entered the study (17 men, 18 women, aged 17–64, mean 37, median 38). The diagnosis was based on typical endoscopic, radiological and histological findings (including 17 persons with previous history of bowel surgery). Bone metabolism was assessed by measuring serum osteocalcin (by EIA), collagen-I carboxyterminal propeptide [PICP] (by EIA), parathyroid hormone (using immuno-chemiluminiscence), 1,25-OH-vitamin D<sub>3</sub> (by RIA), urine hydroxyprolin (using spectrophotometry) and urine free deoxypyridinoline (by EIA). Bone density was measured by peripheral broadband ultrasound attenuation (using CUBA, McCue, UK). Data were statistically treated (t-test, Mann-Whitney, Spearman Correlation) using Jandel Scientific. *Results.* Peripheral bone density was decreased in 22/35 patients (63 per cent). Serum osteocalcin was increased (mean 6.66 – std. dev. 3.15 \b5g/l) as well as the urine excretion of deoxypyridinoline (median 6.90, interquartile range 5.43–11.08 nM/mM of creatinine). Serum PICP was in the upper part of reference values (mean 121.7 – 47.53 \b5g/l). Serum 1,25-OH-vitamin D<sub>3</sub> (mean 33.3 – 14.4 ng/l) and parathyroidal hormone (mean 24.6 – 14.6 ng/l) were within normal range (except 3 patients). There was no significant correlation between bone density, biochemical markers of bone turnover, disease duration and cumulative dose of corticosteroids. *Conclusions.* The bone metabolism is often heavily disturbed in Crohn's disease. The incidence of osteopenia and osteoporosis is high in these patients. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy Nutrition: Metabolism }" "Bone Metabolism and Remodelling in Crohn's Disease"

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"P P 42 0958" P 42 0958 **Low Body Fat and Risk for Osteoporosis in Crohn's Disease**

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<sup>1</sup> Department of Gastroenterology, University Hospital Maastricht, The Netherlands

<sup>2</sup> Nuclear Medicine, University Hospital Maastricht, The Netherlands

Reduced bone mineral density (BMD) has a reported prevalence of 13 to 31% in patients with Crohn's disease (CD). Several risk factors and risk conditions have been proposed. The aim of the study was to estimate whether body composition is correlated to bone mineral density (BMD) in patients with CD. *Methods:* Fifty-seven out-patients with CD (17 M, 40 F, age 18–72, mean 43 yrs.) were investigated using total body dual X-ray absorptiometry (DXA). Total body BMD (TBBMD), lumbar spine (LS) BMD and hip BMD (neck, Wards triangle (WT), trochanter (Troc)), and body fat percentage (% BF) were measured. BMD was expressed in T- and Z-score. Body mass index (BMI) was calculated. Serum 25-OH-vitamin D (vit D) levels were determined. *Results:* The prevalence of osteopenia in this group of patients, defined as Z-score < -1 SD, was 54% (31/57). BMI was correlated with TBBMD-T ( $r = 0.35$ ,  $p < 0.01$ ), and TrocBMD-T ( $r = 0.37$ ,  $p < 0.025$ ). There was a significant correlation between % BF and TBBMD-T ( $r = 0.59$ ,  $p < 0.001$ ), TBBMD-Z ( $0.31$ ,  $P < 0.05$ ), TrocBMD-T ( $r = 0.32$ ,  $p < 0.025$ ) and WT BMD-T ( $0.29$ ,  $p < 0.05$ ). There was a significant correlation between % BF and vit D levels ( $r = 0.43$ ,  $p < 0.025$ ). *Conclusion:* Crohn's disease patients with low BMI and low body fat percentage are at higher risk for osteopenia. Body mass index is a simple clinical parameter which can be helpful in selecting patients at risk for osteopenia in Crohn's disease. Intestinal disorders: IBD, basic Nutrition: Metabolism Clinical practice: Epidemiology (non cancer) } "Low Body Fat and Risk for Osteoporosis in Crohn's Disease"

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"P P 42 0959" P 42 0959 **Prothrombin Fragment (F<sub>1+2</sub>) and Fibrin Degradation Products (FbDP) in Peripheral and Splanchnic Circulation in Crohn's Disease (CD) Patients**

\*J. Kjeldsen<sup>1</sup>, J.F. Lassen<sup>2</sup>, M. Rasmussen<sup>3</sup>, O. Kronborg<sup>3</sup>, O.B. Schaffalitzky de Muckadell<sup>1</sup>

<sup>1</sup> Dept. of Medical Gastroenterology, Odense University Hospital, Denmark

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Coagulation and fibrinolysis is activated in patients with active inflammatory bowel disease. The granulomatous vasculitis demonstrated in CD is accompanied by intravascular fibrin deposition. *Aim:* To study if the systemically demonstrated activation of coagulation and fibrinolysis is present locally in the gut of CD patients. *Method:* 10 patients (6 females) who underwent resection of CD affected gut (in 4 due to active inflammation, in 3 because of stricture, in 3 due to stricture and inflammation) participated. During surgery blood was drawn simultaneously from a cubital vein and a vein draining diseased area of the gut. *Results:* Median (range) Plasma F<sub>1+2</sub> (nmol/l) Plasma FbDP (µg/l) Cubital vein Splanchnic vein Cubital vein Splanchnic vein Crohn's 1.32\* 1.68<sup>#</sup> 292.2\* 289.2\* disease, n = 10 0.(0.64–5.0) (1.20–12.51) (154.5–2872) (156.4–787.7) Healthy 1.60 159.4 controls, n = 30 (0.63–2.41) (90.3–675.9)\*p < 0.05 vs. controls. <sup>#</sup>p = 0.058 vs. cubital vein. *Conclusion:* Splanchnic and cubital plasma FbDP in CD patients were significantly higher compared to controls. Plasma F<sub>1+2</sub> was marginally higher in splanchnic than in cubital blood, but F<sub>1+2</sub> in cubital blood in CD patients was lower than in controls. Fibrinolysis is enhanced systemically and locally in the gut of CD patients. Activation of the coagulation cascade, as assessed by F<sub>1+2</sub>, is not evident in this group of patients with primarily stricturing disease although it may be more pronounced in close proximity to the inflammatory process. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: Splanchnic circulation, ischemia } "Prothrombin Fragment (F<sub>1+2</sub>) and Fibrin Degradation Products (FbDP) in Peripheral and Splanchnic Circulation in Crohn's Disease (CD) Patients"

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**"P P 42 0960" P 42 0960 Change of Clinical, Laboratory Parameters and Clearance-Alpha-1-Antitrypsin in the Chronically Active Patient's with Crohn's Disease** Nj. Jojic, D. Necic, B. Dapcevic

Zvezdara University Center, Gastroenterology Unit, Belgrade, Yugoslavia Practical value of clinical, laboratory and intestinal parameters for the estimation of the total activity, was analyzed in the group of chronically active patients with Crohn's disease. Forty patients were tested, 16 with Crohn's colitis, 12 patients with extensive small bowel disease and 12 patients with ileocolonic disease. Clinical parameters were measured by modified Best index (CDAI), laboratory parameters with acute phase reactants (CRP and orosomuroid) and intestinal activity with Clearance-alpha-1-Antitrypsin (Cl- $\alpha$ -1-At). All parameters were determined at the beginning of testing and after 3, 6, 9 and 18 months. Initially, all patients were clinically active (CDAI > 200) as well as laboratory active (CRP, orosomuroid and Cl- $\alpha$ -1-At were above the normal values). Mean values of CDAI in each quarter were statistically different significantly (Freedman test;  $\chi^2 = 13.4$ ; which is higher than 13.27;  $p < 0.01$ ). Relapse was considered when the patients had CDAI values 50 points higher compared to previous measurements. Mean values ( $\bar{X}$ ; - SD) of orosomuroid (1.7 - 0.2 g/l) and Cl- $\alpha$ -1-At (82 - 12 ml/24 h) were increased during entire period, but there was no significant difference statistically during relapse. Mean CRP values were statistically much higher during relapse ( $t = 2.91$ ;  $p < 0.05$ ). These results mean that constantly increased values of orosomuroid and Cl- $\alpha$ -1-At indicate chronically activity in this group of patients. Increase in CRP values indicated relapses. Intestinal disorders: IBD diagnosis, monitoring } "Change of Clinical, Laboratory Parameters and Clearance-Alpha-1-Antitrypsin in the Chronically Active Patient's with Crohn's Disease"

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"P P 42 0961" P 42 0961 **Anti-Saccharomyces Cerevisiae Antibodies (ASCA): A New Serological Marker to Differentiate Crohn's Disease (CD) from Ulcerative Colitis (UC)** J.F. Quinton, B. Sendid, D. Reumaux, A. Cortot, D. Poulain,

\*J.F. Colombel

C.R. Inserm 4U004B et Laboratoire de Parasitologie-Mycologie, CH et U Lille, France

INSERM U 42, Lille, France

D\ 'e9p. d'H\ 'e9matologie-Immunologie, CH Valenciennes, France *Bakground/aim:* A search for serological tests to differentiate between CD and UC has been underway for a long time. Antineutrophil cytoplasmic auto-antibodies (ANCA) are well recognized marker for UC. We have recently shown that antibodies to oligomannosidic epitopes of the yeast *Saccharomyces cerevisiae* (ASCA) were associated with CD [1]. The aim of this study was to evaluate the value of detecting ANCA in diagnosing UC and ASCA in diagnosing CD by single or combined use of these tests. *Methods:* Serum samples were obtained from 68 patients with CD (40 F, 28 M, mean age 30 yrs) and 81 patients with UC (43 F, 38 H, mean age 42 yrs). Determination of ANCA was performed using the standardized indirect immunofluorescence technique. Determination of ASCA was performed using ELISA [1]. *Test results* for determining either UC or CD in patients with inflammatory bowel disease (IBD) are given in the following table: Se = sensitivity, Sp = specificity, PPV = positive predictive value. Test UC CD Se Sp PPV ASCA + 12 45 68% 85% 88% ANCA + 44 11 65% 83% 72% ASCA +/- ANCA { - } 2 36 55% 97% 97% ASCA { - } / ANCA + 39 3 57% 95% 89% No relationship was observed between the presence of ASCA and ANCA and any clinical parameters including UC or CD activity and location. *Conclusion:* ASCA and ANCA either used single or combined may help diagnosis of IBD. The remarkable PPV observed when combining both tests might be particularly useful in patients with unclassified colitis and should be confirmed in a prospective study.

Reference: Sendid B et al. Clin Diag Lab Immunol 1996; 3: 219–26. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, basic } "Anti-Saccharomyces Cerevisiae Antibodies (ASCA): A New Serological Marker to Differentiate Crohn's Disease (CD) from Ulcerative Colitis (UC)"

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"P P 43 0962" P 43 0962 **Role of the Viscosity of Therapeutic Milk on Digestibility and Tolerance of Lactose in Adults with Hypolactasia**

\*T. Vesa, P. Marteau, F. Briet, A. Briend, B. Flouri, J.C. Rambaud

INSERM U290, Hospital Saint Lazare, Paris, France Subjects with lactose maldigestion including malnourished children digest more efficiently lactose from fermented milk than from milk. It has been hypothesised that differences in viscosity could play a role. Therapeutic enriched milks are developed for the nutrition of malnourished children, but a problem often encountered in rehabilitation is lactose intolerance. *The aim* of this study was to evaluate whether increasing the viscosity of a therapeutic milk would enhance the digestibility of its lactose content. *Methods*: Thirteen healthy adult volunteers with hypolactasia ingested three different test milks in random order with one week interval between each test. The therapeutic milks were prepared from the same milk formula to which rice starch and/or maltodextrin were added to modify the viscosity without modifying the caloric content. Viscosity ranged from that of usual milk (TM1) to approximately that of stirred yoghurt (TM3). Each test milk (500 ml) contained 14 g protein, 21 g fat, 50–55 g carbohydrates including 18 g lactose, and 1886–1969 kJ (450–470 kcal). Test milks were ingested in the morning after a 12-hour fast. Digestion of lactose was measured by hydrogen (H<sub>2</sub>) breath test during 6 h, and intolerance symptoms were recorded. The Wilcoxon test was used for statistical comparisons. *Results*: (means – SD): There were no significant differences between the milks concerning digestion of lactose, oro-caecal transit time, nor symptoms (Table). TM1 TM2 TM3 Maltodextrin content (g) 35 17 0 Rice starch content (g) 0 17 35 Viscosity (cps) 33 80 1892 AUC H<sub>2</sub> (ml) 51 – 35 55 – 37 50 – 40 Oro-caecal transit time (min) 180 – 83 163 – 80 180 – 85 Sum of symptoms 13 – 16 11 – 13 11 – 13 *Conclusion*: moderate increase of meal viscosity does not enhance the digestion or tolerance of lactose from a therapeutic milk in adults. The breath H<sub>2</sub> excretion and intolerance signs were relatively low with the 3 milks, possibly owing to their high caloric and fat content. Other hypothesis should explain the good digestibility of fermented milks in hypolactasic subjects. Intestinal disorders, absorption: Malabsorption syndromes Nutrition: Metabolism } "Role of the Viscosity of Therapeutic Milk on Digestibility and Tolerance of Lactose in Adults with Hypolactasia"

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"P P 43 0963" P 43 0963 **Digestion and Tolerance of Lactose from Yoghurt and Semi-Solid Fermented Dairy Products — Is Bacterial Lactase Important?**

\*T.H. Vesa, P. Marteau, S. Zidi, F. Briet, P. Pochart, J.C. Rambaud

INSERM U 290, Hospital Saint-Lazare, Paris, France Lactase-deficient subjects digest lactose better from fermented dairy products than from milk. Three hypothesis which do not exclude each other have been proposed. Slower gastric emptying and intestinal transit (probably due to physical differences), stimulation of the endogenous residual lactase, and action of the bacterial lactase *in vivo* in the gastrointestinal tract. The specific role of each of these factors is debated. *The aim* of this study was to compare the digestibility and tolerance of three fermented dairy products with the same amount of lactose, and physical state (semi-solid), but different lactase and bacterial contents. *Methods*: 14 lactase-deficient healthy volunteers consumed, on 4 different days and in random order, after a 12-h fast, 3 semi-solid test meals containing 18 g of lactose, and 10 g of lactulose which allowed calculation of lactose malabsorption. The 3 meals were: yoghurt, a fermented milk containing *Lactobacillus acidophilus* and *Bifidobacterium* sp. (Ofilus'), and a similar product enriched with *L. bulgaricus* to increase the lactase content (Bulgofilus). The lactase contents (IU/g product weight) were 0.19 for Ofilus', 0.24 for Bulgofilus, and 0.86 for yoghurt. Breath hydrogen (H<sub>2</sub>) concentration and clinical symptoms were measured for 6 h after consumption of the test meals. *Results*: Symptoms scores were low, indicating a good tolerance of all products. Compared with lactulose, the sum of symptoms was significantly lower for Bulgofilus ( $p = 0.05$ ), and bloating was less severe for Ofilus' ( $p = 0.06$ ). The area under the breath H<sub>2</sub> curve was significantly lower for each fermented milk when compared to lactulose ( $p < 0.0001$ ). There were no differences in symptoms between the fermented milks. The degree of maldigestion of lactose did not differ significantly between them and was 18 – 3% (range 3–43) for yoghurt, 21 – 3% (range 6–52) for Ofilus', and 21 – 3% (range 6–44) for Bulgofilus. *Conclusion*: Despite the differences in the lactase and bacterial contents, lactose was as well digested and tolerated from the 3 different fermented milks. This argues against a major role for lactase in the digestibility of semi-solid fermented dairy products. Intestinal disorders, absorption: Malabsorption syndromes Nutrition: Metabolism } "Digestion and Tolerance of Lactose from Yoghurt and Semi-Solid Fermented Dairy Products / Is Bacterial Lactase Important?"

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"P P 43 0964" P 43 0964 **Lactase and Sucrase-Isomaltase Expression in the Duodenum during Development in Children**

\*E.H. Van Beers, H.A. B\|fcller, E.H.H.M. Rings, A.W.C. Einerhand, J. Dekker

Pediatric Gastroenterology & Nutrition, Acad. Med. Ctr, Amsterdam, The Netherlands *Purpose:* A large number of diseases affect the integrity of the intestinal epithelium, which harbors a number of very important digestive enzymes. Particularly the brush border enzymes lactase and sucrase-isomaltase (SI) are essential for the digestion of milk-based lactose during early childhood and plant-based sucrose and starch later in life respectively. Clinical evaluation of the effects of epithelial damage on intestinal ability to digest carbohydrates is very important for diagnosis and therapy. Since the regulation of these brush border enzymes in health and disease is inherently very important for survival, we have studied the expression of both these enzymes at the mRNA and protein levels in children. *Methods:* 85 Caucasian children (3 mnth–18 y) were studied with normal or affected duodenal mucosae. Villus atrophy was scored in 3 classes. Endoscopic forceps biopsies were taken in duplicate from both proximal and distal duodenum in each child. One of these duplicate biopsies was used in immunohistochemistry (IHC) with anti-lactase or anti-SI antibodies, and the staining of the brush border membrane of the villus enterocytes was measured semi-quantitatively. The duplicate biopsies were used to isolated RNA, and the lactase and SI mRNAs were quantified. Lactase and SI mRNA levels were expressed relative to Gapdh mRNA. *Results:* The biopsies from the proximal and distal region of the duodenum of each patient yielded very similar results in every aspect. In healthy tissue the mRNA and IHC levels of both lactase and SI remained similar in all age-groups. Likewise, when the ratio lactase mRNA/SI mRNA was determined per biopsy, no differential gene expression was noted between these enzymes: The mean mRNA-ratios remained similar at all ages. However, increasing villus atrophy correlated with decreasing expression of both enzymes, measured by mRNA levels or IHC. Despite similar mean levels of lactase and SI in healthy tissue among the age-groups, a large variety was found in the individual levels of the enzymes: Individuals were found with high lactase levels and low SI levels, and vice versa. Also at the epithelial level no correlation was found between individual cells in their expression levels of lactase or SI using IHC. *Conclusions:* There are no longitudinal expression gradients in the duodenum for lactase or SI. There seems to be no age-related regulation of either enzyme in Caucasians, and the relative levels of these enzymes remain similar. Both enzymes are affected negatively during epithelial damage. Nevertheless, large varieties were observed in enzyme levels in individuals as well as at the cellular level, strongly indicating that the expression of the enzymes is largely independently regulated. Endoscopy, general: Endoscopy: children Nutrition: Metabolism Nutrition: Nutrition: children } "Lactase and Sucrase-Isomaltase Expression in the Duodenum during Development in Children"

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"P P 43 0965" P 43 0965 **Reproducibility of a Combined Lactose-<sup>13</sup>C-Glycine Breath Test to Study Gastric Emptying, Orocaecal Transit Time, and Lactose Digestion**

\*F. Briet, P. Marteau, T. Vesa, A. Briend, B. Flouri, J.C. Rambaud

INSERM U290, Hospital Saint Lazare, Paris, France Gastric emptying and oro-caecal transit time (OCTT) influence lactose digestion. *Our aim* was to set-up a combined test and assess its reproducibility to study gastric emptying, OCTT, and lactose digestion in lactose maldigesters. *Subjects & methods:* After an overnight fast, 13 lactose maldigesters ingested 500 ml of milk containing 18 g of lactose and supplemented with <sup>13</sup>C-glycine (99 AP). Breath gas samples were collected every 15 min for 6 h, and gastrointestinal symptoms were recorded using visual analogue scale. A second test was repeated for each subject after one week. Breath excretion of H<sub>2</sub> and <sup>13</sup>CO<sub>2</sub> were measured using an electrochemical cell and an isotopic mass spectrometer respectively. The <sup>13</sup>CO<sub>2</sub> excretion curves were fitted using non-linear regression models to calculate the gastric emptying parameters: half emptying time (t<sub>1/2</sub>), time of maximal gastric emptying (t<sub>max</sub>), and gastric emptying coefficient (GEC) (Maes et al. 1994). The area under curve of breath H<sub>2</sub> excretion (AUC H<sub>2</sub>) was calculated, and the OCTT was assessed by the appearance of H<sub>2</sub> excretion in breath. Results were compared using the Wilcoxon test. *Results:* (means – SD) t<sub>1/2</sub> (min) t<sub>max</sub> (min) GEC AUC H<sub>2</sub> (ml) OCTT (min) Test 1 87 – 14 40 – 12 2.6 – 0.3 64 – 30 122 – 41 Test 2 84 – 18 39 – 12 2.6 – 0.4 51 – 35 180 – 83 p 0.60 0.78 0.79 0.17 0.06 Almost significant decrease was seen between the first and second test concerning abdominal pain (4.6 – 7.5 vs 1.3 – 3.9, p = 0.05), flatulence (6.0 – 6.3 vs 3.8 – 4.4, p = 0.07), and the sum of symptoms (24.6 – 25.3 vs 12.9 – 15.6, p = 0.07). *Conclusion:* This new test allows simultaneous assessment of gastric emptying, intestinal transit time, and lactose digestion. Repeated measures showed a good reproducibility and the absence of a period effect for gastric emptying. Since there was a trend towards a period effect for the assessment of the intestinal transit time and intolerance signs, studies using repeated measures of lactose digestion and tolerance in the same subject should always randomise treatment periods. Intestinal disorders, absorption: Malabsorption syndromes Motility, specific: Small bowel Motility, specific: Stomach } "Reproducibility of a Combined Lactose-<sup>13</sup>C-Glycine Breath Test to Study Gastric Emptying, Orocaecal Transit Time, and Lactose Digestion"

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"P P 43 0966" P 43 0966 **The Clinical Significance of Mucosal Lactase Deficiency: Correlation with Serum Glucose Levels and Symptoms during Lactose Tolerance Test**

\*U. Nieminen<sup>1</sup>, M. Rautio<sup>3</sup>, M. Saxelin<sup>2</sup>, A. Siitonen<sup>3</sup>, T. Vesa<sup>4</sup>, H. Jousimies-Somer<sup>3</sup>, R. Korpela, M. F\ 'e4rkkil\ 'e4<sup>1</sup>

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<sup>2</sup> Valio Research Center, Helsinki, Finland

<sup>3</sup> National Public Health Institute, Helsinki, Finland

<sup>4</sup> Foundation for Nutritional Research, Helsinki, Finland *Purpose:* To study the correlation of duodenal mucosal lactase activity with the results of the lactose tolerance test and symptoms in patients with primary lactase deficiency. *Methods:* The study group consisted of 30 patients with primary lactase deficiency; lactase concentration half of the normal determined by duodenal lactase measurement with normal histology. The exclusion criteria were: coeliac disease, inflammatory bowel diseases, active duodenal or ventricular ulcer disease, cholecystolithiasis, diabetes mellitus, and intense symptoms suggesting of an irritable bowel syndrome. The standard lactose tolerance test was performed with 50 g of lactose liquid. The bowel transit time was determined using 1 g of carmine red to mark the lactose liquid. The symptom score during the lactose test and during the 6-hours follow-up was calculated using a questionnaire. The correlation of duodenal mucosal lactase activity with the results of the lactose tolerance test, and with the symptoms in patients during the test were analyzed using the regression analysis test. *Results:* The symptoms in the patients varied largely during the lactose tolerance test. No correlation of the duodenal mucosal lactase activity was found with patients' symptoms during the lactose test ( $r = -0.03$ ), or with the rise of glucose in the test ( $r = 0.28$ ). Moreover, there was no correlation of the mucosal lactase activity with the bowel transit time ( $r = -0.013$ ). The symptoms in patients' did neither correlate with the rise of blood glucose during the lactose test ( $r = -0.04$ ). *Conclusions:* The duodenal lactase activity was detected as an insignificant factor to define the result in the lactose tolerance test and the intensity of symptoms during the test. Intestinal disorders, absorption: Malabsorption syndromes Motility, general: Functional GI disorders Endoscopy, specific: Stomach, duodenum } " "The Clinical Significance of Mucosal Lactase Deficiency: Correlation with Serum Glucose Levels and Symptoms during Lactose Tolerance Test"

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## "P P 43 0967" P 43 0967 Lactose Malabsorption Adult Type in Brazil

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Lactose malabsorption adult type (LMA) has different prevalences in distinct ethnic groups. Brazil has 150 million people distributed in 5 regions of different ethnic and genetic admixture. Indians are the aboriginal. Since the 16<sup>th</sup> century mixture has occurred with other races. Whites came from Europe as settlers. Negroes came from Africa since 1538 as slaves. Later on many immigrants arrived: Europeans and Orientals. The Southeast (SE) has 64 million people of an intermediate mix of Portuguese, Spanish, Italians, Syrians and Japanese. The Northeast (NE) has 43 million people of intense interracial genetic admixture, mainly Indigenous, Negroids and Portuguese, then they are considered trihybrids. The South (S) has 23 million people with poor genetic admixture and the strongest European influence, specially German, Italian and Portuguese. The other 2 regions, North and Middle West, are less populated, only 13%. Our investigation was undertaken to clarify the LMA prevalence in the different Brazilian regions, thus establishing a complete picture of our country. A lactose tolerance test consisting of the administration of 50 g lactose as a 10% aqueous solution was applied to healthy adults, nonconsanguineous, with no secondary lactase deficiency: 80 (40 Caucasoids, 20 Negroids and 20 mongoloids of Japanese ancestry) born in SE; 70 (48 Caucasoids and 22 Negroids) from S and 37 (trihybrids) from NE. The results of prevalence of LMA are summarised in the table:

Brazilian Population	Caucasoids	Negroids	Japanese	Trihybrid	region	(n)	(%)	(%)	(%)	(%)					
SE	64 000 000	45 85	100	NE	43 000 000	76	23 000 000	37.5	68	Total	130 000 000	41	76	100	76

We conclude that Brazilian Caucasoids have an intermediate prevalence of LMA, whereas Negroid, Japanese and trihybrid Brazilians have a high prevalence of LMA. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport }

"Lactose Malabsorption Adult Type in Brazil"

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## "P P 43 0968" P 43 0968 Lactose Intolerance: Role of the Colon and of Changes in Motor Activity in the Occurrence of Symptoms

\*P. Jou\ 'ebt, J.M. Sabat\ 'e9, B. Flour\ 'e9, Y. Bouhnik, B. Coffin, C. Franchisseur, J.C. Rambaud

INSERM U290, Hospital Saint Lazare, 75010 Paris, France In lactose intolerance, symptoms are attributed to the colonic fermentation of unabsorbed lactose. However, in the small bowel unabsorbed lactose could also produce symptoms via its osmotic load. Mechanisms of symptoms are unsettled. They could be related to the occurrence of motor events induced in the small intestine by the osmotic load and/or in the colon by the bacterial fermentation of unabsorbed lactose. *We compared* in healthy volunteers the effects of lactulose, a nonabsorbable sugar biochemically similar to lactose, taken orally or directly infused into the colon in order to bypass its possible effects on the small bowel. *Methods:* During two periods separated by one month, 8 healthy volunteers swallowed a multilumen tube consisting of 9 perfused catheters, and 1 infusion catheter. After migration of the tube, the infusion catheter was in the cecum, at least 3 perfused catheters were in the jejunum, and 3 in the colon. After an overnight fast, subjects ingested a 500 kcal liquid meal containing either 40 g lactulose or 40 g saccharose; in this last case, the 40 g lactulose was infused directly into the colon 45 min after the beginning of the meal for 4 hrs at flow rates pre-established in 2 ileostomized patients. Motor activity was recorded for 5 hours. Symptoms were also recorded and graded hourly for 10 hrs and their occurrence was marked on the motility records. *Results:* Neither the score for each symptom, nor the overall score (29 – 6 vs 30 – 4;  $p = 0.7$ ; mean – SEM) were significantly different between the 2 periods. Out of the 48 reported symptoms, only 18, i.e. 38%, (11/25 borborygmi, 4/14 abdominal pains, 3/9 flatus) coincided in time with a particular colonic motor event: propagated contractions were associated with borborygmi (8), abdominal pains (3) and flatus (3), waves of localized contractions were associated with borborygmi (2), whereas prolonged waves of contractions that occurred simultaneously on several catheters were associated with borborygmi (1) and pains (1). No symptom coincided with a particular small bowel motor event. *Conclusion:* In healthy subjects, symptoms induced by a nonabsorbable sugar are similar when this sugar is ingested orally and when it is infused directly into the colon. This shows that symptoms originate from the colon. However, symptoms were not clearly correlated with particular motor events. This suggests that nonrecorded motor events (for example tonic variations) or other factors could be involved in the occurrence of symptoms. Motility, specific: Small bowel Motility, specific: Colon, anorectum Intestinal disorders, absorption: Malabsorption syndromes } " "Lactose Intolerance: Role of the Colon and of Changes in Motor Activity in the Occurrence of Symptoms"

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"P P 43 0969" P 43 0969 **Intestinal Mucosal Permeability to Lactulose, L-Rhamnose in Adult Patients with Chronic Diarrhoea** Mohamed A. Nafeh<sup>1</sup>, Ahlam M. Ahmed<sup>1</sup>, Soad M. Abdel-Ghany<sup>2</sup>,

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<sup>1</sup> Department of Tropical Medicine, Assiut University Hospital

<sup>2</sup> Department of Biochemistry, Faculty of Medicine, Assiut University Intestinal permeability to lactulose (La) and rhamnose (rham) was studied to show integrity of the small intestine in chronic diarrhoea. Thirty-six patients with chronic diarrhoea as well as 14 healthy controls were studied. The aetiologic diagnosis of diarrhoea was settled through a set up for management of chronic diarrhoea in the Department of Tropical Medicine, Assiut University Hospital. According to the histopathological changes in the proximal intestine, patients were classified into 2 groups. A group with normal histological appearance (9 patients); showed a significant increase in La/rham ratio in comparison to controls (0.07 – 0.02 vs. 0.04 – 0.02). On the other hand, those with histopathological changes in the proximal intestine (27 patients), showed significant increase in the mean La/5 h (23.3 – 9.9 vs. 11. – 7.8) and highly significant decrease in rham/5 h (23.6 – 12.9 vs. 51.1 – 14.5) compared with controls. All patients had higher la/rham ratios without overlap with the normal range and the mean ratio was statistically highly significant (0.25 – 0.17 vs. 0.044 – 0.022 for controls). We conclude that the la/rham permeability test — in addition to being non-invasive technique — is a sensitive index of small intestinal integrity. We hope that it may replace the endoscopic biopsy and histopathologic study or at least decreases the need for such invasive procedures. Intestinal disorders, absorption: Epithelial transport Intestinal disorders, absorption: Malabsorption syndromes } "Intestinal Mucosal Permeability to Lactulose, L-Rhamnose in Adult Patients with Chronic Diarrhoea"

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"P P 43 0970" P 43 0970 **Longitudinal Mapping of Sodium-Glucose Transport and Disaccharidase Activity in Human Small Intestine**

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Faculty of Medicine & Health Sciences, United Arab Emirates University, Al Ain,

U.A.E. *Purpose:* We have used vesicles prepared from resection specimens to map the profile and properties of some brush border membrane proteins along the length of human small intestine

*Methods:* Sodium-dependent glucose uptake and sucrase-isomaltase activity were determined in brush border membrane vesicles (BBMVs) prepared from duodenum, jejunum, mid and terminal ileum by differential centrifugation and Mg precipitation. A potential role of ras in regulating non receptor-mediated transport of glucose was investigated by conversion of membrane-bound ras to the GDP form by treatment with neurofibromin. All tissues used had normal histological appearance and were obtained fresh from patients undergoing surgery for non-inflammatory benign disease or localized malignancy. *Results:* BBMVs prepared from all 4 regions had comparable diameter (142–160 – 9 nm) and a similar appearance on EM examination. Purity was confirmed by the 7–12 fold enrichment in alkaline phosphatase and 3–5 fold depletion in basolateral membrane potassium-stimulated ATPase. Recovery and enrichment of sucrase ranged between 17–29 fold and 27–47% respectively. Vesicles from all four regions of small bowel supported sodium-dependent transport of <sup>14</sup>C-labeled D-glucose as revealed by a substantial overshoot in the presence of NaSCN. Diffusional uptake of D-glucose was not influenced by KSCN. Peak rates of D-glucose uptake in the duodenum, jejunum, mid and terminal ileum were 168, 829, 352, and 169 pmol/mg protein respectively. Corresponding values for the specific activity of sucrase were 0.3, 1.6, 3.6 and 2.4 μmol/mg protein/min. Vesicles prepared in the presence of an excess of neurofibromin displayed rates of glucose uptake similar to control. *Conclusions:* These data reveal the regional differences along the human small intestine with respect to membrane-bound disaccharidase and transmembrane monosaccharide transport. Sucrase activity was maximal in the mid ileum but substantial activity was still present in the terminal ileum. Sodium-dependent glucose uptake was maximal in the jejunum (initial rate 126 – 9 pmol/mg protein/sec) and was unaffected by inhibition of ras. Intestinal disorders, absorption: Epithelial transport Intestinal disorders: IBD, etiology and genetics Nutrition: Techniques of nutrition } "Longitudinal Mapping of Sodium-Glucose Transport and Disaccharidase Activity in Human Small Intestine"

"P P 43 0971" P 43 0971 **Celiac Disease and Autoimmune Thyroid Disease**

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The association of Celiac Disease (CD) and Thyroid Disease (TD) has previously been described. However, being most of the published data based on retrospective studies or case note review, the exact frequency of thyroid disorders in CD is as yet unclear. We prospectively examined a cohort of adult CD patients drawn from a defined geographical area in Central Italy. *Patients and methods:* the study group comprised 92 CD patients diagnosed between April 1992 and March 1996 (26 M, 69 F; mean age at diagnosis 38.3 yr, range 15–78). The diagnosis of CD was based on the clinical history, laboratory and histological findings, and a good clinical response to a gluten free diet. Age and sex matched controls were selected from among outpatients with HCV-related chronic hepatitis, consecutively referred to our center for interferon therapy. Total and free T<sub>3</sub> and T<sub>4</sub>, and TSH were measured by standard RIAs to assess thyroid function; thyroid microsomal (TM) and thyroglobulin (TG) antibodies were determined by indirect immunofluorescence and agglutination techniques. *Results:* an associated thyroid disorder was found in 15.2% of patients and 2.3% of controls (Chi square,  $p < 0.001$ ): 7 patients (7.6%) were hypothyroid, 3 (3.3%) were hyperthyroid, and 4 (4.3%) had TG and/or TM antibodies with a normal thyroid function. The mean age of patients with both CD and TD was significantly higher than that of those with just CD (49.1 vs. 29.5 yr: Student's *t* test,  $p < 0.001$ ). In 6 of the 14 patients with both diseases the TD had presented first: 2 patients with Grave's disease and 3 with hypothyroidism had received adequate treatment and were euthyroid at the time of examination; in a further hypothyroid patient chronic diarrhoea was thought to be a complication of thyroxine supplementation. Moreover, in 3 patients a prior diagnosis of CD delayed the recognition of the symptoms of hypothyroidism (2 cases) or hyperthyroidism (1 case). All the others were found to have overt TD or TG and TM autoantibodies at the time their CD was diagnosed. *Conclusions:* we have shown that the association of CD and TD is clinically important and more frequent than previously recognized. Since both diseases can present with similar clinical manifestations, we believe that thyroid function and autoantibodies should be checked routinely in all celiac patients at presentation. Intestinal disorders, absorption: Gluten enteropathy } "Celiac Disease and Autoimmune Thyroid Disease"

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"P P 43 0972" P 43 0972 **Gluten Free Diet (GFD) Induces Regression of T-Cell Activation not Only in Duodenum but also in Rectum of Adult Patients with Coeliac Disease (CD)** J.P. Cervoni<sup>1</sup>, C. Cellier<sup>1</sup>, N. Patey<sup>3</sup>, M. Leborgne<sup>3</sup>, S. Chaussade<sup>2</sup>, J.Ph. Barbier<sup>1</sup>, N. Cerf-Bensussan<sup>4</sup>, N. Brousse<sup>3</sup>

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<sup>4</sup> INSERM U 429 Paris, France An increase in the number of intraepithelial lymphocytes (IEL) has been described in rectal biopsies of patients with active CD, and after rectal challenge in treated CD patients. However this data is not available concerning variation of IEL induced by GFD in rectal mucosa. *Aims:* To assess the effect of a GFD on the number of IEL and local signs of T-cell activation in rectal mucosa of CD patients. *Patients and Methods:* Duodenal and rectal frozen biopsies were available in 4 adult coeliac patients (1 M, 3 F, mean age = 39 years) before and after 7 to 24 months of GFD. Monoclonal antibodies directed against CD3, CD25 and HLADR were used for each biopsy. Numbers of labelled IEL were estimated by counting the peroxidase stained cells per 100 epithelial cells. Four normal duodenal and rectal biopsies were used as controls. *Results:* Results of immunostaining Median CD3 CD 25+ HLADR +Duodenum before GFD 78 4/4 4/4 after GFD 55 3/4 2/4 controls 18 0/4 0/4 Rectum before GFD 24 4/4 2/4 after GFD 12 0/4 0/4 controls 13 0/4 0/4 median CD3 = median of intraepithelial lymphocytes for 100 endothelial cells CD25 and HLA DR are expressed as the number of positive patients in each group *Conclusion:* These results suggest that gluten driven T-cell activation is not restricted to proximal part of this intestine but is present on the whole intestinal length. Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption syndromes } "Gluten Free Diet (GFD) Induces Regression of T-Cell Activation not Only in Duodenum but also in Rectum of Adult Patients with Coeliac Disease (CD)"

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"P P 43 0973" P 43 0973 **Immunoglobulin Deficiency in Coeliac Disease: A Single Institution 25 Year Experience**

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Immunoglobulin deficiency, especially deficiency of IgA has been described in coeliac patients. Between 1971 and 1996, over 700 coeliac patients have been treated at this institution. Immunoglobulins have been measured on at least one occasion in 604 of these. Case notes of these patients were reviewed to determine the prevalence of Immunoglobulin deficiency states in this population. *Aims:* To examine the clinical characteristics of coeliac patients found to be deficient in IgA, and to compare them with a group of age and sex matched coeliac patients with normal IgA levels. *Results:* 14 cases (8 women and 6 men) were identified as being selectively deficient in IgA. One man had common variable immunodeficiency. Mean age at diagnosis was lower in the IgA deficient group (17.52 versus 26.12 yrs.). Anaemia was present in 8/14 IgA deficient patients compared with 3/14 controls,  $p = 0.121$ . Abdominal pain was more prevalent among coeliac controls, (5/14) versus (1/14) IgA deficient coeliacs, ( $p = 0.167$ ). Recurrent infection and an increased prevalence of autoimmune conditions was noted in the IgA deficient group, but the difference was not significant. Response to gluten free diet was similar in both groups. No difference was found in the prevalence of HLA B8 and DR3 among the two groups. No IgA deficient coeliac was deficient in any IgG subclass. *Conclusions:* The prevalence of IgA deficiency in west of Ireland coeliacs is 2.31/100. This is similar to other coeliac groups and 13–18 times greater than the general population. These are a distinct group of coeliac patients with unique characteristics, and should be followed closely. We also suggest that all coeliacs be monitored for this state.

Intestinal disorders, absorption: Pathophysiology of diarrhea  
Intestinal disorders, absorption: Gluten enteropathy  
Intestinal disorders, absorption: Malabsorption syndromes }

"Immunoglobulin Deficiency in Coeliac Disease: A Single Institution 25 Year Experience"

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"P P 43 0976" P 43 0976 **Gastric Intraepithelial Lymphocytes (GIELs) and Lymphocytic Gastritis (LG) in Adult Celiac Patients**

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<sup>3</sup> Ist. Chirurgia Generale, IRCCS-Ospedale Policlinico, Università di Milano, Italy *Background and aims.* LG has been associated with H. pylori infection and with celiac disease. The prevalence of LG in adult celiac patients from the Mediterranean area is still unknown. The aims were to correlate GIEL concentration and the prevalence of LG and H. pylori infection in adult celiac patients. *Patients and methods:* Two or more antral gastric biopsies were taken prospectively in a consecutive series of 49 celiac patients (37 on free diet, 12 on gluten free diet for 6 months at least) and compared with those from 22 non celiac patients comparable for sex and age. Biopsies were examined separately by 2 observers and assessed for the presence of gastritis and H. pylori infection. LG was diagnosed if 25% GIELs were counted in at least 300 surface epithelial cells per biopsy. GIELs were also identified by antibody anti-CD3 and anti-CD20. *Results.* LG was not diagnosed in any patient or control. Mean (range) GIEL concentration was 3 (1–20)% in celiac patients on free diet, 2 (1–10)% in those on gluten free diet and 1 (0–6)% in controls ( $P < 0.001$ ). H. pylori infection was observed in 25% patients and 32% controls. *Conclusions.* LG may be rare in adult celiac patients from the Mediterranean area. Genetic factors may affect the immunological status of these celiac patients. Whether patients with and without increased GIELs differ in response to gluten free diet and in risk of intestinal lymphoma should be investigated. *Intestinal disorders, absorption: Gluten enteropathy Immunology and microbiology: GI infections in adults Immunology and microbiology: Inflammation }* "Gastric Intraepithelial Lymphocytes (GIELs) and Lymphocytic Gastritis (LG) in Adult Celiac Patients"

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"P P 43 0977" P 43 0977 **Eating Habits of Children with Down Syndrome**

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<sup>4</sup> Dutch Down Syndrome Foundation, The Netherlands Children with Down syndrome (DS) frequently have feeding problems which can predispose to an inadequate dietary intake. *Aims:* 1. To study the eating habits and nutrient intake of 44 children with DS (0–4 year). 2. Compare them to that of 37 healthy control children, matched for age and sex. 3. Investigate whether the Recommended Dietary Allowances (RDA) (1) are appropriate for these children. *Methods:* The food intake was assessed by the dietary history method. Data from patients and controls were compared using the ANOVA analysis. The data from the children with DS were compared to the RDA by means of the Student-t test. *Results:* The mean weight of the children with DS was 9.7 – 2.7 kg (P25) versus 11.7 – 3.6 kg (P50) in the controls. The mean height of the children with DS was 78.5 – 10.5 cm (P50) versus 83.6 – 13.4 cm (P25) in the controls ( $p < 0.01$ ). The median age at introduction of bread, of hard pieces of fruit and of warm meals was significantly older among the children with DS (12, 30 and 24 months respectively) than in the controls (8, 12 and 12 months respectively). No significant differences were found in the energy intake from macronutrients. The daily intake of vitamins B2, B6 and calcium of the children with DS was significantly lower than in the controls, but in agreement with the RDA. The energy intake per kg body weight of the children with DS reaches the RDA. *Conclusions:* The most important difference in the eating habits of children with DS versus controls is the age at introduction of solid food. The fact that the energy intake per kg body weight of the children with DS reaches the RDA can be explained by the significant lower body weight of the children with DS compared to the controls ( $p < 0.01$ ). Dietetic advice to DS children should be based on the body weight and on the developmental age of the child and not on their chronological age. (1). The Netherlands food and Nutrition Council. The Recommended Dietary Allowances 1989 in the Netherlands. 1992, 2nd edition, The Hague. Nutrition: Nutrition: children } "Eating Habits of Children with Down Syndrome"

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## "P P 43 0978" P 43 0978 Cow's Milk Allergy and Down Syndrome

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The board of the Dutch Down syndrome Foundation (DDF) suspected children with trisomy 21 (DS) to have cow's milk allergy (CMA) more often than children in the general population (1.7–2.8%) [1]. *Aim.* The DDF asked us to establish the frequency of CMA in their young members. *Design.* Experimental, prospective, double-blind, food intervention study. *Patients.* All 109 families living in the western part of the Netherlands were invited. Inclusion criteria: having a child with DS, age 0–4, home-reared, not diagnosed as having CMA, not being breast-fed. *Methods.* The diagnosis of CMA was based on the gold standard of double blind food intervention: improvement of symptoms on cow's milk protein (CMP) elimination and worsening of the same symptoms on CMP introduction. A positive elimination-introduction-re-elimination test was considered diagnostic. During the whole study the children followed a CMP-free diet based on an adapted hypo-allergenic whey hydrolysate milk formula (Nutrilon Pepti Plus, Nutricia Nederland BV). CMP was double-blind introduced by adding 1.5 g CMP per 100 ml CMP-free formula. Before and after each food intervention the symptoms compatible with CMA (respiratory, dermatological, gastrointestinal) were scored. *Results.* Data on CMA before the study were available in 92 children: in 3 of them CMA had already been diagnosed, but not according to the elimination-introduction-re-elimination principle. 44 children participated in our study (41%, 22 boys. Mean age: 21 – 11 months). The main reason to participate (63%) was to exclude CMA. Reasons for not participating were too great a burden on the family (13%), no suspicion of CMA (12%), a critical clinical condition (7%) and unknown reasons (27%). CMA was proven in 1 child (2.8%; 95% CI: 0.1%–14.5%). *Conclusion.* In a selected group of children with DS (meanly parents suspecting their child to have CMA participated) we found CMA only in 1 of 109 children (1%; 95% CI: 0%–5.1%). The frequency of CMA in children with DS seems to be similar to the one reported in the general Dutch child population.

Reference: Eur J Pediatr 1993; 152: 640–4. Clinical practice: Epidemiology (non cancer) Nutrition: Nutrients and gut function Nutrition: Nutrition: children } "Cow's Milk Allergy and Down Syndrome"

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"P P 43 0979" P 43 0979 **Acute Diarrhoea in France Probably Due to Rotavirus during Winter: A Case-Control Approach**

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<sup>3</sup> Département de Gastro-entérologie, Hôpital Rothschild, Paris, France *Background*—The surveillance data gathered from the *Sentinelles* Network at a national level indicates that acute diarrhoea (AD) occurs with an endemic pattern usually including an epidemic winter outbreak [1]. We estimate that 670 000 cases of AD were diagnosed in general practice in January 1996. However the determinants of AD during the winter period are not well established in France. *The aim* of this study was to ascertain risk factors of AD: mode of transmission (consumption of shellfish, of soft water; recent contact with a case of diarrhoea) and facilitating factors (drug consumption; association with influenza or ear infection; underlying chronic disease). *Methods*—A case-control study was conducted with incident cases matched to controls for age class; 588 cases and 568 controls were included among the patients of sentinelle practitioners between December 24, 1995 and January 31, 1996. Conditional logistic regression was used for statistical analyses. *Results*—There was no association between AD and any shellfish consumption — e.g. raw oysters (OR = 1.1 [0.9; 1.4]) — or soft water drinking (OR = 0.7 [0.5; 1.0]). Factors significantly associated with AD were: an intra-familial contact with a case of diarrhoea within the last ten days (OR = 4.4 [3.0; 6.3]); an estimated delay inferior to 3 days between the time of contact and the date of consultation (OR = 10.8 [4.9; 23.8]); and cohabitation with a child under two (OR = 1.9 [1.3; 2.7]). *Conclusion*—These results stress the major role of person-to-person transmission in the occurrence of winter acute diarrhoea epidemics. The nature of the factors significantly associated with the risk of AD is suggestive of a viral etiology. Rotavirus, because of its infantile epidemiology and its incubation period usually inferior to 3 days, is one of the most plausible causes of winter diarrhoea.

Reference: Flahault et al. Sentinelle traces of an epidemic of acute gastroenteritis in France. *Lancet* 1995; 346: 162–3. Clinical practice: Epidemiology (non cancer) Immunology and microbiology: GI infection, children Immunology and microbiology: GI infections in adults }  
"Acute Diarrhoea in France Probably Due to Rotavirus during Winter: A Case-Control Approach"

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"P P 43 0980" P 43 0980A **French Survey on Epidemiology and Management of Acute Diarrhoea** H. Allemand<sup>1</sup>,

\*M. Amouretti<sup>2</sup>, J.F. Colombel<sup>3</sup>, J. Frexinos<sup>4</sup>, P. Rampal<sup>5</sup>, M. Robaszekiewicz<sup>6</sup>, P. Bordet<sup>7</sup>

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<sup>7</sup> Janssen Cilag, Paris, France Although acute diarrhoea is a common problem, little is known about its epidemiology, management and socio-economic impact. *Method:* 6-month survey, using 2 previously validated questionnaires (Q) via Minitel: this system allows real-time follow-up and validation of data. 176 of 277 practitioners (GPs) who initially agreed on participating throughout France, completed <sup>1</sup> over 6 months: *phase-1* Q in all patients (pts) (> 15 yrs) presenting with acute diarrhoea (≥ 3 stools per days, max 72 hrs) and <sup>2</sup> during 2 defined periods: *phase-2* Q on outcome of diarrhoea in 5 consecutive pts (4 – 3 days after phase 1). *Results.* Information was generated in 4200 patients by 176 GPs (age 42 (15–98) yrs, ratio M/F 42/58, 48.4% had profession). Seasonal variations were not observed. The main associated symptom was abdominal pain (84%). Vomiting was reported in 39%, fever in 33%, mucus in stools in 9% and dehydration in 3%. The cause was thought to be viral in 51%, alimentary 23%, drug-induced 8%, bacterial 6.5% and parasitic 0.7%. The duration of episode varied mostly 1–3 days. Self-medication was initiated by 1 of 3 pts prior to consultation. Management was mainly handled by GP's, with few investigation (8% stool culture; 3.5% other), rare referral (2%) or hospitalisation (– 1%). Medication was prescribed in 95% of pts. Diarrhoea (mainly high stool frequency, fever and severe symptoms) lead to absenteeism at work in 1 of 3 pts, usually of short duration (– 3 days). Direct costs of management were the lowest in case of Imodium prescription, but indirect costs (days of sick-leave) appeared not to be affected by type of medication prescribed. *Conclusion.* Diarrhoea is a common condition, leading to relatively low direct health care costs per pt, but frequent work loss of short duration. Clinical practice: Epidemiology (non cancer) Clinical practice: Management strategy } "A French Survey on Epidemiology and Management of Acute Diarrhoea"

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## "P P 43 0981" P 43 0981 Comparison of Loperamide-Oxide and Acetorphan in Acute Diarrhoea

\*J. Frexinos<sup>1</sup>, J.-R. Sallenave<sup>2</sup>

<sup>1</sup> Hopital Rangueil, Toulouse, France

<sup>2</sup> Janssen-Cilag and GP's Cooperative Group, France Loperamide-oxide (LOX), a new loperamide derivative with higher mucosal (antisecretory) than myenteric (motility-inhibiting) properties, was compared with acetorphan (ACE), an antidiarrheal without effects on gut peristalsis and thought to give less constipation than loperamide. *Method:* Randomized, double-dummy placebo (PLA)-blinded study in 574 adult outpatients (pts) with acute diarrhoea (lasting 12 hrs and 72 hrs; 3 (semi-)liquid stools/day). Pts received LOX, 2 tabs of 1 mg at start and 1 tab after each unformed stool (max 8 tabs/day), plus 3 PLA caps identical to ACE, or ACE 100 mg tid, plus LOX-identical PLA tabs. Hospitalization, blood in stools, fever (> 38.5°C), severe infection, chronic diarrhoea, IBD, and intake of antibiotics or other antidiarrhoeals were excluded. Treatment lasted until the end of diarrhoea or max 96 hrs. *Results.* Diarrhoea was resolved in 53% LOX pts, vs 48% ACE pts within 24 hrs, and in almost equal % within 48 hrs (– 87%) and 96 hrs (– 98%). There were no significant differences in mean duration of diarrhoea (26.8 hrs for LOX, vs 28.9 hrs for ACE) or daily number of unformed stools. The number of unformed stools, however, was lower with LOX than with ACE during the total 3-day period ( $p < 0.03$ ), until resolution of diarrhoea ( $p < 0.06$ ) and in the responding pts ( $p < 0.01$ ). Overall response was in favour of LOX when rated by physicians ( $p < 0.01$ ), a difference not found among the pts' assessments. Both drugs were well tolerated, but less aggravation of bloating occurred with LOX ( $p = 0.02$ ). Quality of life was comparable in both groups during the 1st and 2nd day, but in favour of LOX during the 3rd day (less pts with incapacitating symptoms or interrupting work,  $p < 0.05$ ). *Conclusions.* Overall, LOX and ACE are almost equally effective and tolerated; results for some limited parameters slightly favour LOX. Motility, general: Functional GI disorders Clinical practice: Management strategy } "Comparison of Loperamide-Oxide and Acetorphan in Acute Diarrhoea"

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"P P 43 0982" P 43 0982 **Bacterial Overgrowth of the Small Bowel (BOSB) and Malabsorption of Low Weight Sugars in Isolated IgA Deficiency** M. Romeo, G. Balducci, G.F. Sasso, G. Mattiacci, F. Lintas, B. Ceccanti, P. Santini, M. Ceccanti

Dept. Clinical Medicine, University of Rome "La Sapienza" In isolated deficiency of IgA patients BOSB is frequent, leading to chronic diarrhea. The reference method for BOSB was the demonstration of a large number of microbial colonies ( $> 2 \times 10^5$ /ml) in cultures of jejunal fluid. Recently, H<sub>2</sub>-breath test (HBT) was found useful: a good correlation between jejunal-fluid culture data and the fasting basal levels of H<sub>2</sub> in expired air ( $> 10$  ppm) was reported. Relevant lactose malabsorption was demonstrated by our group in chronic alcoholics, frequently affected by diarrhea and impairment of IgA function. In this study, a series of patients affected by primary IgA deficiency was tested by HBT, to confirm the relationship between fasting basal overproduction of H<sub>2</sub> and BOSB, and to assess the frequency of low weight sugars (LWS) malabsorption. *Materials and methods.* A series (A) of 27 patients (14 male, 0.13 female; age 33–46 y., m – SD = 39.9 – 17.16) affected by primary IgA deficiency, without any detectable parasite in the gut were investigated. Controls (C) were 38 healthy people, matched for age, sex and dietary habits. All the subjects were taken at a low-fiber diet for two days before the test. Body weight and height were measured. HBT was performed in the morning (starting about at 8 a.m.) after a 12-hour fasting. Basal H<sub>2</sub>-level in expired air was assayed; lactose (20 g/H<sub>2</sub>O 100 ml) was administered; samples of expired air were taken each 30 min for 4 hours. The diagnosis of lactose malabsorption was established if in at least 3 consecutive samples the H<sub>2</sub>-levels were  $> 20$  ppm higher than basal levels. Statistical evaluation was performed by  $\chi^2$ -test and Tau-C Kendall's test, for Area Under Curve (AUC) evaluation, by Mann-Witney's test. *Results.* Basal H<sub>2</sub>-level was 8.5 – 9.0 ppm [confidential interval (ci) = 3.9 – 7.2] in group A and 5.6 – 5.2 ppm (ci = 4.99 – 12.08) in the group C. The frequency of malabsorption was 78.6% in group A and 41.0% in group C: H<sub>2</sub>-AUC was 12,741.72 – 11,497.15 (ci = 8,283.30 – 17,199.56) in group A and 3,185.77 – 3,617.92 (ci = 2,012.97 – 4,358.56) in group C. Body Mass Index (BMI, body weight/body height<sup>2</sup>) was 22.96 – 3.17 (ci = 21.73 – 24.19) in group A, 24.18 – 3.28 (ci = 23.12 – 25.25) in group C. *Conclusions.* According to our data, basal H<sub>2</sub>-levels are increased in IgA deficiency respect to controls, suggesting BOSB (p < 0.001). Also the frequency of malabsorption is increased in IgA deficiency, as confirmed by AUC values (p < 0.001). LWS malabsorption leads to lowered BMI in IgA deficiency, suggesting impaired LWS utilization. These clinical findings may be related to: 1) modifications of intestinal microenvironment, specific for IgA deficiency (both congenital and acquired), leading to H<sub>2</sub>-consuming bacteria decrease and to saccharolytic bacteria increase, producing the increased H<sub>2</sub>-levels in the colon; 2) small bowel mucosa impairment, frequent in IgA deficiency patients, leading to reduced activity of brush border enzymes, promoting increased frequency of malabsorption; 3) increased osmolarity of stool and increased production of volatile fatty acids (with cathartic activity) in the colon, leading to increased frequency of diarrhea, promoting the BMI decrease (p < 0.001) observed in IgA deficiency patients. Intestinal disorders, absorption: Malabsorption syndromes } "Bacterial Overgrowth of the Small Bowel (BOSB) and Malabsorption of Low Weight Sugars in Isolated IgA Deficiency"



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## "P P 43 0983" P 43 0983 Efficacy of Two Antibiotics and a Probiotic in the Treatment of Small Intestinal Bacterial Overgrowth

\*A. Attar, Y. Bouhnik, B. Flourie, C. Franchisseur, P. Crenn, F. Briet, J.C. Rambaud

Department of Gastroenterology, Saint-Lazare, Paris, France Although antibiotics are widely used in the treatment of small intestinal bacterial overgrowth (SIBO), no controlled trial has been performed to test their efficacy. *In this study* we compared 3 treatments: 1) amoxicillin-clavulanic acid (Am-c) which is *in vitro* the most efficient antibiotic against aerobic and anaerobic bacteria isolated from jejunal contents of patients with SIBO (Bouhnik et al., *Gastroenterology*, 1993, 104, A237), 2) norfloxacin (Nor) which is only efficient against aerobic bacteria, 3) *Saccharomyces boulardii* (Sb), a probiotic agent whose efficacy has been reported in children with SIBO. *Methods*: Ten patients suspected to have SIBO (predisposing conditions, chronic diarrhea, malabsorption syndrome) and a positive H<sub>2</sub> breath test (H<sub>2</sub>BT) were enrolled and received for five 7 days periods no treatment (basal period), a *placebo* (Pla) and then, in a random order and double blinded fashion, Nor (800 mg/d), Am-c (1500 mg/d) and Sb (1500 mg/d). The main criteria of efficacy was the mean daily number of stools reported on the last 3 days of each periods. When the treatment was considered efficient, patients were followed until worsening of diarrhea and were then included in the next period. A H<sub>2</sub>BT was performed on the first and the last day of each period. *Results*: (m – SD) compared to basal period, Nor and Am-c led to a significant reduction in the mean daily number of stools (4.2 – 2.2 vs 2.3 – 1.2 and 3.0 – 1.5; P < 0.01, respectively) whereas Pla and Sb had not effect (3.9 – 1.9 and 3.8 – 1.6). Benefit of Nor and Am-c occurred after respectively 2.0 – 1.4 and 1.2 – 0.4 days and was maintained for 6.1 – 3.7 and 14.2 – 23 days after withdrawal; however, H<sub>2</sub>BT became negative in only 30 and 55% of patients during Nor and Am-c periods respectively. Nor and Am-c reduced the number of stools in 9 and 6 patients out of 10. Hydrogen excreted in breath decreased during Nor and Am-c periods (from 37 – 24 to 12 – 14 ml/2 h, P < 0.01 and from 24 – 19 to 8 – 14 ml/2 h, P = 0.01) but was not modified during Pla and Sb periods. *Conclusion*: Norfloxacin and amoxicillin-clavulanic acid are effective in the treatment of diarrhea induced by SIBO but more patients responded to norfloxacin in spite of a narrower spectrum and inefficiency against anaerobic bacteria. The improvement of diarrhea is associated with a reduction in the abnormal bacterial metabolic activity in the small intestine, but not necessarily with its removal. Intestinal disorders, absorption: Malabsorption syndromes Clinical practice: Management strategy } "Efficacy of Two Antibiotics and a Probiotic in the Treatment of Small Intestinal Bacterial Overgrowth"

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## "P P 43 0984" P 43 0984 The Ursodeoxycholic Acid-p-Aminobenzoic Acid Loading Test, a New Diagnostic Tool in the Bacterial Overgrowth Syndrome

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**Introduction:** Contaminated small bowel syndrome (CSBS) is frequently associated with different clinical symptoms, among which meteorism and diarrhoea are common. Meteorism is due to excessive gas formation, while diarrhoea is a result of bacterial toxins and pathological fermentative processes. These mechanisms include abnormal splitting of carbohydrates, and deconjugation and dehydroxylation of bile salts. Some bacteria capable of metabolizing bile salts have been shown to release *p*-aminobenzoic acid (PABA) from an ursodeoxycholic acid (UDCA)-PABA conjugate. The present aim was to determine the possible complementary role of the UDCA-PABA test in the diagnosis of intestinal bacterial overgrowth. **Patients and methods:** The H<sub>2</sub> breath and UDCA-PABA tests were performed simultaneously in 68 patients with suspected CSBS, and in 5 healthy control subjects. The H<sub>2</sub> breath test involved was performed by oral loading of 25 g lactose and or 10 g lactulose. The UDCA-PABA test was carried out by the oral loading of 250 mg UDCA-PABA conjugate, followed by measurement of the amount of urinary excreted PABA. The diagnosis of bacterial overgrowth was considered to be established when either the H<sub>2</sub> breath test or the UDCA-PABA test yielded proved pathological results. **Results:** 35 of the 68 patients proved to have CSBS. In 13 of the 35, only the enhanced urinary PABA excretion (11.7 – 1.42 mg vs 3.6 – 0.68 mg) indicated the bacterial overgrowth. 15 of the 35 gave only a positive H<sub>2</sub> breath test, and in the remaining 7 cases the results of both tests were pathological. In 8 CSBS patients, the urinary excretion of PABA decreased significantly following a 10-day Tinidazole treatment (5.5 – 1.29 mg vs 13.1 – 2.07 mg). **Conclusion:** The UDCA-PABA test is to be a valuable clinical adjunct to the H<sub>2</sub> breath test for the detection of intestinal bacterial overgrowth: the H<sub>2</sub> production alone failed to reveal bacterial overgrowth in 37% of the cases. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Malabsorption syndromes } "The Ursodeoxycholic Acid-p-Aminobenzoic Acid Loading Test, a New Diagnostic Tool in the Bacterial Overgrowth Syndrome"

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"P P 43 0985" P 43 0985 **Bacterial Colonisation of the Upper Gastrointestinal Tract Is Related to Severity of Illness**

\*C.J. O'Boyle, A. Gilliam, R. Williamson, P. Buckley, C.J. Mitchell, J. MacFie

Combined Gastroenterology Unit, Scarborough General Hospital, Scarborough, North Yorkshire The upper gastrointestinal tract is usually regarded as being sterile. The occurrence of bacterial colonisation in the upper gastrointestinal tract may predispose to septic morbidity. It has been suggested that this occurs more frequently in critically ill or immunocompromised patients. The aim of this study was to assess changes in gastric flora and to attempt to relate these to severity of illness. We have prospectively evaluated proximal gut microflora in 279 surgical patients by culturing aspirates obtained aseptically from indwelling nasogastric suction tubes. Severity of illness was assessed using the 'POSSUM' physiological scoring system. Eighty five (31%) aspirates yielded no growth, eighty four (30%) patients grew one organism type and 110 (39%) grew multiple organism types. *Candida albicans* was the most abundant organism cultured and was present in 104 (37%) of aspirates. This was followed by *E. Coli* 38 (14%), *Strep. Sp.* 33 (12%), *Lactobaccillus* 27 (10%) and *Strep. Fecaelis* 23 (8%). Forty eight percent (175) of bacteria isolated would not commonly be associated with intestinal colonisation. Multiple organism colonisation occurred in significantly fewer patients with low (< 20) POSSUM scores than those with high (> 30) scores (35% vs 67%,  $p < 0.02$ ,  $\chi^2 = 7.09$ ) and was associated with an increase in septic morbidity. We conclude that upper gastrointestinal tract colonisation is common in surgical patients and that bacterial overgrowth is related to the degree of physiological stress and may predispose to septic morbidity. Immunology and microbiology: Host defense mechanisms Immunology and microbiology: GI infections in adults } "Bacterial Colonisation of the Upper Gastrointestinal Tract Is Related to Severity of Illness"

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"P P 43 0986" P 43 0986 **Prophylaxis of Mucosal Damage with Sucralfate During Cancer Therapy**

\*L. Franz<sup>1</sup>, G. Edbom, B. Zackrisson, R. Henriksson

Dept. of Oncology, Umea University Hospital, S-901 85 Umea, Sweden *Purpose.* Radiotherapy and chemotherapy of different malignancies may be complicated by a variety of side effects, some of which may be related to mucosal damage. The value of sucralfate in the prevention of radiation induced symptoms was suggested by the results of two open studies one with prostate and urinary carcinomas and the second with gynaecological cancer treated with radiotherapy. *Methods.* A double-blind randomised placebo-controlled study in patients treated with curative intent for prostate and urinary bladder cancer with external radiotherapy and the study included 70 patients. The other study also double-blind, placebo-controlled included 50 patients receiving irradiation against the head and neck region with curative intent. *Summary of the results.* For the head and neck patients the mucosal reactions were significantly worse for the placebo group at week 1, 2 and 3, but at other observation times the differences did not reach statistical significance. The results of the pelvic treated patients showed that the frequency of diarrhoea, stool consistency and the number of patients requiring symptomatic therapy with loperamide were significantly in favour of sucralfate group. *Conclusion.* The studies demonstrated that sucralfate can be of value in reducing radiation induced bowel and oral symptoms during and following radiotherapy of the head and neck and pelvic region. Oncology, specific: Oesophagus Oncology, specific: Stomach Oncology, specific: Colon, rectum } "  
"Prophylaxis of Mucosal Damage with Sucralfate During Cancer Therapy"

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## "P P 43 0987" P 43 0987 H<sub>2</sub> Starch Breath Test in the Study of Functional Gastrointestinal Disorders

\*M. Ventrucci, G.M. Ubalducci, A. Cipolla, E. Roda

Dept. of Gastroenterology, University of Bologna, Italy Many patients with irritable gut experience gastrointestinal distress after starch ingestion. We studied the oro-cecal transit and absorption of starch by means of a H<sub>2</sub> breath test in 121 H<sub>2</sub> producers: 106 patients with functional gastrointestinal disorders (72 with dyspepsia, 17 with constipation, and 17 with diarrhea) and 15 healthy volunteers. Breath samples were taken every 30 min for 9 hours after ingestion of 100 g of starch in the form of white bread. H<sub>2</sub> breath tests with lactulose (10 g), lactose (20 g) and fructose (25 g) were also carried out in 34, 76 and 67 subjects, respectively. Results are expressed as medians and interquartile ranges (25–75%). *Results:* Incomplete absorption of starch (peak rise in breath H<sub>2</sub> > 10 ppm) was present in 11/15 healthy controls (73%) and in 76/106 patients (72%). Starch ingestion caused gastrointestinal symptoms in only 11 patients of whom 7 showed starch malabsorption. The 9 hour H<sub>2</sub> excretion (area under the curve) after starch ingestion was significantly lower ( $p < 0.05$ ) in patients (42 ppm{\'d7}h, 26–82) than in controls (82 ppm{\'d7}h, 36–126). The oro-cecal transit time of starch did not significantly differ between the two groups (330 min, 270–390 in patients and 300 min, 180–300 in controls), but was significantly lower ( $p < 0.01$ ) in patients with diarrhea (240 min, 180–330) when compared with those suffering from dyspepsia (330 min, 270–405). An inverse relationship was found between H<sub>2</sub> output and transit time in patients ( $\rho = \{-\}0.65$ ), but not in controls ( $\rho = \{-\}0.22$ ). No relationship was found between the H<sub>2</sub> excretion or transit time measured after starch and those after lactulose. The H<sub>2</sub> excretion after starch was not significantly different between the 36 patients with lactose malabsorption (43 ppm{\'d7}h, 29–82) and the 40 patients with normal lactose response (35 ppm{\'d7}h, 15–78). In the 33 patients with fructose malabsorption in the H<sub>2</sub> excretion after starch was higher (55 ppm{\'d7}h, 29–96,  $p = 0.06$ ) than in the 34 with a normal fructose breath test (36 ppm{\'d7}h, 17–75). *Conclusions:* The H<sub>2</sub> starch breath test needs further investigation before it can be used for the diagnosis of functional gut disorders. According to our results gastrointestinal distress after starch ingestion in patients with irritable gut cannot be attributed to excessive H<sub>2</sub> intestinal production. Motility, general: Functional GI disorders Intestinal disorders, absorption: Malabsorption syndromes }" "H<sub>2</sub> Starch Breath Test in the Study of Functional Gastrointestinal Disorders"

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## "P P 43 0988" P 43 0988 Treatment with Lidocaine Gel Enema for Ulcerative Colitis

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<sup>1</sup> Second Department of Internal Medicine, School of Medicine, The University of Tokushima, Tokushima, Japan

<sup>2</sup> First Department of Pathology, School of Medicine, The University of Tokushima, Tokushima, Japan  
*Purpose:* Neuropeptides liberated from enteric neurons have been suggested to contribute to the inflammatory process in ulcerative colitis (UC). Furthermore, inhibitory effects of lidocaine on the responses elicited by neuropeptides were also studied. We studied the efficacy of lidocaine gel enema (LG), reported in 1989 by Bjork, for UC. *Methods:* The subjects of this study were 10 patients who underwent LG at our department. Eight of 10 patients were the left colitis type and two were proctitis type. The conditions before the start of LG were the followings. Seven patients had poorly controlled on sulfasalazine. One became in worse condition during progressive reduction of steroid dosage. One could not reduce the dose level of steroid. One had to stop the steroid therapy because of the side effect. LG was performed as follows. 40 ml (10 ml in the morning, 10 ml in the daytime and 20 ml at night) of 2% lidocaine gel was administered into the rectum. Endoscopy was carried out immediately before and 2 weeks after the start of LG, and biopsy samples of the rectum were examined histologically. *Results:* In all cases, rectal discomfort disappeared within 5 days, and viscous bloody feces disappeared within 2 weeks after the start of LG. Endoscopically, the disappearance of rectal ulcers and a reduction in rectal erosion were observed after 2 weeks of LG. The numbers of crypts and goblet cells were increased, and the inflammation was reduced after 2 weeks of LG. Substance P immunoreactive for nerve fibers slightly increased after 2 weeks of LG. None of the patients complained about any side-effects of LG. *Conclusion:* LG is easy to do and is expected to reduce inflammation, probably through suppressing the release of neuropeptides. LG will be a promising new therapy for UC. Intestinal disorders: IBD, therapy } "Treatment with Lidocaine Gel Enema for Ulcerative Colitis"

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"P P 43 0989" P 43 0989 **Interleukin-8 Induced Neutrophil Activation is Suppressed by the Thiol Modulating Anti-Colitis Agent OR-1384**

\*E. Nissinen, J. Kaivola, I.-B. Lind

Orion Pharma Research, Espoo, Finland The extensive infiltration of neutrophils into the inflamed mucosa plays a major role in the pathogenesis of inflammatory bowel disease. One of the most powerful inflammatory mediators responsible for the attraction and activation of neutrophils is interleukin-8 (IL-8). OR-1384 {3-[(4-methylsulfonyl)phenyl]methylene-2,4-pentanedione} is a novel locally acting agent, which is protective in various animal colitis models at doses of 0.3 { - } 10 mg/kg. OR-1384 forms reversible adducts with free thiol groups, which are essential for the proper function of the specific IL-8 receptor on the surface of neutrophils. *The aim* of this study was to evaluate how the reversible thiol modulating compound OR-1384 can affect IL-8 binding and subsequent neutrophil activation. *Methods:* Human neutrophils were isolated from buffy coats. The neutrophils ( $2 \times 10^6$  cells) were treated with different doses of OR-1384 or reference compounds and incubated with  $^{125}\text{I}$ -IL-8. The free and bound  $^{125}\text{I}$ -IL-8 were separated and the specific binding of  $^{125}\text{I}$ -IL-8 to the neutrophils was measured. The nature of OR-1384 binding to the IL-8 receptor (IL-8R) was evaluated by adding glutathione to the incubation mixture containing OR-1384. Elastase release from the neutrophils ( $20 \times 10^6$  cells) was used as an IL-8 induced functional assay. *Results:* OR-1384 dose-dependently prevented IL-8 binding to the neutrophils ( $\text{IC}_{50} = 70 \text{ nM}$ ) while the analogue of OR-1384 without thiol modulating properties was ineffective. The reversible nature of OR-1384 binding to the IL-8 receptor was confirmed by the addition of glutathione. The neutrophil functional assay showed that elastase release was effectively inhibited by OR-1384 ( $\text{IC}_{50} = 18.9 \text{ nM}$ ). 5-ASA did not inhibit IL-8 binding but showed some effect on elastase release at high mM concentrations. *Conclusions:* The thiol modulating compound OR-1384 was shown to prevent IL-8 binding to neutrophils and interfere with the neutrophil activation process determined as inhibition of elastase release. The effects were clearly dependent on the thiol modulating properties of OR-1384. However, unlike other thiol reactive compounds the effect was reversible. In addition to the previously shown suppression of cytokine formation in inflammatory cells, OR-1384 is likely to exert its effect by inhibiting IL-8 induced neutrophil-mediated deleterious effects in the inflamed gut. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Interleukin-8 Induced Neutrophil Activation is Suppressed by the Thiol Modulating Anti-Colitis Agent OR-1384"

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"P P 44 0990" P 44 0990A **Pair of Twins with Myo-Neuro-Gastrointestinal Encephalopathy (MNGIE) Syndrome**

\*D. Katsaros<sup>1</sup>, A. Papadimitriou<sup>2</sup>, R. Divari<sup>2</sup>, N. Rossolimos<sup>1</sup>, K. Goumas<sup>1</sup>

<sup>1</sup> Gastroenterology Dept., Red Cross Hospital, Athens, Greece

<sup>2</sup> Neurology Dept., Red Cross Hospital, Athens, Greece MNGIE syndrome is a rare multisystem mitochondrial disorder affecting the nervous system and Gastrointestinal (GI) tract. Here we report a pair of male twins, 45 years old, suffering from this syndrome. Both were short, thin, almost cachectic (35–40 kgs) and stated intermittent diarrhoea since childhood, leading to malabsorption, which deteriorated recently. The one of them had been treated for coeliac disease, without success, until we considered his neurological findings, which had gradually become prominent and consisted in bilateral eyelid ptosis, neurosensory hearing loss, nasal speech and mild limb weakness. Laboratory GI investigation did not reveal specific pathological findings, except malabsorption. However brain MRI showed severe leucoencephalopathy. Muscle biopsy showed scattered ragged red fibers and denervation. Mitochondrial enzyme analysis showed significant deficiency of cytochrome-c-oxidase. Southern blot analysis and PCR showed no deletion of mitochondrial DNA. Investigation of the second patient revealed similar findings. Both patients died recently, within 3 months the one from the other. Their parents, two older brothers and one sister are alive in good health. MNGIE syndrome seems to be a separate nosological entity in the spectrum of mitochondrial encephalomyopathies affecting also the GI tract. However, although gastrointestinal symptoms are firstly presented and last for years, this syndrome has been reported only in the neurological literature, in four cases only, and never in twins. Intestinal disorders, absorption: Malabsorption syndromes } "A Pair of Twins with Myo-Neuro-Gastrointestinal Encephalopathy (MNGIE) Syndrome"

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"P P 44 0991" P 44 0991 **Vasoactive Intestinal Peptide Is Involved in the Interleukin-1 $\beta$  Inhibitory Action on the Acetylcholine-Induced Jejunal Contraction**

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Human Nutrition Research Center: INSERM, Nantes, France

<sup>1</sup> Human Nutrition Research Center: INRA, Nantes, France We have previously shown that interleukin-1 $\beta$  (IL-1 $\beta$ ) decreased the acetylcholine (ACh)-induced intestinal contractility through an action on the enteric nervous system. However, the neuromediators potentially involved are poorly known. The aim of the present study was to determine the possible involvement of the three main noncholinergic, nonadrenergic relaxant mediators: nitric oxide (NO), vasoactive intestinal peptide (VIP) and adenosine triphosphate (ATP) in the inhibitory effect of IL-1 $\beta$  on the ACh-induced intestinal contractility. *Methods.* Isometric contraction of rat jejunum longitudinal muscle-myenteric plexus (LM-MP) preparations, bathed in Krebs solution was recorded by a force transducer. IL-1 $\beta$  (10 ng/ml) was added to the bath for 90 minutes. The effect of potentially inhibitory agents on the LM-MP jejunal motor response to ACh ( $10^{-5}$  M) was investigated before and after exposure to IL-1 $\beta$ . The following drugs were used: N<sup>G</sup>-nitro-L-arginine methyl ester (L-NAME); N<sup>G</sup>-amino-L-arginine (L-NNA); N<sup>G</sup>-monomethyl-L-arginine (L-NMMA); vasoactive active intestinal peptide (VIP) 10–28; [4-Cl-D-Phe<sup>6</sup>, Leu<sup>17</sup>] VIP and suramin to inhibit NO synthase, VIP and ATP effect respectively. *Results.* L-NAME ( $3 \times 10^{-4}$  M), L-NNA ( $3 \times 10^{-4}$  M) and L-NMMA ( $3 \times 10^{-4}$  M) did not prevent the inhibition of ACh-induced jejunal contraction caused by IL-1 $\beta$ , but increased the ACh response of smooth muscle when administrated alone. Moreover, suramine ( $3 \times 10^{-4}$  M) failed to affect the inhibition induced by IL-1 $\beta$ . On the contrary, addition of VIP 10–28 ( $10^{-5}$  M) or [4-Cl-D-Phe<sup>6</sup>, Leu<sup>17</sup>] VIP ( $10^{-5}$  M) to the bath abolished the inhibitory effect of IL-1 $\beta$ . The effect of IL-1 $\beta$  on the ACh-induced jejunal contraction was partly reproduced by VIP ( $10^{-6}$  M). *Conclusions.* In LM-MP jejunal preparation, neither NO nor ATP are involved in the inhibitory effect of IL-1 $\beta$  on ACh-induced contractility. This inhibitory effect seems to be mediated by VIP. Immunology and microbiology: Inflammation Motility, specific: Small bowel } " Vasoactive Intestinal Peptide Is Involved in the Interleukin-1 $\beta$  Inhibitory Action on the Acetylcholine-Induced Jejunal Contraction "

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"P P 44 0992" P 44 0992 **Is Small Bowel Motility Induced by Duodenal Enteral Nutrition Dependent on Osmolality?**

\*T. Schmidt, T. Wandersleb, A. Pfeiffer, H. Kaess

Department of Gastroenterology, Hospital Bogenhausen, Munich, Germany *Background/Aim:* Recently, we have demonstrated that upper small intestinal motility induced by duodenal nutrition with an isoosmolar nutrient solution is not dependent on the amount of calories administered (Gastroenterology, May 1996: abstract). The aim of the present study was to investigate, whether the intestinal fed pattern induced by duodenal enteral nutrition is dependent on osmolality. *Methods:* Duodenal infusion (5 ml/min) of an enteral nutrition (2.64 kcal/min; 17% proteins, 59% carbohydrates, 24% lipids) at 3 different osmolalities (160, 300, and 600 mosmol/kg obtained by the addition of sodium chloride) on three consecutive days in a randomized order in 8 healthy volunteers. Duodenal infusion started 10 min after a phase III activity and was continued for 90 min. Motility was recorded with a digital data logger and 6 catheter-mounted miniature pressure transducers located around the duodenojejunal flexure. Recordings underwent visual and computer-aided analysis (Scand J Gastroenterol 1994; 29: 1076–82). *Results* (means – SEM): Osmolality [mosm/kg] 160 300 600 Contraction frequency [min<sup>-1</sup>] 1.95 – 0.21 1.94 – 0.28 1.92 – 0.27 Contraction amplitude [mm Hg] 20.7 – 0.3 21.3 – 0.9 20.6 – 0.6 Propagated contractions [%] 36 – 3 37 – 4 34 – 5 Propagation distance [cm] 4.1 + 0.2 4.2 + 0.2 4.1 + 0.2 *Conclusion:* Small intestinal motility induced by duodenal enteral nutrition is not influenced by osmolalities ranging from 160 to 600 mosm/kg. Nutrition: Nutrients and gut function Nutrition: Techniques of nutrition Motility, specific: Small bowel } "Is Small Bowel Motility Induced by Duodenal Enteral Nutrition Dependent on Osmolality?"

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"P P 44 0993" P 44 0993 **Enteric Dysmotility Revealed by Computer Analysis of Prolonged Small Bowel Manometry**

\*D.L. Wingate, F.D. Castillo, D.F. Evans, M.J. Benson

GI Science Research Unit, St Bartholomew's and The Royal London School of Medicine & Dentistry, London, UK Prolonged ambulant small bowel manometry (PSBM) has been shown to discriminate *groups* of patients (Chagas' disease, HIV) from *groups* of normal controls, and the precision of PSBM is increased by computer analysis. However, its value in the diagnosis of *individual* patients remains to be determined. We analysed PSBM in 37 patients who were tertiary referrals. The commonest cause of referral was suspected chronic idiopathic intestinal pseudo-obstruction (CIIP), with differential diagnoses of CIIP, mechanical obstruction, irritable bowel syndrome, or chronic intractable abdominal pain. Three patients with intractable post-vagotomy diarrhoea and 4 diabetic patients with diarrhoea and abdominal pain were included in the cohort. After intubation with a multi-channel pressure-sensitive catheter under fluoroscopic control, recording on a portable datalogger continued for 17–24 hours with the patient freely ambulant at home or in hostel accommodation. In 5 patients, all with CIIP, endoscopic assistance was required to position the catheter; recording was unsuccessful in 2 patients with disabling CIIP because the recording catheter was not retained in the proximal small bowel. The fasting data recorded from each patient was characterised by computer analysis, and the values obtained were compared with control values derived from 47 comparable recordings in healthy volunteers. Abnormal motor activity was found in 13/28 patients with suspected CIIP, in 4/4 diabetics and in 3/3 vagotomised patients. The commonest abnormality was increased nocturnal contractile activity. There was a significant ( $p = 0.005$ ) excess of prolongation and/or diminished migration velocity of Phase 3 of the migrating motor complex (MMC) in CIIP, suggesting myenteric plexus damage: this was not seen in the other groups where there was, however, a significant ( $p = 0.05$ ) excess incidence of accelerated Phase 3 migration velocity. We conclude that systematic analysis of prolonged small bowel manometry promises to be an important clinical tool in the diagnosis of enteric neuropathology. Motility, specific: Small bowel Motility, general: Functional GI disorders Motility, general: Innervation } "Enteric Dysmotility Revealed by Computer Analysis of Prolonged Small Bowel Manometry"

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## "P P 44 0994" P 44 0994 Computer Programmes Disagree in Measurement of Small Bowel Contractions Recorded by Ambulatory Manometry

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*Introduction:* Computer analysis of small bowel manometry has been shown to give discordant results for different programmes with regard to qualitative recognition of contractile events [1]. It is unclear to what extent different programmes agree with regard to quantitative measurement of contractions. *Methods:* Six ambulatory test records with normal intestinal motility patterns including fasting and postprandial motility were analyzed by three computer programmes: SBMA 1.41, (Krankenhaus München-Bogenhausen), Motan 3.3 (Gatehouse ApS), Multigram 6.31 (Synectics Medical AB). The method of comparison has previously been described [1]. Amplitude, area under the curve (AUC) and duration of contractions, that were recognized by all programmes, were subjected to analysis. Correlation coefficient (r) and slope of linear regression with confidence intervals (CI) were calculated for each pair of programmes. *Results:* 2385 contractions were recognized by all programmes, and thus subjected to analysis, out of a total of 4287 contractions recognized by at least one of the programmes. Programmes SBMA vs Motan\* Motan vs Multigram\* Multigram vs SBMA\* r slope L.CI U.CI r slope L.CI U.CI r slope L.CI U.CI Amplitude 0.81 0.55 0.54 0.56 0.82 1.51 1.49 1.53 0.94 1.09 1.08 1.09 AUC 0.66 0.36 0.36 0.37 0.63 3.25 3.15 3.35 0.88 0.55 0.54 0.56 Duration 0.39 0.90 0.89 0.91 0.28 1.78 1.75 1.81 0.21 0.52 0.51 0.53\*first programme y, second programme x for regression; L. and U.CI: lower and upper 95% confidence limits *Conclusion:* The degree of agreement between different computer programmes in measuring contractions is unexpectedly low, showing that the outcome depends critically on the algorithms applied. Difficulties are encountered particularly in the analysis of duration of contractions.

Reference: Gastroenterology 1996; 110 A683 Motility, specific: Small bowel } "Computer Programmes Disagree in Measurement of Small Bowel Contractions Recorded by Ambulatory Manometry"

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## "P P 45 0995" P 45 0995 **The Importance of Immune Genetic Test in the Study of the Pathogenesis of Chronic Pancreatitis**

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Donetsk State Medical University, Donetsk Diagnostic Centre, Donetsk Station of Blood Transfusion, Ukraine

*Aim.* To deepen knowledge about the pathogenesis of chronic pancreatitis (CP), its use in the diagnosis and treatment of the disease. *Task.* To study the immune genetic predisposition to CP in connection with the specialty of its manifestation. *Material.* The frequency of occurrence of erythrocyte antigens (ABO-system and rhesus-factors – CcDEe) and leucocyte antigens (HLA-system) with a calculation of the risk of the disease was studied on 52 patients of CP and 56 non-patients. *Results.* The risk of the development of CP was high in those belonging to blood group A0 by 3.23 times. Antigens of the HLA-system A<sub>1</sub>, B<sub>8</sub>, B<sub>18</sub>, Bw<sub>22</sub> rise of the risk in the development of the disease in 2.79, 3.51, 3.52 and 3.44 times correspondingly. These antigens were associated with disregulation between the T- and B-branches of the immune system with a deficit of T-suppressors with a marked cell autosensibilisation to pancreas tissue. In the presence of the phenotype Bw<sub>40</sub> the risk of developing CP rose by 6.47 times which was connected to a rise in the blood concentration of natural killers. Antigen B<sub>13</sub> was associated with a fall in the debit part of lipase and B<sup>27</sup> with a rise in the echogram of pancreas in sonography i.e. with fibrosis of the tissue of the organ. The risk of developing CP in patients having the phenotype of the antigens rose correspondingly by 3.17 and 3.38 times. Antigen protectors were A<sub>2</sub>, B<sub>5</sub>, Cw<sub>4</sub>. *Conclusion.* In part of the patients with CP immune genetic predisposition to the development of the disease has a place, and separate antigens were associated with its pathogenetic branches. This information in perspective can be used in the diagnosis and treatment of CP. Pancreas: Pancreatitis, chronic Clinical practice: Management strategy Immunology and microbiology: Host defense mechanisms } "The Importance of Immune Genetic Test in the Study of the Pathogenesis of Chronic Pancreatitis"

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**"P P 45 0996" P 45 0996 Comparison of the Preventive Effects of Somatostatin and SMS 201-995 in ERCP-Induced Hyperamylasemia**  
G\ 'f6rg\ 'fcl Ahmet, Kayhan Bur\ 'e7ak, Mentec  
B\ 'fclent, Ak\ 'e7ali Zafer, \ 'dcnal Selahattin

G\ 'dcTF Ankara, T\ 'fcrkiye The aim of this study was to compare the preventive effects of SMS 201-995 and somatostatin in ERCP-induced hyperamylasemia. *Materials and Methods:* 120 patients who underwent ERCP were included in our study and were divided in to 3 equal groups. After an overnight fast, the patients were sedated with 10 mg midazolam and duodenal relaxation was achieved with 40 mg hyoscine-n-butylbromide, intravenously (iv). Group I was treated with SMS 201-995 (3 \ 'b4} 100 \ 'b5g/day sc on the ERCP day) and the second group was treated with somatostatin (3.5 \ 'b5g/kg iv bolus with the start of ERCP, and then 250 \ 'b5g i.v infusion for 4 hours). The control group received only iv saline. Contrast material was same in all groups. Serial blood samples were withdrawn pre-ERCP and at timed intervals after ERCP (4<sup>th</sup> hour, 24<sup>th</sup> hour, 48<sup>th</sup> hour). Serum amylase and isoamylase levels were determined. The results are shown in the table. GROUP Pre- Post- Post- Post- Pre- Post- Post- Post- ERCP ERCP ERCP ERCP ERCP ERCP ERCP ERCP amylase amylase amylase amylase iso- iso- iso- iso- SU/dl at 4<sup>th</sup> at 24<sup>th</sup> at 48<sup>th</sup> amylase amylase amylase amylase hours hours hours U/dl at 4<sup>th</sup> at 24<sup>th</sup> at 48<sup>th</sup> hours hours hours hours hours  
1 116 + 44 186 + 44 220 + 28 202 + 36 69 + 11 107 + 12 99 + 7 81 + 112 94 + 7 147 + 42  
116 + 17 149 + 26 55 + 9 81 + 2 73 + 12 73 + 93 152 + 69 232 + 44 236 + 88 186 + 37 88 + 45  
195 + 74 145 + 40 109 + 24 *Conclusion:* According to this study, somatostatin was more potent than SMS 201-995 for inhibiting ERCP-induced hyperamylasemia. Pancreas: Secretion, regulation Pancreas: Pancreatitis, acute Endoscopy, specific: Pancreatic } "Comparison of the Preventive Effects of Somatostatin and SMS 201-995 in ERCP-Induced Hyperamylasemia"

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"P P 45 0998" P 45 0998 **Prognostic Factors in the Therapeutic Approach to Pseudocysts of the Pancreas**

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Dept. of Gastroenterology, University Hospital "Sestre Milosrdnice", Croatia

<sup>1</sup> Pliva Pharmaceutical Co., Research Institute, Biomedical Dept., Zagreb, Croatia *Purpose:* This study was performed to test the prognostic value of etiology, location and the amount of liquid in the pancreatic pseudocyst (PC), as well as the concentration of biochemical parameters (LDH, glucose, proteins, sodium, potassium, bilirubin and lipase) of the PC contents and the serum of the patients regarding the efficiency of ultrasound (US)-guided percutaneous evacuation (PE) as a possible method of therapeutic approach. *Methods:* After obtaining informed consent, a total of 43 patients with histories of acute pancreatitis and PCs persisting for more than 6 weeks were included in the study. The diagnosis was made by US examination and CAT scan. The PC content samples were obtained using a Chiba needle of 21-gauge under US control. Biochemical parameters were determined by standard laboratory methods. *Results:* Concerning the various etiologic factors, no differences were noted in the outcome of PE. PE was a successful method of treatment for the PCs located in the tail of the pancreas, while those located in the head of the pancreas had a significantly lower healing rate. The amount of liquid taken during the PE was significantly lower in patients successfully treated by PE (median 96.5 ml) compared to the PC liquid amount in the patients with the failed treatment (median 222 ml). Concerning the biochemical parameters, unlike the serum data, significantly lower values of proteins, potassium and lipase in the PC liquid were found in successfully treated patients. *Conclusion:* It can be concluded that the analysis of the mentioned parameters (location, the amount of liquid, proteins, potassium and lipase concentrations in the evacuated material) can allow an early decision concerning the therapeutic approach to patients with PC. **Pancreas: Pancreatitis, acute Radiology and ultrasound: Therapy Echoendosonography: Therapy }** "Prognostic Factors in the Therapeutic Approach to Pseudocysts of the Pancreas"

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"P P 45 0999" P 45 0999 **Long-Term Effects of ONO-3403, A New Oral Protease Inhibitor, on Experimental Chronic Pancreatitis in Rats**

\*M. Shiozaki, Y. Takeda, T. Itabashi, K. Katsu

Second- Department of Internal Medicine, Osaka Medical College, Takatsuki City, Osaka, Japan *Purpose:* ONO-3403 is a potent newly developed oral protease inhibitor. In rats, long-term administration of ONO-3403 has a pancreaticotrophic effect. We therefore evaluated the protective effect of chronically administered ONO-3403 against the development of pancreatic fibrosis in a rat model of chronic pancreatitis. *Methods:* Rats were injected intraductally with zeinoleic acid solution. After three days in the acute phase, there was progressive pancreatic atrophy, leading to diffuse fibrosis by day 28. Some of the rats were fed a diet containing 0.1% ONO-3403 from day 2 or 4 until day 28. Histologic findings and pancreatic enzyme contents of ONO-3403-treated rats were compared with untreated controls. *Results:* On day 2 there was no acinar cell loss and the fibroblasts appearing in the interstitium were immature. On day 4 acinar cell loss and proliferation of stromal fibroblasts were evident. ONO-3403 given from day 4 did not significantly prevent pancreatic fibrosis by day 28. However, in the group given ONO-3403 from day 2, acinar cells showed regeneration and interstitial fibrosis was almost absent, indicating a marked protective effect of ONO-3403. *Conclusion:* To prevent pancreatic fibrosis, chronic treatment with ONO-3403 should be started from the early stage of acute pancreatitis when there is no acinar cell loss, CCK receptors on acinar cell membranes are well preserved, and stromal fibroblasts are immature. Institution of long-term ONO-3403 therapy immediately after the attack of abdominal pain may prevent the progression of pancreatic fibrosis and consequent impairment of exocrine pancreatic function. *Pancreas: Pancreatitis experimental* *Pancreas: Pancreatitis, chronic }* "Long-Term Effects of ONO-3403, A New Oral Protease Inhibitor, on Experimental Chronic Pancreatitis in Rats"

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"P P 45 1001" P 45 1001 **Micronutrient Status in Tropical Pancreatitis** Paul Laboi<sup>1</sup>,

\*K.T. Shenoy<sup>2</sup>, C. Jayakumar<sup>1</sup>

<sup>1</sup> Dept. of Medicine, Medical College, Trivandrum, India

<sup>2</sup> Dept. of Gastroenterology, Medical College, Trivandrum, India *Objective:* To study micronutrient status in Tropical pancreatitis (TP). *Study design:* Case control study. *Subjects:* 25 cases of TP with either pancreatic calculi or diabetes mellitus with exocrine pancreatic insufficiency and 25 age matched controls with no pancreatic disease. *Study variables:* Clinical evaluation, biochemical parameters (albumin, alkaline phosphatase, transaminases, blood glucose and glycated haemoglobin) and nutritional assessment (nutrient intake and BMI). *Outcome measures:* Serum levels of zinc, copper and iron estimated by atomic absorption spectrophotometry. *Data analysis:* Odd's ratio (OR) and 95% confidence interval (CI) using cut offs, difference in the means by independent 't' test and regression analysis using micronutrient level as dependent and age as independent variable. *Results:* 12 males and 13 females were recruited. Age ranged from 21 to 41 years. Baseline characteristics were similar among cases and controls. Variable OR 95% CI P value Copper  $\mu\text{g/dl}$  ( $< 100$  vs  $\geq 100$ ) 0.06 0.06–0.015 0.001 Zinc  $\mu\text{g/dl}$  ( $< 100$  vs  $\geq 100$ ) 9.04 1.74–1.88 0.011 Iron  $\mu\text{g/dl}$  ( $< 100$  vs  $\geq 100$ ) 0.62 0.20–1.88 0.396 Copper/zinc ratio was 0.25 in cases and 1.088 in control. Serum zinc of  $> 140 \mu\text{g/dl}$  was 9 times more at risk of developing tropical pancreatitis than age matched controls. Level of zinc was independent of age and sex. *Conclusion:* Tropical pancreatitis is associated with low serum copper and high zinc levels and further studies are needed to explain the pathology of tropical pancreatitis using this micronutrient hypothesis. Pancreas: Pancreatitis, chronic } "Micronutrient Status in Tropical Pancreatitis"

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"P P 45 1002" P 45 1002A **Randomised Controlled Trial of Antioxidants (Antoxid) in Tropical Pancreatitis\***

\*K.B. Leena, K.T. Shenoy

Dept. of Gastroenterology, Medical College, Trivandrum, India *Objective:* To test the hypothesis that a combination of antioxidants is effective in reducing lipid peroxides and pain relief in tropical pancreatitis. *Design:* Randomised double blind cross over trial using either Antoxid or placebo. Each capsule of Antoxid contains Beta carotene 50 mg, Vitamin A 2500 i.u., Vitamin E 10 i.u., Vitamin C 50 mg and Zinc sulphate monohydrate 27.45 mg and was given thrice daily for 30 days followed by placebo capsule or vice versa. A washout period of 2 weeks was given. *Sample size:* 15 patients with tropical pancreatitis. *Co-Intervention:* Treatment of diabetes mellitus with soluble insulin; pancreatic enzyme preparation and analgesics for relief of pain. *Measurements:* Clinical and biochemical (lipid peroxides, red cell enzymes, vitamin C and blood glucose) at the baseline and during each treatment period. Pain and global improvement were scored by visual analogue scale. *Outcome measures:* Improvement in blood glucose and reduction in lipid peroxides and other red cell enzyme changes; subjective improvement in pain and global improvement. *Compliance to treatment:* Consumption of more than 80% of capsules was assessed as good and more than 90% as excellent. *Data analysis:* Descriptive and independent \quotet\rquote test and Mann Whitney U test to detect difference between the two groups in the basal state. Wilcoxon matched pair signed rank test to detect the treatment effect ( $\alpha = 0.05$ ). *Results:* 8 received Antoxid and 7 received placebo as the first drug. Compliance was 100%. Baseline characteristics were similar. Significant reduction in lipid peroxides ( $P = 0.001$ ), red cell glutathione ( $P = < 0.05$ ) and pain scores ( $P = < 0.001$ ) were noted with Antoxid. Surgery could be avoided in 70%. Global improvement was marked with Antoxid. *Conclusion:* Antoxid is a promising drug for pain relief of tropical pancreatitis and surgery could be avoided in majority of TP. \* Study funded by American Remedies Ltd, Madras. Pancreas: Pancreatitis, chronic Clinical practice: Management strategy }" "A Randomised Controlled Trial of Antioxidants (Antoxid) in Tropical Pancreatitis\*"

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## "P P 45 1003" P 45 1003 **Computed Tomography in Tropical Pancreatitis**

\*K.B. Leena, K.T. Shenoy

Dept of Gastroenterology, Medical College, Trivandrum, India *Objective:* To determine the morphology of pancreas and other organs by computed tomography (CT) in tropical pancreatitis (TP). *Methods:* 102 patients with TP had CT performed. Calcification, ductal diameter and dilatation, lipomatous atrophy, fluid collection, focal and diffuse enlargement of pancreas, peripancreatic tissue planes, hepatobiliary and vascular involvement, renal changes were studied. *Results:* Calcific 64, non calcific 18 and pancreatic malignancy with TP 30 were observed. *Calcific:* Calcification was seen in 54 patients in the whole pancreas, 5 in the body and 5 in the tail. Ductal dilatation was seen in 14 patients and main ductal diameter was 5–18 mm (mean 8.8 mm). Margins of the pancreas were smooth in 38 patients and irregular in 26. Pancreas was atrophic in 20 patients and lipomatous atrophy was noted in 18. Fluid collection was noted in 18 patients, localised in 12; peripancreatic in 4 and remote in 2. Gall stones were noted in 9, choledochal cyst in 1, renal calculi in 3, horse shoe kidney in 1 and hepatic haemangioma in 1. *Non calcific:* Of the 18, 4 had calculi and 9 had ductal dilatation and lipomatous atrophy and 4 had pancreatic fluid collection as pancreatic ascites. *Pancreatic malignancy with TP:* Mass lesion with calcification and obstructed duct located in the head in 18 and diffuse in 12. Involvement of the peripancreatic planes was noted. Hepatic metastasis was noted in 50%. *Conclusion:* CT is useful in studying the morphology of pancreas pathology in tropical pancreatitis. Even in non calcific cases, pancreatic calcification could be documented at CT and hence the division of calcific and non calcific by radiology may not reflect actual pathology. Pancreas: Pancreatitis, chronic Radiology and ultrasound: Diagnosis } "Computed Tomography in Tropical Pancreatitis"

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"P P 45 1004" P 45 1004 **Elements Influencing the Evolution of the Pancreatic Pseudocysts**

\*A. Tudora, C. Duta, F. Miculit, R. Sarandan

University of Medicine and Pharmacy-Timisoara, Romania To assess the elements which influence the evolution of the pancreatic pseudocysts we have followed 40 patients between 1991–1995: 14 with chronic pancreatitis (CP) and 26 with acute pancreatitis (AP). The evolutive possibilities in the patients with CP were as follows: spontaneous resolution in 2 cases (14%), persistence of the pseudocysts with clinical symptoms (1 case) and appearance of complications (5 cases = 36%)-obstruction of the bowel or biliary tree (2 of these cases associated the abscesses formation). The acute pancreatic pseudocysts resolve spontaneously in 9 cases (35%), the rest presented complications that required intervention: 2 (8%) intracystic hemorrhage, 11 (42%) obstruction phenomena, 3 (11%) abscesses formation and 1 case-the portal vein thrombosis. The pseudocysts in the cephalic area were associated with a spontaneously resolution (65% in the cases with AP respectively 69% for CP). The size under 3 cm (for the acute pseudocysts), respectively 4.5 cm was significantly correlated with the resolution. The number of the pseudocysts (single or multiple) has no influence over the evolution. *Conclusions:* The predictive factors which indicates the resolutive evolution in the pseudocysts during the acute and chronic pancreatitis are the size (under 3 cm respectively 4.5 cm) and the localisation in the cephalic area. In these cases the pseudocysts resolved either spontaneously or persisted asymptomatic or pauci-symptomatic requiring only a follow-up. Pancreas: Pancreatitis, acute Pancreas: Pancreatitis, chronic } "Elements Influencing the Evolution of the Pancreatic Pseudocysts"

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"P P 45 1005" P 45 1005 **Can Gastroprotected Pancreatic Extracts (GPPE) Improve Undernutrition Criteria in Elderly People? A Double Blind Anthropometric and Biochemical Study** F. Dyard<sup>1</sup>,

\*J. Moreau<sup>2</sup>, F. B\'e9ziat<sup>3</sup>, S. Lauque<sup>3</sup>, B. Vellas<sup>3</sup>, J.L. Albareyre

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Involution of pancreatic enzyme and bicarbonate secretions have been demonstrated among people over 70th and particularly when malnutrition was present. Clinical consequences of these findings are unknown and the potential benefit of pancreatic enzymes supplementation had never been assessed in this population. The *aims* of this study was thus to evaluate the effect of GPPE on anthropometric and biochemical data among undernourished elderly subjects during a 3 month follow-up period. *Methods*: 52 patients (46 women) with a mean age of 87 – 6 years were included. Their caloric intake calculated by a dietician on three consecutive days by using Euronut' program (on average 1,082 kcal/d) was 30% lower than RDA. Main inclusion criteria were BMI (kg/m<sup>2</sup>) (< 21 – 3) and low serum albumin (32 – 3.3 g/l). GPPE 2 caps tid or placebo were administered in a randomised and double blind fashion. Patients were examined at D15, D30, D60, D90 for dietary intakes, anthropometric and biochemical assessment. *Results*: At inclusion, the two groups were similar for age, sex, BMI, albumin and other biological variables. Evolution of caloric intakes and body weight were not different between the two groups. Conversely, serum prealbumin level at D90 was higher in the GPPE group compared to placebo (0.23 – 0.06 g/l vs 0.19 – 0.06 g/l respectively; p  $\{ \backslash a3 \}$  0.05). In addition, there was a trend in favour of the GPPE for retinol binding protein (0.043 – 0.0013 g/l vs 0.038 – 0.011 g/l respectively; p = 0.09). *Conclusion*: These data suggest that the administration of pancreatic extracts may improve several nutritional parameters in undernourished elderly subjects. Further studies are needed to confirm these results on a large scale. Nutrition: Metabolism }" "Can Gastroprotected Pancreatic Extracts (GPPE) Improve Undernutrition Criteria in Elderly People? A Double Blind Anthropometric and Biochemical Study"

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"P P 45 1006" P 45 1006 **Impact of Continuing Alcohol Addiction on the Results of Resective Surgery for Chronic Pancreatitis** B. Chareton, M. Foglia, O. G\'e9rard, C. Stasik,

\*G. Spiliopoulos, J.P. Campion, B. Launois

Department of Digestive Surgery and Transplant Unit, CHR Pontchaillou, Rue Henri Le Guilloux, 35033 Rennes, France *Materials and methods:* Between 1972 and 1991, 149 patients underwent resective surgery for chronic pancreatitis. Surgical procedures included 87 pancreaticoduodenectomies and 62 distal splenopancreatectomies. Excluded from the study were 5 patients lost to follow-up and 10 patients having died in the post-operative period. *Results:* 46 patients had continuing alcohol addiction (OH+) and 88 patients had been weaned for alcohol (OH{-}). Post-operative comfort was poor in 3.5% of OH{-} versus 30.4% of OH+ patients, medium in 26.7% of OH{-} patients versus 30.4% of OH+ patients and good in 69.8% of OH{-} versus 39.2% of OH+ patients. Pain was present in 8% of OH{-} versus 57% of OH+ patients. Body weight was stable or increased in 100% of OH{-} versus 47% of OH+ patients. 53% of OH+ patients experienced weight loss. Return to normal activity was 85% in OH{-} versus 50% in OH+ patients. 5, 10 and 20 year survival for OH{-} and OH+ patients was 90% vs 75%, 85% vs 60% and 70% vs 30% respectively. Following pancreaticoduodenectomy, 5, 10 and 20 year survival for OH{-} and OH+ patients was 95% vs 70%, 90% vs 50% and 60% vs 50% respectively. Following distal splenopancreatectomy 5, 10 and 20 year survival for OH{-} and OH+ patients was 90% vs 90%, 70% vs 70% and 70% vs 15% respectively. Late deaths occurred in 21 of 46 patients in the OH+ group: 5 oropharyngeal/oesophageal tumors, 2 cardiovascular conditions, 9 acute alcohol related complications, 5 "other" causes. Late deaths occurred in 17 OH{-} patients, 5 oropharyngeal/oesophageal tumors, 6 cardiovascular conditions, 9 acute alcohol related complications, 6 "other" causes. *Conclusions:* The best results of pancreatic resection for chronic pancreatitis are obtained in those patients who can be weaned from alcohol. Comfort, return to normal activities and survival are improved. **Pancreas: Pancreatitis, chronic Liver and bile ducts, 1: Hepatotoxicity, ethanol }** "Impact of Continuing Alcohol Addiction on the Results of Resective Surgery for Chronic Pancreatitis"

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"P P 45 1007" P 45 1007 **Resection in Chronic Pancreatitis. A Retrospective Study with 154 Patients with Special Reference to 20 Years and 10 Years Survival** B. Chareton, M. Foglia, O. G'érard,

\*C. Stasik, G. Spiliopoulos, J.P. Campion, B. Launois

Department of Digestive Surgery, CHR Pontchaillou, Rue Henri Le Guilloux, 35033 Rennes, France

We retrospectively studied results in 154 patients who underwent pancreatic resection.

*Methods:* Between September 1972 and December 1994, we performed 87 cephalic pancreatoduodenectomy (30 with pylorus conservation), 62 spl'eanopancreatectomy (SPC) and 4 total pancreatectomy for chronic pancreatitis. Patients with simultaneous neoplasia at

histological control were not included. Mean age was 44 years (range 20–70 years). The most common reason for a resection was intractable pain often associated with jaundice, duodenal

compression, segmental portal hypertension, suspicion of pancreatic neoplasia. 140 (90%) patients were male. Chronic ethylism was the most common aetiology. We could establish a

score of comfort based on pain, diabetes, diarrhea and weight increase in 60% of patients. Median follow up was 10 years. Cause of death was determined in all patients. *Results:* Perioperative

mortality was 4.5% in Whipple procedure, 9.6% in splenopancreatectomy and 50% in total pancreatectomy. Survival after duodenopancreatectomy at 10 and 20 years was 72 and 54%.

Survival after splenopancreatectomy at 10 and 20 years was 68 and 38%. In both groups 20 years survival was significantly higher among patients who stopped alcohol intake (62 vs 52% for Whipple

and 72 vs 16% for SPC). Low comfort score was clearly associated with alcohol intake after pancreatic resection. Among patients who underwent Whipple operation comfort score was

higher with pylorus conservation than in patients without pylorus conservation but this difference disappeared when patients who didn't stop alcohol consumption were excluded. None of the

patients in whom we carried out Whipple operation needed another surgical procedure for pancreatic pathology while 9% of the patients splenopancreatectomy group were operated again.

ENT neoplasia (10 cases) and cardiovascular accident (8 cases) were the major causes of long term mortality. *Conclusion:* However pancreatoduodenectomy in chronic pancreatitis seems an

heavy procedure its operative morbidity and mortality are low. A good and long term comfort is obtained in most of the patients. As for any ethylic patient screening for ENT neoplasia should

be the rule ... Clinical practice: Management strategy Pancreas: Pancreatitis, chronic }"

"Resection in Chronic Pancreatitis. A Retrospective Study with 154 Patients with Special Reference to 20 Years and 10 Years Survival"

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"P P 45 1008" P 45 1008 **The Risk of Occurrence of Diabetes Mellitus is Influenced by the Type of Elective Pancreatic Surgery in Patients with Chronic Pancreatitis**

\*D. Malka, P. Hammel, P. Levy, A. Sauvanet, J. Belghiti, P. Ruszniewski, P. Bernades

Fédération Médico-Chirurgicale d'Hépatogastro-Entérologie, Hospital Beaujon, Clichy, France Whether elective pancreatic surgery (EPS) in patients with chronic pancreatitis (CP) influences the occurrence of diabetes mellitus is unclear. *Aim:* to assess if patients with CP who underwent EPS had an increased risk of diabetes as compared to those who did not. *Methods:* 482 patients with CP (men: 85.3%; alcoholics: 84.6%) followed 8.0 years (1–32) were studied. Among them, 222 who underwent EPS were compared to 224 who did not. Thirty-six patients who underwent a non-elective pancreatic surgery were excluded. *Results:* prevalence of diabetes was of 40.7% (insulin-dependent: 19.9%) in the whole group of 446 patients and increased with time of follow-up [48.4% (26.8%) and 60.1% (37.2%) after 5 and 10 years, respectively]. The actuarial rate of diabetes: a) was not influenced by EPS (35.6% vs 43.3% at 15 years); b) was higher in patients who underwent pancreatic resection [n = 95 (distal pancreatectomy: n = 56)] than in those treated by derivation (n = 126) [51.8% (distal pancreatectomy: 64.3%) vs 37.4% at 15 years,  $p < 0.01$  ( $p < 0.001$ )] and in those not operated on ( $p < 0.05$ ); c) was lower in patients treated by pancreatic drainage (n = 42) than in those not operated on (20.9% vs 32.8% at 10 years,  $p < 0.02$ ). *Conclusions:* distal pancreatectomy is the only procedure of EPS which increases the risk of diabetes in patients with CP. By contrast, pancreatic drainage seems to delay the onset of diabetes. Pancreas: Pancreatitis, chronic } "The Risk of Occurrence of Diabetes Mellitus is Influenced by the Type of Elective Pancreatic Surgery in Patients with Chronic Pancreatitis"

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"P P 45 1009" P 45 1009 **Spatial Blood Flow Distribution in the Normal and Chronically Inflamed Human Pancreas**

\*M.K. Schilling, C. Redaelli, P. Reber, H. Friess, M.W. B\fcchler

Dept. Visceral and Transplantation Surgery, Univ. Berne, Switzerland In experimental models many pancreatic diseases namely acute and chronic pancreatitis are accompanied by, caused or aggravated by microcirculatory changes. In this study we assessed blood flow as well as the flow curve pattern in the pancreas of patients undergoing laparotomy for non pancreatic diseases as well as patients undergoing pancreatic head resection for chronic pancreatitis by laser doppler flowmetry (LDF). *Methods:* In 13 patients undergoing laparotomy, EBF was assessed by LDF on the normal pancreas as well as in 9 patients with chronic pancreatitis. Blood flow was recorded for at least 30 seconds after a stable signal was obtained. Post sampling data processing included calculation of systolic and mean blood flow and pulse curve analysis with pulsatile index and integral under the curve calculations. *Results:* Results (for the normal pancreas) in perfusion units (upper row: systolic/diastolic flow, middle row: mean flow – SD, lower row: pulsatile index).

*Discussion:* A typical spatial distribution of pancreatic blood flow was found, correlating with the anatomical vascular supply and lowest flow over the mesenteric vein, the water shed area between pancreaticoduodenal sup/inf and splenic arterial blood supply. Furthermore blood flow and blood flow pattern was significantly decreased in chronic pancreatitis, most pronounced in the pancreatic head. } "Spatial Blood Flow Distribution in the Normal and Chronically Inflamed Human Pancreas"

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## "P P 45 1011" P 45 1011 Transforming Growth Factor Beta Mediates Both Fibrogenesis and Hyperglycemia in Patients with Chronic Pancreatitis

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<sup>2</sup> Semeiotica Chirurgica, Università degli Studi di Padova, Italy Transforming growth factor beta (TGF $\beta$ ) has suggested to mediate liver fibrosis which can be monitored by the serum determination of the N-terminal peptide of type III procollagen (PIIP) and laminin. Fibrogenesis is also an important phenomenon found in patients with chronic pancreatitis (CP), for which no data are available on TGF $\beta$  or PIIP and laminin patterns. The aims of our study were to compare the serum patterns of PIIP, laminin and TGF $\beta$  in patients with LC and CP and to verify if there were any correlation between these indices. We studied 81 subjects; 20 were controls (CS), 23 patients had CP, 17 viral cirrhosis (VC), 11 alcoholic cirrhosis (AC) and 10 primary biliary cirrhosis (PBC). In the sera of all subjects we measured PIIP and laminin (IRMA and RIA assays, CIS-France) and TGF $\beta$  (ELISA, Boehringer Mannheim, Germany). PIIP and laminin increased in VC and AC in comparison with CS, CP and PBC (Anova one-way:  $F = 8.86$ ,  $p < 0.001$  and  $F = 11.57$ ,  $p < 0.001$  respectively). In CP high levels of PIIP and laminin were found in 7/23 and 5/23 patients. TGF $\beta$  significantly decreased in patients with VC ( $45 \pm 3$  ng/mL, mean  $\pm$  SEM), AC ( $54 \pm 9$ ) as compared to CS ( $101 \pm 6$ ) ( $F = 11.29$ ,  $p < 0.001$ ). High levels of TGF $\beta$  were found in 6/23 patients with CP. In patients with CP, PIIP varied independently from laminin ( $r = 0.358$ ,  $p$ : ns), but correlated with TGF $\beta$  ( $r = 0.481$ ,  $p < 0.05$ ). On the contrary in LC patients PIIP and laminin varied consensually ( $r = 0.709$ ,  $p < 0.001$ ) and the variations of PIIP were inversely correlated with those of TGF $\beta$  ( $r = \{-\}0.374$ ,  $p < 0.05$ ). In CP, a reduced exocrine function (PABA test) was associated with an increment of laminin values ( $r = \{-\}0.519$ ,  $p < 0.05$ ). Fasting serum glucose was correlated with TGF $\beta$  ( $r = 0.884$ ,  $p < 0.001$ ), while HbA1c was correlated with C-peptide values ( $r = \{-\}0.570$ ,  $p < 0.01$ ). 18 patients with CP were followed up for a median period of 7.5 yrs (4–12 yrs range). TGF $\beta$  significantly decreased during follow-up (Student's  $t$  test:  $t = 3.09$ ,  $p < 0.01$ ). A trend towards a decrement was found also for PIIP. *Conclusions:* 1. biochemical markers of liver fibrosis can be considered of limited value in assessing pancreatic fibrosis; 2. in LC, the existence of a feed-back regulation of TGF $\beta$  mediated by the fibrogenetic process may be hypothesized; 3. this feed-back does not seem to be present in CP, where TGF $\beta$  seems to be involved in favouring fibrosis on the one hand and the development of hyperglycemia on the other; 4. pancreatic fibrotic phenomena, more marked when exocrine function is severely impaired, seem to go towards quiescence in long term follow-up. Pancreas: Pancreatitis, chronic } "Transforming Growth Factor Beta Mediates Both Fibrogenesis and Hyperglycemia in Patients with Chronic Pancreatitis"

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## "P P 45 1012" P 45 1012 Is the Pancreas Able to Adapt to Repeated Caerulein-Induced Pancreatitis?

\*Z. Warzecha, A. Dembinski, P. Ceranowicz, J. Jaworek, J. Bilski, S.J. Konturek

Institute of Physiology, Collegium Medicum of Jagiellonian University, Krakow, Poland Acute pancreatitis with tissue damage and acinar cells loss is followed by recovery. We studied biochemical, histological and functional regeneration of pancreatic tissue after repeated caerulein-induced pancreatitis. Caerulein-induced pancreatitis was evoked in rats by s.c. infusion of caerulein (10  $\mu$ g/kg/h) for 5 h. After infusion, rats were divided into three groups. First group was infused with caerulein one time, in the second group infusion of caerulein was repeated 10 days later. The third group was infused with caerulein 3rd time 10 days after the 2nd infusion. Rats were sacrificed at time sequence of 0, 12, 24, 48, 72 hours and at 5th, and 10th day after last infusion. Pancreatic blood flow was measured using laser Doppler flowmeter. Plasma and pancreatic amylase, pancreatic weight, RNA and DNA contents, and histological changes were determined. We found that DNA and RNA content, as well, as histological changes in 1st group were showing progress of regeneration after 3 days. Regeneration after caerulein induced-pancreatitis was almost completed within 10 days and amylase content in the tissue and plasma amylase level returned close to normal values. Repeated infusion of caerulein caused significantly less pronounced destruction of the pancreatic tissue however regeneration occurred progressively later then after 1st or 2nd infusion. Tissue repair after 2nd infusion started after 5 days while that after 3rd infusion after 10 days. Pancreatic blood flow dropped after first induction of pancreatitis by 50% of control. Repeated acute pancreatitis was accompanied by lower and shorter decrease in pancreatic blood flow. *Conclusion:* Our results indicate that the pancreas is able to adapt to repeated induction of pancreatitis what is manifested by cumulative reduction of pancreatic damage. This effect is correlated with reduced significantly when compared to initial value and this effect is connected with the preservation of pancreatic blood flow. Pancreas: Pancreatitis experimental Pancreas: Acinar, duct cell function Pancreas: Pancreatitis, acute } "Is the Pancreas Able to Adapt to Repeated Caerulein-Induced Pancreatitis?"

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## "P P 45 1013" P 45 1013 Studies of Exocrine Pancreatic Function in Patients with Sjögren's Syndrome

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Department of Internal Medicine, Matsunami General Hospital, Gifu University, Gifu Japan

Sjögren's syndrome (SJS) is a chronic, slowly progressive autoimmune disease, involving principally the salivary and lachrymal glands and occasionally other exocrine glands such as the gastrointestinal and pancreatic glands. The special aim of this study was to elucidate the relation between salivary or lachrymal gland destruction and diminished exocrine pancreatic function in SJS. We studied the exocrine pancreatic function in 25 consecutive patients (2 M/23 F, age 55.6 – 2.2 yrs, M – SE) with SJS (15 primary SJS/10 secondary SJS). All of the patients had xerostomia and dry eyes. Diagnostic evaluation of the salivary and lachrymal glands hyposecretion included sialography (n = 18) and Schirmer's I test (using a mean value of the both sides) (n = 24). The bentiromide test (n = 24) and secretin test (100 U, iv) (n = 9) were performed to assess exocrine pancreatic function. To evaluate the endocrine pancreatic function in SJS, a standard oral 75 gGTT was also performed in 15 of the patients. Furthermore, endoscopic retrograde pancreatography (ERP) (n = 17) was performed to obtain the pancreatic ductal images. ERP findings were classified by using the criteria of Kasugai. Epigastric pain was complained in 14 patients. None of the patients had liver cirrhosis, chronic renal failure and alcoholism. The value of Schirmer's I test was then related to the results of bentiromide test and secretin test. The bentiromide test showed abnormality in 13 of 24 patients (54%). In the secretin test, 4 of 9 patients (44%) were abnormal and the maximal bicarbonate concentration (MBC) was low in 2 patients. One showed markedly decreased 3 factors (MBC, volume output and amylase output). According to the WHO criteria, 2 of 15 patients were diagnosed having diabetes, 3 showed impaired glucose tolerance and the rest were normal. As to the ERP findings, 8 of 17 patients showed minimal pancreatitis, 7 moderate pancreatitis, 1 advanced pancreatitis and the rest was normal. Sixteen patients were diagnosed as chronic pancreatitis (8 definite/8 probable). A significantly positive correlation between the MBC in secretin test and the value of Schirmer's I test was found (n = 9, p < 0.01). In chronic pancreatitis, a good correlation between the results of bentiromide test and the value of Schirmer's I test was also demonstrated (n = 15, p < 0.05). The value of bentiromide test in the severe change of sialogram was significantly lower than that in the slight change of sialogram (p < 0.05). High incidence of exocrine pancreatic dysfunction was found in SJS. The exocrine pancreatic damage in SJS may be caused by an autoimmune mechanism via the common antigen between the salivary or lachrymal gland and the pancreatic gland. Pancreas: Acinar, duct cell function Pancreas: Pancreatitis, chronic }

"Studies of Exocrine Pancreatic Function in Patients with Sjögren's Syndrome"

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## "P P 45 1014" P 45 1014 **Detection of Macroamylase in Serum by a Rapid Assay**

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Dept of Gastroenterology, University of Bologna, Italy

IRCCS S. Matteo, University of Pavia-Italy Simple procedures are currently available for the determination of amylase isoenzymes in serum which are based on the specific inhibition of salivary isoamylase. Unfortunately, they are not able to detect macroamylasemia and in the majority of these cases they erroneously indicate an increase of pancreatic isoenzyme. In 1982 a new test was described which readily distinguishes macroamylase by means of a PEG precipitation technique. In the present study we combined this technique with a widely used automated assay for amylase and isoamylase determination in order to establish the clinical utility of this combination. *Methods.* We studied 18 sera previously found positive and 61 negative for macroamylase using gel filtration chromatography (Sephadex G-100); of the latter, 32 had normal and 29 elevated amylase activity. Total amylase concentration was estimated using a colorimetric method (Amyl, Boehringer Mannheim). Pancreatic isoamylase was determined after inhibition of the salivary fraction by two monoclonal antibodies (P-Amyl, Boehringer Mannheim). The precipitation of macroamylase was obtained by adding PEG 6000 followed by incubation at 37°C for 10 min. *Results.* Sera positive for macroamylase showed precipitation of at least 71% of the amylase activity (89.6% – 7.2, mean – SD), while sera without macroamylase exhibited a maximum of 61% precipitated amylase activity (27.8% – 15.2). No significant difference in precipitation rates was found between sera with normal (25.4% – 15.5) and those with elevated amylase levels (30.3% – 14.7). Eleven of the 18 sera with macroamylase and 15 of the 61 without macroamylase were also tested with a precipitation technique using another chromogenic method for amylase assay (Phadebas, Pharmacia); the results were similar to those obtained using the automated method. All the sera but one with macroamylase showed an elevation in pancreatic isoamylase using the immunoinhibition test; this isoenzyme was found to be the prevalent fraction (> 50% of the total amylase activity) in 11 of these sera. *Conclusion.* The results demonstrate that PEG precipitation procedure is a simple and reliable technique for quick detection of macroamylase. This test can be easily applied to automated assays for amylase and should be carried out whenever dealing with hyperamylasemia of unclear origin. Pancreas: Pancreatitis, acute } "Detection of Macroamylase in Serum by a Rapid Assay"

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## "P P 45 1015" P 45 1015 Pancreatic Secretion and Gastrin Release in Response to Intraduodenal Ammonia

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Recent studies have suggested that *Helicobacter pylori* caused persistent elevations in the ammonia content in stomach leading to the development of G-cell hyperfunction and enhanced level of plasma gastrin. In patients with *Helicobacter pylori* infection, interdigestive pancreatic enzyme secretion was increased. The aim of this study was to evaluate the effect of ammonia on plasma gastrin and exocrine pancreatic secretion in conscious dogs equipped with pancreatic fistulas and *in vitro* on secretory activity of isolated pancreatic acini. Ammonia given intraduodenally (0.5, 1.0, 2.0, 4.0, 8.0 mM/L) resulted in increased pancreatic protein output, reaching respectively 9%, 10%, 19%, 16% and 17% of caerulein maximum and in a strong increase in gastrin plasma level. Ammonia (8 mM/L, i.d.) given during intravenous infusion of secretin (50 pmol/kg-h) and cholecystokinin (50 pmol/kg-h) reduced the protein and bicarbonate output by 37% and 35% respectively, as compared to control response obtained with those peptides alone. When pancreatic secretion was stimulated by ordinary feeding the same load of ammonia decreased the protein and bicarbonate responses by 47% and 78% respectively and has no significant effect on plasma gastrin. In isolated pancreatic acini, increasing concentrations of ammonia ( $10^{-7}$  M– $10^{-4}$  M) produced a dose-dependent stimulation of amylase release reaching about 45% of caerulein induced maximum. When ammonia was given together with submaximal dose of caerulein ( $10^{-12}$  M) enzyme secretion was reduced by 30%. Conclusions: 1. ammonia affects pancreatic enzyme secretion; 2. Rise in gastrin plasma level may be responsible for stimulation of basal pancreatic secretion in conscious animals. 3. Effects of ammonia on pancreatic secretion may be mediated in part by its direct action on pancreatic acini. Pancreas: Acinar, duct cell function Pancreas: Secretion, regulation Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Pancreatic Secretion and Gastrin Release in Response to Intraduodenal Ammonia"

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## "P P 45 1016" P 45 1016 **Effect of Dose Escalation of Pancreatic Enzymes on Steatorrhoea in Patients with Pancreatic Insufficiency**

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In patients with cystic fibrosis increasing the dose of pancreatic enzymes will further and significantly reduce steatorrhoea. However, it is not known whether this is also true for patients with pancreatic insufficiency due to chronic pancreatitis. Therefore we have studied the effect of two different regimens of pancreatic enzyme supplementation (Pancrease<sup>®</sup>, lipase 3 {\'b4} 10,000 U daily versus lipase 3 {\'b4} 20,000 U daily) each dose for 2 weeks combined with omeprazol 40 mg/day, in a double blind, randomized cross-over study. Results were compared with those obtained during control period. Sixteen patients (13 male, 3 female; age 22–75 yr) with chronic pancreatitis (alcoholic n = 9; idiopathic n = 7) and exocrine insufficiency (fecal fat > 10 g/24 h) participated in the study. Food intake, fecal parameters (weight, fat, stool frequency) were measured and subjective abdominal symptoms were scored. *Results:* Fecal fat Fecal weight Fat absorption (%) (g/24 h) (g/24 h) control 36 – 7 400 – 70 49 – 143 {\'b4} 10,000 lipase 18 – 5\* 260 – 40 75 – 5\*3 {\'b4} 20,000 lipase 18 – 7\* 290 – 50 75 – 6\*\* \*p < 0.05 versus control Enzyme supplementation significantly (p < 0.05) reduced abdominal symptoms: pain score from 3.2 – 0.6 (control) to 1.3 – 0.4 and 1.3 – 0.4 during low and high doses lipase respectively. General well being increased significantly from 4.8 – 0.4 (control) to 6.1 – 0.4 and 6.2 – 0.4 during low and high doses lipase. It is concluded that dose escalation from 30,000 U to 60,000 U lipase daily does not further improve fat absorption or abdominal symptoms in patients with pancreatic insufficiency due to chronic pancreatitis. Pancreas: Pancreatitis, chronic Intestinal disorders, absorption: Malabsorption syndromes Clinical practice: Management strategy } "Effect of Dose Escalation of Pancreatic Enzymes on Steatorrhoea in Patients with Pancreatic Insufficiency"

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"P P 45 1017" P 45 1017 **Non-Alcoholic Chronic Calcifying Pancreatitis (NA-CCP): Is it Less Severe than Alcoholic CCP?** R. Dani, C.E.D. Nogueira, A. Cardoso Jr., A.M.S. Reis

Santa Casa de Misericórdia, Belo Horizonte, Brazil Non-alcoholic chronic calcifying pancreatitis (NA-CCP) represents in our experience 11% of chronic calcifying pancreatitis (CCP) cases. Some authors claim that NA-CCP have a more benign course than alcoholic CCP (ACCP). The aim of this study is to report on the behavior of NA-CCP as observed in our service. *Material.* From 1963 to 1996 we have cared for 528 cases of CCP: 473 (89%) were alcoholics, 42 (8%) idiopathic, 10 (1.9%) nutritional, and 3 (0.6%) were cases of hereditary CCP. The mean age of the 55 cases of NA-CCP at the moment of the diagnosis was 26 – 17.3 years (range 1–75), with 34 males (61.8%) and 21 females (36.2%), from which 32 were white (58.2%), 19 (34.5%) colored and 4 (7.3%) negroes. Pancreatic calcifications were noticed in 39 cases (70.9%). Age at the beginning of the symptoms was 20.8 – 18.1 years (range 1–74). The main symptoms were weight loss in 49 patients (89%), pain in 38 (69%), diabetes in 18 (33%), obstructive jaundice in 14 (26%), steatorrhea in 14 (26%), cysts and pseudocysts in 7 (13%), and other pancreatitis complications in 17 cases (31%). Surgery was undertaken in 28 cases at patients' mean age of 32.3 – 18.5 years (range 1–75). The main indications were clinically uncontrollable pain in 12 cases (43%) and pain associated to pancreatitis complications in 16 patients (29%). Nine patients were reoperated upon (16%) due to recurrence of pain (4 cases) or pain plus pancreatitis complications (5 cases). *Results.* From the 28 initially operated on patients 12 are dead (57%), with a mean survival of 15 months. The other 9 cases were doing well (mean follow-up of 12 years). Pancreatic carcinoma (PC) was diagnosed in 7 patients with idiopathic CCP\* (17%) and in 1.7% of ACCP cases. *Conclusion.* NACCP is a severe disease, showing morbidity and mortality comparable to ACCP. All deceased. Pancreas: Pancreatitis, chronic } "Non-Alcoholic Chronic Calcifying Pancreatitis (NA-CCP): Is it Less Severe than Alcoholic CCP?"

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## "P P 45 1018" P 45 1018 Portal Venous Obstruction in Chronic Pancreatitis. A Prospective Longitudinal Study of a Medical-Surgical Series of 482 Patients

\*L. Sosa Valencia, P. Hammel, J. Belghiti, P. Ruszniewski, P. Bernades

F\ 'e9d\ 'e9ration M\ 'e9dico-Chirurgicale d'H\ 'e9pato-Gastroent\ 'e9rologie, Hospital Beaujon, 92118 Clichy Cedex, France *Aim of the study:* a prospective search for portal venous obstruction (PVO) in a medical-surgical series of 482 patients with chronic pancreatitis who were followed up a mean time of 6.6 years. *Patients (pts) and methods:* PVO was systematically searched for using abdominal ultrasound and CT scan, and then confirmed by endoscopic ultrasound, echodoppler or angiography. Patients with cirrhosis were excluded. *Results:* PVO was found in 19 patients (4%). Only 4 patients were symptomatic and presented with fever. Obstruction involved the portal vein alone in 7 patients, the portal vein and the splenic vein in 3, the portal vein and the mesenteric vein in 3 and the portal vein and the spleno-mesenteric axis in 6. The total prevalence of PVO alone or in combination with other veins was 1.5% (7/482) and 2.5% (12/482) respectively. Acute pancreatitis and pseudocysts were the probable cause of PVO in 84% of cases. Three patients had chronic non calcifying pancreatitis and 2 had duodenal cystic dystrophy. Esophageal varices were found in five patients (grade I n = 4, grade III n = 1) occurring 6 months to 11 years after PVO diagnosis. No gastric varices were diagnosed. At the end of analysis, 16 patients had portal cavernoma, demonstrated by computed tomography and abdominal ultrasound in all cases and by endoscopic ultrasound in 11 patients. Liver biopsies were performed in 6 cases and reported 3 steatosis and cholestasis and 3 fibrosis. Liver dystrophy was shown in 10 patients, half of them with right lobe atrophy. Only one patient was operated on due to severe gastrointestinal hemorrhage from colic variceal bleeding and died, 11 were operated on for causes not related to PVO, four of them more than once (distal splenopancreatectomy n = 4, cephalic pancreatectomy n = 1, cystogastroenteroanastomosis n = 3, enteral bypass n = 4, and surgical shunts n = 2). Eighteen patients have been followed after PVO diagnosis, without bleeding. Only chronic pancreatitis and post-operated related complications were observed. *Conclusions:* PVO prevalence is 4% in this series, the risk of digestive variceal bleeding is very low and surgical treatment of portal hypertension is not indicated. *Key words:* chronic pancreatitis, portal vein obstruction, digestive bleeding. Pancreas: Pancreatitis, chronic }" "Portal Venous Obstruction in Chronic Pancreatitis. A Prospective Longitudinal Study of a Medical-Surgical Series of 482 Patients"

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"P P 45 1019" P 45 1019 **Helicobacter Pylori Infection in Patients with Chronic Pancreatitis and Duodenal Ulcer**

\*T. Niemann, N. Thorsgaard

Medical Department, Herning Central Hospital, Denmark *Purpose:* The prevalence of duodenal ulcer (d.u.) is increased in ptt. with chronic pancreatitis (c.p.). Previous investigations including measurement of the pH in the upper gastrointestinal tract have not yielded a convincing explanation. Ptt. with d.u. without c.p. are mostly infected with *Helicobacter pylori* (H.p.), and the prevalence of IgG antibodies (IgG) against H.p. is > 90%. *Methods:* H.p. IgG was measured retrospectively in all ptt. who had their exocrine pancreas function investigated with a Lundh meal test in the period 1988–95, and in a control group with d.u. in whom H.p. were not eradicated. The Lundh meal test was done in 68 ptt.. In 35 of them the final diagnosis was c.p., and 9 of these have had d.u. (26%). In none of these 9 ptt. H.p. were eradicated. In the remaining 33 ptt. the final diagnosis was non organic dyspepsia. A control group of 21 ptt. with d.u. was included. *Results:* dyspepsia c.p. d.u. 17 d.u. +Hp+ 9 6 6 18 Hp 17 24 20 3 3 Total 33 26 9 21 *Conclusion:* Patients with c.p. have an increased prevalence of d.u. compared to a group with non organic dyspepsia. The H.p. IgG prevalence in ptt. with c.p. and d.u. was increased compared to the group with c.p. and no ulcer ( $p = 0.05$ ), but not as high as in the d.u. control group (n.s.). The H.p. IgG level in the group with c.p. but not d.u. was almost identical to the background population. *Helicobacter pylori* infection contributes, but may not be the only cause of duodenal ulcer in patients with chronic pancreatitis. **Pancreas: Pancreatitis, chronic Oesophageal gastric duodenal disorders: Helicobacter Pylori }** "Helicobacter Pylori Infection in Patients with Chronic Pancreatitis and Duodenal Ulcer"

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"P P 45 1020" P 45 1020 **Postprandial Release of Glucagon-Like Peptide-1 (GLP-1) with and without Pancreatic Enzyme Substitution in Pancreatic Insufficiency**. Larsen, E.K. Philipsen, J.J. Holst

Department of Gastroenterology F, Glostrup Hospital

Department of Medical Physiology, Panum Institute, University of Copenhagen, Denmark

Secretion of glucagon-like peptide 1 (GLP-1), a gastrointestinal hormone with insulinotropic action and inhibitory action on gastrointestinal secretion and motility is stimulated by ingestion of a meal. Both metabolizable and non metabolizable sugars may stimulate secretion, but it is unknown how pancreatic enzyme substitution affects GLP-1 release in pancreatic insufficiency.

*Methods.* Eight patients with pancreatic insufficiency (meal-stimulated intraduodenal lipase and amylase < 5% of normal mean concentrations) ingested a mixed meal containing 2100 kJ with 50 g carbohydrate. Each participant were studied twice at random without or with pancreatic enzyme substitution (50 KU lipase and 45 KU amylase). Plasma GLP-1 (7–36) determined by RIA, C-peptide (ELISA) and blood glucose were measured over 300 min.

*Results.* (Means – SE). No significant differences were found in meal stimulated blood glucose, C-peptide and GLP-1 responses (area under curve) with and without pancreatic enzyme supplementation. Peak GLP-1 levels were observed after 146 – 37 min and 73 – 21 min with and without enzyme supplementation, respectively (not significant). Peak glucose was observed after 69 – 12 min and 68 – 9 min and C-peptide after 116 – 9 min and 112 – 11 min with and without enzyme supplementation, respectively. Area under curve Meal without Meal with 0 to 300 min. enzyme enzyme Glucose 1914 – 140 1888 – 122 (mmol.min/l) C-peptide 264 – 47 260 (48) (nmol.min/l) GLP-1 4834 – 653 5727 (648) (pmol.min/l) Means – SE, no significant difference on any data

*Conclusions.* In pancreatic insufficiency secondary to chronic pancreatitis meal stimulated GLP-1 release is preserved and not influenced to a greater extent by enzyme supplementation. Thus, nutritional absorptive processes may be of minor importance for GLP-1 secretion, which seems primary stimulated by the presence of nutrients in the gut lumen.

Pancreas: Secretion, regulation } "Postprandial Release of Glucagon-Like Peptide-1 (GLP-1) with and without Pancreatic Enzyme Substitution in Pancreatic Insufficiency"

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## "P P 45 1021" P 45 1021 NBT-PABA Pancreatic Function Test Using a Novel Dual Isotope Technique and Gas Chromatography-Mass Spectrometry

\*B. Larsen, S. Ekelund, L. Jørgensen, A. Bremmelgaard, N.T. Pedersen

Department of Clinical Chemistry, Aalborg Hospital, Aalborg

Department of Medicine, Herning Hospital, Denmark We present a tubeless test of exocrine pancreatic function based on a new dual isotope technique using NBT-PABA (N-benzoyl-tyrosyl-p-aminobenzoic acid) as substrate for intestinal chymotrypsin activity and the stable isotope  $^{13}\text{C}$ -PABA (p-aminobenzoic acid) as pharmacokinetic marker. We have developed a gas chromatography-mass spectrometry (GC-MS) method for analysis of PABA and  $^{13}\text{C}$ -PABA in serum. Ten healthy volunteers and 10 patients with exocrine pancreatic insufficiency were orally administered 500 mg NBT-PABA and 50 mg  $^{13}\text{C}$ -PABA together with a standard meal after an overnight fast. The test doses corresponded to 1.103 mmol PABA and 0.349 mmol  $^{13}\text{C}$ -PABA. Blood samples were drawn at specified intervals. Serum concentrations of PABA and  $^{13}\text{C}$ -PABA were measured and the ratio of PABA to  $^{13}\text{C}$ -PABA was calculated. The analytical procedure showed good precision with a CV% 5.3 for the ratio. Best separation between the two groups was found 12; hour after administration of the test mixture. The average ratios were  $2.64 \pm 0.15$  (mean  $\pm$  SEM) and  $1.26 \pm 0.22$ , respectively. The cut off limit of normal was calculated to 1.72 (mean  $\pm$  2SD), giving sensitivity 0.90 and specificity 1.00 in this material. Introducing a stable isotope and GC-MS in the NBT-PABA test, allows a very sensitive and specific identification in serum of the test substances in serum. We found good separation between healthy controls and patients with pancreatic insufficiency. Further studies of applicability and diagnostic efficiency are justified. Pancreas: Pancreatitis, chronic } "NBT-PABA Pancreatic Function Test Using a Novel Dual Isotope Technique and Gas Chromatography-Mass Spectrometry"

## "P P 45 1022" P 45 1022 **Postprandial Duodenal pH is Abnormally Low in Patients with Exocrine Pancreatic Insufficiency: A Preliminary Study**

\*P. Bovo, V. Di Francesco, M. Marcori, B. Vaona, M. Filippini, G. Talamini, M.P. Brunori, L. Frulloni, M.T. Leardini, E. Dall'O, G. Cavallini

Gastroenterology Unit, University of Verona, Italy

Increases in basal and pentagastrin-stimulated acid output and abnormally low postprandial pH (pH-metry method) have been reported in the course of chronic alcoholic pancreatitis, though it is still debatable whether or not any correlation exists between duodenal pH and exocrine pancreatic insufficiency. The aim of this study was to assess the circadian variations in intraduodenal pH in 16 hospital patients with chronic pancreatitis (mean age: 50.2 – 7.2 years) and in 8 controls (mean age 41.4 – 12 years); pHmetry was performed by using specially designed 2- or 4-channel monocrystalline antimony electrodes (Monocrystant mod.0011) connected up to a recorder (Digitrapper Synectis MK-II and MK-III, respectively). The detectors were placed under fluoroscopic control in the gastric corpus in the duodenal bulb and/or in the second portion of the duodenum. The evaluation parameters considered, expressed as mean – SD values were: 24-h, postprandial, orthostatic and clinostatic median pH. The chronic pancreatitis patients were also submitted to the Secretin-Cerulein test (lipase output at 60–90 min) for assessment of the exocrine pancreatic insufficiency and to the Pancreolauryl test as proof of maldigestion. *Results:* 1) The chronic pancreatitis patients presented a significantly greater degree of acidification in the postprandial phase at the level both of the bulb (pH: 2.6 – 1.1;  $P < 0.02$ ) ( $n = 8$ ) and the second portion of the duodenum (pH: 3.4 – 1.2;  $P < 0.05$ ) ( $n = 13$ ) as compared to the control group (pH: 5.1 – 1.0 and 5.1 – 1.6 respectively). 2) There was a correlation between the median duodenal pH values and both output of bicarbonates ( $R = 0.72$ ;  $P < 0.04$ ) and Pancreolauryl test ( $R = 0.61$ ;  $P < 0.04$ ). *Conclusions:* Duodenal acidity, exocrine pancreatic insufficiency and maldigestion appear to be correlated in chronic pancreatitis. Pancreas: Pancreatitis, chronic }" "Postprandial Duodenal pH is Abnormally Low in Patients with Exocrine Pancreatic Insufficiency: A Preliminary Study"

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"P P 45 1024" P 45 1024 **Evidence for Potentiative Interaction between Vagal Cholinergic M1 Fibers and Cholecystokinin (CCK) as Mediators of the Pancreatic Protein Secretion**

\*E. Niebergall-Roth, S. Teysen, M. Hartel, D. Wetzel, C. Beglinger<sup>1</sup>, M.V. Singer

Univ. Hosp. of Heidelberg at Mannheim, Germany

<sup>1</sup> Univ. Hosp. of Basel, Switzerland In six conscious dogs with gastric and pancreatic fistulas we compared the effect of the muscarinic M1-receptor antagonist telenzepine (TEL; 20.25, 40.5 and 81.0 nmol/kg/h iv.), of the CCK-antagonist L-364,718 (L; 0.025, 0.05 and 0.1 mg/kg/h iv.) and combinations of both on the pancreatic protein response to graded loads of intraduodenal tryptophan (TRP; 0.37–10.0 mmol/h), given against a background of secretin (S; 20.5 pmol/kg/h iv.). The 180-min integrated protein response (IPR, g) to all loads of TRP was calculated.

**Results:** All loads of TRP significantly ( $p < 0.05$ ) increased the pancreatic protein output over that seen with secretin alone (data not shown). When given singly, the two highest doses of TEL and L significantly decreased the IPR by 70 to 97%. All combinations of TEL + L abolished the IPR before and after TV. In the case of the lowest doses of TEL and L, the inhibitory effect of their combination was significantly greater than the sum of the effects when given singly. An interaction between two agents given together resulting in a greater effect than the sum of the effects of the two agents given singly was defined as a potentiated interaction. Table: 180-min. IPR (g) to all loads of TRP TEL (20.25) + L (0.025): 0.8\*Control: 25.2 TEL (20.25) + L (0.05): { - }0.2\*TEL (20.25): 15.2 TEL (20.25) + L (0.1): 0.2\*TEL (40.5): 7.3\* TEL (40.5) + L(0.025): 0.4\*TEL (81.0): 7.5\* TEL (40.5) + L (0.05): { - }0.2\*L (0.025): 12.6 TEL (40.5) + L (0.1): 0.8\*L (0.05): 6.7\* TEL (81.0) + L (0.025): 1.0\*L (0.1): 0.8\* TEL (81.0) + L (0.05): 0.8\* TEL (81.0) + L (0.1): 0.6\*Results are means (n = 6); \* $p < 0.05$  vs. control **Conclusion:** Potentiation exists between the inhibitory actions of the M1 antagonist TEL and the CCK-A-antagonist L on the endogenously stimulated pancreatic protein output. We interpret these data as indicating a potentiative interaction between vagal cholinergic M1 fibers and CCK as mediators of the pancreatic enzyme response to intraduodenal amino acids. Pancreas: Secretion, regulation }" "Evidence for Potentiative Interaction between Vagal Cholinergic M1 Fibers and Cholecystokinin (CCK) as Mediators of the Pancreatic Protein Secretion"

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"P P 45 1025" P 45 1025 **ERCP-Induced Necrotizing Pancreatitis. Is It a More Severe Disease?**

\*A.S.Y. Fung, G.G. Tsiotos, M.G. Sarr

Mayo Clinic, Rochester, MN, USA Acute necrotizing pancreatitis (ANP) is a rare but serious complication of ERCP. *Aim:* To compare disease severity, clinical course, and outcome of ERCP-induced ANP versus ANP induced by other causes. *Results:* 72 patients with ANP underwent operative treatment at the Mayo Clinic. ANP was caused by ERCP in 6 patients (8%). When compared to the remaining group of 66 patients with ANP induced by other causes (gallstone – 27; alcohol – 6; postoperative – 8; familial – 1; idiopathic – 24), the ERCP-induced group had a higher admission APACHE-II score (13 – 3 vs 10 – 1;  $\bar{x}$  – SEM), more extensive estimated pancreatic parenchymal necrosis (55 vs 47%), a greater rate of postoperative gastrointestinal or pancreatic fistulas (50 vs 33%), and a longer postoperative hospitalization (84 – 38 vs 53 – 5,  $\bar{x}$  – SEM;  $p < 0.05$ ). In addition, the ERCP-induced group required necrosectomy earlier in the hospital course and had a higher rate of infected necrosis (100 vs 75%). Although mortality rate of ERCP-induced ANP was lower (17 vs 29%), these patients were considerably younger (50 – 4 vs 62 – 2,  $\bar{x}$  – SEM;  $p = 0.02$ ) and all survivors had residual long-term morbidity (e.g. exocrine or endocrine pancreatic insufficiency) or decreased functional ability. *Conclusions:* ERCP-induced ANP is usually severe, presents in a more fulminant state, and carries a poorer prognosis concerning short- and long-term morbidity than ANP of other etiologies. Infection introduced during the ERCP may, in part, account for the more aggressive nature of this disease. Pancreas: Pancreatitis, acute } "ERCP-Induced Necrotizing Pancreatitis. Is It a More Severe Disease?"

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"P P 45 1026" P 45 1026 **Obstructive Jaundice: Comparison between Spiral CT and Cholangio-MR, after Failure of ERCP** G.A. Rollandi, A. Talenti,

\*E. Biscaldi, E. Bonifacino, N. Gandolfo, R. Perrone

Institute of Radiology, University of Genoa *Introduction:* In spite of improvements of CT and US techniques, the direct vision of the biliary tree is always important in case of obstructive jaundice, for a good choice of the therapy. At the moment Contrast Media for intravenous cholangiography are no more produced; conventional radiographic studies are then impossible. While ERCP and PTC are examination with high specificity and sensitivity, but they are also quite invasive and have frequent complications. Recently a new MRI technique for cholangiography has been described. It is based on the detectability of the bile by MR sequences, without any introduction of contrast medium. *Purpose:* We wanted to evaluate the diagnostic informations from Cholangio-MR (C-MR) in patients with obstructive jaundice, already examined by Spiral CT, and after failure to obtain a ERCP. *Materials and Methods:* 13 jaundiced patients, with US diagnosis of dilatation of biliary tree and with failure to obtain a ERCP (4 non successful attempts, 3 gastric resections, 6 difficulties of management in emergency) were submitted to Spiral CT of the upper abdomen and to C-MR, before surgical treatment. Spiral CTs were performed with a volumetric scan with 10 mm collimation, 3 mm of index of reconstruction, pitch 1, 300 mAs, 120 kV, i.v. injection (4 cc/s) of non ionic c.m. (370 I g/100 ml). C-MR examinations were performed with a 0.5 T magnetic strength, TR6000, TE200, ETL16, matrix 160–256, Nex5, MIP reconstruction. *Results:* In 12 cases C-MR reached the correct diagnosis; only in 1 case a little stone (2 mm) at the papilla was lost. In 6 cases (4 primary tumours of biliary tree and 2 pancreatic cancers) C-MR didn't give any more informations than CT. In 4 cases (biliary stones) C-RM provided more diagnostic information-sa than CT. In 2 cases of chronic pancreatitis, with pseudocysts of the head of pancreas only C-RM allowed the correct diagnostic identification as the cause of jaundice. *Conclusions:* C-MR has high diagnostic sensitivity and specificity in the diagnostic evaluation imaging of jaundice. Spiral CT is more useful only in neoplastic diseases. Oncology, specific: Liver, biliary Radiology and ultrasound: Diagnosis } "Obstructive Jaundice: Comparison between Spiral CT and Cholangio-MR, after Failure of ERCP"

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## "P P 45 1031" P 45 1031 Preoperative Cyst Fluid Analysis for the Differential Diagnosis of Cystic Lesions of the Pancreas

\*P. Hammel, H. Voitot, V. Vilgrain, P. L'evy, J.F. Fl'e9jou, P. Ruzzniewski, P. Bernades

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The nature of cystic lesions of the pancreas (CLP) is often difficult to determine preoperatively since imaging techniques do not give correct diagnosis in 30% of cases. We have previously shown that cyst fluid analysis for carcinoembryonic antigen (CEA), carbohydrate antigen (Ca) 19.9 and amylase is useful for the differential diagnosis of CLP. *Aim:* to assess the reliability of preoperative lipase, Ca 72.4 and M1 mucin antigen analysis, in addition to that of amylase, CEA and Ca 19.9, in cyst fluid obtained by fine-needle aspiration for pathological diagnosis in a large series of CLP. *Methods:* cyst fluid was obtained for 96 CLP [26 mucinous cystadenomas or cystadenocarcinomas (MC), 14 serous cystadenomas (CS) and 56 pseudocysts (PC) complicating well-documented chronic pancreatitis]. Cutoffs of biochemical and tumor markers were determined so that the three types of CLP could be differentiated as accurately as possible. Sensitivity (se), specificity (spe), positive and negative predictive values (PPV and NPV) of these markers were calculated for this purpose. *Results:* dg se sp PPV NPV % % % % Amylase > 5000 U/ml PC 93 86 91 89 Lipase > 26,000 U/ml PC 89 89 92 85 CEA > 400 ng/ml MC 54 100 100 100 CEA < 4 ng/ml SC 100 93 70 100 Ca 19.9 > 50,000 U/ml MC 65 89 68 87 Ca 72.4 > 25 U/ml MC 63 97 94 80 M1 mucins > 600 UM1/ml MC 62 96 81 82 *Conclusion:* Our study confirms that high amylase levels, high Ca 19.9 levels and low CEA levels are indicative of PC, MC and SC, respectively. Moreover, high Ca 72.4 and M1 mucins levels are strongly indicative of MC. *Clinical practice:* Management strategy Oncology, general: Screening, prevention Oncology, specific: Pancreas }

"Preoperative Cyst Fluid Analysis for the Differential Diagnosis of Cystic Lesions of the Pancreas"

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## "P P 45 1032" P 45 1032 Does Nonoperative Management of Pancreatic Pseudocysts Increase the Risk of Misdiagnosis?

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The worldwide diffusion of nonoperative alternatives to surgical management of pancreatic pseudocysts might lead to an increase of diagnostic errors with consequent inappropriate treatment of unrecognized cystic neoplasms. The aim of this retrospective study was to ascertain the clinical incidence of diagnostic errors in a series of nonoperatively managed pseudocysts. Data from 64 patients (49 males and 19 females; mean age: 57.3 years, range: 26–80) bearing one or more pancreatic pseudocysts who underwent a percutaneous ultrasound-guided drainage were reviewed and analysed. The pre-treatment workup included: medical history, physical examination, ultrasound (US) and computed tomography (CT) scans, determination of tumor markers and pancreatic enzymes in the serum and in the cystic fluid, chemistry and cytology. All patients were entered into a combined clinico-ultrasonographic follow-up. Sixty patients underwent a percutaneous catheter drainage and 4 repeated fine needle aspirations. A total of 4 neoplastic lesions were overlooked after the initial workup (4/64, 6.2%). Two cancer-associated pseudocysts were identified within the treatment period (2/64 3.1%). Four patients died soon after the treatment while the remaining 58 were followed-up for a mean of 41 months (range: 10–132). A third cancer and a mucinous cystic tumor (2/58, 3.4%), fully communicating with the main duct, were further detected during this period. Data from our experience confirm the existence of a misdiagnosis risk in the nonoperative management of pancreatic pseudocysts and support the need for a thorough followup with continuous reassessment of each patient. The nature of any pseudocyst with atypical clinical history or behaviour should be questioned and, when doubts persist, the patient should be referred for surgical exploration.

Oncology, specific: Pancreas  
Clinical practice: Management strategy }

"Does Nonoperative Management of Pancreatic Pseudocysts Increase the Risk of Misdiagnosis?"

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## OT40 1034 Proximal Esophageal pH-Metry in Controls and in Patients with Reflux or Otolaryngologic (ORL) Symptoms. A Multicenter Study in Italy

\*F. Baldi, M.L. Brancaccio, R. Cappiello, M. Dinelli, L. Fei, S. Mattioli, G. Missale, S. Passaretti, R. Sablich, S. Sottili, V. Stanghellini, I. Vantini

G.I.S.M.A.D.-Italy We studied 22 healthy subjects (9 M; 50.1 – 12.0 yrs) [Gr. I]; 114 patients with typical reflux symptoms from 6 months (72 M; 48.8 – 14.1 yrs) [Gr. II] and 116 patients with unexplained ORL symptoms from 6 months (67 M; 52.1 – 12.6 yrs) [Gr. III]. All subjects underwent an upper GI endoscopy, an ORL examination and a 24-hr esophageal pH-metry performed with 2 glass electrodes (Ingold M 4.40, M 1.40) connected to a portable data-logger and positioned 5 cm above the LES and 1 cm below the UES localized by manometry, respectively. *Parameters:* N. of GER episodes (pH < 4 5 sec.; GER) and acid exposure time (% T pH < 4; % T) were calculated for the 24-hr period at the two recording sites. The proximal distribution of reflux (% of distal GER reaching the proximal site; % P) was calculated for the 24-hr, upright and supine periods. Statistical analysis was performed with a Student T test or Mann-Whitney U test. *Results:* data are expressed as mean – SD and reported in Table-1 and 2. The subdivision of the patients according to the presence of esophagitis or of ORL lesions didn't show significant differences between the reflux values assessed at the proximal site. Table 1 GER %T Prox Dist. Prox. Dist. Gr. I 2.5 – 2.9\* 21.0 – 14.1\* 0.1 – 0.1\* 1.0 – 0.9\* Gr. II 12.5 – 14.1 83.0 – 79.6 1.3 – 2.2 9.6 – 9.0 Gr. III 16.6 – 42.5 59.4 – 73.1° 1.3 – 2.2 5.0 – 5.3° \*p < 0.01 vs Gr II and Gr III; °p < 0.01 vs Gr I Table 2 % P 24-hr Upright Supine Gr. I 16.1 – 20.4 31.0 – 65.1 1.9 – 6.7 Gr. II 20.9 – 24.2 21.7 – 30.2 14.6 – 22.7° Gr. III 28.6 – 35.6\* 27.9 – 29.6 37.5 – 84.4\* \*p < 0.05 vs Gr I and Gr II; °p < 0.05 vs Gr I *Conclusions:* proximal acid GER was significantly higher in both patient groups, in comparison with controls. Patients with ORL symptoms had a significantly higher frequency of refluxes that reached the proximal esophagus, particularly during the night. Oesophageal gastric duodenal disorders: EG Reflux }" "Proximal Esophageal pH-Metry in Controls and in Patients with Reflux or Otolaryngologic (ORL) Symptoms. A Multicenter Study in Italy"

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## OT40 1035 Sensitivity to Acid and Distension in Gastro Oesophageal Reflux Disease (GORD) and the Acid Hypersensitive Oesophagus

\*S. Bruley des Varannes, G. Shi, C. Scarpignato, J.P. Galmiche

Dept of Gastroenterology, University of Nantes, 44035 Nantes, France Although mechanical receptors are present in the oesophageal wall, the investigation of oesophageal sensitivity in GORD and some functional related disorders has been usually limited to the acid perfusion test. We therefore compared the oesophageal sensitivity to both acid and mechanical stimuli in patients with GORD and with the newly described acid hypersensitive oesophagus (AHO) syndrome (Gut 1995; 37: 457–64). *Methods.* One hundred and twenty four patients referred for 24-h oesophageal pH monitoring for symptoms suggestive of GORD were submitted to an oesophageal acid perfusion test (APT) and to an oesophageal balloon distension test (BDT). The probability that symptoms and reflux episodes occurred simultaneously by chance was calculated. APT was considered positive when perfusion induced retrosternal burning or the spontaneously reported pain. The balloon volume inducing pain (VIP) was determined; BDT was considered positive when VID was  $\geq 7$  ml (95% IC of 10 healthy subjects). *Results.* Patients were divided into 3 groups: normal acid exposure (< 4.2% of total recording time) with no significant relation between symptoms and reflux episodes (group Functional Dyspepsia (FD)), and with significant relation between symptoms and reflux episodes (group AHO), abnormal acid exposure (group GORD). The results of APT and BDT are in the table (Chi<sup>2</sup>, Mann-Whitney; P < 0.05 compared a: with volunteers; b: with GORD, c: with FD). Volunteers AHO GORD FD (n = 10) (n = 27) (n = 29) (n = 68) Age (mean yrs) – Sex (M/F) 41 – 4/6 51 – 9/18 48 – 25/4 55 – 20/48 APT positive (%) 30 63c 62c 37 VIP (ml, median – range) 11.2 (6 – 15) 7 (4 – 12)a 12 (5 – 15) 9 (3 – 15)a BDT positive (%) 10 59a, b, c 14 24 *Conclusion.* Compared to healthy volunteers or dyspeptic patients without reflux, a) patients with GORD exhibit a high sensitivity to acid but are poorly responsive to mechanical distension, b) in contrast, patients with AHO are sensitive to both stimuli therefore suggesting that the primary disorder is rather a visceral hyperalgesia than a true motility disorder. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, general: Functional GI disorders } "Sensitivity to Acid and Distension in Gastro Oesophageal Reflux Disease (GORD) and the Acid Hypersensitive Oesophagus"

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## OT40 1036 **Lanzoprazole Versus Omeprazole in Long Term Maintenance Treatment of Refluxoesophagitis. A Scandinavian Multicentre Trail**

\*L. Carling, C. Axelsson, H. Forsell, A. Stubberud, K. Kraglund, U. Bonnevie, P. Ekstrand

Med. Dept. of Bollnäs-Sörms Hospital, Bollnäs, Sweden  
This double-blind multicentre study recruited 289 patients who were treated with 30 mg lansoprazole for 8 weeks or as most 12 weeks. When cured the patients were randomized to either treatment with 20 mg omeprazole or 30 mg lansoprazole each day for 48 weeks or until relapse (t.i. at least grade II esophagitis or/and severe refluxsymptoms). The baseline distribution of esophagitis was: Grade II 194 (67%), grade III 74 (26%), grade IV 19 (7%). Grade II corresponds to: Erosive and exudative confluent lesions without circumferential extensions. The demographic data was similar in the two treatment groups. To the maintenance part 266 patients were recruited and 131 got lansoprazole 30 mg o.m. and 125 omeprazole 20 mg o.m. treatment. They were followed every 12 weeks.  
**Results:** After 8 weeks 84% of the patients were cured and the cumulative figure after 12 weeks was 90%. Grade II patients healed to grade 0 in 82.5%. Maintenance part  
Lanzo 30 mg Omeprazole 20 mg  
Patients evaluated 124 120  
Relapse (total) 12 (9.7%) 11 (9.2%)  
week 0–12 3 4 week 12–24 5 4 week 24–26 3 2 week 36–48 1 1  
 $p = 0.94$  NS  
Eighteen patients relapsed to grade II oesophagitis. Only two patients got a symptomatic relapse. There were no differences in adverse events in the both treatment groups.  
**Conclusion:** Both lansoprazole 30 mg o.m. and omeprazole 20 mg o.m. gives low and similar relapse rates in maintenance treatment in moderate and severe refluxoesophagitis. Oesophageal gastric duodenal disorders: EG Reflux  
Clinical practice: Management strategy  
Endoscopy, specific: Oesophagus }  
"Lanzoprazole Versus Omeprazole in Long Term Maintenance Treatment of Refluxoesophagitis. A Scandinavian Multicentre Trail"

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## OT40 1039 Somatostatin Prevents Meal Induced Alterations in Lower Esophageal Sphincter Function

\*J.W. Straathof, S. Tieleman, C.B.H.W. Lamers, A.A.M. Masclee

Dept. of Gastroenterology, University Hospital Leiden, The Netherlands Somatostatin (SST) inhibits gastrointestinal secretion and motility. SST reduces gastric acid secretion and is of potential clinical interest in acid related disorders. It is not known, however, whether SST influences lower esophageal sphincter (LES) function. Therefore we evaluated the effect of SST on LES characteristics. Six healthy subjects (2 M, 4 F; age 19–53 yr) were studied after an overnight fast on 4 separate occasions in random order under fasting conditions during 1) SST infusion (250 µg/h) or 2) saline i.v. (control) and after meal stimulation during 3) SST infusion (250 µg/h) and 4) saline i.v. (control) for 240 min. LES pressure, transient LES relaxations (TLESR), as the most important reflux mechanism, and acid reflux were measured by combined esophageal pH metry and manometry (Dent-sleeve). The meal consisted of carbohydrates only (500 Kcal) in order to prevent gastro-intestinal hormone secretion. *Results:* under fasting conditions SST did not affect LES pressure and LES pressure during SST (range 25 – 4 to 29 – 6 mmHg) was not significantly different from control (range 23 – 4 to 26 – 1 mmHg). TLESR frequency under fasting conditions during SST infusion (2.2 – 0.6 per hour) was not significantly different from control (2.4 – 0.5 per hour). Meal ingestion significantly ( $p < 0.05$ ) increased TLESR frequency from 2.4 – 0.5 to 4.8 – 0.5 in the first postprandial hour. However, this meal induced increase in TLESR frequency did not occur during SST infusion. Acid reflux time was low (fasting 0.1%; meal 0.2%) and not influenced by SST. It is concluded that 1) somatostatin does not affect fasting LES pressure and TLESR-frequency, 2) but meal induced decreases in LESP and increases in TLESR's do not occur during somatostatin infusion; 3) somatostatin prevents meal induced alteration in LES function that permit reflux. The effect of somatostatin in patients with reflux disease therefore deserves further evaluation. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Somatostatin Prevents Meal Induced Alterations in Lower Esophageal Sphincter Function"

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## OT41 1040{ a}-Interferon in Chronic C Hepatitis: Is Antipyrine Metabolism a Predictor of Response?

\*A. Grieco, R. Castellano, A. Matera, S. Marcocchia, A. Giancaterini, P. Di Rocco, B. Alfei, P. Marino, A. Bianco, G.B. Gasbarrini

Inst. Internal Medicine-Catholic Univ.-Rome-Italy{ a}-interferon (IFN) treatment is today the only evaluated therapy for hepatitis C able to induce a biological remission. The determination of predictive factors of response is essential in planning IFN treatment. Cirrhosis is a negative predictor of response and it is also associated with decreased antipyrine metabolism. A positive correlation has been recently observed between the liver metabolic capacity and the response to { a}-IFN in pts with chronic hepatitis C [1]. We assessed the antipyrine test in pts with chronic hepatitis C, who underwent { a}-IFN therapy. We enrolled 45 pts (22 males, 23 females, median age 47, range 25–70) with histological diagnosis of CAH; 20 were classified as having CAH with mild or no fibrosis (group A), and 25 as CAH with severe fibrosis or cirrhosis (group B). The antipyrine metabolism test (18 mg/kg in water p.o.; blood samples drawn 3 and 24 hrs after administration for spectrophotometrical analysis) was administered to all patients before treatment with recombinant { a}-IFN2b (9 MU/week/6 months). The therapeutic response was assessed in terms of ALT normalisation. We observed a complete response to IFN therapy in 19/45 pts (42%) and the response rate was higher in Group A (16/20, pts-80%) than in Group B (3/25 pts-12%). Pts of group A had significantly better clearance (0.405 – 0.1 ml/min/Kg) than those of group B (0.22 – 0.15 ml/min/Kg) ( $p < 0.001$ ). Baseline antipyrine clearance for the group of responders (0.412 – 0.15 ml/min/kg) was significantly higher than that of the non-responders (0.242 – 0.14) ( $p < 0.001$ ). 13/19 responders had an antipyrine clearance over a cut-off  $> 0.30$  ml/min/Kg (78%). We confirm the relationship between hepatic drug metabolism, explored by antipyrine metabolism, and the response to IFN therapy in pts with C hepatitis. We suggest the use of this test in pts clinical baseline evaluation, especially when liver histology is not available.

Reference: S. Coverdale et al *Hepatology* 1995; 21: 298–304. Liver and bile ducts, 1: Hepatitis viral, diagnosis Liver and bile ducts, 1: Hepatitis, viral, treatment }" "alpha-Interferon in Chronic C Hepatitis: Is Antipyrine Metabolism a Predictor of Response?"

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OT41 1041 **Therapy of Chronic Hepatitis C Non Responders to Alfa-Interferon: A Preliminary Report of Intravenous Natural Beta-Interferon (IFN)** A. Cartabellotta, P. Campagna, G. Anastasi, L. Giannitrapani, M. Fulco, M. Soresi, F. Bascone, G. Montalto

Cattedra di Medicina Interna, Universit\`e di Palermo *Background:* { a}-IFN has been shown to be effective in the treatment of chronic viral C hepatitis, but its efficacy remains unsatisfactory; in fact only 20–25% of patients will have a sustained response and 50% are non-responders. In these patients alternative treatment (ribavirin, ursodeoxycolic acid, phlebotomy) have not been effective. Recently efficacy of beta-IFN, ineffective when administered by I.M. route, has been proven when administered by intravenous infusion. *Aims:* To evaluate in patients with chronic hepatitis C non-responders to previous treatment with { a}-IFN, efficacy and safety of intravenous beta-IFN. *Patients and methods:* 9 patients, (8 M/1 F) mean age 36 – 1.4 SD years (range 21–50), with histologically proven chronic active hepatitis C without cirrhosis, HCV-RNA positive and non responders to previous treatment with { a}-IFN (recombinant or lymphoblastoid or leukocyte-derived), with mean basal ALT value 222 – 194 UI/L (range 65–359), received 6 MU of beta-IFN daily for 6 days a week for 8 weeks, by an intravenous infusion in 100 ml of saline. *Results:* After 8 weeks of treatment 5 pts (55%) showed complete normalization of ALT values and became HCV-RNA negative on serum. Therapy was well tolerated and the beta-IFN dose did not have to be interrupted or reduced due to side effects in all patients, but one due to severe neutropenia. *Conclusion:* Intravenous beta-IFN can be a well tolerated effective treatment for patients with chronic hepatitis C non-responders to { a}-IFN. Nevertheless to define the optimum dose and schedule of treatment to achieve eradication of HCV infection, longer follow-up of these patients are necessary. Liver and bile ducts, 1: Hepatitis, viral, treatment }" "Therapy of Chronic Hepatitis C Non Responders to Alfa-Interferon: A Preliminary Report of Intravenous Natural Beta-Interferon (IFN)"

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OT41 1042 **Ribavirin Monotherapy in Patients with HCV Related Chronic Hepatitis or Liver Cirrhosis: A Retrospective Study of 95 Patients** F. Zoulim, J. Haem, F. Habersetzer, S. Si Ahmed, F. Bailly, C. Trépo

Hotel Dieu Hospital, Lyon, France Ribavirin is a purine analog which inhibits the replication of a variety of RNA viruses and was shown to have a transient efficacy in chronic hepatitis C during short term therapy. We have analyzed retrospectively its efficacy in 95 patients suffering from liver biopsy proven chronic hepatitis C. All patients had raised ALT levels and were positive for serum HCV RNA by PCR prior to therapy. Liver histology showed chronic active hepatitis in 50 and cirrhosis in 45. Sixty patients had received a previous course of IFN and 35 were naïve of any antiviral treatment. Patients were treated with Ribavirin with a dose of 600 mg–1200 mg/day for a mean duration of 11 months. ALT levels returned to normal values in 38 patients (40%), and decreased by more than 50% in 20 other patients (21%). HCV RNA clearance from serum was observed in 7 patients (8%). The rate of ALT normalization was higher in patients with chronic hepatitis (54% = 27/50) than in those with cirrhosis (11/45 = 24%) ( $p = 0.0001$ ). HCV RNA clearance was observed in 5/50 (10%) patients with chronic hepatitis versus 2/45 (4%) patients with liver cirrhosis ( $p = 0.03$ ). The delay of ALT normalization was 2.7 months in patients with chronic hepatitis and 4.4 months in patients with cirrhosis. In the group of 42 patients who were non-responders to a previous course of Interferon alpha, ALT returned to normal in 11 (26%) or decreased by more than 50% in 10 other patients (24%), and HCV RNA became negative in 1 (2.5%). Paired liver biopsy samples were available in 17 patients. The histologic activity index improved in 8/10 responders, 2/3 partial responders and 2/4 non responders. Side effects were mild but more pronounced in cirrhotic patients. In *conclusion*, the rate of ALT normalization and liver histology improvement after long term administration suggest that Ribavirin monotherapy may be beneficial in controlling HCV associated liver disease. This may represent an alternative therapy in patients contra-indicated to Interferon therapy. Liver and bile ducts, 1: Hepatitis, viral, treatment Clinical practice: Management strategy } "Ribavirin Monotherapy in Patients with HCV Related Chronic Hepatitis or Liver Cirrhosis: A Retrospective Study of 95 Patients"

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**OT44 1044 Which Anastomosis Following Proctectomy and Total Mesorectal Exision TME for Rectal Cancer? Low Colorectal (LCRA) or Colonic Pouch-Anal Anastomoses (CPAA)**

\*N. Dehni, J.D. Singland, R.D. Schlegel, M. Guiguet, E. Tiret, R. Parc

Centre de chirurgie digestive, Hospital Saint Antoine, Paris, France After TME for low rectal cancer, the decision to perform LCRA or CPAA is made per-operatively depending on the tumor distance from the anal verge. The functional results of these operations are thought to be equal 1–2 years after operation. This consideration led us to compare the long term functional results of these two operations. *Methods* from 87 to 92, 173 patients underwent anterior resection and TME for cancers between 2–12 cm from the anal verge. All patients alive without recurrence were contacted by telephone for their functional results. There were 47 patients with CPAA and 34 patients with LCRA. Minimal follow up was 3 years for all patients (mean 5 years). *Results* the 2 groups were well matched for sex, age, histologic stage and adjuvant therapy. Functional results figure herein

Function	CPAA	LCRA	p*	n = 47	n = 34
No. bowel movements/day	1.57	1.79	– 1	0.001	
Irregular transit	30%	71%	0.003		
Fragmented defecation	41%	65%	0.06		
Diarrhea/constipation	31%	59%	0.02		
Incontinence for feces	13%	12%	1.0		
Use of Loperamide	4%	21%	0.03		
Restricted diet	14%	41%	0.01		

\*Wilcoxon or Fisher test *Conclusion* quality of life at long term follow up seems better with CPAA than LCRA after radical treatment of rectal cancer. Preservation of a short rectal segment does not offer any clinical advantages. These results are importants to be considered because of the high morbidity currently reported [1] following LCRA.

Reference: Karanjia et al. Br J Surg 1994, 81: 1224–1226. Oncology, specific: Colon, rectum }  
"Which Anastomosis Following Proctectomy and Total Mesorectal Exision TME for Rectal Cancer? Low Colorectal (LCRA) or Colonic Pouch-Anal Anastomoses (CPAA)"

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## OT44 1046 Stool DNA Yield and the Detection of K-ras Mutations in Patients with Colorectal Cancer Using the Amplification Refractory Mutation System

\*N.R. Cruickshank<sup>1</sup>, J.C. Fox<sup>2</sup>, G. Ellison<sup>2</sup>, N.R. Charlesworth<sup>2</sup>, A. Jones<sup>3</sup>, R. Cobb<sup>3</sup>, D. Morton<sup>1</sup>, J.P. Neoptolemos<sup>1</sup>

<sup>1</sup> Dept. of Surgery, Queen Elizabeth Hospital, Birmingham

<sup>2</sup> Cancer Diagnostics Research & Development, Zeneca Diagnostics

<sup>3</sup> Birmingham Heartlands NHS Trust Molecular analysis of stool DNA has the potential of providing a non invasive screening test for colorectal neoplasia. This study evaluates the extraction of human DNA from stool combined with the identification of K-ras mutations using the Amplification Refractory Mutation System (ARMS). 35 consecutive matched stool and tumour samples were analysed. Stool samples were collected on admission to hospital prior to surgery, 2–4 gms of stool being used in each silica based DNA extraction. The human DNA extracted from stool was evaluated by serial dilution and PCR amplification using three common human specific primer sequences; exons 1 of the cystic fibrosis,  $\alpha_1$  antitrypsin and K-ras genes. Tumour DNA and matched stool DNA were then evaluated using ARMS allele specific amplification for 7 common K-ras mutations in codon 12 and 13. Human DNA was isolated in 55/61 stool samples and quantified by serial dilution and PCR amplification (range 1/5 to 1/1000 dilutions). 23 out of 61 tumours were K-ras positive (38%), 21 tumours had sufficient stool DNA recovered to allow analysis with the corresponding mutation identified in 13/21 stool samples (62%) and 12/17 (70%) of left sided lesions. In the K-ras positive stool samples all 8 samples which had a stool DNA quality greater than 1 in 200 had the correct mutation identified, compared to 5/15 in those samples with a stool dilution yield of less than 1 in 100 ( $2p = 0.0047$  – Fisher's exact probability test). These results suggest that DNA yield is essential to successful stool DNA mutational analysis. In the presence of a high DNA yield from stool, this can provide a sensitive and specific test for colorectal cancer, but progress in this novel screening method will be dependant on developing improved extraction techniques. Oncology, general: Screening, prevention Oncology, general: Molecular biology, genetics Oncology, specific: Colon, rectum } "Stool DNA Yield and the Detection of K-ras Mutations in Patients with Colorectal Cancer Using the Amplification Refractory Mutation System"

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## OT44 1047 Is It Possible to Assess the Quality of Rectal Excision for Cancer?

\*M. Pocard, Y. Panis, J. Nemeth, P. Hautefeuille, P. Valleur

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After rectal excision for cancer, the great variability in the reported incidence of local recurrence (from 4 to 35%) suggests that surgery is crucial for the prognosis. To date, no objective criteria have been reported to assess the quality of proctectomy for cancer. *The aim of this work* was to assess, in patients (pts) undergoing curative resection of rectal carcinoma, the impact on survival and local recurrence rates, of the number of lymph nodes (involved or not) founded on the resected specimen. *Patients and Methods:* From 1982 to 1992, 180 pts underwent curative proctectomy (i.e. without synchronous metastase or distal lymph node invasion): 117 pts without lymph node invasion (NO) and 63 pts with proximal nodes invasion (N+). Mean follow up was 55 – 40 months (extr. 0–152). Mean number of lymph nodes on the specimen was 12 – 8 (extr. 0–42). According to the number of nodes (N), we studied the survival and local recurrence (LR) rates at 10 years, and for N+, the mean number of positive nodes (N+). *Results:* NO patients (n = 117) N+ patients (n = 63)

N pts	LR	Survival	N pts	LR	Survival
0–4	27 19%	72%	0–4	6 0%	1.8 60%
5–9	32 19% <sup>(a)</sup>	70%	5–9	19 11%	2 54%
> 10	58 5% <sup>(a)</sup>	77%	> 10	38 34%	4.4 33% <sup>(a)</sup>

(a) p < 0.05; preoperative radiotherapy (29 pts NO and 12 N+) did not influence the results. Only the mean number of lymph nodes was reduced in case of radiotherapy: 7.4 vs 12.3 (NO) and 9.3 vs 13.5 (N+). *Conclusions:* a) in NO patients, local recurrence rate was significantly higher if < 10 nodes were founded. Whatever the cause (insufficient excision or carcinoma with low level of nodes reaction), the high rate of recurrence observed in these cases underline the need of a careful postoperative follow up; b) in N+ patients, a small number of lymph nodes on the specimen could suggest that the risk of nodes invasion is probably low (and that the prognosis is better) rather than an insufficient rectal excision. Oncology, specific: Colon, rectum Oncology, general: Therapy }

"Is It Possible to Assess the Quality of Rectal Excision for Cancer?"

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## OT45 1049 Families with a Strong History of Colorectal Cancer but with Tumours Lacking the Mutator Phenotype

\*J.R. Jass, V. Pokos, J.L. Arnold, D.S. Cottier, P.J. Browett, I.M. Winship, M.R. Lane

University of Auckland, Auckland, New Zealand Clinical and pathological features of families with a strong family history of colorectal cancer but lacking tumours with the mutator phenotype were studied with the aim of distinguishing a new syndrome of hereditary bowel cancer. In eight families fulfilling the Amsterdam criteria for hereditary non-polyposis colorectal cancer (HNPCC), at least two out of two cancers per family showed DNA repair proficiency as indicated by a lack of microsatellite instability at up to six loci. Colonoscopic findings in at-risk family members, together with clinical and pathological features in affected family members were compared with genuine HNPCC families (12). The overall tumour burden in the eight families included 38 colorectal cancers, one ovarian cancer, but no uterine, gastric, pancreatic, small intestinal or upper urinary tract cancers. Despite the fact that at least one family member was aged less than 50 years, the mean age at onset of cancer was 57 years. The majority of cancers developed in the left colon and rectum (80%). Only one subject had multiple colorectal cancer and there was no increased frequency of mucinous (14%) or poorly differentiated (10%) cancer. At-risk family members had more adenomas at colonoscopy than at-risk members of HNPCC families ( $p = 0.095$ ) and a higher adenoma:carcinoma ratio (13:1 versus 7:1). No families showed features of attenuated FAP. The preceding data suggest that there may be hereditary colorectal cancer syndromes (?autosomal dominant) distinct from HNPCC and FAP.

Oncology, specific: Colon, rectum  
Oncology, general: Screening, prevention  
Endoscopy, specific: Colon, rectum } "Families with a Strong History of Colorectal Cancer but with Tumours Lacking the Mutator Phenotype"

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## OT45 1051 Thyroid Carcinoma in Patients with Familial Adenomatous Polyposis in the Netherlands

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Familial adenomatous polyposis (FAP) is known to be associated with several extracolonic cancers. In the literature a 25–160 times higher relative risk of developing thyroid carcinoma (TC) has been reported, especially in women. The aims of the present study were to assess the incidence of TC in the Dutch FAP Registry and to evaluate the value of screening of the thyroid. *Methods:* The registry contains 155 families including 601 patients (339 men and 262 women). The diagnosis of FAP was confirmed by endoscopy, histology, mutation analysis or a medical report. For risk assessment, patients were studied with respect to their risk of developing TC from birth until date of last contact, death, date of diagnosis, or closing date of the study (January 1, 1996). The age-specific relative risk (RR) was defined as the ratio between the observed and expected number of tumours. The expected numbers were calculated by multiplying the person-years by corresponding age-specific incidence rates obtained from the Dutch National Cancer Registry of 1991. *Results:* Screening for TC revealed 5 cases which were all female. The mean age at diagnosis was 36 years (range 16–62). In 3 patients TC appeared to be the presenting symptom. Histology revealed 2 follicular carcinomas and 2 mixed papillar/follicular carcinomas. In one patient histology was not available. The RR of TC in female FAP patients was 32 (95% confidence interval 13–76). At the age of 74 the cumulative incidence in these patients was 17% versus 0.22% in non-FAP women. None of the FAP patients died from TC. *Conclusions:* Female FAP patients are more likely to develop TC especially at relative young age. Moreover, TC may be the presenting symptom of FAP. However, the prognosis remains good. Therefore, as swelling of the thyroid can easily be detected by palpation we recommend periodic physical examination in female FAP patients. Other screening procedures are not appropriate as the prognosis of TC in FAP appears to be good. Oncology, general: Epidemiology Oncology, specific: Colon, rectum Oncology, specific: Endocrine } "Thyroid Carcinoma in Patients with Familial Adenomatous Polyposis in the Netherlands"

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## OT46 1054 Early Diagnosis of Extrahepatic Bile Duct Cancer with Mr Cholangiopancreatography

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<sup>2</sup> Department of Radiology, Juntendo University, Tokyo, Japan *Objectives:* Purpose of this study was to determine the efficacy of MR Cholangiopancreatography (MRCP) in the early diagnosis of extrahepatic bile duct cancer. *Subjects and Methods:* From July 1995 to April 1996, 56052 patients visited our outpatient clinic, and 192 patients suspected of having pancreatobiliary diseases were examined with MRCP. Male to female was 114: 78, with an average age of 53 years. MRCP was performed with a 1.5 T scanner (TOSHIBA VISART). Two dimensional heavily T2 weighed MRCP images were obtained in breath-hold of 3 seconds using Fast Asymmetric Spin Echo Sequence (FASE). *Results:* In 34 patients, MRCP demonstrated extrahepatic bile duct stenosis which was confirmed by ERCP or PTC. Ten patients were eventually diagnosed to have bile duct cancer which was confirmed by surgery (n = 6) or PTCD and cytology (n = 4). Two patients were non-icteric, and one patient had no bile duct dilatation. In one patient tumor was limited to the muscular layer and in 2 patients to the perimuscular connective tissue. A curative resection based on histological findings was possible in 2 patients. *Conclusion:* MRCP is a useful method to diagnose early stage of extrahepatic bile duct cancer. Oncology, specific: Liver, biliary Radiology and ultrasound: Diagnosis } "Early Diagnosis of Extrahepatic Bile Duct Cancer with Mr Cholangiopancreatography"

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## OT46 1055 Combined Modality Therapy (CMT) in the Primary Cholangiocarcinoma of the Confluence: Czech Experience in 219 Patients

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1st Medical Department, Charles University, Prague, Czech Republic Primary cholangiocarcinoma of the confluence (hilar cancer, HC) is the most common biliary tree malignancy in Central and Eastern Europe in the elderly. If untreated, its prognosis remains dismal, with the median survival 98.7 days. *Aims:* This study was performed to assess the feasibility of CMT in HC palliation. *Patients:* Since Jan 1990 to Jan 1996, 219 consecutive jaundiced pts with HC (121 males, 98 females, mean age 58.7 years) were entered into the prospective study. In all pts, nonsurgical stenting of the CBD was performed, followed by regional chemotherapy (RCHT) in 63 cases or by intraluminal radiotherapy (ILRT) in 36 pts. *Results:* Median survival in pts, treated by stenting alone, was 236 days. In those, treated by stents and RCHT or ILRT, median survival reached 594 days. In pts, treated by stents, RCHT and ILRT in combination, median survival was 711 days. We were not able to demonstrate any weighty side effects, either local or systemic. Early and/or late complications of stenting did not exceed 2.1%. *Conclusions:* On the basis of the results mentioned is possible to conclude, that CMT in preoperative HC palliation is the method of choice, nowadays. *Supported by grant 2227 of IGA MH CR Oncology, specific: Liver, biliary Oncology, general: Therapy }* "Combined Modality Therapy (CMT) in the Primary Cholangiocarcinoma of the Confluence: Czech Experience in 219 Patients"

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## OT47 1056 Inhibition of Cholera Toxin-Induced Secretion by Substance P Antagonist

\*J.L. Turvill, M.J.G. Farthing

DDRC, St Bartholomew's & The Royal London School of Medicine, UK *Introduction.* Substance P (SP) is known to evoke neuronally mediated small intestinal fluid secretion accompanied by the release of vasoactive intestinal polypeptide (VIP). 5-hydroxytryptamine (5-HT) release, the activation of the enteric nervous system and VIP release are all implicated in cholera toxin (CT)-induced secretion. Since 5-HT receptors are located on sensory SP neurons we tested the hypothesis that SP antagonists would prevent CT-induced secretion. *Methods.* Anaesthetised male Wistar rats (180–220 g) were pretreated with: either (i) SP antagonist D Pro<sup>2</sup> D Trp<sup>7,9</sup> SP (PTT SP) 0.1, 0.3, 1.0 or 3.0 mg/kg ip; (ii) NK-1 antagonist (sendide) 0.1, 0.3, 1.0 or 3.0 mg/kg ip; (iii) NK-2 antagonist (GR83074) 1.0 mg/kg ip; or (iv) saline ip. 25 µg CT in 2 ml saline was instilled into 25 cm segments of small intestine isolated between cannulae. After 2 h incubation, *in situ* perfusion was performed with plasma electrolyte solution (Na 140, K 4, Cl 104, HCO<sub>3</sub> 40 mM) containing [<sup>14</sup>C]-polyethylene glycol as a non-absorbable marker. 3 × 10 min collections were made after 30 min equilibration and net fluid (µl/min/g dw) and electrolyte movements were determined. *Results.* Net fluid movement (med { } 102 (IQR { } 75 to { } 147) n = 14) was reduced by 0.3 mg/kg ( { } 38 ( { } 14 to { } 67) n = 6), 1.0 mg/kg ( { } 76.5 ( { } 40 to { } 83) n = 7) and 3.0 mg/kg PTT SP ( { } 10.4 ( { } 4 to { } 42.5) n = 7); p = 0.0011 (Kruskal Wallis) but not by 0.1 mg/kg ( { } 135 ( { } 133 to { } 141.7) n = 5). The NK-1 antagonist also inhibited secretion at doses of 0.1 mg/kg ( { } 24.8 ( { } 16.1 to { } 39.7) n = 6), 0.3 mg/kg ( { } 49.4 ( { } 27.5 to { } 57.5) n = 8) and 1.0 mg/kg ( { } 29.4 ( { } 2.4 to { } 81.5) n = 8); p = 0.0017, as did the NK-2 antagonist ( { } 38 ( { } 13 to { } 39) n = 4); p = 0.0046 (Mann Whitney). Electrolytes parallel fluid movements. *Summary.* The SP antagonist PTT SP significantly inhibits CT-induced secretion. Antagonism of NK-1, which is SP's preferred receptor, similarly inhibits secretion. In addition, the NK-2 receptor is involved in the mediation of CT-induced secretion. Intestinal disorders, absorption: Pathophysiology of diarrhea } "  
"Inhibition of Cholera Toxin-Induced Secretion by Substance P Antagonist"

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**OT47 1057 Expression of the VIP 1 Receptor during Enterocytic Differentiation of Human Colon Cancer Cells (Caco-2): Regulation at the mRNA Level. Couvineau, J.J. Maoret, I. Carrero, C. Rouyer-Fessard, M. Laburthe**

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The human colon adenocarcinoma cell line Caco-2 in culture spontaneously differentiates into enterocytes and expresses the VIP 1 receptor. In Caco-2 cells, a dramatic increase of VIP 1 receptor concentration has been observed when cells undergo differentiation (Laburthe et al., 1987, *J. Biol. Chem.*, 262: 10180–10184). Scatchard analysis of <sup>125</sup>I-VIP binding to Caco-2 cell membranes revealed an increase of VIP receptor concentration from undifferentiated cells at day 5 culture (15 fmol/mg of protein; K<sub>d</sub> = 0.2 nM) to differentiated cells at day 28 of culture (128 fmol/mg of protein; K<sub>d</sub> = 0.07 nM). We report here the study of VIP 1 receptor mRNA expression during enterocytic differentiation of Caco-2 cells. Analysis of VIP 1 receptor mRNA expression by 1) RNase protection assay revealed the presence of a high level of mRNA in differentiated cells (Day 25) and a very low level of mRNA in undifferentiated cells (Day 5). In contrast, β actin mRNA level was the same in both conditions; 2) RT-PCR detection of mRNA followed by southern blot using a VIP 1 receptor cDNA probe also revealed a much higher amount of VIP 1 receptor mRNA in Caco-2 cells at day 25 than at day 5. These results strongly suggested that the expression of VIP 1 receptor during enterocytic differentiation of Caco-2 cells was regulated at the mRNA level. In order to determine the half-life and transcription rate of VIP 1 receptor mRNA, the following experiment were performed: 1) cells were treated at different time with actinomycin D (a specific inhibitor of RNA polymerase II) and VIP 1 receptor mRNA was detected by RNase protection assay. The half-life of VIP 1 receptor mRNA was 10 hours in the two conditions of culture (day 5 and day 25); 2) runoff transcription was performed on isolated nuclei from differentiated and undifferentiated Caco-2 cells, showing that VIP 1 receptor mRNA were transcribed at 5-fold higher rate in differentiated cells than in undifferentiated cells. It is concluded that the expression of the VIP 1 receptor during enterocytic differentiation of Caco-2 cells is regulated at the transcriptional level.

Hormones and receptors: Receptor characterization  
Hormones and receptors: Molecular biology  
Oncology, specific: Colon, rectum  
} "Expression of the VIP 1 Receptor during Enterocytic Differentiation of Human Colon Cancer Cells (Caco-2): Regulation at the mRNA Level"

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## OT47 1058 Functional Characterisation of Neurokinin Receptors Mediating Ion Transport in Porcine Jejunum

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Substance P (SP) and neurokinin A (NKA) are the major tachykinin neurotransmitters in the porcine small intestine. Tachykinins seem to be involved in the secretory actions of *Clostridium difficile* toxin A, and in inflammatory bowel disease, in which alterations in ion transport constitute part of the pathophysiology. Thus, tachykinin receptor antagonists might have a therapeutic potential. The aim of the present study was to characterise neurokinin (NK) receptors, involved in ion transport, in porcine jejunum, as this tissue exhibits functional similarity to human upper small intestine. **Methods:** Stripped porcine jejunal tissue preparations with intact mucosa and submucosa were mounted in Ussing chambers containing Ringer-solution. The tissue was short-circuited and corresponding values of electrical parameters (resistance and open circuit potential difference) were measured and calculated by computer. Compounds were added to the serosal side. **Results:** SP produced a concentration dependent increase in short-circuit current (SCC), the curve having a double sigmoidal form. The NK-1 antagonist CP 99,994 totally abolished the first sigmoidal response, indicating the presence of an NK-1 receptor. This was further supported by a concentration-dependent response of the NK-1 agonist [Sar<sup>9</sup> Met(O<sub>2</sub>)<sup>11</sup>]-SP (Sar<sup>9</sup> SP) with an EC<sub>50</sub> value of 235.0 nM – 53.9. Increasing concentrations of CP 99,994 (0.1 μM, 0.3 μM and 1 μM) produced a parallel dextral shift of the Sar<sup>9</sup> SP curve with a slope of the Schild regression (1.59) different from unity. Another NK-1 antagonist, RP 67,580, and the inactive enantiomer of CP 99,994, CP 100,263, did not change the response to SP. The NKA concentration response curve (EC<sub>50</sub> value of 68.87 nM – 16.23) was not significantly changed by the NK-2 antagonists, SR 48,968 or GR 94,800. However, CP 99,994 totally inhibited NKA responses at 0.5 μM and higher concentrations. The NK-2 agonist, [D-Ala<sup>8</sup>]NKA<sub>4-10</sub>, caused only in μM concentrations an increase in SCC, whereas the NK-3 agonist, senktide, did not elicit a response. **Conclusion:** SP and NKA mediate ion transport in porcine jejunum through NK-1 receptors. Tachykinins might also activate a new unclassified receptor. However, this needs to be further substantiated and clarified using structural studies. Species dependent heterogeneity of NK-1 receptors might explain the lack of effect of RP 67,580. Intestinal disorders, absorption: Epithelial transport

Hormones and receptors: Receptor characterization } "Functional Characterisation of Neurokinin Receptors Mediating Ion Transport in Porcine Jejunum"

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## OT47 1059 Effect of Continuous Jejunal Application of Soluble Fiber on Cholecystokinin and Neurotensin Release in Men

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<sup>3</sup> Sandoz Nutrition, Bern, Switzerland We have shown, that a liquid diet with soluble guar fiber (Sunfiber [SF]) given as bolus for 7 days increase fasting cholecystokinin (CCK) concentrations (JPEN, 1993, 231–235). Whether a continuous jejunal application of the same diet also affects CCK secretion is not well defined. The aim of this study was therefore to assess the effect of continuous feeding on plasma CCK and neurotensin (NT) release. *Methods:* 23 patients after upper gastrointestinal surgery received continuously a liquid diet by jejunostomy over 16 days. 9 standard liquid diet (SLD), 14 the same diet with 20 g SF/L (SFD). At day 16 basal and postprandial (after perfusion of 500 ml diet) CCK and NT concentrations were assessed. Blood was drawn at regular intervals and CCK and NT concentrations were measured by specific radioimmunoassays (Pancreas, 1991, 260–265). *Results:* Data are in pg/ml (mean – SEM). N Basal 30 min 50 min 70 min 90 min 1) CCK SFD 14 0.35 – 0.1 3.1 – 1.3 4.0 – 2.1 4.0 – 2.2 2.6 – 1.0 SLD 9 1.3 – 0.4 4.6 – 1.6 4.4 – 1.6 4.3 – 1.6 4.6 – 1.5 2) NTS SFD 14 9.0 – 2.0 78 – 15 102 – 24 104 – 19 88 – 17 SLD 9 6.4 – 1.3 71 – 33 99 – 28 101 – 34 106 – 43 No difference was seen for basal and postprandial concentrations between the two diets. Furthermore the area under the curve were not significantly different. *Summary:* After 16 days continuous feeding basal CCK and NT levels were similar for both diets and comparable to healthy volunteers. Furthermore the postprandial response was similar for both diets. *Conclusion:* In contrast to orally bolus feeding regimens continuous feeding of a SF containing liquid diet does not change basal CCK and NT concentrations. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Nutrition: Nutrients and gut function Hormones and receptors: Clinical disorders } "Effect of Continuous Jejunal Application of Soluble Fiber on Cholecystokinin and Neurotensin Release in Men"

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## OT50 1061 Association of Serum Antibodies Against P53 Protein with Poor Survival in Zollinger-Ellison Syndrome Patients

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Villejuif *Background/Aims:* Long-term survival of patients with Zollinger-Ellison syndrome is largely determined by the presence or the absence of liver metastases. However, because of the lack of precision of this criteria, the development of further indicators is still required. The recent evidence that auto-antibodies directed against the p53 protein could predict a poor survival for some types of cancers, has prompted us to investigate the presence of such antibodies in sera from Zollinger-Ellison syndrome patients and their potential value as survival indicator.

*Methods:* The detection of anti-p53 antibodies was carried out in sera from 44 consecutive Zollinger-Ellison syndrome patients using both an ELISA assay and Western-blotting. The mean follow-up of these patients was 92 months. *Results:* Anti-p53 antibodies were detected in 7 out of the 44 Zollinger-Ellison syndrome patients (16%) both by ELISA and by Western-blotting. Univariate and multivariate analysis demonstrated that the presence of anti-p53 antibodies ( $P = 0.0009$  and  $P = 0.017$  respectively) and liver metastases ( $P = 0.0009$  and  $P = 0.012$  respectively) were independently associated with a shorter survival. *Conclusions:* Our results suggest that anti-p53 antibodies are an indicator of survival and could be used in combination with staging for determining poor prognosis Zollinger-Ellison syndrome patients requiring reinforced therapy. Oncology, specific: Pancreas Oncology, general: Molecular biology, genetics } "Association of Serum Antibodies Against P53 Protein with Poor Survival in Zollinger-Ellison Syndrome Patients"

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## OT50 1062 Follow-Up Program after Curative Resection of Colorectal Carcinoma

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Portugal  
*Background:* After curative surgery for colorectal carcinoma, intensive follow-up has been implemented in many Centers. Its primary goal is the detection of recurrence in the asymptomatic stage hoping to increase the possibility of new curative resection and to prolong survival. The type and the effectiveness of such follow-up programs has been controversial.

*Aims:* To evaluate the sensitivity of diagnostic methods and the efficacy of a follow-up program on recurrence detection, treatment and survival after curative resection of colorectal carcinoma.

*Material and Methods:* Between 1989 and 1993, 218 patients were submitted to curative colorectal resection and underwent regular examinations according to a defined schedule which included: clinical examination, tumoral markers (TM) – CEA and CA19-9, liver function tests (LFT), chest roentgenography and abdominal ultrasonography (US) every four months during the first two years and half-year until the fifth. All patients were submitted to annual colonoscopy to detect metachronous tumors or anastomotic recurrences. Those with rectal cancer also

performed computerized tomography (CT) at the fourth postoperative month for basal determination. *Results:* Tumor recurred in 54 patients (25%), with 61% of them having tumor associated symptoms. The sensitivity of the diagnostic methods was: TM-85%; CT-91%; US-75%; LFT-40%. A second resection with curative intent was performed in 13 patients (24%): anastomotic-40%; hepatic metastases-29%. The five year survival rate after colorectal resection was 70% and survival was prolonged after curative resection of tumor recurrence ( $p = 0.038$ ) but was not different between symptomatic and asymptomatic recurrences. *Conclusions:* The TM seems to be the best test for recurrence detection because of its low cost and high sensitivity.

Despite the elevated number of asymptomatic recurrences detected, this did not lead to more effective treatment, neither did it prolong survival. Further controlled prospective studies are needed to confirm the efficacy of follow-up programs. Oncology, specific: Colon, rectum  
Clinical practice: Management strategy } "Follow-Up Program after Curative Resection of Colorectal Carcinoma"

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## OT50 1063 Germline Mutations of Mismatch Repair Genes (MMR) in Early Onset Colonrectal Cancer Patients

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<sup>6</sup> Cattedra di Genetica Medica, Universit'e0 di Bari, Bari

<sup>4</sup> IRCCS Castellana, Bari Hereditary non polyposis colorectal cancer (HNPCC), is an autosomal dominant disorder that account for 4–13% of all cases of colorectal carcinomas. It is characterized by early age of occurrence, prevalence of proximal localization, higher risk of multiple tumors (synchronous and metachronous). For HNPCC diagnosis the so called "Amsterdam criteria" must be fulfilled. Frequently families or individuals are observed which do not meet the rigorous Amsterdam criteria, but are highly suggestive as having HNPCC (HNPCC like syndrome). HNPCC is due to defects in genes coding for mismatch repair system (MMR): hMSH2, hMLH1, hPMS1, hPMS2. The aim of our study is to define the clinical features and the mutational status at MMR genes, of young cancer patients with colorectal tumor not fulfilling Amsterdam criteria or without a family history indicative for HNPCC. Blood and paraffin embedded tumor tissue have been collected from 33 individuals who developed the disease before 40 years of age. Mutational analysis was carried out by a non radioactive single strand conformation polymorphism (SSCP) made more sensitive by a acrylamide gradient, followed by direct DNA sequencing where a aberrant migration pattern was observed. Preliminary and partial analysis demonstrates the presence of four mutations in hMSH2 (exons 5, 16, 14) and two mutations in hMLH1 (exons 5, 16) in individuals under 40 years of age. Our result indicate that mutations at MMR genes can be responsible of colorectal cancer in young patients even in situations not fulfilling Amsterdam criteria, and suggest the necessity of establishing new criteria for identifying individuals to be tested for mutations at MMR genes. Oncology, general: Molecular biology, genetics Oncology, specific: Colon, rectum Oncology, general: Screening, prevention } "Germline Mutations of Mismatch Repair Genes (MMR) in Early Onset Colonrectal Cancer Patients"

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OT50 1064 **K-Ras-2 Gene Mutations in Colorectal Adenomas and the Risk of Metachronous Adenomas** G. Nusko, R. Sachse, U. Mansmann, Ch. Wittekind, E.G. Hahn

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Mutations of K-ras-2 gene and tumor suppressor genes have been found in colorectal adenomas and carcinomas. The aim of this study was to investigate the prognostic value of K-ras-2 gene mutations found in initial colorectal adenomas predicting the risk of metachronous adenomas.

*Material and Methods:* Genomic DNA was extracted from the formalin fixed and paraffin embedded adenomas larger than 5 mm in diameter removed during 1980 and 1986 at the initial total colonoscopy. All patients had a colonoscopic follow-up for at least six years. The sequence of the exon 1 of the K-ras-2 oncogene was amplified using PCR and screened for mutation by single strand conformation polymorphism (SSCP). All suspected mutations were confirmed by direct sequencing. The predictive value was assessed by logistic regression analysis.

*Results:* Out of 54 patients 39 (72%) were male and 15 (28%) female. At the time, where the initial adenoma was removed, 31 (57%) patients were younger than 60 and 23 (43%) were equal to or older than 60 years. Point mutations of the K-ras-2 oncogene were found in the index adenoma of 15 (27.7%) patients. Mutations were found more frequently in large (> 20 mm) adenomas and in adenomas with severe dysplasia ( $p = 0.0011$  and  $p = 0.0310$ , respectively). There were no significant associations between anatomical location, histological type or number of synchronous initial lesions and K-ras-2 mutations. Mutations were found predominantly at codon 12 with transversions from GGT to GAT (36%), from GGT to GTT (57%) and from GGT to TTT in one patient. The one mutation found at codon 13 showed a transversion from GGC to GAC. There were significant associations of size (> 20 mm) and K-ras-2 mutation of the initial adenomas and the size (> 5 mm) of metachronous adenomas ( $p = 0.0259$  and  $p = 0.0265$ , respectively). But multivariate analysis revealed that K-ras-2 did not provide a significant additional contribution to the prognostic value of the size (odds ratio 7.62; 95% CI: 1.68–34.48) and the amount of villous structure (odds ratio 0.22; 95% CI: 0.0–0.90) of the initial adenoma.

*Conclusions:* Patients with large (> 20 mm) adenomas and adenomas harbouring K-ras-2 mutations at the initial examination are of a significant higher risk for developing large (> 5 mm) metachronous adenomas during surveillance. But the risk of metachronous colorectal adenomas can be estimated sufficiently by the size and the histological type of the largest initial adenoma.

Oncology, specific: Colon, rectum  
Oncology, general: Molecular biology, genetics }

"K-Ras-2 Gene Mutations in Colorectal Adenomas and the Risk of Metachronous Adenomas"

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## OT51 1065 Antibiotic Prophylaxis (AbP) for the Prevention of Bacterial Infections in Cirrhotic Patients with Gastrointestinal Bleeding (GB): A Meta-Analysis

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In cirrhotic patients with GB, the AbP decreases the incidence of infections but no randomized controlled trial (RCT) showed an increase in survival. *Aim of the meta-analysis:* to assess the efficacy of AbP for the prevention of bacterial infections and the effect of AbP on survival rate in cirrhotic patients with GB. *Methods:* An overview of RCTs assessing the efficacy of an AbP for the prevention of infection in cirrhotic patients with GB. RCTs including patients without bleeding or comparing 2 antibiotics were excluded. Meta-analysis used Peto and Der Simonian methods. *Results:* Four RCTs including 414 patients, 204 treated with an AbP and 210 without AbP were identified. The AbP used oral, non absorbable antibiotics during 4 days (n = 68), or norfloxacin during 7 days (n = 60), or the association of amoxicillin-clavulanic acid and ciprofloxacin during 4 days (n = 30), or ofloxacin for 10 days with an IV bolus of amoxicillin-clavulanic acid before each endoscopy (n = 46). The end point of each RCT was the prevention of bacterial infection during 10 to 14 days. The mean percentage of patients free of bacterial infection was 85% in patients treated with an AbP vs 55% in non treated patients. This difference was significant (mean rate difference: 32%, 95% confidence interval (CI): 19–44, p < 0.001), without significant heterogeneity. The mean percentage of patients free of bacteremia and/or spontaneous bacterial peritonitis (3 RCTs) was 91% in treated patients vs 74% in non treated patients. This difference was significant (mean rate difference: 15%, 95% CI: 8–22, p < 0.001), without heterogeneity. The mean percentage of patients free of infection caused by enteric bacteria (2 RCTs) was 95% in treated patients vs 75% in non treated patients, this difference was significant (mean rate difference: 19%, 95% CI: 10–28, p < 0.001). The mean survival rate was 87% in patients treated with an AbP vs 77% in non treated patients. This difference was significant (mean rate difference: 9.2%, 95% CI: 2.4–16.0, p < 0.008), without heterogeneity. Sensitivity analysis without the RCT using non absorbable antibiotics showed similar results, but the difference concerning survival rate was not significant (mean rate difference: 7.4%, 95% CI 0–16, p = 0.07). *Conclusions:* In cirrhotic patients with GB, the AbP significantly decreases the incidence of bacterial infection and significantly increases short term survival rate. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: GI bleeding } "Antibiotic Prophylaxis (AbP) for the Prevention of Bacterial Infections in Cirrhotic Patients with Gastrointestinal Bleeding (GB): A Meta-Analysis"

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**OT51 1068 Evaluation of Portal Hypertension and Haemodynamic Risk Factors for Variceal Bleeding by Color Doppler Sheir S. Baddar,**

\*M. Osman, S. Shalaby, M.M. Hendi

Internal Medicine Department, Ain Shams University, Cairo, Egypt Seventy patients were included in this work. Ten normal control subjects, thirty patients with evidence of portal hypertension with no history of bleeding from oesophageal varices, and thirty patients with evidence of portal hypertension with history of oesophageal variceal bleeding. Real time US, Color Doppler examination and upper endoscopy were done for all the subjects. Color Doppler U.S. was found to be more sensitive and specific than real-time U.S. in diagnosing portal hypertension regarding increase in congestion index (CI), better visualization of collaterals and more accurate diagnosis of P.V. thrombosis. CI more than 0.09 cmXsec was 100% specific and 100% sensitive in diagnosing portal hypertension, compared to 100% specificity and 93% sensitivity considering portal vein flow velocity < 12 cm/sec, 100% specificity and 85% sensitivity considering portal vein diameter > 13 mm, and 100% specificity and 88% sensitivity considering the visualization of collaterals. P.V. thrombosis was better detected by Color Doppler as 40% of the thrombosed PV were missed using real time U.S. Color Doppler allowed better visualisation of the collaterals as 70% only of the visualised cases could be detected using real time U.S. Study of the collateral haemodynamics revealed that the most reliable protector against bleeding varices was the presence of adequate splenorenal shunt with partial flow reversal in the splenic vein and incomplete flow reversal in the left gastric vein. Recanalization of para-umbilical vein was not directly related to the presence of varices, yet the larger the diameter and the more the flow the less will be the risk of bleeding. The risk factors bleeding varices were: 1) PV "CI" more than 0.12 cmXsec. 2) Absence of adequate collaterals specially splenorenal shunt. 3) PV thrombosis. 4) Complete flow reversal in left gastric vein. }

"Evaluation of Portal Hypertension and Haemodynamic Risk Factors for Variceal Bleeding by Color Doppler"

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## OT53 1070A Population Based Study on the Familial Aggregation of Inflammatory Bowel Disease

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*Introduction:* Recent studies have shown variable degrees of familial aggregation in inflammatory bowel disease (IBD). In our study the prevalence of Crohn's disease (CD) and ulcerative colitis (UC) in first degree relatives of IBD patients, living in a well-defined area, was studied. *Methods:* All known prevalent IBD patients living in the study area (148.250 inhabitants) were asked about the occurrence of IBD in their first degree relatives. In case of a positive family history, medical information was requested to verify the diagnosis. A control group of 616 persons without IBD was recruited in co-operation with the Registration Network family Practice. *Results:* The family pedigrees of 245 patients consisted of 1571 first degree family members. Sufficient information was available of 1554 cases: 485 parents, 756 siblings, and 313 children. IBD was reported and confirmed in 16 first degree relatives by 11 (4.5%) patients: 7 (5.3%) of the 132 patients with CD and 4 (3.5%) of the 113 patients with UC. Prevalence of IBD was highest for siblings (1.5%) and children (1.3%) while only 0.2% of the parents were affected with IBD. Affected family members of the index patients showed a 88% disease concordance concerning either CD or UC. Among first degree relatives of the control subjects, IBD was observed in 0.8% (vs. 4.5% in IBD patients), resulting in an odds ratio of 5.7 (95% C.I. 2.0–16.7). *Conclusion:* In this population based study, the observed risk of IBD for first degree relatives of IBD patients was higher than in controls. However, the prevalence in our population is lower than has been reported by other centres, possibly reflecting the population based character of our study. Intestinal disorders: IBD, etiology and genetics } "A Population Based Study on the Familial Aggregation of Inflammatory Bowel Disease"

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## OT53 1071 **Inflammatory Bowel Disease in a Danish Twin Register**

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Institute of Preventive Medicine, Copenhagen University Hospital, Genetic Epidemiology Research Unit, Institute of Community Health, University of Odense, Denmark

Previous population studies have shown a 10 fold increased risk of inflammatory bowel disease (IBD) among first degree relatives of patients with ulcerative colitis and Crohn's disease. To further investigate the heridity of these diseases a twin study was performed. A questionnaire was sent to all 34,076 twins included in a new twin register, which comprises all twins born in Denmark 1953 through 1982 (34,188), who had been identified and who had accepted to participate in studies. If a twin stated to suffer from IBD, the diagnosis was confirmed or excluded by applying the classical criteria to medical records from hospitals or private physicians. A total of 29,430 (86%) twins answered the questionnaire. Among these, 93 twin pairs with at least one suffering from IBD were observed (Crohn's disease: 36, ulcerative colitis: 57). In the Crohn's disease group three of 11 monozygotic pairs were concordant for the disease, while none of the 25 dizygotic pairs were concordant. In the ulcerative colitis group one of 15 monozygotic pairs and one of 42 dizygotic pairs were concordant for the disease. The proband concordance rate among monozygotic pairs was 38.5% for Crohn's disease and 6.7% for ulcerative colitis. The frequency of IBD in the twin register was 1.5 time the expected as estimated from the age-specific rates in the background population. The frequency of IBD among twins of patients with IBD was 36 times the expected. In conclusion, this study further strengthens the hypothesis of a genetic predisposition for development of IBD, a predisposition which may be stronger for Crohn's disease than for ulcerative colitis.

Intestinal disorders: IBD, etiology and genetics  
Clinical practice: Epidemiology (non cancer) } "Inflammatory Bowel Disease in a Danish Twin Register"

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## OT53 1072 Signal Transduction Role of Nuclear Factor (NF)-Kappa B in the Regulation of Pro-Inflammatory Cytokine Secretion by IL-10 in IBD Granulocytes

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<sup>1</sup> Tularik, San Francisco, USA *Background:* Pro-inflammatory cytokines (IL-1{ b}, TNF-{ a}, IL-8, IL-1ra) are secreted in large amounts by IBD monocytes, macrophages and granulocytes (PMN, abstract 5<sup>th</sup> UEGW). IL-10 is a major inhibitor of pro-inflammatory cytokine secretion. NF-Kappa B is thought to be a major player in pro-inflammatory signal transduction. The *Aim* of this study was to evaluate mechanisms by which pro-inflammatory cytokine secretion by PMN can be regulated. *Methods:* PMN from 25 patients with ulcerative colitis (UC), 21 patients with Crohn's disease (CD) and 15 normal volunteer controls (NC) were obtained from peripheral blood by dextran sedimentation and density centrifugation. Release of pro-inflammatory cytokines (ELISA) into culture supernatants as well as mRNA (semiquantitative RT-PCR) were assessed. Formation of activated NF-Kappa B was assessed by gel shift or western Blot, respectively, from nuclear and cytosolic extracts. *Results:* In IBD patients enhanced secretion of pro-inflammatory cytokines by PMN coincides with detection of activated NF-Kappa B in nuclear extracts, which is absent in NC PMN. During in vivo (IBD) as well as in vitro activation of normal cells (i.e. by TNF, PMA or LPS) NF-Kappa B p65 is activated and translocated from cytosol to nucleus (Western Blot). In vitro treatment with IL-10 reverts those changes: NF-Kappa B is shifted back from nucleus to cytosol and can no longer be detected by gel shift in nuclear extracts. *Conclusions:* Activation and nuclear translocation of NF-Kappa B may provide a signal transduction mechanism by which IBD PMN are induced to secrete enhanced levels of pro-inflammatory cytokines. Moreover, IL-10 appears to induce deactivation of NF-Kappa B and evasion of the factor from the nucleus back to cytosolic compartment. This mechanism provides insights into signal transduction events influenced by IL-10 and may also suggest novel targets for future immunomodulatory strategies. Supported by DFG SCHR 2-1. *Graphic missing*  
Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, therapy } "Signal Transduction Role of Nuclear Factor (NF)-Kappa B in the Regulation of Pro-Inflammatory Cytokine Secretion by IL-10 in IBD Granulocytes"

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## OT53 1073 **No Exceeding Malignancy Prevalence in Relatives of IBD Patients: Comparison with Colon-Cancer Patients and Controls**

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The relation between Inflammatory Bowel Diseases (IBD) and colon-cancer (CC) is not clearly defined. The colon cancer is considered to be more frequent in longstanding extensive ulcerative colitis (UC) and in Crohn disease of colon (CD). However, some investigators suggest that extensive colitis patients have a genetic predisposition to colorectal cancer and longstanding inflammation is not of primary importance in the promotion of cancer in UC. We report a prospective investigation on malignancy prevalence in relatives of an initial series of 225 IBD patients (178 UC; 47 CD), as well as 491 colon cancer pts. (CC) and 220 orthopedic pts. (ORT) as controls. In all patients (UC, CD, CC) as well as in controls (ORT) the prevalence of colon (A), extracolonic digestive (B) and extradigestive (C) malignant tumours in the first degree relatives has been evaluated. Results are shown in table.

number of relatives	A	B	C
UC	1194	5 (0.42%)	10 (0.84%)
CD	271	0 (0.00%)	3 (1.11%)
CC	3484	60 (1.72%)	25 (0.72%)
ORT	1489	6 (0.40%)	10 (0.67%)

36 (2.42%)  
In this initial series no difference in malignancy prevalence or tumours spectrum among UC, CD and ORT patients was observed. The relative risk of colon cancer in relatives of CC patients versus ORT was 4.3. Partially supported by grant of 60% MURST  
Intestinal disorders: IBD, etiology and genetics  
Oncology, specific: Colon, rectum  
Oncology, general: Epidemiology }  
"No Exceeding Malignancy Prevalence in Relatives of IBD Patients: Comparison with Colon-Cancer Patients and Controls"

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## OT54 1074 **Anti-Tumor Necrosis Factor Antibody cA2 Treatment Induces Clinical Remissions in Patients with Active Crohn's Disease**

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<sup>6</sup> Centocor Inc, Malvern, USA TNF has been implicated in the pathogenesis of Crohn's disease (CD), and preliminary studies have suggested that administration of anti-TNF antibodies causes rapid clinical responses in patients with steroid-refractory CD. The present study is a double blind placebo-controlled trial in patients with active CD designed to assess the magnitude and duration of response to cA2 treatment. One hundred and eight patients with a CDAI between 220–400 were randomized to receive either placebo, 5 mg/kg, 10 mg/kg, 20 mg/kg or 20 mg/kg of cA2 as a single 2 hour intravenous infusion. Patients receiving concomitant therapy with corticosteroids, 6-mercaptopurine, or 5-ASA continued treatment throughout the 12 week trial. Patients in the different treatment groups were well matched for demographic and disease-related baseline characteristics. cA2 treatment resulted in a significantly larger reduction of the CDAI at 4 weeks ( $\{-\}$  110.4 – 102.6) than placebo ( $\{-\}$  12.8 – 79.3) ( $p < 0.001$ ) and these differences were sustained throughout the study period. The number of patients achieving a clinical remission (CDAI < 150) was 16% in the placebo group versus 45.8% in cA2 treated patients ( $p = 0.022$ ), and the number of patients responding to cA2 therapy (reduction of CDAI > 70) was 24% versus 69.9% respectively ( $p < 0.001$ ). cA2-treated patients had a significant reduction in CRP levels, and an increase in the IBDQ scores. These data indicate that anti-TNF therapy has a high clinical efficacy in patients with CD, including those not responding to standard therapy. }" "Anti-Tumor Necrosis Factor Antibody cA2 Treatment Induces Clinical Remissions in Patients with Active Crohn's Disease"

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## OT54 1075 Ciprofloxacin Vs Mesalazine in the Treatment of Active Crohn's Disease

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*France***Background:** Evidence is accumulating for bacterial participation in the pathogenesis of (CD). Despite this, few controlled trials using broad-spectrum antibiotics have been conducted in CD. Ciprofloxacin (Cipro) has shown promising results in the treatment of CD with perineal disease and fistulae. The aim of this randomized controlled study was to investigate the efficacy of Cipro compared with 5-aminosalicylate (Pentasa<sup>R</sup>) in treating moderately active CD.**Methods:** Forty patients (25 F, 15 M, mean age 28 years) with moderate flare-up of CD (mean CDAI: 217, range 160–305) were randomized to receive Cipro 500 mg twice daily or Pentasa<sup>R</sup> 4 g/day for 6 weeks. Clinical remission was defined as a CDAI  $\leq$  150 associated with a decrease in CDAI ( $\Delta$  CDAI)  $>$  75 at 6 weeks. Partial remission was defined as: 1) a CDAI  $\leq$  150 with a  $50 < \Delta$  CDAI  $<$  75; 2) a CDAI  $>$  150 with a  $\Delta$  CDAI  $>$  50 at 6 weeks.**Results:** Clinical remission was obtained in 10/18 Cipro patients (56%), and in 12/22 Pentasa<sup>R</sup> patients (55%). Partial remission was obtained in 13/18 Cipro patients (72%), and 13/22 Pentasa<sup>R</sup> patients (59%)(ns). C-reactive protein decreased from 32 – 29 to 9 – 5 ( $p = 0.027$ ) in Cipro patients and from 33 – 22 to 21 – 16 in Pentasa<sup>R</sup> patients (ns). Three patients on Cipro (17%) and 7 on Pentasa<sup>R</sup> (32%) were considered as treatment failure because of deterioration or insufficient improvement (ns). Two patients receiving Cipro (11%) were withdrawn from the study for minimal side effects and absence of compliance. Two patients on Pentasa<sup>R</sup> (9%) were withdrawn because of the absence of improvement at 3 weeks.**Conclusion:** This study suggests that Cipro 1 g/day is at least as effective as Pentasa<sup>R</sup> 4 g/day in treating moderately active CD. Intestinal disorders: IBD, therapy } "Ciprofloxacin Vs Mesalazine in the Treatment of Active Crohn's Disease"

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## OT54 1076 **Balsalazide is More Effective and Better Tolerated than Mesalazine in Acute Ulcerative Colitis (UC)**

\*J.R.B. Green, C.D. Holdsworth, A.J. Lobo, R. Leicester, J.A. Gibson, G.D. Kerr, H. Hodgson, K.J. Parkins, M.D. Taylor, P.D.I. Richardson, ABACUS Investigator group

Gastroenterology units in Stoke, Sheffield, London, Stafford, Shrewsbury and Astra Pharmaceuticals Ltd., Kings Langley, U.K. This study compared the tolerability and efficacy of balsalazide (mesalazine prodrug) and mesalazine (pH-dependent delayed release) in acute UC. Patients (101 total, 99 evaluable) (62 male) aged 41 – 13 years (mean – SD) with grade 2 (erythema + loss of vascular pattern + contact bleeding: 55% of patients), 3 (+spontaneous bleeding: 32% of patients) or 4 (+frank ulceration: 13% of patients) (extent > 12 cm; left-sided disease 80%) sigmoidoscopically verified, symptomatic (moderate 69% or severe 31%) UC were randomised, double blind, to receive balsalazide 2.25 g t.i.d. (equivalent to 0.78 g mesalazine) (n = 50) or mesalazine 0.8 g t.i.d. (n = 49) for 4, 8 or 12 weeks, as necessary. Rectal hydrocortisone p.r.n. was provided as relief medication. Both groups were comparable at entry. A greater proportion of patients achieved symptomatic remission (none/mild symptoms) at 2 (64% vs 43%,  $p < 0.05$ ), 4 (70% vs 51%,  $p > 0.05$ ), 8 (78% vs 45%,  $p < 0.001$ ) and 12 weeks (88% vs 57%,  $p < 0.001$ ) after balsalazide treatment compared to mesalazine. Similarly, more patients achieved complete remission (none/mild symptoms, sigmoidoscopy grade 0 (normal) or 1 (erythema with loss of vascular pattern) with no steroid use in previous 4 days) in the balsalazide group after 4 (38% vs 12%,  $p < 0.01$ ), 8 (54% vs 22%,  $p < 0.005$ ) and 12 weeks (62% vs 37%,  $p < 0.05$ ) with greater patient satisfaction (12 weeks: 91% vs 63%,  $p < 0.005$ ). Diary card analysis showed that patients taking balsalazide experienced more days with complete symptom relief (using no steroid) during the first 4 weeks of treatment (24% vs 14%,  $p < 0.01$ ) and took less time to achieve their first completely symptom free day (median: 10 vs 25 days,  $p < 0.005$ ) compared to those taking mesalazine. One patient in each group discontinued due to an unacceptable adverse event (AE) however, all 4 serious AEs (complications of UC) occurred in the mesalazine group and fewer patients in the balsalazide group reported AEs (48% vs 71%,  $p < 0.05$ ). Analysis of prognostic factors identified low ulcerative colitis grade at entry ( $p < 0.05$ ) and treatment with balsalazide ( $p < 0.01$ ) as increasing the probability of complete remission after 12 weeks. In conclusion, balsalazide 2.25 g t.i.d. was more effective and better tolerated than mesalazine 0.8 g t.i.d. in achieving remission of acute ulcerative colitis. Intestinal disorders: IBD, therapy }  
"Balsalazide is More Effective and Better Tolerated than Mesalazine in Acute Ulcerative Colitis (UC)"

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## OT54 1077 **Ridogrel for the Treatment of Mild to Moderate Ulcerative Colitis. A Placebo-Controlled Trial**

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An increased colonic production of eicosanoids has been documented in patients (pts) with Inflammatory Bowel Disease (IBD). Thromboxane (TXA<sub>2</sub>) may play an active role in the development of chronic inflammatory lesions in the bowel. Ridogrel (RID), a combined TXA<sub>2</sub> synthetase inhibitor (low dose) and TXA<sub>2</sub>/PGEND receptor blocker (high dose), might therefore be useful in IBD. *Methods:* 79 pts with mild to moderately active ulcerative colitis (UC) were randomized to 8-week double-blind treatment with either placebo (PLA) or one of three dose schedules of oral RID: 5 mg od, 25 mg bid, or 150 mg bid. Endoscopic assessments were performed every 4 weeks, with an additional assessment at week 2 in pts who had not improved clinically at week 2. Pts were subsequently withdrawn from the trial if there was no endoscopic improvement. *Results:* At endpoint, 3/20 PLA-treated pts, 9/21 RID 5 mg od treated pts, 6/17 RID 25 mg bid treated pts and 11/21 RID 150 mg bid treated pts had improvement by **1** grade on endoscopy. Significant differences in efficacy between RID and PLA were detected. Thirteen pts from the PLA group, 9 from the RID 5 mg od, 7 from the RID 25 mg bid and 6 from the RID 150 mg bid group had discontinued the therapy at week 2 due to insufficient response. More pts in the RID 5 mg od (n = 7) and RID 150 mg bid (n = 8) groups reached a clinically quiescent disease state at endpoint than the pts in the RID 25 mg bid (n = 4) or PLA (n = 3) groups. At endpoint the investigator rated the results of treatment as good or excellent in 3/20 of PLA-treated pts, 8/21 of RID 5 mg-treated pts, 6/17 of RID 25 mg-treated pts and 10/21 of RID 150 mg-treated pts. Adverse events, whether or not related to treatment, were reported by 9 to 11 pts in the three RID groups and in 6 pts in the PLA group. *Conclusion:* All three RID doses were well tolerated and were equally effective in relieving the inflammation associated with mild to moderate UC. Lower doses of RID, known to only inhibit TXA<sub>2</sub> synthetase activity without blocking the TXA<sub>2</sub>/PGEND receptor, need to be tested for the treatment of acute exacerbations of UC. Intestinal disorders: IBD, therapy }"  
"Ridogrel for the Treatment of Mild to Moderate Ulcerative Colitis. A Placebo-Controlled Trial"

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## OT55 1078 Three-Days Metronidazole (MET) and Clarithromycin (CLA) in Triple Therapy with Omeprazole (OME) for Cure of H. Pylori (HP) Infection

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Elisabeth Hospital, Essen, Germany

<sup>1</sup> Institute of Pathology, Bayreuth, Germany *Purpose:* Triple therapy with OME, MET and CLA (OMC) has become a standard in our clinic for cure of HP infection, as OMC poses currently an optimum in terms of efficacy, safety and cost effectiveness. Shorter than one-week schedules of modified classic triple have proved to be effective, so we intend to test the hypothesis that the treatment with MET and CLA can be shortened to three days in OMC without loss of efficacy. *Methods:* In a prospective, randomised, and controlled ongoing study, patients with indication to HP cure are assigned to one of the following two groups: Group 3D-OMC: OME 20 mg bid on days 1–7, MET 400 mg tid on days 2–4, CLA 250 mg tid on days 2–4. Group 7D-OMC: OME 20 mg bid, MET 400 mg bid, and CLA 250 mg bid, all on days 1–7. The HP status is determined before and at least 4 weeks after OMC by urease test, histology, culture, and UBT; antimicrobial HP resistance is assessed by E-Test (AB-Biodisk, Solna, Sweden). *Results:* At present, 60 patients (mean age 51 years) were randomised into the study. 31 patients have meanwhile completed the protocol. 16 of 17 patients in group 3D-OMC had been cured of HP infection versus 13 of 14 patients in group 7D-OMC. Pretherapeutic culture and testing of resistance was successful in 26 patients. The one patient with persisting HP infection in group 3D-OMC harboured a MET resistant strain. *Conclusions:* These preliminary data indicate no difference of HP cure rate between a 7-days OMC scheme and a 3-days OMC scheme with enhanced daily antimicrobial dosis. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Three-Days Metronidazole (MET) and Clarithromycin (CLA) in Triple Therapy with Omeprazole (OME) for Cure of H. Pylori (HP) Infection"

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## OT55 1079 Do Physicians from Different Countries Treat *H. Pylori* Positive Ulcer Disease Differently; A Comparison between America and Germany

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<sup>4</sup> Univ. of Magdeburg, Germany *Purpose:* The aim of this study was to determine the first line treatment used by two groups of physicians (gastroenterologists (GE) and family practitioners (FP)) in *H. pylori*-positive ulcer disease in two different countries. *Methods:* Cross-sectional study, mail questionnaire. *Results (to date):* 1125 US and 538 German physicians responded: Regimen\* GE (USA) GE (FRG<sup>186</sup>) FP (USA) FP (FRG<sup>186</sup>) (n = 645) (n = 301) (n = 480) (n = 237) PPI based triple 36% 42% 14% 22% Standard triple 16% <1% 25% <1% PPI based quadruple 16% – 11% -PPI/CLA 11% 1% 8% 3% H<sub>2</sub> based quadruple 9% – 10% -PPI/AMO 4% 51% 5% 53% other (insufficient) 8% 6% 26% 22% \*PPI (Proton pump inhibitor), AMO (Amoxicillin), H<sub>2</sub> (H<sub>2</sub>-inhibitors), CLA (Clarithromycin), MET (Metronidazole) BIS (Bismuth); PPI based triple (PPI plus combination of two antibiotics (AMO, CLA, MET)); Standard triple (BIS, MET, TET/AMO), PPI based quadruple (PPI plus standard triple); H<sub>2</sub> based quadruple (H<sub>2</sub> plus standard triple). <sup>186</sup>FRG (Federal Republic of Germany) *Conclusion:* The frequently used standard triple therapy based regimens in the US are almost non existent in Germany, whereas the most frequently used regimen in Germany (PPI/AMO) plays only a minor role in the US. We conclude that treatment of *H. pylori* positive peptic ulcer disease differs substantially in the two countries. This can be explained due to different recommendations of the researchers in the field of *H. pylori* treatment in the two countries. Nearly 25% of the FP in each country treat *H. pylori* positive ulcer disease with ineffective regimens. This emphasizes that knowledge acquisition of newly recommended therapies for *H. pylori* infection is not optimal. Researchers in the field have to make sure that dissemination of currently recommended therapies is a continuous process. Oesophageal gastric duodenal disorders: Helicobacter Pylori Clinical practice: Management strategy } "Do Physicians from Different Countries Treat H. Pylori Positive Ulcer Disease Differently; A Comparison between America and Germany"

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## OT55 1080 Eradication of Hp Infection after Triple Therapies Failure: A Quadruple Schedule Approach

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<sup>3</sup> Dept of Gastroenterology, Genoa, Italy Overall triple therapies eradication rate against *Helicobacter pylori* infection is commonly high (about 80 to 90%). Still unsolved problem remains what to do with symptomatic patients after an unsuccessful triple therapy. Indeed microbiologic culture to test antibiotic resistance is not widely spread. The problem is even more relevant in patient with history of peptic ulcer which needs to be cured. The aim of this study was to establish an effective quadruple therapy which can be widely used without testing antibiotic resistance. *Material and Methods:* we enrolled 15 consecutive outpatients (mean age 51; range 33–69, M/F 8/7) referred to our endoscopy unit for Hp related gastritis resistant to triple therapies. Hp status was evaluated by three different test (histology, CLO test and serology). Study design: endoscopy with multiple biopsies were performed at immission time and two months after the end of the treatment (Omeprazole 20 mg b.i.d., Metronidazole 250 mg q.i.d., Amoxicillin 250 mg q.i.d. and Bismuth citrate 125 mg q.i.d. for 14 days). Hp eradication was considered successful when both histology and CLO test resulted negative. *Results:* overall results were calculated by intention to treat (ITT) and per protocol analysis (PP). Over 15 patients only 2 subjects remained Hp positive after the treatment (PP 85.7%; ITT 80%). Only one patient had side effects (diarrhea). *Conclusions:* 1) A 14 days quadruple therapy cured 85% of the Hp triple therapies resistant infected patients. 2) Side effects were less than 2% and compliance was very high (93%). } "Eradication of Hp Infection after Triple Therapies Failure: A Quadruple Schedule Approach"

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## OT57 1085 Repeat Resection of Liver Metastasis from Colorectal Cancer

\*R. Adam, H. Bismuth, F. Navarro, D. Castaing, A. Abascal

Hepato-Biliary Surgery and Liver Transplant Research Center, Paul Brousse Hospital, Villejuif, France It is estimated that about 60% of patients (pts) submitted to hepatic resection of metastasis from colorectal cancer will present a recurrence. This recurrence is limited to the liver in about 30% of cases. Repeat hepatectomy has been used increasingly in relation to the low mortality and morbidity of hepatic resection. However, the risk of these repeat hepatectomies, their long-term results as well as the rationale for patient selection need to be clarified. For this purpose, we have analyzed over a period of 12 years (1983–1995) the results of 57 re-hepatectomies performed in 44 pts with hepatic metastasis from colorectal cancer (2 hepatectomies: 44, 3 hepatectomies: 10, 4 hepatectomies: 3). These repeat hepatectomies represented 19.5% of the 282 liver resections performed during the same period for the same indication. The time interval between first and second hepatectomies was over 1 year in 23 pts (52%). Extra hepatic disease was associated to hepatic recurrence in 11 pts (25%). Major hepatectomy (> 3 segments) was performed in 50% of first resections, 36% of second resections and only 15% of third and fourth resections. There was no post-operative mortality within two months. Post-operative bleeding was not increased as compared to that of first resections. Post-operative morbidity was 11% (6/55) comparable to that of first resections. Overall survival after repeat resection was 44% at 5 years with no difference related to Dukes classification of initial colorectal tumor, to synchronous versus metachronous metastasis or to local versus distant hepatic recurrence. *Conclusion:* Repeat resection of liver metastasis from colorectal cancer allows a long-term survival at least equal to that of first resection with no mortality and comparable morbidity. This policy is warranted when repeat hepatectomy is potentially curative. } "Repeat Resection of Liver Metastasis from Colorectal Cancer"

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## OT57 1086 Liver Regeneration after Partial Hepatectomy is Depressed by Kupffer Cell Depletion

\*C. Meijer<sup>1</sup>, H.J. Schouten<sup>1</sup>, A.H.W. Van Maurik<sup>1</sup>, A.P.J. Houdijk<sup>1</sup>, N. Van Rooijen<sup>2</sup>, S. Meijer<sup>1</sup>, C.D. Dijkstra<sup>2</sup>, P.A.M. Van Leeuwen<sup>1</sup>

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*Purpose.* After partial hepatectomy, activation of Kupffer cells (KC) by circulating gut-derived endotoxin results in a rapid release of inflammatory mediators. Some of these mediators are thought to play a role in the induction and regulation of liver regeneration. We therefore hypothesized that KC are important for liver regeneration and investigated the effect of KC-depletion on liver regeneration after partial hepatectomy (phx).  
*Methods.* All animals (36 Wag/Rij rats, male, 200–220 gram) underwent a twothird liver resection. The rats were randomized in 2 groups: 48 hours prior to phx, KC-depletion was performed in 18 rats by intravenous (i.v.) administration of 1 ml liposome-encapsulated dichloromethylene diphosphonate (CL<sub>2</sub>MDP). The 18 control rats received 1 ml normal saline (NaCl) i.v. Directly after phx 1/4 dosage of the i.v. treatments was readministered. One week prior to phx, splenectomy was performed in all rats to eliminate the effect of liposome-encapsulated CL<sub>2</sub>MDP on macrophage populations in the spleen. Every 24 hours after phx 50 mg/kg bromodeoxyuridine (BrdU) was administered by 1 ml intraperitoneal injection. Animals were sacrificed at 24, 48 and 96 hours (n = 6 per group) after phx. To confirm KC-depletion, cryostat liver sections were stained with the monoclonal antibody ED2, a marker for resident tissue macrophages. Liver cell proliferation was determined by the BrdU labeling index in liver sections. Weight of the remnant liver was expressed in percent of calculated initial liver weight.  
*Results.* KC depletion was confirmed in sections of the resected liver. Proliferation of parenchymal liver cells 48 hours after phx was significantly depressed in KC-depleted rats when compared with control rats (p < 0.05). Also, weight increase of the remnant liver, determined 96 hours after phx, was significantly delayed (p < 0.05) in KC-depleted rats.  
*Conclusion.* KC are important for liver regeneration after partial hepatectomy. Immunology and microbiology: Host defense mechanisms Liver and bile ducts, 1: Cell biology, collagen, fibrosis Oncology, specific: Liver, biliary } "Liver Regeneration after Partial Hepatectomy is Depressed by Kupffer Cell Depletion"

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**OT57 1087 Unresectable Hepatic Metastases from Colorectal Cancer: Results of a Combined Approach by Chemotherapy and Subsequent Resection**  
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Resection is the sole curative treatment of hepatic metastases from colorectal cancer. However, it may be achieved in only 10% of patients (pts) since most pts have at the first irresectable lesions associated with a poor prognosis. Over the past 6 years, we have managed these pts with a new protocol of chemotherapy with the aim to perform subsequent curative liver resection. From April 1988 to March 1994, 53 out of 337 pts (16%) with liver metastases initially considered as non resectable were subsequently submitted to hepatic resection with a curative intent. All pts have been treated by intravenous chronomodulated chemotherapy combining 5 Fluorouracil, Folinic acid and Oxaliplatinum, a non nephrotoxic platinum complex. To optimize dose intensities and tolerance, drug delivery was sinusoidally modulated along the 24 hour-scale with peak flow rates at 04.00 hours for 5-FU and Fol and at 16.00 hours for Oxa, using an ambulatory programmable-in-time pump. Initial non resectability was assessed by the same surgical team and was related either to technical impediment due to large (n = 8), multinodular (n = 24) and central ill-located tumours (n = 8) or to the presence of extrahepatic disease (n = 13 – Peritoneum (6), Epiploon (3), Lungs (4)). Pts received 3 to 29 courses of chemotherapy (mean = 10) for 2 to 29 months (mean = 8 months) before surgery. *Results:* An objective reduction in tumour size was observed following chemotherapy in all pts subsequently submitted to liver resection. A significant reduction of tumor markers was also demonstrated. A major hepatectomy (> 3 segments) was performed in 37 pts and a minor resection in 16. There was no operative mortality within 2 months. Post operative complications included 2 infected collections that needed non operative drainage, 1 transient biliary fistula and 1 reoperation for bleeding. Chronomodulated chemotherapy was routinely continued post operatively in all pts for 6 courses at less. Associated procedures included repeat hepatectomy (15), pulmonary resection (11), hepatic cryotherapy (8), splenectomy (1) nephrectomy (1), resection of the diaphragm (2), repeat resection of colon cancer recurrence (2). Twenty eight pts are presently alive (of whom 16 without disease) with a mean follow of 2.5 years (range 1.3–6.4). Median survival is 3.2 years with a patient survival rate of 61% at 3 years. *Conclusion:* Resection may be achieved in some unresectable pts with the help of an efficient chemotherapy. The benefit in survival seems comparable to that obtained with liver resection for initially resectable liver metastases. This therapeutic strategy involves a multimodality approach including repeat hepatectomy and extrahepatic surgery. }

"Unresectable Hepatic Metastases from Colorectal Cancer: Results of a Combined Approach by Chemotherapy and Subsequent Resection"

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## OT63 1088 Increased Human Gastric Endothelial Cell COX-2 Expression during Angiogenesis

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**Introduction:** Angiogenesis plays an important role in gastric ulcer healing. Prostaglandins (PGs) promote angiogenesis *in vivo* and non-steroidal anti-inflammatory drugs (NSAIDs) reduce vascularity of gastric ulcer granulation tissue and delay healing. However, it is not known whether gastric ulcer angiogenesis is associated with changes in endothelial cell cyclooxygenase (COX) expression. Therefore we investigated COX expression during *in vitro* angiogenesis using human gastric endothelial (HuGE) cells which were obtained using an immunomagnetic separation technique developed in our laboratory.

**Methods:** HuGE cells were isolated from normal gastric mucosa using anti-PECAM-1 antibody-coated Dynabeads. HuGE cells were cultured routinely on 1% gelatin in Medium 199 + 30% FCS + 90  $\mu$ g/ml heparin + 40  $\mu$ g/ml ECGS until plating onto basement membrane matrix (Matrigel) or addition of 1  $\mu$ M phorbol 12, 13 dibutyrate (PdBu). COX-1 and COX-2 expression were investigated by RT-PCR, western blotting and indirect immunofluorescence studies. PGE<sub>2</sub> levels in cell-conditioned medium were measured by ELISA.

**Results:** PdBu induced formation of cell extensions and "ring" structures in HuGE cells at 4 hours which was associated with increased COX-2 expression and PGE<sub>2</sub> production. COX-2 was localized predominantly in the nuclear envelope. At 24 hours COX-2 expression had declined. There was no change in COX-1 expression after addition of PdBu. Formation of "tube-like" structures by HuGE cells on Matrigel was associated with an increase in COX-2 (and COX-1) mRNA expression and PGE<sub>2</sub> production which was maintained at 24 hours.

**Conclusion:** In this model of angiogenesis, HuGE cell differentiation (formation of "tube-like" structures) rather than proliferation was associated with induction of COX-2 and COX-1 expression. This process may be impaired by NSAIDs during gastric ulcer healing. These findings suggest that specific COX-2 inhibitors may also impair angiogenesis and delay gastric ulcer healing.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic

Hormones and receptors: Molecular biology }

"Increased Human Gastric Endothelial Cell COX-2 Expression during Angiogenesis"

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## OT63 1089 Gene Expression of Metalloproteinases (MMP-1, -2, and -3) and Their Tissue Inhibitors (TIMP-1 and -2) during Experimental Gastric Ulcer Healing

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Increasing evidence indicates that extracellular matrix (ECM) degradation plays a crucial role not only in tumor invasion but also in the process of wound repair. We analyzed the spatial and temporal pattern of expression of three major members of the metalloproteinase (MMP) family, namely MMP-1, MMP-2 and MMP-3, and of their specific tissue inhibitors TIMP-1 and -2, in an experimental model of gastric ulcer healing. *Methods:* chronic gastric ulcers were induced in rats by acetic acid injection and groups of 5 rats each were sacrificed before and at 1, 3, 7, 14, 28 and 56 days after the ulcerogen. Gene expression of MMPs and TIMPs was examined by in situ hybridization with <sup>35</sup>S-labeled RNA probes and the autoradiographic signal was quantified by an image analysis system. *Results:* in the normal rat stomach, there was no evidence of MMP-1 and TIMP-1 expression, while low amounts of MMP-2, MMP-3 and TIMP-2 RNA transcripts were present in some mesenchymal cells of the lamina propria, submucosa and muscularis propria. MMP gene expression was dramatically up-regulated after ulcer induction, starting at 24 h and peaking at 3–7 days (e.g. when lesions undergo transition into true "chronic" ulcers). With the completion of ulcer healing, MMP mRNA expression progressively returned toward normal; however, higher than normal levels of MMP-1 and MMP-3 mRNA persisted at sites of excessive ECM deposition and prominent histologic abnormalities. The spatiotemporal pattern of distribution of TIMP-1 and -2 essentially followed that of MMPs; in contrast with MMP expression, however, low amounts of TIMP-1 and -2 mRNA were also noted on some epithelial cells of gastric glands. *Conclusions:* the up-regulation of MMPs, by degrading basement membranes around migrating proliferating cells and removing the excess of matrix transiently accumulated in the granulation tissue, may play a crucial role in gastric ulcer healing promoting the re-epithelialization of the ulcer crater, angiogenesis, and the final remodelling of regenerated tissue.

Hormones and receptors: Molecular biology  
Oesophageal gastric duodenal disorders: GD disorders, acid peptic }  
"Gene Expression of Metalloproteinases (MMP-1, -2, and -3) and Their Tissue Inhibitors (TIMP-1 and -2) during Experimental Gastric Ulcer Healing"

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## OT63 1090 Acute and Chronic Gastrointestinal Effects of Selective Cyclooxygenase-2 Inhibition in Rats

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<sup>1</sup> Gastrointestinal Unit, Univ. Hospital, Inselspital, Bern, Switzerland

<sup>2</sup> Dep. of Exp. Clinical Medicine, Ruhr-University, Bochum, Germany **Background:** Non-selective cyclooxygenase (COX) inhibitors induce gastrointestinal ulcers and delay gastric ulcer healing. It has been reported that the selective COX-2 inhibitor L-745,337 causes less gastrointestinal side-effects, but this drug has not been tested in a reliable chronic ulcer model. **Methods:** Dose-response for indomethacin, diclofenac, and L-745,337 was assessed. Inflammatory PG-E2 was measured 5 hrs after implantation of carrageenin-soaked sponges. Rats (8 per dose and group) with gastric cryoulcers were treated twice daily for 15 days and delay in ulcer healing (incl. histologic changes) and intestinal perforation rate were assessed. **Results:** 5 mg/kg L-745,337 reduced ( $P < 0.05$ ) PG-E2 concentration in inflammatory exudates (COX-2) by 88%. Indomethacin but not L-745,337 (20 mg/kg) caused severe gastric ulcerations 5 hrs after dosing. In chronic models, however, L-745,337 caused dose-dependently profound delay of gastric ulcer healing, decrease of angiogenesis/maturation of granulation tissue, and intestinal perforation comparable to traditional NSAIDs such as indomethacin and diclofenac. Indomethacin Diclofenac L-745,337 Daily dose/kg (2 weeks) 2 times; 0.5 mg 2 times; 2.5 mg 2 times; 5 mg Gastric 6-keto-PG-F1 { a } { - } 42% \* { - } 88% \* { - } 27% n.s. Ulcer size on day 15 + 81% \* +111% \* + 107% \* Angiogenesis in ulcer bed { - } 55% \* { - } 59% \* { - } 55% \* Thickness of ulcer bed +78% \* +94% \* +105% \* Intestinal perforation rate # 5% 45% 36% \* data compared with placebo,  $P < 0.05$ ; # absolute data. **Conclusion:** L-745,337 is not ulcerogenic in acute studies but delays healing of gastric ulcers and causes intestinal perforation in chronic studies comparable to traditional NSAIDs. Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Acute and Chronic Gastrointestinal Effects of Selective Cyclooxygenase-2 Inhibition in Rats"

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## OT63 1091 Expression of Epidermal Growth Factor (EGF) and Transforming Growth Factor Alpha (TGF- $\alpha$ ) during Ulcer Healing-Time Sequence Study

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Dept. Med I, Univ Erlangen-Nuremberg, Germany

Inst. Physiol. Jagiell. Univ. Med. Sch. Krakow, Poland *Background:* Growth factors such as EGF and TGF- $\alpha$  have been shown to share common receptor (EGFr) and to accelerate ulcer healing due to stimulation of cell proliferation but expression of EGF and TGF $\alpha$  during ulcer healing has been little studied. In this study, the rate of cell proliferation, the gastric secretion and the gene expression of mRNA EGF and TGF $\alpha$  were determined during ulcer healing. *Material and Methods:* Chronic gastric ulcers were induced in 150 Wistar rats by serosal application of 100% acetic acid (ulcer area 20 mm<sup>2</sup>). Separate groups of rats with acetic acid ulcers were equipped with gastric fistula for the assessment of gastric secretion during ulcer healing. The animals were sacrificed at 0, 2, 4, 6 and 8 days after ulcer induction and the area of ulcer was determined by planimetry. The mucosal sections with gastric ulcer was immunostained for proliferating cell nuclear antigen (PCNA) – an index of cell proliferation, and for EGF, TGF $\alpha$  and EGFr using specific antibodies. Expression of mRNA EGF and mRNA TGF- $\alpha$  was determined in the ulcer margin by reverse-transcriptase polymerase chain reaction (RT-PCR). Five micrograms of total RNA extracted from gastric mucosa with ulcer was used to synthesise a first strand cDNA by enzyme MMLV-RT and then amplified by the PCR method with specific primers. RT-PCR products were stained with ethidium bromide and separated on 1.5% agarose gel. *Results:* At 2, 4, 6 and 8 days after ulcer induction, the area of gastric ulcers was gradually reduced from initial size (day 0) by 10%, 33%, 58% and 87%, respectively, and this was accompanied by rise in PCNA with the maximum at day 4. Following induction of gastric ulcers a marked decrease in gastric acid and pepsin secretion was observed at day 2, by 55% and 43%, respectively, but then secretion tended to return at day 8 to normal value. Immunohistochemical expression of EGF, TGF $\alpha$ , and EGFr was negligible at the day 0 but increased significantly during the healing, reaching the peak at day 4. Expression of RT-PCR mRNA TGF $\alpha$  was detected at 2, 4, 6 and 8 day, whereas RT-PCR mRNA EGF was detected at day 2, 4 and 6 after ulcer induction with the most intense signals observed at day 2. *Conclusions:* 1) Enhancement in cell proliferation and suppression of gastric secretion during ulcer healing is mediated by expression of EGF and TGF $\alpha$ ; 2) Expression of EGF and TGF $\alpha$  mRNA precedes the overexpression of these growth factors during ulcer healing; 3) Overexpression of growth factors during healing coincides with the inhibition of gastric secretion probably mediated by these growth factors. *Hormones and receptors: Growth factors }* "Expression of Epidermal Growth Factor (EGF) and Transforming Growth Factor Alpha (TGF-alpha) during Ulcer Healing-Time Sequence Study"

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**OT65 1092 Gliadin Specific, HLA-DQ2 Restricted T Cells are Frequently Found in the Small Intestinal Mucosa of Coeliac Disease Patients'** d8. Molberg, K. Kett, H. Scott, L.M. Sollid, E. Thorsby,

\*K.E.A. Lundin

Institute of Transplantation Immunology, Medical Department A, and Institute of Pathology, The National Hospital and University of Oslo, Oslo, Norway Coeliac disease (CD) is an immune-mediated disorder of the small intestine with a very strong HLA association to a particular HLA-DQ2 variant. More than 90% of the patients carry this variant. We previously showed that T cells from the small intestinal mucosa of patients on a gluten-free diet could respond to gluten when presented by the disease associated HLA-DQ2 molecules (Lundin et al. J Exp Med 178: 187–196, 1993). The purpose of the present study was to examine if this is a general phenomenon in CD. Lamina propria-derived T cells from 22 consecutive patients, all being HLA-DQ2+, were studied. 19 patients had a gluten-free diet, 3 patients had a normal diet. Small intestinal biopsies were challenged in vitro with wheat flour gliadin proteins, activated T cells were isolated by an immunomagnetic method and cultured without further gliadin stimulation. We succeeded in establishing gliadin-specific T cell lines from all the 22 patients, but not from disease controls. Inhibition studies with anti-HLA monoclonal antibodies demonstrated predominant HLA-DQ2 restriction in polyclonal T cell lines from 11 of the patients. Gliadin-specific T cell clones were established from several of the patients. Nine T cell clones could be studied in detail, all of them showed HLA-DQ2 restriction. Our results indicate that presence of gliadin-specific T cells is a general phenomenon in the small intestine of coeliac disease patients. Intestinal disorders, absorption: Gluten enteropathy Immunology and microbiology: Inflammation } "Gliadin Specific, HLA-DQ2 Restricted T Cells are Frequently Found in the Small Intestinal Mucosa of Coeliac Disease Patients"

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**OT65 1093 Distinctive Activated Cellular Subsets in Colon from Patients with Ulcerative Colitis and Crohn's Disease.**

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<sup>3</sup> Dpt. of Nephrology, University of Western, Ontario, Canada

**Introduction.** A comparative study on in situ preactivated lymphocytes in Crohn (CD) and ulcerative colitis (UC), and in non-inflammatory controls (C) was assessed, with special reference for T-cell activation markers and lymphocyte homing molecules. **Study design.** IL-2 expanded cell-lines (n = 43) were generated from colon biopsies obtained by endoscopy. 4 patients with active CD, 5 with active UC and 6 controls were included. Cell-lines were characterized by FACS analysis. Results are expressed as % positive cells (mean value) and compared using Wilcoxon rank sum test. **Results.** Control Crohn disease Ulcerative colitis 1. **Cellular distribution clonality** CD3+ (T-cells) 52.7% 27.3% 30.7% CD8+/CD4{ - } 64.0% 21.1% 39.3% CD4+/CD8{ - } 36.0% 68.9%<sup>4</sup> 60.7%<sup>4</sup> CD4{ - }/CD8{ - } 10.0% 3.0% 8.0% { a } { b } TCR+ 90.0% 90.0% 97.0% CD3{ - }/CD56+ (LAK-cells) 69.2% 64.0% 41.4%<sup>2</sup> 2. **Activation marker** CD4+/CD30+ 5.5% 9.9% 21.6%<sup>2</sup> CD8+/CD30+ 27.6% 12.1% 35.5% 3. **Adhesion molecules** Lymfocytes/{ a }<sup>4</sup>{ b }<sup>7</sup> 86.4% 37.1%<sup>1,4</sup> 41.8%<sup>4</sup> CD4/{ a }<sup>4</sup>{ b }<sup>7</sup>+ 91.0% 58.9%<sup>1,4</sup> 55.0%<sup>4</sup> CD8/{ a }<sup>4</sup>{ b }<sup>7</sup>+ 91.5% 42.7%<sup>1,4</sup> 53.3%<sup>4</sup> CD3+/HML-1 ({ a }<sup>E</sup>{ b }<sup>7</sup>) 6.4% 26.9%<sup>1,4</sup> 11.1%<sup>4</sup> CD4/HML-1+ 13.9% 10.9% 5.5% CD8/HML-1+ 10.3% 36.1% 32.3% CD3+/LEU8+ 25.0% 16.8% 49.3%<sup>3</sup> CD8/LEU8+ 22.4% 12.1% 36.5%<sup>1</sup> C-CD (p < 0.05);<sup>2</sup> C-UC (p < 0.05);<sup>3</sup> CD-UC (p < 0.05);<sup>4</sup> C-CD + UC (p < 0.05) **Conclusions.** In IBD, an increase in CD4/CD8 ratio, a decrease in { a }<sup>4</sup>{ b }<sup>7</sup> expression (critical in homing LPL) and an increase in { a }<sup>E</sup>{ b }<sup>7</sup> expression (expressed on majority of IEL) were observed. In contrast to Crohn's disease, an increase in CD30 (preferentially expressed by Th2 cells) and Leu-8 (L-selection) expressions on T-helper cells were only documented in UC with a significant underexpression of CD56 LAK cells. These findings suggest clear differences in activation and homing mechanisms. Intestinal disorders: IBD, basic } "Distinctive Activated Cellular Subsets in Colon from Patients with Ulcerative Colitis and Crohn's Disease."

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**OT65 1094 Anti-Endomysium Antibodies on Human Umbilical Cord: An Improved Method for Diagnosis and Follow-Up of Coeliac Disease** S.B. Grosso, M. Bruno, S. Grosso, G. Caula,

\*C. Sategna-Guidetti

Cattedra di Gastroenterologia, Università di Torino, Italy Although anti-endomysium antibodies (EmA) are, to date, the most reliable serological marker of coeliac disease (CD), both the high cost of monkey oesophagus (MO) and the ethical problems connected with killing of endangered species, limit their routine application. *Aim:* In this study we investigated the use of human umbilical cord (HUC) as an alternative substrate to MO in EmA determination. *Method:* IgA EmA were appraised, by indirect IF on MO and HUC, on sera from 104 untreated biopsy proven CD patients, 40 healthy volunteers and 48 disease controls (inflammatory bowel disease and irritable bowel syndrome). One year after gluten withdrawal 44 out of 104 CD patients underwent a second intestinal biopsy and EmA appraisal. *Results:* A) IgA EmA sensitivity and specificity were 95% and 100% respectively on both substrates, with a diagnostic efficiency of 97.4%. B) One year after a gluten free diet (GFD) 38/44 (86%) patients still had histological alterations. EmA positivity on MO was found in only 10/38 (26%), while on HUC it persisted in 29/38 (76%). The agreement between histology and EmA was respectively 40% on MO and 79% on HUC. *Conclusion:* A) HUC can replace MO as substrate for IgA EmA detection with comparable diagnostic efficiency, lower costs and sparing of monkeys. B) HUC seems to be a more suitable substrate than MO in EmA detection during a GFD because of its higher agreement with histological pattern. Intestinal disorders, absorption: Malabsorption syndromes Intestinal disorders, absorption: Gluten enteropathy } "Anti-Endomysium Antibodies on Human Umbilical Cord: An Improved Method for Diagnosis and Follow-Up of Coeliac Disease"

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## OT65 1095 TNF $\alpha$ and LPS Increases Human Peripheral Blood Lymphocyte Adhesion to HIMECs Which Is Partially Blocked with Monoclonal Antibody to $\alpha_4$

\*R. Thompson, J. Wilson, J.R. Rhodes, S.L. Bloom

Dept of Medicine, University of Liverpool, Liverpool, UK *Purpose* Bacterial Products may play a fundamental role in the pathogenesis of Inflammatory Bowel Disease (IBD). A weakened mucoid barrier may allow the influx of bacterial products into the lamina propria which may have a direct effect on endothelium and result in increased lymphocyte recruitment. Using Human Intestinal Microvascular Endothelial Cells (HIMECs), we measured the effect of TNF $\alpha$ , butyrate, lipopolysaccharide (LPS) and f-Met-Leu-Phe (fMLP) on the adhesion of  $^{51}\text{Cr}$  labelled human lymphocytes. *Methods* Normal and inflamed colon ( $n = 3$ ) obtained from patients undergoing resection for colonic cancer or IBD were used to isolate HIMECs, as described (Gut 38 (4): A635). HIMECs were plated onto 24 well plates, grown to confluency and incubated with butyrate, LPS, fMLP or TNF $\alpha$ . Peripheral blood lymphocytes (PBLs), from healthy volunteers, were isolated using "Lymphoprep" and labelled with  $^{51}\text{Cr}$ . The PBLs were incubated with monoclonal antibody to  $\alpha_4$  (Serotec), a lymphocyte integrin which is expressed on the majority of PBLs, and incubated with the HIMECs for one hour. Gamma counts in the supernatant, the standardised washes and the monolayers, removed by detergent, were used to calculate percentage lymphocyte adhesion. *Results* The adhesion of PBLs to nonstimulated HIMEC monolayers was 27% (SD = 3) (3 wells) Preincubation with TNF $\alpha$  (10 ngml $^{-1}$ ) and LPS (10  $\mu\text{gml}^{-1}$ ) increased this to 74% (SD = 4  $p < 0.01$  Mann Whitney) and 52% (SD = 9  $p < 0.05$ ) though various concentrations of butyrate and fMLP had no effect. Preincubation with Anti  $\alpha_4$  reduced adhesion by 25% ( $p < 0.05$ ) on TNF $\alpha$  and 15% ( $p < 0.05$ ) on LPS stimulated cells. *Conclusions* TNF $\alpha$  and LPS have a direct effect on HIMECs which results in increased PBL adhesion. Preincubation with antibody to  $\alpha_4$  reduced adhesion significantly but not substantially suggesting that other molecules or mechanisms may facilitate adhesion of PBLs to TNF $\alpha$  and LPS stimulated endothelium. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "TNF $\alpha$  and LPS Increases Human Peripheral Blood Lymphocyte Adhesion to HIMECs Which Is Partially Blocked with Monoclonal Antibody to  $\alpha_4$ "

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## "P P 46 1102" P 46 1102 Gastric Functions and Dyspeptic Symptoms in Reflux Esophagitis

\*B. Salvioli, V. Stanghellini, C. Tosetti, S. Mattioli, F. D'Ovidio, M. Pastina, B. Misitano, R. Cogliandro, N. Monetti, R. Corinaldesi

Depts. of Internal Medicine & Gastroent., Surgery, Nuclear Medicine, University of Bologna, Italy

The relationship between gastric functions and dyspeptic symptoms in reflux esophagitis (RE) is poorly investigated. We evaluated scintigraphic gastric emptying of solids (GE; 638 kcal,  $^{99m}\text{Tc}$ -chicken liver) in 68 (51 M, 51 – 13 yrs; m – SD) RE pts. Results were expressed as half-times (T<sub>1/2</sub> min) and GE rates (k; %/h). Gastric acid secretion (BAO, PAO; mEq/h) was also evaluated in 50/68 RE pts (40 M, 49 – 14 yrs). Fifty healthy volunteers served as controls (HC; T<sub>1/2</sub> = 101 – 20 min, k = 40 – 11%/h, BAO = 3 – 2 mEq/h, PAO = 21 – 7 mEq/h). RE pts presented delayed GE (T<sub>1/2</sub> = 153 – 86 min, P < 0.01; k = 32 – 13%/h, P < 0.01) and increased acid secretion (BAO = 5 – 5 mEq/h; PAO = 32 – 15 mEq/h, p < 0.01) compared to HC (Mann Whitney U test). Delayed GE and increased acid secretion were observed respectively in 32% and 40% of pts. Increased acid secretion was present in 19% of pts with delayed GE and in 50% of pts with normal GE, while delayed GE was present in 15% of pts with increased secretion and in 43% of pts with normal secretion (P < 0.05, X<sup>2</sup>). Epigastric pain/burning, postprandial fullness, nausea, vomiting were each graded 0 to 3 according to their influence on usual activities. Dyspepsia (total score  $\geq 3$  with at least one symptom  $\geq 2$ ) was observed in 64% of pts: 26% of them presented prevalent pain (pain  $\geq 2$  with any other symptom  $\leq 1$ ), 44% prevalent discomfort (postprandial fullness and/or nausea and/or vomiting  $\geq 2$ , with pain  $\leq 1$ ) and 30% resulted unclassifiable. Gastric emptying (n = 68) Acid secretion (n = 50)

Category	Delayed	Normal	Increased
Dyspepsia (total)	74%	58%	60%
Prev. pain	12%	35%	42%
Prev. discomfort	71%	27%	33%
Unclassifiable	17%	38%	25%

\*P < 0.005 vs normal gastric emptying; X<sup>2</sup>. **Conclusions:** RE pts as a whole present delayed GE and increased acid secretion compared to HC, but gastric motor and secretory abnormalities are not usually associated. Dyspeptic symptoms are frequent in these patients. RE patients with delayed GE present more often prevalent discomfort compared to patients with normal GE. Oesophageal gastric duodenal disorders: EG Reflux Motility, general: Functional GI disorders } "Gastric Functions and Dyspeptic Symptoms in Reflux Esophagitis"

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"P P 46 1103" P 46 1103 **Recordings of Duodeno-Gastro-Oesophageal Reflux in Supine (Sleeping) GORD Patients with Fiberoptic Bilirubin Monitoring Are at Least as Good as 24-Hours Recording.** H. Geldof

IJsselland Hospital, Capelle a.d. IJssel, The Netherlands *Aim.* Oesophageal fiberoptic bilirubin monitoring quantifies the duodeno-gastro-oesophageal reflux (DGOR), which seems to be relevant for the pathogenesis of GORD and its complications such as Barrett oesophagus and oesophageal carcinoma. To improve this method, the value of recordings in supine (sleeping) patients (average 8 hours) is compared with that of 24-hours recordings. *Method.* Measurements were made with a fiberoptic sensor and portable dataprocessing unit (Bilitec 2000, Synectics medical Inc.). The fiberoptic electrodes were placed 5 cm above the lower oesophageal sphincter. The absorbance threshold was set to 0.14, corresponding to 10  $\mu$ M of bilirubin. Studies were performed in 11 patients with uncomplicated GORD, 10 patients with GORD complicated by intestinal metaplasia below the squamo-columnar mucosal junction, and in 13 patients with a Barrett oesophagus. *Results.* The table below shows the mean percentages of the recording time of oesophageal exposure to bilirubin. Total recording time Supine patients Uncomplicated GORD 11% 8% Intestinal metaplasia 55% 71% Barrett oesophagus 60% 69% Comparisons between uncomplicated GORD and GORD with metaplasia or Barrett oesophagus;  $p < 0.001$  *Conclusions.* Fiberoptic measurements of bilirubin concentrations shows large differences in the oesophageal bilirubin exposure between uncomplicated GORD, and GORD with metaplasia or Barrett oesophagus. Shorter recordings (average 8 hours) from patients in the supine (sleeping) position yield probably better information than 24-hours recordings. Moreover, the 8-hours supine recordings are much more convenient for the patients. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus Motility, specific: Stomach } "Recordings of Duodeno-Gastro-Oesophageal Reflux in Supine (Sleeping) GORD Patients with Fiberoptic Bilirubin Monitoring Are at Least as Good as 24-Hours Recording"

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## "P P 46 1104" P 46 1104 Exertional Gastroesophageal Reflux (GER) and Angina Pectoris

\*E. Vincent, F. Romand, N. Claudel, J. Desbaumes

Service de Gastro-Entérologie, HIA Desgenettes, 69998 Lyon ArméeThe aim of the study was to evaluate the role of GER in recurrent pain in patients on treatment for coronary artery disease. 16 patients (14 M/2 F, mean age 60.5 years) underwent graded bicycle exertional ECG during 24-hours esophageal pH-monitoring (pH-24). GER was defined by pH < 4 and pain was considered as GER related if it occurred within 2 mn. PH-24 was interpreted according to Stein's criteria. Exertional GER appears only in refluxers in pH-24 (table 1: pH-W exertional pH-metry). Table 1 pH-24 Refluxers Non refluxers Total pH W exertional GER 7 0 7 no exertional GER 6 3 9 total 13 3 16 12 patients (75%) presented with at least 1 pain during the study (table 2). During pH-24 4 patients (25%) experienced pain (5 events including 1 GER related). During pH-W 10 patients (62%) experienced pain, including 4 GER-related, without ECG signs of ischemia. Table 2 Symptom index in pH-24 (0) 0% 50% total pH W no pain (0) 4 2 2 unrelated pain 6 6 related pain 2 1 1 4 total 12 3 1 16 GER is frequent (81%) in patients with angina pectoris suffering despite treatment. Exertional pH-metry confirms GER responsibility or its contribution to pain in 25% of patients versus 6% in pH-24. 50% of patients experienced pain without relation to GER nor ECG signs of ischemia. Oesophageal gastric duodenal disorders: EG Reflux } "Exertional Gastroesophageal Reflux (GER) and Angina Pectoris"

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"P P 46 1105" P 46 1105 **Clinical Importance of Esophageal 24 Hours-pH-Manometry** P. Netzer,

\*A. Gut, N. Gries, S. Hurlimann, F. Halter, W. Inauen

Gastroenterology Unit, Inselspital, University of Berne, Switzerland *Aim:* Ambulatory 24 hr-pH-manometry has been validated by several studies since the early 1990ies but its clinical relevance remains to be defined. In a retrospective study we analyzed indications, findings and therapeutic consequences of all 24 hr-pH-manometries performed at our unit. *Patients and methods:* We analyzed a total of 220 complete 24 hr-pH-manometry measurements which have been performed in 180 patients between 1991 and 1995. Mean patient age: 52 years; f:m = 1:1.1. Recording device: Gastroscan II (MIC). Probes: Ingold glass electrode combined with Sentron catheter (4 pressure microsensors) or Unisensor catheter (4 pressure microsensors and integrated Ingold glass electrode). *Results:* Indications (246; > 1/patient possible) and findings: Indications Findings normal reflux motility reflux + mot Total disorder disorder Pre-/postop. 11 30 5 25 71 (29%) Dysphagia 8 3 24 10 45 (18%) Reflux 7 20 2 11 40 (16%) Chest pain 11 11 3 7 32 (13%) Collagen dis. 1 4 9 13 27 (11%) Achalasia 0 1 13 2 16 (7%) Aspiration 2 3 0 3 8 (3%) Miscell. 1 0 3 3 7 (3%) Total 41 (17%) 72 (29%) 59 (24%) 74 (30%) 246 (100%) *Motility disorders* (54% of all patients): nonspecific motility disorders 53% (of which 69% had reflux), secondary motility disorders due to collagen disease 21%, achalasia 17%, diffuse esophageal spasm 3%, nutcracker esophagus 2%, miscellaneous 4%. *Therapeutic consequences:* recommendation of one or more measures in 71%, no new recommendation in 29%. *Conclusions:* 24 hr-pH-manometry showed in 83% of our cases pathological findings and led in 71% of our cases to a change in management. These results confirm that 24 hr-pH-manometry is a useful complementary investigation for specific indications. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Clinical Importance of Esophageal 24 Hours-pH-Manometry"

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"P P 46 1107" P 46 1107 **Effect of White Wine on Gastroesophageal Reflux in Patients with Reflux Disease**

\*C. Pehl, A. Pfeiffer, B. Wendl, H. Kaess

Dept. of Gastroenterology, Hospital Bogenhausen, Munich, Germany White wine provokes heartburn in patients with gastroesophageal reflux disease (Gastroenterology 1995; 108: 125–31). In healthy volunteers, we recently demonstrated that white wine induced gastroesophageal reflux (GER) in contrast to a comparable ethanol solution and to tap water (Dig Dis Sci 1993; 38: 93–6). The aim of the present study was to investigate whether these results could be reproduced in patients with reflux disease. *Methods:* 15 GER patients (6 F, 51–86 yrs) received in a random order 300 ml white wine or tap water together with a standardised lunch. Because of the taste of wine the patients could not be blinded. Therefore, their pH-measurements were coded and analysed in a blinded fashion. The fraction time esophageal pH < 4 (FT) was calculated for three hours after ingestion of the two beverages. *Results:* Median and range; Wilcoxon test for paired data. Wine Water FT (%) median 23.1 12.4 Range 0–88.8 0–44.9 significance p < 0.01 *Conclusion:* In accordance with the results obtained in healthy volunteers (Dig Dis Sci 1993; 38: 93–6) white wine provokes an increase in GER also in patients with reflux disease. Therefore, patients with GER disease should be advised to avoid the ingestion of white wine. Clinical practice: Epidemiology (non cancer) Nutrition: Nutrients and gut function Motility, general: Functional GI disorders } "Effect of White Wine on Gastroesophageal Reflux in Patients with Reflux Disease"

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"P P 46 1108" P 46 1108 **Decaffeinated Coffee Reduces Gastroesophageal Reflux in Patients with Reflux Disease**

\*C. Pehl, A. Pfeiffer, B. Wendl, A. Kaess

Dept. of Gastroenterology, Hospital Bogenhausen, Munich, Germany Coffee provokes heartburn in patients with gastroesophageal reflux disease (Gastroenterology 1995; 108: 125–31). In healthy volunteers, we recently demonstrated that regular coffee induced gastroesophageal reflux (GER) compared with tap water. GER could be reduced by decaffeination of regular coffee (Aliment Pharmacol Ther 1994; 8: 283–7). The aim of the present study was to investigate whether GER induced by ingestion of regular coffee taken together with a standardised breakfast could also be reduced by decaffeination of coffee in patients with reflux disease. *Methods:* 17 GER patients (7 F, 45–85 yrs) received in a double-blinded study design 2 cups (300 ml) of regular coffee (207 mg caffeine) and coffee decaffeinated by supercritical carbon dioxide extraction together with a standardised breakfast. The fraction time esophageal pH < 4 (FT) was calculated for three postprandial hour. *Results:* Median and range; Wilcoxon test for paired data. Regular coffee Decaff. coffee FT (%) median 16.4 1.6 Range 0–70.6 0–38.0 significance  $p < 0.01$  *Conclusion:* The GER induced by regular coffee in patients with reflux disease can be reduced by the decaffeination of coffee. Oesophageal gastric duodenal disorders: EG Reflux Nutrition: Nutrients and gut function Motility, general: Functional GI disorders } "Decaffeinated Coffee Reduces Gastroesophageal Reflux in Patients with Reflux Disease"

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"P P 46 1109" P 46 1109 **Apparently Life Threatening Events (ALTE) and Gastroesophageal Reflux (GOR) on Medical Treatment in Infants** F. Benkebil, P. Roy,

\*D.C. Belli

Gastroenterology Unit; Pediatric Department, HUG, Geneva, Switzerland *Introduction:* GOR is a frequent disease among infants, which may induce severe complications, such as ALTE. The prevalence of this association seems to increase with the supine sleeping position. The aim of this retrospective study was to analyze the potential association of GOR in 33 successive infants with ALTE, as well as their pH-metry and their evolution on medical treatment alone. *Patients and Methods:* 33 successive infants, median age = 28 days (3–185), were investigated by a clinical story and a 24 hr-pH monitoring (pH-m) following ALTE. They were born at a term. pH-m was realized with a DigitrapperMKIII (Synectics') on a 24 hr basis. pH-m criteria studied: % overall reflux, % sleep reflux, % awake reflux, clearance in total, pre-prandial and postprandial periods. control pH-m was performed on medical treatment (Cisapride: 1 mg/kg BW/d + Ranitidine: 300 mg/1.73 m<sup>2</sup>/d) before leaving hospital. *Results:* In medical story, 23 infants had frequent regurgitations, 6 had respiratory symptoms, 6 had previous ALTE without hospitalisation. The median duration of ALTE was 2 min (1–45). Position at the time of ALTE was similar to usual position: Supine Prone Lateral. On the total period reflux index basis, results of pH-m disclosed 2 groups: Gr A with GOR (n = 25) and Gr B (n = 8) without GOR. Both groups had no differences in clinical presentation. Gr A pH-m: % Index % Sleep % Awake Clearance Gr A 12.3 + 5.6 12.1 – 6.6 14.1 – 11.9 1.6 – 0.6 Among the 33 infants, 6 had GOR only and 10 mainly in awake, 8 only and 4 mainly in sleep period. Furthermore, the vast majority of GOR was post-prandial. On medical treatment, all patients had presented a good evolution, with normalized pH-m in Gr A. With a 5-months follow-up, no patient presented with a new episode of ALTE. *Conclusion:* GOR and ALTE can be associated. GOR was observed in both awake and sleep periods. ALTE is not related to GOR in 25% of cases. Finally, a medical treatment alone can safely be proposed to resolve this problem. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: EGD disorders in children } "Apparently Life Threatening Events (ALTE) and Gastroesophageal Reflux (GOR) on Medical Treatment in Infants"

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"P P 46 1110" P 46 1110 **The Value of Repeat Ambulatory pH Tests in the Diagnosis of GORD in Patients with No or Equivocal Oesophagitis** Thomas C.B. Dehn

Royal Berkshire Hospital, London Road, Reading, Berkshire, UK  
GORD symptoms may show daily variation: symptom severity may be greater than endoscopic oesophagitis. A normal pH test may not be representative. *Aim* Assess use of repeat pH tests in diagnosis of GORD. *Patients* 34, age 13–72 with grade 0 or 1 endoscopy (OGD). *Gp A*, (n = 15), normal acid exposure time (AET < 4.3%) and fewer than normal symptoms experienced on day of test 1. *Gp B* (n = 17) with super-sensitive oesophagus (grade 0 OGD, normal AET, symptom index (SI) > 33%). *Gp C* (n = 2) atypical symptoms, grade 0 OGD. *Results: Gp A* OGD grade 0 = 10. I = 5) normal (0–3.8%) {'} abnormal AET (6.3–11.8%) n = 4, outcome – 4 anti reflux surgery (ARS): normal {'} normal AET n = 9: no treatment 6, medical 2, achalasia 1: abnormal (4.6–8.2%) {'} normal AET = 2: no treatment 1, ARS 1 (SI 70 & 71%). *Gp B* normal (0.3–4.2%) {'} abnormal AET (4.6–8.2%) n = 3, ARS 2, medical 1. Normal {'} normal AET 2 & SI (50–83%) {'} SI (54–97%) = 13, ARS 11, medical 2. Normal {'} normal AET 2 & SI (42%) {'} normal SI (0%) = 1, no treatment. *Gp C* abnormal (5.1–14.8) {'} abnormal AET (7.0–10.0%) = 2, ARS 2. *Conclusion* 7/34 patients (20.5%) had abnormal AET on 2nd test and 13/18 confirmed supersensitive oesophagus. Repeat pH tests should be contemplated in patients with persisting symptoms, especially if endoscopy negative. Oesophageal gastric duodenal disorders: EG Reflux }" "The Value of Repeat Ambulatory pH Tests in the Diagnosis of GORD in Patients with No or Equivocal Oesophagitis"

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"P P 46 1111" P 46 1111 **Helicobacter Infection in Esophageal Reflux (ER) Disease**

\*O. Galimov, S. Fyodorov, M. Nurtdinov, A. Scumkin

Bashkir State Medical University, Ufa, Russia *Aim:* Establishing the conditions maintaining chronic local inflammatory process in the abdominal esophagus. *Methods.* Biopsy fibroesophagoscopy was carried out. Haematoxylin and eosin as well as Warthin-Starry staining technique was used in morphologic study of lower third mucosa biopsies. Urease test was carried out the same time. Two groups of patients were studied: group 1 (18 patients) ER resistant to the therapy performed, group 2 (25 ER patients) in which conservative treatment appeared effective within usual therapy time. *Results.* Helicobacter pylori (HP) in group 1 was determined in 66.7% cases and gastric metaplasia was revealed in 83.3%. The similar evidence was observed in group 2 in 16% and 24% cases respectively. Urease test was found to be positive in 16% cases (group 1) and 4% (group 2). HP revealed marked polymorphism closely adhering to the epithelial cells on the pit fundus and glands lumen. Chronic inflammatory process activation in mucosa was observed. HP was not revealed in degeneration process and pronounced active inflammation in metaplasia mucosa as well as in areas of stratified scaly noncornified epithelium irrespective of its state. Following the antireflux treatment in combination with antihelicobacter therapy no HP were revealed in all group 1 patients after control morphologic study. Positive therapy effect was obtained in 77.8% patients. Clinical evidence of esophagitis persisted in 22.2%. *Discussion.* Thus HP is significant in ER pathogenesis the fact that is supported by ineffective routine therapy. Therefore ER patients should undergo esophagus biopsy (1–4 cm from cardia) with subsequent morphologic study for HP presence. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, specific: Oesophagus } "Helicobacter Infection in Esophageal Reflux (ER) Disease"

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"P P 46 1112" P 46 1112 **Serum Prolactin Levels in Childhood Gastro-Oesophageal Reflux Disease Treated with Cisapride**

\*I. Korponay-Szab<sup>1,3</sup>, J.B. Kov<sup>1</sup>cs, A. Nagy, M. L<sup>1</sup>őrincz

Heim P<sup>1</sup> Children's Hospital, Budapest, Hungary As serotonin and cholinergic stimuli may enhance prolactin (PRL) output, effect of cisapride treatment was studied in gastro-oesophageal reflux disease (GORD). *Methods:* Serum PRL was determined in 137 children with GORD newly diagnosed by pH-metry (age 0.15–19.8 years, mean: 5.05). 83 of them had also a prospective follow up of 6–36 months with at least one control PRL during continuous cisapride (0.2 mg/kg four times i.d.) intake > 2 months, checked between 9:00–11:00 a.m. Additional antacid/ranitidine use was allowed, but those with any therapy with dopamin antagonist drugs were excluded. *Results:* Mean PRL was 10.9 ng/ml (2.3–51.64) in the untreated pts, 17.6% (24/137) had pathologically high PRL levels (Group A) and further 8 pts (5.8%) PRL levels at the upper limit of normal range for age (Group B). Mean age of Group A was 2.15 years (0.15–13.81),  $p < 0.01$  vs. Group B and the remaining pts. During cisapride treatment, there was apparently no significant change in the frequency of high PRL results (16.8%), however, in Group A and B, serum PRL level has been decreased in all but one patients to normal values, whereas other 13 pts newly exhibited high PRL. None of them had clinical signs of hyperprolactinaemia and all were well controlled regarding GORD. Continuing with the same treatment schedule and resampling after 2–3 weeks before the morning dose of cisapride, normal values were obtained in 13/13 of them. (There were no other known differences regarding fed state or time between other circumstances of samplings). Among 39 pts, who had been instructed already before the first control PRL determination to leave out the morning dose just before sampling, no high PRL occurred. *Conclusions:* High serum PRL levels are common among untreated infants and toddlers with GORD. Effective treatment normalized PRL. Cisapride did not caused long lasting hyperPRL, however, it may play some role in the still unclear PRL-related (compensative?) mechanisms. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: EGD disorders in children Hormones and receptors: Brain gut axis } "Serum Prolactin Levels in Childhood Gastro-Oesophageal Reflux Disease Treated with Cisapride"

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"P P 46 1113" P 46 1113 **Epidemiology of Gastroesophageal reflux: Predictive Factors for the Course of the Disorder and Treatment Demand** S. Bruley des Varannes<sup>1</sup>, J.-C. Grimaud<sup>2</sup>, P. Ruzsniwski<sup>3</sup>, T. Vallot<sup>4</sup>, A. Richard<sup>5</sup>, F. Gentin<sup>6</sup>

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<sup>6</sup> Gastroenterology Department, Laboratoire Glaxo Wellcome Paris The frequency of the symptoms of gastroesophageal reflux (GORD) is high and affects approximately 2/3 of individuals. The severity of the symptoms and perception by the patient obviously play a role in the request for medical care, while the reasons for medical consultation and/or following a course of treatment still remain unclear. The objective of this study was to examine the course of GORD and treatment demand, and to determine the predictive factors thereof for follow-up of a specific patient population over a period of six months. *Method:* a specific population of patients having experienced at least one episode of heartburn in the course of the past 15 days, who were consulting their general practitioner and had a history of such episodes were followed up over a period of six months. Investigation of predictive factors was conducted by multiple logistic regression and Poisson distribution. *Results:* 1115 patients were included in the study. Patients had been suffering from heartburn for 4 years and the mean duration of previous episodes was less than 1 month for 61%, between 1 and 3 months for 26% and more than 3 months for 13%. Heartburn was the main reason for consultation on DO for 86%. The mean duration of the current episode of heartburn was 3 weeks. The patients evaluated the symptoms of the current episode as causing slight discomfort (6%), discomfort (60%) great discomfort or incapacitating (34%). On D90, 4% of patients claimed they felt no discomfort due to heartburn; 51%, slight discomfort; 32%, moderate discomfort, and 6%, great discomfort. The predictive factors for discomfort on D90 were: the duration of episodes prior to DO, the frequency of the episodes and the severity of the symptoms on DO. The predictive factors for discomfort on D180 were: discomfort related to heartburn on D90, the length of time the patient had been suffering from GORD, and the main reason for consultation on DO; patients for whom heartburn was not the main reason for consultation on DO experienced a greater level of discomfort. The predictive factors for the extent of treatment demand over six months were: the levels of stress and anxiety measured on DO, age, discomfort related to heartburn on D90, severity on DO, and the frequency of episodes prior to the episode on DO. In conclusion, the severity of GORD after three and six months seems to be clearly related to the severity of previous episodes and the severity of the symptoms on DO. These criteria are not in themselves sufficient to explain the level of treatment demand. The levels of stress and anxiety of the patient appear to be closely related to future demand for treatment and further examination. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: EG Reflux }" "Epidemiology of

Gastroesophagealreflux: Predictive Factors for the Course of the Disorder and Treatment Demand"

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"P P 46 1114" P 46 1114 **Gastroesophageal Reflux Disease and Moderate to Severe Asthma. Prevalence and Clinical Management** J. Leit<sup>o</sup>,

\*A. Pinto, J. Canena, J. Reis, A. Santos, G. Lucas, M. Gomes, M. Quina

Cl<sup>inica</sup> Universit<sup>ria</sup> de Medicina Interna e Gastreterologia, Hospital de Pulido Valente, Lisbon, Portugal *Purpose:* To determine the prevalence of gastroesophageal reflux disease (GERD) in a population with moderate to severe asthma and the efficacy of anti-reflux therapy in symptoms, corticoid use and pulmonary function tests. *Methods:* We studied 29 asthmatic patients (46.2 years) with moderate to serious disease (daily steroid use/bad control of symptoms). They had previous diagnosis of asthma since 17 years, and GERD symptoms for 8.4 years. Patients were submitted to: 1) upper gastrointestinal endoscopy with biopsy of the lower esophagus; 2) 24-hour ambulatory esophageal pH recording; 3) pulmonary function tests; 4) daily registration of symptomatic score, anti-asthma medication and peak expiratory flow. Patients with GERD defined by Richter criteria were treated for 8 weeks with omeprazole 20 mg bid. After that patients were submitted to another session of pulmonary function tests. In the following 20 weeks, treatment was changed to omeprazole 20 mg once a day. By the end of this period corticoid use was checked. Statistical analysis were made with the Wilcoxon,  $\chi^2$ , and the t-Student tests. *Results:* We found a prevalence of abnormal distal acid exposure in 17 (58.6%) of asthmatics. 52.9% had upright reflux, 17.7% had supine reflux and 29.4% both. In these 17 patients 53% had hiatus hernia and 41.2% esophagitis at the endoscopy. Histopathology found esophagitis in 47.1% of the 17 patients. After medical treatment all patients became asymptomatic; Symptomatic score ( $p < 0.02$ ) and steroid use ( $p < 0.03$ ) showed statistical improvement. Although there was some improvement in pulmonary function tests this was not statistical significant. *Conclusions:* 1) High prevalence of GERD was found in the studied asthmatic population; 2) Anti-reflux medical therapy significantly improve symptomatic score and corticoid using; 3) Results highly suggest the importance of detecting abnormal acid exposure in patients with asthma, specially in those with moderate to severe disease Oesophageal gastric duodenal disorders: EG Reflux }" "Gastroesophageal Reflux Disease and Moderate to Severe Asthma. Prevalence and Clinical Management"

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"P P 46 1115" P 46 1115 **The Role of Bile in the Genesis of Oesophageal Reflux Symptoms**

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*Introduction.* Gastro-oesophageal reflux (GOR) of acid is known to be associated with oesophageal pathology as well as symptomatology. The role that duodenal contents play is not well known. Bilitec 2000, a spectrophotometric bilirubin detector, allows for the first time ambulatory monitoring of duodeno-gastro-oesophageal reflux, so symptoms can now be related to the presence of duodenal contents as well as acid in the oesophagus.

*Methods.* 59 patients referred for investigation of symptomatic GOR underwent oesophageal manometry and combined oesophageal pH and Bilitec monitoring. No patients had a primary motility disorder. All symptom events described as regurgitation or heartburn were analysed for the presence of pH < 4 and bilirubin absorbance > 0.14 in the two minutes either side of the symptom. Total, upright and supine periods were analysed for acid (pH < 4) shift and bilirubin absorbance > 0.14.

*Results.* 38 patients (64%) had significant acid reflux on pH testing, and 21 patients (36%) did not. 40 patients (68%) had significant bile reflux on Bilitec monitoring and 19 patients (32%) did not. There was good correlation between total bile and acid reflux ( $p < 0.05$  Spearman rank correlation). 394 symptom events were identified (range 1–24 events per patient). Symptoms were associated with reflux thus: Acid reflux Bile reflux Both acid & Neither alone alone bile reflux

Reflex Type	No. of events	Percentage
Acid reflux	147	37%
Bile reflux	24	6%
Both acid & bile reflux	45	11%
Neither alone	178	45%

Of the 178 symptom events that were not associated with either an acid or a bile reflux episode, 127 (71%) occurred in patients with no significant acid or bile reflux. The majority of events occurred in the upright interprandial period (173 events, 44%), 165 events (42%) occurred during the postprandial period, 42 events (10%) in the supine period and 14 events (4%) during meals.

*Conclusions.* 32% of patients had no significant acid or bile reflux, so presumably there was another pathology to account for their symptoms. Despite good correlation between acid and bile reflux, acid and bile reflux episodes do not always occur simultaneously. However, symptoms are more frequently associated with acid reflux than bile reflux, and bile does not seem to be a major cause of reflux symptoms. Oesophageal gastric duodenal disorders: EG Reflux }

"The Role of Bile in the Genesis of Oesophageal Reflux Symptoms"

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## "P P 46 1116" P 46 1116 The Incidence of Gastro-Oesophageal Reflux Disease Based on Non-Specific Symptoms in Instituted Intellectually Disabled

\*C.J.M. Bartim'e9us, M.C. Niezen-de Boer<sup>1</sup>, E.C. Klinkenberg-Knol<sup>2</sup>, S.G.M. Meuwissen<sup>2</sup>

<sup>1</sup> Bartim'e9us, Zeist, The Netherlands

<sup>2</sup> Free Univ Hosp, Amsterdam, The Netherlands The prevalence of GOR in randomly selected instituted intellectually disabled (IQ < 50) in the Netherlands is 48.2% and of oesophagitis 64.5%. In this study we investigated the incidence of GOR and RO in a population with non-specific reflux symptoms such as: behaviour difficulties as automutilation, food refusal, fear and restlessness, vomiting, regurgitation and rumination. Also predisposing factors were evaluated. In one institute 110 persons underwent a 24 hour oesophageal pH test and were scored for predisposing factors and non-specific reflux symptoms. A pathological pH test was defined as a pH < 4 > 4.5% of the measured time. Subjects with a pathological pH test (patients) were compared to those with a normal pH test (controls). In 7 cases (6.4%) the test failed for technical reasons. In 57 (55.3%) cases a pathological pH test was found, compared to 48.2% in the earlier mentioned at random population (ns). In this group non-ambulancy, the use of anticonvulsive medication, cerebral palsy and a history of GOR appear to be predisposing factors, while the suggested non-specific reflux symptoms did not discriminate for GOR. At endoscopy RO was diagnosed in 33 patients (57.9%), of which: 12 (36.4%) grade I, 15 (45.5%) gr II, 6 (18.2%) gr III/IV (Savary-Miller classification). Barrett's esophagus was found in 2 (6.1%) and 1 (3.0%) showed a peptic stricture. *In conclusion:* reflux of acid gastric contents was demonstrated in 55.3% intellectually disabled with non-specific reflux symptoms, while 57.9% of them showed RO. Subjects with non-ambulancy, the use of anticonvulsive medication, cerebral palsy and a history of GOR are at risk to develop GOR. But non-specific symptoms as behaviour problems and vomiting do not discriminate for GOR. This study demonstrate that GOR and RO are major clinical problems in intellectually disabled persons. Oesophageal gastric duodenal disorders: EG Reflux Clinical practice: Epidemiology (non cancer) Endoscopy, specific: Oesophagus } "The Incidence of Gastro-Oesophageal Reflux Disease Based on Non-Specific Symptoms in Instituted Intellectually Disabled"

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## "P P 46 1117" P 46 1117 **The Prevalence of Gastro-Oesophageal Reflux and Reflux Oesophagitis in Instituted Intellectually Disabled in the Netherlands and Belgium**

\*C.J.M. B\|f6hmer, M.C. Niezen-de Boer<sup>1</sup>, E.C. Klinkenberg-Knol<sup>2</sup>, J.H.S.M. Nadorp<sup>3</sup>, S.G.M. Meuwissen<sup>2</sup>

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GOR was estimated to be present in 10–15% of the intellectually disabled population (Sondheimer '79). Therefore, we investigated the prevalence of GOR among the inhabitants, with an IQ < 50 (n = 1607), of 6 institutes in the Netherlands and Belgium. At random 435 persons underwent a 24 hour oesophageal pH test and were scored for predisposing factors, characteristic reflux symptoms and other possible risk factors. Subjects with a pathological pH test (patients), defined as a pH < 4 > 4.5% of the measured time, were compared to those with a normal pH test (controls). In 49 cases (11.3%) the test failed for technical reasons. In 186 (48.2%) cases a pathological pH test was found (median duration of pH < 4: 12.7%). As predisposing factors scoliosis, cerebral palsy, the use of anticonvulsive medication or other benzodiazepines, and an IQ < 35 were indicated, while as reflux symptoms haematemesis, rumination, depression, and restlessness were found. As other risk factors a history of GOR, the presence of Barrett's oesophagus, and Down's syndrome were significant more often present. At endoscopy RO was diagnosed in 127 GOR patients (68.3%), of which: 58 (45.7%) grade I, 44 (34.6%) gr II, 25 (19.7%) gr III/IV (Savary-Miller). Barrett's oesophagus was found in 14 (11.0%) and 4 (3.1%) showed peptic strictures. *In conclusion:* reflux of acid gastric contents was demonstrated randomly in 48.2% intellectually disabled, while 68.3% showed RO of which 19.7% of severe degrees or with complications. Subjects with scoliosis, cerebral palsy, the use of anticonvulsive medication, an IQ < 35, haematemesis, rumination, restlessness, depression, a history of GOR, Barrett's oesophagus or Down syndrome are at risk to develop GOR. This study demonstrate that GOR and RO are major clinical problems in intellectually disabled persons. Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Oesophageal gastric duodenal disorders: EG Reflux } "The Prevalence of Gastro-Oesophageal Reflux and Reflux Oesophagitis in Instituted Intellectually Disabled in the Netherlands and Belgium"

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## "Dental Erosions and Gastro-Oesophageal Reflux in Intellectually Disabled"

\*C.J.M. Bartim'e9us, E.C. Klinkenberg-Knol<sup>2</sup>, M.C. Niezen-de Boer<sup>1</sup>, S.G.M. Meuwissen<sup>2</sup>

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Gastro-oesophageal reflux (GOR), recurrent vomiting and regurgitation may lead to erosions of the teeth. In the intellectually disabled population these conditions are frequently found. Therefore, we investigated the presence of dental erosions and GOR among intellectually disabled inhabitants, with an IQ < 50 (n = 409), recruited from 2 institutes in the Netherlands. At random 88 individuals underwent a 24 hour oesophageal pH test, dental screening and were scored for possible predisposing factors and reflux symptoms. A pathological pH test was defined as a pH < 4 > 4.5% of the measured time. Subjects with dental erosions (patients) were compared to those without dental damage (controls). 25 individuals were toothless (28.4%). In 29 out of 63 (46.0%) cases dental erosions were found. In 19 (65.5%) patients GOR was diagnosed, compared to 9 (26.5%) controls (p = 0.04), while 16 (55.2%) patients showed had a history of GOR in comparison with 7 (20.6%) controls (p = 0.008). In patients the mean duration of pH < 4 was 15.6% compared to 6.3% in controls 9 (p = 0.02). As predisposing factor an IQ < 35 (p < 0.0001) was found, while symptoms as vomiting, rumination, regurgitation, swallow difficulties and gnashing one's teeth did not increase the risk to develop these dental erosions. *In conclusion:* in this population of 63 instituted intellectually disabled persons dental erosions were diagnosed in 46%, while over 65% of them had also GOR or a history of GOR. Individuals with longer duration of pH < 4 and with an IQ < 35 are at higher risk to develop dental erosions. This study shows that dental erosions are often atypical manifestations of GOR in the intellectually disabled population. Oesophageal gastric duodenal disorders: EG Reflux  
Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Dental Erosions and Gastro-Oesophageal Reflux in Instituted Intellectually Disabled"

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"P P 46 1119" P 46 1119 **Respiratory Symptoms Due to Gastro-Esophageal Reflux Disease (GERD), a Comparative Study**

\*J.B. Van den Bogaerde, H. Van der Walt

Department of Surgery, & Gastroenterology, University of Pretoria, South Africa *Purpose:* This study compares patients with GERD and respiratory symptoms (RS), to GERD patients without RS. *Methods:* Patients with GERD, unresponsive to medical therapy underwent laparoscopic anti-reflux surgery. Pre-operative symptom scoring, endoscopy, esophageal manometry, 24 hour pH studies and DeMeester (DEM) scores were performed. RS included hoarseness, chronic cough, or asthma. Patients with RS were compared to age and sex matched controls with GERD but no RS. After laparoscopic surgery symptom scoring, endoscopy and manometry were performed. The two-tailed T test was used for statistical analysis and significance was defined as  $p < 0.05$ . *Summary of Results:* A total of 59 patients with GERD and RS were compared to 59 age and sex matched controls. The average age of RS patients and matched controls was 44.5 years (range 18–78). Mean pre-operative lower esophageal sphincter (LES) pressure in the RS group was 5.16 mm Hg and in the control group 5.66 mm Hg. This was not statistically significant. The majority of patients in the RS group had defective LES (90%) compared to 84% of control patients. Mean DEM scores were 53.08 in the RS group and 45.07 in the control group, which was not statistically significant. Clearance was normal in 40% of the RS group and in 32% of the control group (not statistically significant). Laparoscopic anti-reflux surgery was performed and LES pressure normalized in both groups. RS disappeared in all but one patient, but this patient reported a reduction of bronchodilator therapy. This confirmed that RS were caused by GERD in the majority of patients in the RS group. *Conclusion:* Patients with GERD and RS do not have significantly different acid reflux scores, LES pressures, clearance or defective sphincters when compared to those with GERD but without RS. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux Laparoscopic surgery: Therapy } "Respiratory Symptoms Due to Gastro-Esophageal Reflux Disease (GERD), a Comparative Study"

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**"P P 46 1121" P 46 1121 The Presentation of Gastroesophageal Reflux Disease; A Prospective Clinical and Endoscopic Study B. Werdmuller, A.B.M.M. v/dPutten,**

\*R.J.L.F. Loffeld

Department of Internal Medicine, Ziekenhuis De Heel Zaandam, The Netherlands A prospective study was done amongst 1432 consecutive patients referred for upper gastrointestinal endoscopy in order to assess the prevalence and severity of symptoms in patients with oesophagitis (n = 115), hiatal hernia (n = 108), Barrett's oesophagus (n = 29) and functional dyspepsia (n = 439). All patients received a questionnaire consisting 12 questions related to reflux. Eight questions were scored on a linear scale ranging from 1 till 5 (absent = 1, severe = 5). Patients with grades I or II reflux oesophagitis were significantly younger compared with patients with grades III or IV oesophagitis (p < 0.001). Patients with functional dyspepsia were significantly younger than all other patients (p < 0.0001). A concomitant hiatal hernia was present in a substantial number of patients with oesophagitis or Barrett's oesophagus. Mean symptomscore in grade I oesophagitis was 15.3 (SD 5.8); in grade II 15 (SD 6.5); in grade III 8.9 (SD 7); in grade IV 11.4 (SD 5.1); in patients with Barrett's oesophagus 10.3 (SD 6), in hiatal hernia 12.2 (SD 6.8), and in functional dyspepsia 11.5 (SD 6.7). Symptomscore in patients with Grades III or IV oesophagitis was significantly lower compared with grades I or II oesophagitis (p < 0.001). Patients with Barrett's oesophagus and/or hiatal hernia and/or functional dyspepsia had significantly lower symptomscores if compared with grades I or II oesophagitis, 10.3 (SD 6) versus 15.2 (SD 6) (p < 0.001) and 12.2 (SD 6.8) versus 15.2 (SD 6) (p = 0.01), and 11.5 (SD 6.7) versus 15.2 (SD 6) (p < 0.0001) respectively. No difference in symptomscore was present in comparing grades III or IV oesophagitis, hiatal hernia, Barrett's oesophagus and patients with functional dyspepsia. Patients with grades I or II oesophagitis had a significantly higher number of reflux complaints, mean 5.1 (SD 1.5), compared with grades III or IV oesophagitis, mean 3.5 (SD 1.8), patients with Barrett's oesophagus, mean 3.7 (SD 1.9), patients with hiatal hernia, mean 4.1 (SD 1.9) and dyspeptics with reflux complaints, mean 4.0 (SD 1.9) (p < 0.0001). The prevalence of epigastric pain, retrosternal pain, nocturnal pain, belching, heartburn, retrosternal heartburn and halitosis was significantly higher in patients with grades I or II oesophagitis, while the prevalence of dysphagia was significantly higher in patients with grades III or IV oesophagitis. Patients with grades III or IV oesophagitis had a significantly shorter history compared with all other groups. It is concluded that the presence of a majority of typical reflux symptoms has a high predictive value for the presence of grades I or II oesophagitis, dysphagia is indicative for grades III or IV oesophagitis. In cases of less symptomatology or a low symptomscore it is not possible to distinguish Barrett's oesophagus, hiatal hernia or dyspeptics with reflux complaints. Oesophageal gastric duodenal disorders: EG Reflux Endoscopy, specific: Oesophagus Clinical practice: Epidemiology (non cancer) } "The Presentation of Gastroesophageal Reflux Disease; A Prospective Clinical and Endoscopic Study"

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"P P 46 1122" P 46 1122 **Oscillatory Index in Oesophageal 24 Hour pH Monitoring for Gastroesophageal Reflux** A. Kostovski

Pediatric Clinic, Faculty of Medicine, Skopje, Macedonia Vandenas JPGN 11: 304, 1900), introduced a new parameter: oscillatory index (OI), after him Watanabe (JPGN 19: 50, 1994) used the term prolonged stable pH around 4 (PSPH4). The aim of the study was to determine the incidence and clinical significance of the OI in children investigated for GER and to correlate it with reflux index (RI). In a prospective study were evaluated 53 children (age 52 – 54 months) for GER by 24 h. pH monitoring (24 HpHM). They were separated in three groups: Group A with vomiting and failure to thrive (age 9.7 – 6.9), group B with gastrointestinal symptoms but older (142 – 120 m), and group C with pulmonary manifestations (33.3 – 31.9) GER was considered if RI was > 5%. OI and RI were analyzed, only. *Results:* In group A with RI < 5% OI was 1.23 – 0.95 and with RI > 5 was 7.93 – 4.75% ( $p < 0.05$ ). In B if RI was < 5% we found OI to be 2.28 – 1.65% (within 2 hours postprandial.) and 0.66 – 0.52% (fasting). With RI > 5% OI was 3.90 – 2.91% and 0.94 – 0.56, respectively. In C with RI < 5% OI was 2.16 – 0.96 and 0.82 – 0.87%, respectively. With RI > 5% OI was 6.63 – 3.49 and 2.65 – 4.09%. If RI was > 10% OI was 9.0 – 4.03 and 3.4 – 1.72%. Five pts were with OI > 10%. *Conclusions:* We found that OI correlates with RI (bigger in C group) and with age (group A). Pts in group C with high OI treated with prokinetics solved. So high OI can be a trigger for pulmonary symptoms. Oesophageal gastric duodenal disorders: EG Reflux }" "Oscillatory Index in Oesophageal 24 Hour pH Monitoring for Gastroesophageal Reflux"

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"P P 46 1123" P 46 1123 **Process of *Candida* Infection of the Esophagus**

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<sup>2</sup> Dept. of Clinical Nutrition, Faculty of Medical Professions, Kawasaki University of Medical Welfare, Kurashiki, Japan *Purpose:* Esophageal *Candidiasis* occurs under three conditions; an immunocompromised state (leukemia, AIDS), a fungi overgrowth state (long term administration of antibiotics, diabetes mellitus), and a non-immunosuppressive state (healthy individuals). Our experimental studies using SEM have dealt with the formation (F) process and healing (H) process of *Candida* infection under a non-immunosuppressive state. The aim of the present study was to analyze the process under two other conditions. *Methods:* Antibiotics (tetracycline: TC) and/or immunosuppressive drugs (tacrolimus, prednisolone: PSL, azathioprine: AZP) were administered to rabbits for two weeks, during or following two-week administration of *Candida albicans* suspensions, and the lesions were observed by SEM. *Results:* The F and H process of *Candida* infection was observed under all conditions. The H/F ratios of the same or post administrations of drugs were 83.3% and 80% in TC, 20% and 16.7% in tacrolimus, and 0% and 0% in PSL + AZP. In studies without drugs, there were 83.3% and 100%, respectively. Therefore, the H process was obviously suppressed only under the immunosuppressive conditions. *Conclusion:* *Candida* infection can be classified into two states; a state with H process suppression and one without H process suppression. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Immunology and microbiology: GI infections in adults } "*Process of Candida Infection of the Esophagus*"

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"P P 47 1124" P 47 1124 **Analysis of Esophageal Motility by Fast MR Imaging**

\*Y. Seki, S. Naruse, M. Kitagawa, H. Ishiguro, Y. Nakae, N. Iizuka, H. Ieda, O. Ito, T. Hayakawa<sup>1</sup>, Y. Seo, M. Murakami<sup>2</sup>

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Manometry and radiography are techniques commonly applied to analyze the esophageal motor dysfunctions. In order to find a less invasive method, we have tested a fast MR imaging to analyze esophageal motility in rabbits. <sup>1</sup>H imaging of the esophagus was carried out by using a 4.7 T magnetic resonance spectrometer for animal studies (Biospec ABX 47/40, Bruker, Germany) with a bird-cage RF-coil (inner diameter of 20 cm). Japanese white rabbits (3.0–3.7 kg) were fixed firmly on an animal support in the prone position without anesthesia, and a pair of earplugs was applied to keep out noise from gradient coils. Median sagittal images were taken by a fast gradient-echo imaging (Snapshot) at 3 images/sec. Typical values used were as follows: field-of-view 22.5 cm, data matrix 96<sup>2</sup>, spectral width 72 kHz, relaxation delay 3.4 msec, echo-time 1.9 msec, slice-thickness 6 mm, number of accumulation 1. A 6 Fr. silastic tube with a balloon at the tip was inserted nasally into the upper esophagus just distal to the upper esophageal sphincter. The balloon was then inflated to 1 cm diameter by infusion of 0.6 ml of 0.6% (w/v) ferric ammonium citrate. One to 10 sec after inflations the balloon moved from the upper esophagus to the stomach in 3–30 sec. The maximal velocity was 8.3 cm/sec. The primary peristalsis that followed the voluntary act of swallowing was also visualized. Fast MR imaging allows us to observe clearly a rapid movement of a bolus along the entire length of esophagus during swallowing. Motility, specific: Oesophagus Radiology and ultrasound: Diagnosis } "Analysis of Esophageal Motility by Fast MR Imaging"

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"P P 47 1125" P 47 1125 **Relation between Esophageal Motricity and Phonation: Experimental Study of Upper Esophageal Sphincter (UES) Using Manometry Associated with Phonation Study**

\*L. Bourat<sup>1</sup>, M. Veyrac<sup>1</sup>, S. Hachemane<sup>1</sup>, B. Arnoux-Sindt<sup>2</sup>, C. Masse<sup>1</sup>, B. Guerrier<sup>2</sup>, H. Michel<sup>1</sup>

<sup>1</sup> Service d'Hépatogastroentérologie, CHRU Montpellier, France

<sup>2</sup> Service d'ORL, CHRU Montpellier, France Pharyngeal symptoms of gastrooesophageal reflux disease (GORD) suggest existence of relations between oesophageal motricity and phonation. The aim of the study was to explore those relations in a preliminary work evaluating a new experimental method. *Patients and Methods:* Eight patients (3 m, 5 f), with dysphagia (n = 1) or GORD including 4 with pharyngeal symptoms and vocal overworking, underwent manometry with an electronic probe (GAELTEC CTG-6, diameter 3 mm) associated with vocal study of 6 phonemes, repeated 4 times with the probes studying the UES. A numerical recording of voice pronouncing test sentences was realised before and during manometry to detect a probe-induced modification of the phonation. We analysed the presence, the length and the size of the UES relaxations during phonation, in comparison with UES relaxations induced by a dry swallow. We also studied the motricity of the upper oesophageal third. The voice recordings were studied on a computerised vocal analyser called "EVA". *Results:* Out of 192 phonemes pronounced, 64 induced UES relaxation (33%). The falls in UES pressure were always equal or more than 50% of those induced by dry swallow, and in 25 cases more than 80% of this value. The mean length of relaxation was 1.75 s. Relaxations induced upper oesophageal motricity in 75% to 100% cases in 3 patients, never in the others. Out of 3 of these patients, 2 had no probe-induced phonation modifications. Pharyngeal symptoms didn't influence results. *Conclusion:* This study propose an original investigation method associating vocal and manometric study. It suggests existence of UES relaxations induced by phonation, of which some cases induce upper oesophagus motricity. Motility, specific: Oesophagus } "Relation between Esophageal Motricity and Phonation: Experimental Study of Upper Esophageal Sphincter (UES) Using Manometry Associated with Phonation Study"

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## "P P 47 1126" P 47 1126 Does Lower Esophageal Sphincter Vector Volume Change by Chronic Obstructive Pulmonary Disease?

\*G\ 'f6rg\ 'fcl Ahmet, Kayhan Bur\ 'e7ak, Kayhan Mine<sup>1</sup>, Ak\ 'e7ali Zafer, Kayhan Burhan<sup>2</sup>

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<sup>2</sup> H\ 'dcTF Ankara T\ 'fcrkiye The aim of this study was to investigate the effect of chronic obstructive pulmonary disease (COPD) on the lower esophageal sphincter (LES) vector volume, which is the anatomic and functional pressure profile of LES. *Materials and Methods:* 3 groups of patients were included. The first group consisted of 12 patients with chronic bronchitis, second group 12 patients with emphysema, and the last group 12 healthy volunteers. All the patients and healthy controls lacked gastroesophageal reflux symptoms, any gastrointestinal system disease or other systematic diseases. The smokers were also excluded. All patients underwent esophageal motility testing using a catheter with 6 distal side holes each oriented radially 60\ 'b0 from the other. The catheter was continuously perfused with water at 0.5 ml/min by a low-compliance pneumohydraulic capillary infusion system. Subjects were studied after an overnight fast. The patients received no drugs for 48 hours prior to this study. The LES pressure and vector volume were obtained using the rapid pull-through method and were measured at end-expiration. Serial readings (6 times) were taken from each of the six sensor channels permitting better detection of pressure changes even with asymmetric sphincters. The measurements were evaluated statistically (Mann Whitney U). *Results:* No significant differences existed between the mean vector volumes of group I and group III ( $p = 0.08$ ). The vector volume of group II was significantly less than that of group III (control) ( $p = 0.01$ ). The mean value of group II was also lower than that of group I ( $p = 0.015$ ). *Conclusion:* The results of this study demonstrated that COPD influenced LES vector volume. Motility, specific: Oesophagus }" "Does Lower Esophageal Sphincter Vector Volume Change by Chronic Obstructive Pulmonary Disease?"

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"P P 47 1127" P 47 1127 **Comparison of pH Probe Placement Determined by Manometry Vs a Combined pH and Lower Oesophageal Sphincter Detector** S. Carley, M.S. Gilleney, P. Vales,

\*R.F. McCloy

Department of Surgery, Manchester Royal Infirmary, Manchester M13 9WL The monitoring of oesophageal pH is now widely accepted as the most accurate method of assessing gastro-oesophageal reflux. Continuous monitoring with a probe placed 5 cm above the proximal border of the lower oesophageal sphincter for 24 hours is the agreed standard. Accurate placement of the probe is essential, too low a placement will lead to false positives, too high a placement will result in false negative investigations. The proximal LOS is commonly identified using either manometry or the Acid-Alkali interface. Synectics have developed a pH probe with a water filled lumen that allows measurement of oesophageal intraluminal pressure. Pressure measurement allows the LOS to be identified. A study was undertaken to assess the accuracy of placement of the Synectics probe compared with conventional manometry. *Methods:* Twenty patients undergoing 24 hour pH monitoring were investigated. Conventional oesophageal manometry was performed to identify the LOS. Immediately afterwards the Synectics probe was intubated. The probe was withdrawn in 1 cm steps from 60 cm to 35 cm, the AA was identified at the point that the measured pH rose above 4. A second withdrawal was performed monitoring the intraluminal pressure, the LOS was identified at the point of intraluminal pressure falling below gastric pressure. *Results:* The PM of the LOS as obtained at manometry was taken as the standard, this was compared with the PM of the LOS as determined by the Synectic probe and with the AA interface. Using the LOS detector 75% of probes would be sited between 3 and 7 cm above the PM of the LOS. Using the AA interface alone 33% of probes would be sited between 3 and 7 cm above the PM of the LOS. Use of AA interface alone is significantly less likely to result in acceptable placement of the pH probe ( $p < 0.01$ ). *Discussion:* In departments where formal oesophageal manometry is not available it has been suggested that identification of the AA interface is adequate for the placement of the pH probe. The results show that this would lead to the unacceptably low placement of 77% of probes. Use of the LOS detector reduces the error to 25%. *Conclusion:* Use of the Synectic LOS detector significantly increases the accurate placement of pH monitoring probes over identification of the AA interface alone. Formal manometry is still recommended as the standard for placement of the pH electrode. Oesophageal gastric duodenal disorders: EG Reflux } "Comparison of pH Probe Placement Determined by Manometry Vs a Combined pH and Lower Oesophageal Sphincter Detector"

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"P P 47 1128" P 47 1128 **Esophageal Motor Function in Connective Tissue Diseases** S. Unal, I. Dogan, K. Ozoran<sup>1</sup>, A. Gorgul, B. Sivri, N. Duzgun

<sup>1</sup> Gazi University School of Medicine, Department of Gastroenterology, Ankara, Turkey

Ankara Numune Hospital, Clinic of Rheumatology, Ankara, Turkey The effect of scleroderma (Sc) on esophageal motor functions (EMF) is well known. The aim of this study was to investigate the effect of Sc, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), ankylosing spondilitis (AS), dermatomyositis (DM) or polymyositis on EMF. In all patients EMF was studied by using water-perfused manometry system. Patients were diagnosed as nonspecific esophageal motor disorders (NEMD), nutcracker esophagus (NC), diffuse esophageal spasm (DES), hypertensive lower esophageal sphincter (HLES) and normal, by using the current diagnostic criteria. Table 1: Manometric findings

	Total	Normal	Abnormal	Types of abnormalities (male/female)	n (%)	n (%)	DES	HLES	NC	NEMD	RA			
Scl	37	9	28	13 (2/11)	4 (30)	9 (70)	1	8	AS	8 (8/-)	8 (100)	---	---	Dm
SLE	4	1	3	1 (1/3)	1 (25)	3 (75)	---	3	SLE	8 (1/7)	4 (50)	4 (50)	---	2
MCTD	1	0	1	1 (-/1)	1 (100)	0	---	---	---	---	---	---	---	---
Total	71	21	50	41 (58)	30 (42)	2 (2)	11	16	In 3	manometrically abnormal	of 4 patients with dermatomyositis, low contraction amplitudes have been detected in the 1/3 proximal esophagus consistent with disease, however, it was interesting that with high contraction amplitudes in the 2/3 distal esophagus they were diagnosed as NC. Not in all of the patients with Sc the classical findings of esophagus dysmotility, characteristic for this disease were observed. Manometric findings in the group of patients with RA were heterogeneous in nature. For some of patients with RA, NEMD was diagnosed because of low contraction amplitude in the body of the esophagus. Some other patients were diagnosed as NC due to observed high contraction amplitudes. This study concludes that, as well as Sc, the other connective diseases also have effects on esophageal motor function in various ways. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux }			

"Esophageal Motor Function in Connective Tissue Diseases"

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"P P 47 1129" P 47 1129 **Placebo-Controlled Study of Cisapride in Patients with Nonspecific Esophageal Motility Disorder (NEMD) Accompanied by Delayed Esophageal Transit**

\*C.W. Song, S.H. Um, C.D. Kim, H.S. Ryu, J.H. Hyun, J.G. Choe

Dept. of Internal and Nuclear Medicine, Korea University Hospital, Seoul Korea NEMD represent a difficult therapeutic challenge because of the heterogenous nature of the esophageal motor functions. We studied the effects of cisapride (CIS) on the esophageal symptoms and esophageal motor function in a group of patients (pts.) with NEMD showing delayed esophageal transit. *Method:* 70 eligible pts. were entered into a 4-week, double-blind randomized comparison of 10 mg of CIS or placebo (PLA) q.i.d. Symptom assessment, esophageal manometry following wet swallows and esophageal scintigraphy following intake of a liquid and solid bolus were performed in each patient before and after treatment. *Results:* After 4 wks, both CIS and PLA significantly reduced the symptom scores without statistical difference between the two groups. However, the global efficacy of CIS, as rated by good and excellent responses, was significantly superior to that of PLA ( $P < 0.05$ ). CIS significantly increased the number of esophageal peristaltic contractions ( $P < 0.05$  versus baseline and PLA) and significantly improved esophageal emptying of the solid bolus ( $p < 0.05$  versus PLA), while not of the liquid bolus. PLA did not have any significant effects versus baseline on these parameters. Both PLA and CIS, however, improved the distal esophageal amplitude versus baseline (no significant intergroup differences). *Conclusions:* CIS is effective and well tolerated in pts. with NEMD accompanied by delayed esophageal transit. Its efficacy may be related to its action on the esophageal body by increasing the number of peristaltic contractions and esophageal emptying of solids. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux } "Placebo-Controlled Study of Cisapride in Patients with Nonspecific Esophageal Motility Disorder (NEMD) Accompanied by Delayed Esophageal Transit"

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## "P P 47 1131" P 47 1131 Esophageal Motility and Gastric Tone in Systemic Sclerosis (SSc)

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Gastrointestinal tract is frequently involved in SSc, but only few patients became symptomatic. Esophageal motility abnormalities are reported in 75–90% of patients. Gastric involvement has been poorly studied. The most common SSc classification describes either a limited or a diffuse cutaneous form. *Aims:* to evaluate the esophageal motility pattern and the compliance of the proximal stomach in patients with limited and diffuse SSc. *Methods:* in 14 consecutive patients (13 F, age 32–63, 9 with diffuse SSc) a study of the esophageal motility (constantly perfused multilumen catheter) and gastric compliance (volume/pressure relationship) was performed (electronic barostat). During isobaric distension, the intragastric pressure was increased from 0 to 20 mmHg, up to a maximum of 600 ml or to discomfort. A manometric score was calculated in each patient based on the tracing alterations (1–3). Perception was scored by a specific questionnaire. *Results:* the esophageal motility pattern was impaired in 10 patients (71%). In limited and diffuse SSc patients the manometric score was 1.2 – 0.5 and 2.8 – 0.4 (M – SD), respectively ( $p < 0.05$ ). Volume/pressure relationship (compliance) was studied by linear regression analysis in each patient (correlation coefficient 0.95–0.99). Gastric compliance was larger in diffuse SSc patients than in both limited SSc and 6 controls (78 – 15 vs 51 – 11 e 55 – 15 ml/mmHg (M – SD), respectively;  $p < 0.05$ ). No relationship was found between the manometric score and gastric compliance in each patient. In all patients gastric distention produced gastric symptoms and the perception score was higher than controls (8.1 – 5.4 vs 1.3 – 2.5 (M – SD),  $p < 0.05$ ). No difference was found in perception score between diffuse SSc and limited SSc patients. *Conclusions:* in diffuse SSc patients gastric compliance was larger than limited SSc patients and controls. The proximal stomach could play a role in eliciting dyspeptic symptoms in SSc patients. Motility, specific: Oesophagus Motility, specific: Stomach Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Esophageal Motility and Gastric Tone in Systemic Sclerosis (SSc)"

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## "P P 47 1132" P 47 1132 Coexistence of Gastroesophageal Reflux Disease and Esophageal Dismotility in Non-Cardiac Chest Pain

\*Z. Mungan, S. Kamali, F. Besisik, G. Boztas, O. Yegins\fc, S. Kaymakoglu, R. Sezer

Istanbul Medical Faculty, Section of Gastroenterohepatology, Istanbul,

T\ferkiye Gastroesophageal reflux disease (GERD) is the most important etiologic factor of non-cardiac chest pain (NCCP). But not all NCCP patients with GERD respond to anti-reflux therapy. In a prospective study, we evaluated 43 patients with NCCP to investigate the etiology and the respond to medical therapy. All patients were referred to us from cardiology department. Male/female ratio was 24/19 and the mean age was 41.5 – 9. Patients were evaluated by means of upper GI endoscopy, endoscopic biopsy, 24-hour pH monitoring and conventional manometry. GERD and/or dismotility were diagnosed in 27 cases (62.8%). Dismotility disorders were non-specific, nutcracker, diffuse spasm and hypertensive LES (in 6, 3, 2 and 2 cases, respectively). Patients were treated with H2RA, omeprazole, cisapride or nifedipine where indicated. Fifteen patients had complete resolution of pain. Our results were as follows:  
Diagnose n (%) Respond to therapy GERD 14 (32.6) 11 (78.6) GERD + dismotility 7 (16.3) 2 (28.6) Dismotility 6 (14.0) 2 (33.3) Total 27 (62.8) 15 (55.6) Our results indicated that; 1. GERD is the most important cause of NCCP, 2. Dismotility coexistence with GER was found in 1/3 of GERD patients, 3. Respond to medical therapy is better when GERD is alone. Presence of motility disorder or association of GERD with dismotility is an indicator of poor response of medical therapy in NCCP Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus }" "Coexistence of Gastroesophageal Reflux Disease and Esophageal Dismotility in Non-Cardiac Chest Pain"

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"P P 47 1133" P 47 1133 **24 Hours Oesophageal pH, Pressure Monitoring and ECG in Patients with Non-Cardiac Chest Pain**

\*A. Baniukiewicz, S. Dobrzycki<sup>1</sup>, M. Jedynak, A. Gabryelewicz

Gastroenterology Department, Medical School Bialystok

<sup>1</sup> Cardiology Department, Medical School Bialystok *Aim:* The aim of this study was to report the findings of simultaneous 24-hour oesophageal pH, pressure monitoring and ECG in patients with non-cardiac chest pain. *Material and methods:* The study group consisted of 23 patients (10 male and 13 female, mean age 46.2 years). Long term pH/manometry was performed (within 48 hours after admission and exclusion of ischemic heart disease), using catheter with an antimony electrode and separate catheter with three solid-state pressure transducers. The data were recorded on portable data logger with 2-MByte memory capacity. (Synectics, Sweden). Simultaneous Holter monitoring has been used in the evaluation of cardiac events (Marquette Laser SXP). The analysis of data included: 1) percentage of propulsive, nonpropulsive and simultaneous contractions 2) mean amplitude and duration of contractions, 3) propagation of contractions, 4) time pH below 4.0 (%), 5) total number of reflux episodes (pH < 4.0), 6) total number of reflux episodes longer than 5 min, 7) symptom index for reflux and for dysmotility pain. An upper GI endoscopy and treadmill test were performed in all patients on a separate day. *Results:* A total of 46% of patients were found to have either reflux- or dysmotility- related chest pain. 36% of pain episodes were associated with gastro-oesophageal reflux and 26% with dysmotility. The pain was not related with oesophageal abnormality in 38% of cases. None of these pain episodes were associated with electrocardiogram changes. *Conclusion:* 24-h oesophageal pressure, pH and ECG recording is worthwhile and useful diagnostic tool of non-cardiac chest pain and offers the additional clinically valuable advantages of studying these patients. Partly supported by Medical Academy of Bialystok Grant No 513779 Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "24 Hours Oesophageal pH, Pressure Monitoring and ECG in Patients with Non-Cardiac Chest Pain"

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## "P P 47 1134" P 47 1134 **Visceral Sensitivity of the Esophagus, and Its Relation to Basal Manometric Findings**

\*M. B. Forjesson, T. Eliasson, C. Mannheimer, H. Norrsell, M. Pilhall<sup>1</sup>, P. Rolny

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<sup>1</sup> Dept. of Clinical Physiology, Östra University Hospital, Gothenburg, Sweden *Purpose of the study:* Balloon distention of the esophagus is currently used for assessment of esophageal motility and visceral sensitivity. Recently, a lowered pain threshold on balloon distention could be shown in a subgroup of patients with "non-cardiac" chest pain. However, the relation between the increased visceral sensitivity and motility has received little attention so far. The aim of the study was to study visceral sensitivity of the esophagus and its relation to peristaltic activity as well as the effects of TENS. *Methods:* 18 patients referred for esophageal evaluation, because of chest pain of unknown origin, were investigated with routine esophageal manometry and 24-h pH measurements. A balloon (Medi Tech occlusion balloon catheter 10 ml, 65 mm, USA) was placed 6 cm above the lower esophageal sphincter (LES), and in stepwise fashion filled with air in 1 ml increments, until maximum balloon volume of pain 5/10 on the Borg scale. Basal manometry before balloon distention was compared with manometry at maximum balloon volume for each patient. As a study of the effects of TENS (transcutaneous electrical nerve stimulation) on visceral pain, the balloon provocation was done in two sessions with TENS or placebo-TENS. *Results:* As a result of balloon distention, the peristaltic wave increased proximal of the balloon and decreased distally of the balloon, as shown in earlier studies. The amplitude of the peristaltic wave proximal of the balloon was positively correlated with increased visceral sensitivity ( $p < 0.05$ ). Likewise the amplitude of peristalsis at the level of the balloon was significantly ( $p < 0.05$ ) correlated with increased sensitivity, as was the duration of the peristaltic wave at the level of LES ( $p < 0.05$ ). TENS significantly reduced symptoms during the balloon distention and also had effects on the esophageal motoric activity. *Conclusion:* Esophageal visceral sensitivity was related to basal manometric findings. TENS decreases symptoms during balloon distention and thus may have an effect on visceral sensitivity. The same motoric patterns as induced by the cholinergic drug edrophonium was related to increased visceral sensitivity, thus indicating a possible connection between increased cholinergic activity (autonomic dysfunction) and higher visceral sensitivity of the esophagus. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus Motility, general: Functional GI disorders } "Visceral Sensitivity of the Esophagus, and Its Relation to Basal Manometric Findings"

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"P P 47 1135" P 47 1135 **Esophageal Manometry in Progressive Systemic Sclerosis**

\*L. Correia, R. Palma, P. Ferreira, E. Pires, J. Lopes, A. Carvalhinhos

Department of Medicine II, Santa Maria Hospital, Lisbon Progressive Systemic Sclerosis is a connective tissue disease characterised by esophageal involvement in up to 70%. Severe gastroesophageal reflux and dysphagia follow esophageal dysmotility. Impaired peristalsis of the distal body with low lower esophageal sphincter pressure are the distinguishing features. *Methods:* In order to evaluate the frequency and nature of esophageal dysmotility in PSS, 102 consecutive standard manometry recordings were reviewed (19 males, 83 females). The mean age was 48.9 years (range 17–82 years). Twenty-three (22.5%) patients had no esophageal complaints. Of the remaining 79 patients, 58 (56.9%) had heartburn, 31 of them also had dysphagia. Dysphagia was the main complain in 15 patients. Six patients had other symptoms. *Results:* Fifty (49%) patients showed aperistalsis of the distal esophagus; 14 (28%) of them with simultaneous low LES pressure; 37 (36.2%) had a normal or inespecific motility disorder of the esophageal body; 14 (13.7%) showed low amplitude peristaltic waves and one patient had low LES pressure alone. Fifty-five (69.6%) symptomatic patients and 10 (43.5%) patients without esophageal symptoms presented motility changes suggesting PSS. *Conclusions:* (1) Sixty four per cent (65/102) of our patients showed esophageal involvement by PSS, mainly (49%) smooth muscle aperistalsis; (2) The occurrence of esophageal complaints was highly suggestive of disease involvement, but more than 40% of the asymptomatic patients also presented motor abnormalities suggestive of PSS; (3) Low LES pressure occurred in 14.7% of the patients, almost exclusively (93%) associated with impaired peristalsis of the esophageal body supporting that the primary abnormality in the pathogenesis of the GER in PSS is an abnormal clearance. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: EG Reflux }  
"Esophageal Manometry in Progressive Systemic Sclerosis"

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## "P P 47 1136" P 47 1136 **Esophageal Motor Disorders in Diabetic Patients**

\*N. Pandolfo, F. Gianiorio, L. Spigno, P.L. Bozzano, F.P. Mattioli

Clinica Chirurgica R, University of Genoa, Genoa, Italy *Aim of the study* is to detect the presence of esophageal motor disorders in diabetics and to establish whether their seriousness is related to the kind of diabetes and to the presence of diabetic neuropathy. *Materials and methods:* we studied 16 patients (5 m, 11 f, mean age 44, range 19–67) affected with Diabetes Mellitus. Fourteen of those subjects were suffering from the Insulin-dependent kind of diabetes and were treated with this hormone; two patients were treated with oral antidiabetic drugs. Eight patients were suffering from peripheral neuropathy (the diagnosis was supported by cardiovascular autonomic neuropathy tests); eight subjects were complaining gastro and/or esophageal symptoms (dyspepsia and/or heartburn). A station pull-through was used to perform esophageal manometry. The Arndorfer E8M3R catheter (8 channels, 4 of them radial) was used. This catheter was connected to a computerized poligraph by means of a pneumo-hydraulic system and external transducers. The software used to compute the results was created at our Institute. *Results:* the study of esophageal motility showed the presence of alterations in all patients. In particular, mean LES pressure was lower than normal values (12.8 – 4.3 vs 20.4 – 2.4,  $p < 0.01$ ). In neuropathic patients LES pressure was lower than non-neuropathic patients (10.3 – 4.3 vs 15.4 – 2.6,  $p < 0.05$ ). A good correlation was found between LES pressure and neuropathic score. Esophageal peristalsis was altered in all patients: nine patients had lower-amplitude waves, four had higher-amplitude waves, twelve had multi-peaked waves. The duration of the primary waves was significantly longer in all diabetic patients (5.0 – 1.1 vs 3.7 – 0.5,  $p < 0.01$ ). Four neuropathic patients (score  $\geq 4$ ) had non-peristaltic waves in more than 50% of swallowings. Three of them had 20% of retroperistaltic waves. *Conclusion:* Esophageal manometry can be considered an useful method to evaluate autonomic neuropathy in diabetic patients. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus Nutrition: Metabolism } "Esophageal Motor Disorders in Diabetic Patients"

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## "P P 47 1137" P 47 1137 Oesophageal Gastric and Ano-Rectal Motility Disorders in Patients with Diabetic Neuropathy

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The impairment of the gastrointestinal smooth muscle function as a complication of the diabetes mellitus is well known. The incidence and the predilectory sites of the gastrointestinal motility disorders and its relationship to the autonomic neuropathy remains still poorly investigated. Our *objectives* were to examine the motor function at different levels of the gastrointestinal tract in diabetics. Second, whether the cardiovascular reflex test and/or the sensory tests, which are generally used to establish the degree of autonomy neuropathy in diabetes mellitus, can predict the severity of the gastrointestinal motor dysfunction. *Patients, methods:* 10 diabetics (6 male, 4 female) with different gastrointestinal symptoms were studied. The mean age was 59 (39–72) years. The mean duration of their diabetes was 17 (4–51) years. The gastrointestinal motor function was examined by oesophageal, gastric and anorectal manometry (Polygraph HR, Polygram 5.06C2, Synectics Medical). Parameters studied: Coordination of pharyngeal (PHX) contraction and upper oesophageal sphincter (UOS) relaxation; the amplitude, the duration, the propagation velocity, the wave morphology of oesophageal body (OB) contractions at 3, 8, 13 and 18 cm above the lower oesophageal sphincter (LOS); the mean pressure the relaxation time and rate of the LOS; the fasting type gastric MMC patterns; basal pressure of the external and internal anal sphincters (EAS, IAS), the recto-anal inhibitory (RAI) and contractory (RAC) reflexes, the voluntary contraction and the expulsion. All patients had an initial cardiovascular autonomic neuropathy (CAN) and a sensory neuropathy (SN) test. *Results:* The of the CAN (mean score: 5.1 – 0.8) and SN tests proved a moderate autonomy neuropathy in average. We did not observe any abnormalities of the UOS and the PHX function except one case. In the OB, the amplitude of contractions was frequently decreased (9/10 patients at 18 cm, 7/10 at 3 cm above the LOS) with prolonged duration in 50% of the cases. The rate of simultaneous waves was increased in 4/10 patients. LES abnormalities (pressure and relaxation time) was found in 5/10 cases. The presence of gastric motility disorders was prominent. We observed the absence of MMC phase III. activity in 9/10, of which complete paresis was found in 6 cases. The most frequent abnormality of the rectoanal function was the impairment of the voluntary contraction (7/10). Abnormalities of the baseline EAS and/or IAS pressures; RAC and RAI reflexes were less pronounced (4–5/10). We could not observe close correlation between the result of the CAN test and the alteration of the studied parameters of the gastrointestinal motility. In this small series of patients we can *conclude* that the abnormalities of the sphincters function are less pronounced, than the impairment of the oesophageal body or gastric motility. Second, the presence and/or the severity of the gastrointestinal motor dysfunction in diabetic patients can not be predicted by the standard CAN or SN tests. The study was supported by a grant of Ministry of Social Welfare (ETT: T-02 533/93). Motility, general: Functional GI disorders } "Oesophageal Gastric and Ano-Rectal Motility Disorders in Patients with Diabetic Neuropathy"

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"P P 47 1138" P 47 1138 **Manometric Study of Erosive Esophagitis: Correlation of Manometric Findings with Healing and Symptoms Improvement**

\*D. Kamberoglou, L. Kafadaris, A. Psichos, E. Patrikios, V. Doulgeroglou, V. Tzias, M. Lagoudakis

Endoscopy Department, 1st IKA Hospital, Athens, Greece The aim of this study was to correlate manometric findings with the natural history of gastroesophageal reflux (GER) disease in patients with erosive esophagitis. 33 symptomatic pts (17 F, 18 M; mean age 59, range: 28–82 yrs) underwent, endoscopy and manometry. Symptoms were scored (scale 0–9) before and after treatment. All patients were initially treated with omeprazole 20 mg for 4 weeks (regimen A). If healing was not achieved they continued on 40 mg for another 4 weeks (regimen B). *Results:* In 23 (69.7%) pts (Group A) esophagitis was healed on regimen A and in 25 (75.7%) (Group A1) symptoms were completely abolished. In 10 pts (Group B) esophagitis was improved on regimen A and in 5 of them complete healing was achieved on regimen B (overall healing: 84.8%). In 8 pts (Group B1) symptoms were improved on regimen A and 7 of them were completely asymptomatic on regimen B (overall symptoms eradication: 96.9%). Symptoms score after regimen A was significantly lower compared with the initial score (0.4 – 0.14 vs 5.3 – 0.26;  $p < 0.001$ ). Pts as a whole had hypotensive (8.87 – 0.75 mmHg) lower esophageal sphincter (LES) and in 5 (15%) of them a nonspecific esophageal motor disorder (NEMD) was found. When comparing group A with group B and group A1 with group B1 as far as LES pressure, wave amplitude and duration and velocity of peristalsis, no significant differences were seen. Pts in group B were more likely to have NEMD compared with group A but this was not significant. In contrast pts in group B1 (symptoms improvement) had more frequently NEMD compared with group A1 (asymptomatic) ( $X^2 = 4.1$ ;  $p < 0.05$ ). Hiatus hernia, smoking, alcohol, age and sex did not affect natural history of GER disease. *Conclusions:* 1) In 84.8% of pts with erosive esophagitis complete healing of inflammation is achieved on two-month treatment with omeprazole although nearly all (96.9%) are completely asymptomatic. 2) The presence of NEMD significantly delays symptoms eradication. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Manometric Study of Erosive Esophagitis: Correlation of Manometric Findings with Healing and Symptoms Improvement"

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"P P 47 1139" P 47 1139 **Evaluation of Patients with Gastroesophageal Reflux (GER) Referred for Surgery: The Role of Esophageal Manometry** D. Kamberoglou, L. Kafadaris, E. Patrikios, V. Doulgeroglou, V. Tzias, M. Lagoudakis

Endoscopy Department, 1st IKA Hospital, Athens, Greece GER and its complications is a very common disease in the general population. The aim of this study was to consider manometric findings in patients with GER prior to surgery. Endoscopy and manometry were performed in 55 pts (28 F, 27 M; mean age 57, range: 28–82 yrs) with long-lasting GER symptoms and continuous use of antisecretory and/or prokinetic drugs. Endoscopy showed that 12 pts had esophagitis I, 28 II, 5 III, 7 Barrett's esophagus and in 3 esophagus was normal. 23 (51%) pts had significant sliding hernia (hernia > 3 cm). As far as lower esophageal sphincter (LES) pressure (mean of highest end-expiratory pressures) is concerned, 3 groups of pts were formed: 1) Group A with normal pressure,  $\geq 10$  mmHg: 24 (44%) pts, 2) Group B with low pressure, 6–10 mmHg: 13 (23%) pts and 3) Group C with very low pressure, < 6 mmHg: 13 (23%) pts. Patients as a whole had a mean LES pressure of  $9.63 \pm 0.7$  mmHg (range: 2–24). According to these results an anti-reflux operation (Nissen fundoplication) might benefit 31 pts (group B + C) (56%). Another 7 pts with significant hiatus hernia could also be included increasing the percentage to 69% (38 pts in total). In 8 (14.5%) pts a nonspecific esophageal motor disorder (NEMD) was diagnosed and in 5 (9%) of them who also had a hypotensive LES, an alternative type of surgery might be considered. *Conclusion:* Esophageal manometry is of great value in patients with GER disease prior to surgery since it helps distinguishing the group with normal LES pressure who are unlikely to benefit from it. Nevertheless in 9% of pts with a NEMD a different surgical approach could be considered. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Evaluation of Patients with Gastroesophageal Reflux (GER) Referred for Surgery: The Role of Esophageal Manometry"

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"P P 47 1140" P 47 1140 **Correlation between Esophageal Clearance and Esophageal Motility in Patients with Gastroesophageal Reflux (GER)**

\*D. Kamberoglou, A. Psichos, S. Georgiou, V. Doulgeroglou, V. Tzias, M. Lagoudakis

Endoscopy Department, 1st IKA Hospital of Athens, Greece The aim of this study was to examine the relationship between esophageal clearance expressed by the duration of reflux episodes and parameters of esophageal body motor function. 32 patients (13 F, 19 M; mean age 53, range 22–81 yrs) with symptomatic GER and positive 24 h ambulatory pH study who also underwent endoscopy and manometry entered the study. Mean duration of reflux episodes was calculated by dividing time in min the pH was below 4 by number of episodes (total, upright and supine position). According to motor function patients were classified in two groups: A) with normal manometry (17 pts; 5 F, 12 M mean age 44.3) and B) with abnormal manometric findings (15 pts: 8 F, 7 M, mean age 62.6). 12 pts in group B had a degree of failed peristalsis (mean after 10 wet swallows 85.5%; range 0–92%), 3 abnormal wave amplitude (mean in lower esophageal third after wet swallow < 30 or > 180 mmHg), 1 incomplete lower esophageal sphincter relaxation and 1 triple-peaked contractions. 13 pts (40.6%) had erosive esophagitis and 3 (9%) a hiatus hernia (> 3 cm). All pts had abnormal 24 h pH study (mean total time with pH < 4: 13.6%; range: 4.1–40.7%). Group B pts had significantly longer reflux episodes compared with group A (2.44 – 0.48 vs 1.57 – 0.24; Mann Whitney U test:  $p < 0.05$ ) and this difference seems to be entirely due to the results in supine position (5.28 – 1.25 vs 2.44 – 0.45;  $p < 0.05$ ) since no significant difference was found in upright position (1.28 – 0.12 vs 1.09 – 0.15). No correlation was found between esophageal clearance and wave amplitude ( $r_s = 0.14$ ). Pts with dysmotility were significantly older than those with normal manometry (62.6 vs 44.3 yrs;  $p < 0.01$ ). Age correlated well with esophageal clearance ( $r_s = 0.45$ ;  $p < 0.05$ ). **Conclusions:** 1) Esophageal clearance is significantly prolonged in patients with GER and abnormal manometric findings. 2) Wave amplitude does not seem to affect the duration of reflux episodes in these pts. 3) Age seems to influence esophageal motility and subsequently to prolong esophageal clearance. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus } "Correlation between Esophageal Clearance and Esophageal Motility in Patients with Gastroesophageal Reflux (GER)"

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"P P 47 1141" P 47 1141 **Erythromycin Enhances Esophageal Motility in Patients with Gastroesophageal Reflux** G. Tzovaras,

\*E. Xynos, E. Epanomeritakis, E. Chrysos, J. Tsiaoussis, N. Kariotakis, A. Mantides, J.S. Vassilakis

Dept of General Surgery, University Hospital of Heraklio *Background:* It has been shown that i.v. erythromycin (ER) enhances gastric and esophageal motility in both health and disease, acting either as a motilin agonist or as a cholinergic factor. The *Aim* of the study was to investigate any possible effect of i.v ER on esophageal motility in patients with gastroesophageal reflux (GER). *Patients-Method:* In 15 patients with GER, proven on 24-hour ambulatory esophageal pHmetry, standard esophageal manometry was performed after giving i.v. either placebo or 200 mg ER. lactobionate (Abbot). The calculated manometric parameters of esophageal motility were the lower esophageal sphincter (LES) pressure, the amplitude and duration of peristalsis at 5, 10 and 15 cm proximal to LES and the velocity and strength of peristalsis at distal esophagus. *Results:* ER significantly increased LES pressure from  $16.5 \pm 4.6$  SDmmHg to  $41.3 \pm 9.7$  SDmmHg ( $p < 0.001$ ), without though affecting the postdeglutition relaxation of LES. ER also increased the amplitude (from  $78.5 \pm 34.3$  SDmmHg to  $97.1 \pm 39.5$  SDmmHg;  $p < 0.001$ ), the duration (from  $3.4 \pm 0.6$  SDsec to  $3.8 \pm 0.6$  SDsec;  $p = 0.005$ ) the velocity (from  $3.1 \pm 0.8$  SDcm/sec to  $3.5 \pm 1.1$  SDcm/sec;  $p = 0.0047$ ) and the strength (from  $149 \pm 84$  SDmmHg $\times$ sec to  $200.7 \pm 103$  SDmmHg $\times$ sec;  $p < 0.001$ ) of peristalsis at 5 cm proximal to LES. Similarly, ER increased the amplitude of peristalsis at 10 and 15 cm proximal to LES (from  $69.7 \pm 39.3$  SDmmHg to  $77.4 \pm 36.9$  SDmmHg;  $p = 0.049$  and from  $35.6 \pm 20.4$  SDmmHg to  $48.9 \pm 36.1$  SDmmHg;  $p = 0.004$  respectively) and the duration of peristalsis at the same levels (from  $3.1 \pm 0.6$  SDsec to  $3.3 \pm 0.5$  SDsec;  $p = 0.011$  and from  $2.7 \pm 0.6$  SDsec to  $3 \pm 0.5$  SDsec;  $p = 0.003$  respectively). *Conclusion:* I.V. ER improves the impaired esophageal motility in patients with GER. This observation might be of clinical use. Oesophageal gastric duodenal disorders: EG Reflux Motility, general: Functional GI disorders Motility, specific: Oesophagus }"  
"Erythromycin Enhances Esophageal Motility in Patients with Gastroesophageal Reflux"

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## "P P 47 1142" P 47 1142 Esophageal Motility in Patients with Gastroesophageal Reflux Disease

\*V.D. Pasechnikov, N.A. Kovaleva

Stavropol Medical Academy, Stavropol, Russia Esophageal motility (EM) has been shown to be impaired in patients (pts) with gastroesophageal reflux disease (GERD). The aim of this study was to compare EM parameters in GERD pts with controls (ctls), and to determine the effect of different treatment on lower esophageal sphincter pressure (LESP), amplitude, duration, and velocity of esophageal peristaltic contractions (EPC). EM was studied in 30 GERD pts with and without reflux esophagitis (RE), classified as Savary-Miller grades 1–2, and in 10 healthy ctls. LESP was measured by rapid pull-through technique, measurements of amplitude, duration and velocity of EPC were made at 3, 8, and 13 cm above the LES. All measurements were repeated after resolution of symptoms in pts without RE (grade 0) and after healing of RE in grade 1 and 2 pts. All pts had a significantly lower mean LESP ( $p_{1-3} < 0.05$ ) and EPC amplitude in distal esophagus (DEA) than ctls ( $p_{1-3} < 0.05$ ). Grade 2 RE pts had a significantly lower mean LESP ( $p_{1-3} < 0.05$ ) and DEA ( $p_{1-2} < 0.05$ ), than grade 0 and grade 1 RE pts. The duration and velocity of EPC were decreased in all pts when compared to ctls ( $p_{1-3} < 0.05$ ). The incidence of aperistaltic contractions was presented in 40–45% of test swallows (TS) in grade 2 RE pts, in 30–35% of TS in grade 1, and in 15–20% of TS in grade 0. All distinctable EM disorders did not change after resolution of symptoms in grade 0 pts or healing of RE in grade 1 pts. Cisapride (10 mg tid orally; 4 wks), but not antacids or H<sub>2</sub>-receptor antagonists increased LESP (53%), DEA (20%), duration (8%), of EPC in GERD pts. We conclude that impaired EM in GERD pts is preexistent factor in the pathogenesis of RE. Main EM parameters in GERD pts were significantly improved after 4 wks administration of cisapride 10 mg tid orally and did not changed after treatment by antacids and H<sub>2</sub>-receptor antagonists. Oesophageal gastric duodenal disorders: EG Reflux Motility, specific: Oesophagus Clinical practice: Management strategy } "Esophageal Motility in Patients with Gastroesophageal Reflux Disease"

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"P P 47 1145" P 47 1145 **Clinical and Manometric Response to Intrasphinteric Injection of Botulinum Toxin in Achalasia**

\*D'Onofrio Vittorio, Giardullo Nicola, Iaquinto Gaetano

Gastroenterology and Digestive Endoscopy Service, San G. Moscati Hospital, Avellino Italy Botulinum Toxin (Botox<sup>®</sup>) has been reported to reduce successfully the lower esophageal sphincter pressure (LESP) and achieve significant symptomatic relief in patients with achalasia. Experience so far suggests that Botox is safe and efficacious at least in the short term (NEJM, 332 (12): 774, 1995). *Aim:* We examined the manometric, radiological and symptomatic efficacy of intrasphinteric Botox administration in adult achalasic patients as well as the complications and adverse effects associated with this procedure. *Methods:* 8 consecutive patients (6 women, 2 men, mean age: 59 years) without a previous history of esophageal surgery or dilatation were enrolled in the study. There were 6 classic and 2 vigorous achalasia. All patients had achalasia newly diagnosed using clinical, radiological and manometric criteria. Baseline manometry, symptoms scores, radionuclide emptying test and endoscopy were obtained in all patients within one month prior to Botox, and 4 weeks after. By endoscopy, under direct vision, 100 U of Botox (25 units/ml), were injected to the four quadrants of the lower esophageal sphincter, using a standard sclerotherapy needle. *Results:* Four weeks after the treatment all patients had significant symptomatic improvement with the mean symptom score from 7.5 – 0.7 to 1.9 – 0.3 ( $p < 0.01$ ), and the LESP significantly decreased from 50 – 9 to 25.5 – 11 mmHg ( $p < 0.05$ ). Reappearance of partial peristalsis was observed in 1 of 2 vigorous achalasia but none of the classic achalasia. Neither complications nor adverse effects were booked. Before After Symptom score 7.2 – 0.8 2.8 – 0.5 Weight loss 1.6 – 0.2 0 Dysphagia 3.2 – 0.4 1 – 0.2 Chest pain 1.8 – 0.4 0 Regurgitation 2.3 – 0.7 1.8 – 0.3 LESP (mmHg) 50.4 – 16.4 42 – 8.4 *Conclusions:* 1) Botox injection is safe and effective in the treatment of achalasia. 2) Botox treatment produces significant symptomatic improvement and reduction of LESP. 3) Long term randomized studies will need to compare the efficacy, safety and costs of the different treatment options in achalasia. Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Motility, specific: Oesophagus Endoscopy, general: Instrumentation, therapy } "Clinical and Manometric Response to Intrasphinteric Injection of Botulinum Toxin in Achalasia"

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"P P 47 1148" P 47 1148 **Relationship of Manometric Changes with Symptomatic Response Following Pneumatic Dilation in Achalasia Cardia Patients** H.M. Shahi,

\*Rakesh Aggarwal, A. Misra, D.K. Agarwal, S.R. Naik

Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, India *Introduction:* Achalasia cardia is frequently treated with pneumatic dilation, to reduce the lower esophageal sphincter (LES) pressure. Relationship of changes in esophageal manometric findings following dilation with symptom relief is however unclear. We therefore decided to study this relationship. *Methods:* 16 achalasia patients underwent esophageal manometry before and one month after pneumatic dilation. At each time, LES pressure and body motility were recorded. Mean basal esophagus to gastric pressure gradient (MIEP-MIGP), a measure of esophageal retention, was calculated. *Results:* 12 patients had good dysphagia relief (GR) and four had poor relief (PR). Manometric changes were similar ( $p = ns$ ) in GR and PR groups [data as median (range) in mmHg]:

Parameter	Good relief (n = 12)	Poor relief (n = 4)
LES pressure	42 (17–51)	18 (3–39)
MIEP-MIGP	5.9 { - } 1.9	2.5 { - } 2.9 ( { - } 1.8 to 12.0) ( { - } 5.3 to 3.0) (0.3 to 3.5) ( { - } 5.8 to { - } 1.3)

In PR patients, dysphagia persisted despite reduction in LES pressure and amelioration of esophageal retention as evidenced by reversal of MIEP-MIGP. *Conclusions:* Esophageal manometric changes may not correlate with symptomatic response. Persistent dysphagia in achalasia patients who respond poorly to dilation may be related to abnormal peristalsis than to LES hypertension. Motility, specific: Oesophagus Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Endoscopy, specific: Oesophagus } "Relationship of Manometric Changes with Symptomatic Response Following Pneumatic Dilation in Achalasia Cardia Patients"

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## "P P 47 1149" P 47 1149 Operative Treatment of Achalasia: Our Experience

\*E. Battaglia, L. Dughera, A.M. Serra, V. Debernardi, G. Buonafede, P.R. Mioli, E. Masenti, G. Emanuelli

Dept. of Clinical Pathophysiology, University of Torino In the period January 1985–January 1996, 168 cases of esophageal achalasia (62 m, 106 f, age range 11–85 yr) were referred to our Department for evaluation and treatment. Symptoms' onset was comprised between 3 months and 20 years, and their incidence was as follows: dysphagia (99.5%), weight loss (92.2%), food regurgitation (71.7%), non-cardiac chest pain (57%), pyrosis (30.7%), nocturnal pulmonary aspiration (29.4%), nausea (23%). Radiological abnormalities (esophageal body dilatation, "bird's beaking" of the lower esophageal sphincter (LES), tertiary contractions, etc) were found in 80% of patients. Endoscopic evaluation showed abnormal findings (erosive esophagitis, *Candida* esophagitis, food impaction) in 72% of cases. Esophageal scintigraphy was always abnormal, with a residual of radioisotopic compound of 80–100% after 20 minutes from ingestion. Manometry showed typical aperistaltic features and lack of LES relaxations in all patients, with an average LES pressure of 32.5 – 10 (SEM) mmHg (n.v. 10–40 mmHg): 11 patients (5.6%) had a progression to achalasia from a previous diagnosis of diffuse esophageal spasm. All patients were initially treated with sublingual nifedipine, 10–40 mg/day. Then, most of them (160 pts) underwent an operative treatment, consisting of Heller myotomy associated with anti-reflux procedures (140 pts, 83%), and pneumatic dilatation of cardia (20 pts, 12%). Pneumatic dilatation consisted of 3 sessions, carried out at one-week intervals. Post-operative course was almost uneventful, and 6 complications (4 cases of pneumonia and 2 pleural effusions) were observed; no deaths were reported. Following pneumatic dilatation, one patient underwent surgery due to esophageal perforation. After 6 months, esophageal manometry documented a return of esophageal peristaltic activity in 16 (11%) of patients undergoing surgery. After 1 yr, all patients having a surgical procedure were asymptomatic, whereas only 2 (1%) of those treated by pneumatic dilatation of the cardia were asymptomatic. In our experience, a surgical approach to achalasia is a safe and effective therapeutic option, whereas less convincing results have been obtained with pneumatic dilatation of the cardia. Clinical practice: Management strategy Motility, specific: Oesophagus Endoscopy, specific: Oesophagus } "Operative Treatment of Achalasia: Our Experience"

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## "P P 47 1151" P 47 1151 Achalasia: Results of Esophagomyotomy in Patients Having Failed to Respond to Dilatation Therapy

\*E.P. Cosentini, G. Berlakovich, J. Zacherl, G. Stacher-Janotta, G. Stacher, E. Wenzl

Div. of General Surgery and Psychophysiology Unit, Dept. of Surgery, University of Vienna, Währinger-Gürtel 18–20, 1090 Vienna, Austria

**Introduction:** Balloon dilatation under endoscopic control is commonly accepted as the first choice of treatment for achalasia. However, adequate treatment results are obtained in a significantly smaller proportion of patients than with esophagomyotomy.

**Patients:** We investigated the results of Gottstein-Heller myotomy with or without antireflux procedure in 19 female and 19 male patients, in whom pneumatic dilatation had failed to yield satisfactory results. At the time of investigation the patients' age ranged from 17 to 85 years (median, 54 yr), the time elapsed since the operation from 0.5 to 24 yr (M, 6 yr). In 33 patients the myotomy had been combined with a fundoplication and in 2 with a fundopexy. Before myotomy they had suffered from severe to very severe dysphagia for liquid, semisolid and solid meal constituents and had undergone 1 to 8 dilatations.

**Results:** At the time of investigation 15 patients were entirely symptomfree. Eleven patients could stomach their ingesta only by drinking after each bite; before myotomy, this had been the case in all patients. Three patients had dysphagia of intermediate degree for solid meal constituents and 1 only slightly less severe dysphagia than before the operation. In one patient the operation had not yielded any positive effect. In all except of the two latter patients the body weight had increased by 5 to 45 kg (M, 13.5 kg). Each one patient suffered from reflux esophagitis, a cicatricial hernia, and a sliding hiatal hernia, all of which had arisen after the myotomy. Two patients, who postoperatively had been more or less symptomfree, had recommenced to suffer from dysphagia 2 and 3.5 yr later. Their dysphagia, however, was less intense than before the operation and their weight was markedly higher. In 24 patients the passage through the esophagus of a 10-ml water-bolus labelled with 250 mCi <sup>99m</sup>Tc sulphur colloid could be studied with the patient in the supine position. A normal passage was present in only one patient, and a slightly delayed passage in 2 others. In 8 patients between 23% and 84% of the bolus and in the remaining 13 the entire bolus was still present in the esophagus after 120 s. Manometric investigations performed in 23 patients revealed that the resting pressure of the lower esophageal sphincter was 23% to 29% lower than before myotomy and higher in only one patient, who also suffered from severe dysphagia.

**Conclusion:** It is concluded that the surgical treatment of achalasia yields good results in a high proportion of patients, in whom dilatation treatment had failed to achieve satisfactory results. }

"Achalasia: Results of Esophagomyotomy in Patients Having Failed to Respond to Dilatation Therapy"

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"P P 48 1152" P 48 1152 **Is Routine Conscious Sedation or Topical Pharyngeal Anesthesia Necessarily in Upper Emergency Endoscopy in Bleeding Patients?**

\*S. Mosca, A. Balzano, V.P. Rocco, A. Bove, A. Sergio, T. Gigliotti

Dept. of Gastroenterology A. Cardarelli Hospital Naples Italy Upper emergency endoscopy in bleeding is frequently performed in cirrhotic patients. A routine IV conscious sedation may complicate the status of these patients at high risk of encephalopathy because of the bleeding status. *Patients:* in the last 12 months [May 1995–April 1996] we have performed all the upper emergency endoscopies for bleeding without any routine medication. The patient was reassured and was gently and energetically requested to cooperate for the success of the procedure. With the patients in the left decubitus position, gentle intubation was achieved with an endoscope (generally a 10.5 mm). During the procedure the patients were continuously reassured by the physician or by the assistant. We have performed 583 endoscopies in bleeding patients: of these 192 were performed in cirrhotic patients: 56 patients required sclerotherapy and 26 patients a balloon tamponade. An injective hemostasis was performed for bleeding ulcers in 77 patients. No success of procedure or diagnostic or therapeutic may be imputed to patient cooperation. *Conclusion:* Routine IV conscious sedation or topical pharyngeal anesthesia is unnecessary in upper endoscopy performed for bleeding. The patient may be successfully prepared with verbal assurance by physician and continuously reassured during the procedure or by physician or by technician. This patient preparation may have advantage especially in the group of cirrhotic bleeding patients that are at high risk of complication by IV sedation. Endoscopy, general: Preparation, management Endoscopy, general: GI bleeding } "Is Routine Conscious Sedation or Topical Pharyngeal Anesthesia Necessarily in Upper Emergency Endoscopy in Bleeding Patients?"

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## "P P 48 1155" P 48 1155 Risks, but No Benefits of a Midazolam-Fentanyl Combination as Premedication of ERCP

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The benefit of combining benzodiazepine with an opioid as premedication for more complex endoscopic procedures remains poorly defined. Therefore, we performed a double blind, randomized, placebo controlled study comparing midazolam plus fentanyl with midazolam alone as premedication of ERCP. *Method:* Consecutive in-patients (n = 115) undergoing diagnostic and/or therapeutic ERCP were randomized to receive either an intravenous combination of midazolam (5–15 mg) plus fentanyl (0.05 mg standard dose) or midazolam alone (5–20 mg); midazolam was individually titrated. Oxygen saturation (SaO<sub>2</sub>), blood pressure, heart rate and arrhythmias were monitored continuously, using a multifunction monitor. The degree of sedation during the examination and the patients' acceptance were rated. The two groups were comparable with respect to age, sex, body-weight, risk-group (ASA), initial SaO<sub>2</sub>, indication, type, duration of the procedure and titrated dose of midazolam. *Results* are expressed as median (range). midazolam + fentanyl (n = 58) midazolam + placebo (n = 57) p

Parameter	Midazolam + Fentanyl (n=58)	Midazolam + Placebo (n=57)	p-value
Minimum SaO <sub>2</sub> (%)	88 (70–95)	90 (66–95)	0.013
SaO <sub>2</sub> (%)	7.0 (2–22)	5.0 (3–28)	0.009

Following midazolam-fentanyl SaO<sub>2</sub> dropped below 85% in 16 patients compared to 4 with midazolam (p = 0.004). Besides fentanyl, age and risk-groups II and III were independent predictors of hypoxemia. Transient fall of blood pressure, increase of heart rate, incidence of arrhythmias and patients' acceptance were not significantly different. There was a trend to a more effective sedation in the midazolam-fentanyl group (p = 0.063). In *conclusion*, the combination of midazolam-fentanyl increases the risk of respiratory depression in comparison with midazolam alone. There was no significant difference concerning the benefits, f. e. degree of sedation and patients' acceptance. The theoretical premise that fentanyl used in combination should reduce the dose of midazolam was not confirmed. Endoscopy, general: Preparation, management } "Risks, but No Benefits of a Midazolam-Fentanyl Combination as Premedication of ERCP"

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"P P 48 1176" P 48 1176 **Optimal Number of Biopsy Specimens and Brush Cytology in the Diagnosis of Gastric and Colorectal Malignancies** L. Demirtaş, Y. Yazgan,

\*M. Özcelik, A.K. Güneş, M. Danacı

GATA Haydarpaşa Training Hospital, Istanbul, Turkey

Retrospective studies have indicated that endoscopic biopsies yielded a positive diagnosis in 57–86% and cytology in 71–98% of colon cancers. The aim of our study is to identify the optimal strategy of biopsies and cytology in cases with mass lesions in upper and lower gastrointestinal system.

Group	Cytology alone (%)	4 biopsies (%)	6 biopsies (%)	8 biopsies (%)	10 biopsies (%)
Gastric	75.00	52.08	87.50	89.18	93.28
Colorectal	76.47	79.41	88.24	92.86	94.12

261 patients with gastric or colorectal masses were included in the study. Biopsy specimens were put into 4 vials, with 4 biopsies in the first, 2 in the second, 2 in the third and 2 in the fourth one. Based on our data, 9 discrete combinations of biopsies and cytologies were made and the results shown in the table were found. Lower diagnostic rate in first biopsies was found (52.08%) in gastric malignancies, when compared to the 79.41% in colorectal cancers. The percentage of cytology alone was comparable in both groups (75% and 76% respectively). When cytology was added to the first four biopsies in gastric malignancies, the rate increased to 87.50%, and to 89.18% in colorectal malignancies. There seemed to be no difference between cytology and 10 biopsies in both groups. With combination of biopsy and cytology, diagnosis could not be made in 4–6% of cases. Cytology and 6 biopsies had the same diagnostic range as 10 biopsies did and cytology added to 10 biopsies did not increase this diagnostic range significantly. We conclude that cytology and 6 biopsies appear to be the optimal strategy in the diagnosis of gastric and colorectal malignancies.

Oncology, specific: Stomach  
Oncology, specific: Colon, rectum  
Endoscopy, general: Instrumentation, diagnosis }

"Optimal Number of Biopsy Specimens and Brush Cytology in the Diagnosis of Gastric and Colorectal Malignancies"

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## "P P 48 1183" P 48 1183 Preoperative Parathyroid Imaging Using Echoendoscopy in Primary Hyperparathyroidism: A Prospective Preliminary Study

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<sup>4</sup> Department of Radiology, Hopital Haut-L<sup>\</sup>'e9v\ 'eaeque, 33604 Pessac, France *Purpose:* Parathyroid adenomas responsible for primary hyperparathyroidism (PHPT) are difficult to detect preoperatively. As most of parathyroid adenomas arise below and/or behind the thyroid gland, and as abnormal parathyroid glands are situated in the mediastinum or in a deep cervical location, we assessed the ability of echoendoscopy (EE) to localize parathyroid adenomas. *Methods:* 6 females and 3 men (age 54.4 – 16.5 years) with PHPT (calcium concentration 2.9 – 0.4 mmol/l with inappropriate parathormon levels 297.6 – 284.7 ng/l) were studied. A single eutopic parathyroid adenoma was confirmed at surgery in 7 cases. One patient became normocalcemic after a percutaneous infusion of ethanol in the adenoma. One patient had no lesion at surgery. All patients underwent ultrasonography (US), Tc 99 m sestamibi scanning, CT scanning or magnetic resonance imaging (MRI) and EE before undergoing initial neck exploration. EE was performed by a single physician, under general anesthesia, using 7.5 and 12 Mhz probe (Olympus EUM20). The duration of the exam was 15 minutes. The operative findings were recorded and correlated with the results of preoperative studies. *Results:* 6 of the 8 adenomas were correctly localized using EE and sestamibi scanning. 2 of these tumors were undetectable using CT scanning/MRI. Conversely CT scanning/MRI detected 2 adenomas that were not identified by EE and sestamibi scanning. US correctly localized only 4 adenomas. In one case; sestamibi scanning, MRI and EE visualized a lesion which was not found at surgery. *Conclusion:* the sensitivity of EE to detect parathyroid adenomas was roughly equivalent to that of sestamibi scanning or CT scanning/MRI. Thus, EE may be a useful tool for the preoperative investigation in patients with PHPT. Our results have to be confirmed in larger series of patients, especially in patients with small, and/or abnormal located parathyroid glands and above in patients with persistent or recurrent PHPT after surgery. Echoendosonography: Echoendoscopy }" "Preoperative Parathyroid Imaging Using Echoendoscopy in Primary Hyperparathyroidism: A Prospective Preliminary Study"

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"P P 49 1186" P 49 1186 **Uncommon Locations of Hydatid Disease** M. Safioleas,

\*E. Misiakos, Gr. Kouraklis, Chr. Manti, E. Karanikola, A. Papachristodoulou

2nd Department of Propedeutic Surgery, Athens University Medical School, Laikon General Hospital, Athens, Greece Hydatid disease is still a challenging diagnostic and therapeutical problem especially in endemic countries; the most commonly involved organs are the liver, the lung and less often the spleen. The aim of this study is to present the possibility of other locations of hydatid cysts in solid organs or other anatomic sites rarely encountered. During the last 20 years, 12 patients were operated on for uncommon locations of hydatid disease. There were 6 men and 6 women with a age range of 27 to 86 years (mean age 60.4 years). There were 2 cases with hydatid cysts located in the gallbladder, 4 cases in the pancreas, one case in the kidney, one case in the thyroid gland, one in the breast, one in the pericardium, one in the supraclavicular region and one in the thigh. Clinical symptomatology varied according to anatomic location and preoperative diagnosis was accomplished with radiological examinations, ultrasound or computerized tomography. Surgical treatment included cholecystectomy in the 2 cases with hydatid cysts in the gallbladder, omentoplasty or peripheral resection of the pancreas in the 4 pancreatic cases, nephrectomy in the kidney case, lobectomy in the thyroid case and cyst excision in the rest cases. In all cases histopathological examination of the surgical specimens confirmed the diagnosis. One patient with pancreatic resection died postoperatively, while the remaining 11 patients did not have any significant complications. In conclusion, hydatid disease should be included in the differential diagnosis of cystic masses in solid organs or other anatomic sites especially in endemic countries; hydatid cyst excision is curative and confirms the diagnosis. Radiology and ultrasound: Diagnosis } "Uncommon Locations of Hydatid Disease"

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"P P 49 1187" P 49 1187 **Parasitic Liver Disease**

\*A.E. Mohamed, M.A. Al Karawi, Z. Ghandour

Dept. of Gastroenterology, Armed Forces Hospital, Riyadh, Saudi Arabia Several parasites infest the liver and biliary tree. Ascaris may be present in the liver or in the biliary tree and cause obstructive jaundice due to worms or associated stones. In schistosomiasis the liver may be involved early or later leading to periportal fibrosis and portal hypertension. We have studied 72 patients with hepatosplenic schistosomiasis, liver ultrasound showed periportal fibrosis in 48 and in 30 liver biopsy showed bilharzial granuloma or fibrosis. In amebiasis tender hepatomegally may present during the acute phase while more commonly in chronic carriers, an amebic abscess develops. We have treated 3 patients with amebic liver abscess in two of which percutaneous drainage was done. Hydatid cysts of the liver may be large and cause pressure on the liver or rupture into the biliary tree causing obstruction. In our unit we have introduced endoscopic management for such cases and we have treated successfully 10 patients. Between 1985–1990 we have treated 22 patients with albendazole alone. After 1990 we have introduced combination therapy in 19 patients (Albendazole + Praziquantel) and was found to be more effective than albendazole alone. Ten other patients had percutaneous drainage of a huge liver cysts. Liver flukes infest liver and can cause biliary tree obstruction causing recurrent cholangitis. One of our patients from Thailand had obstructive jaundice and ERCP showed multiple *Clonorchis sinensis* worms and an associated cholangiocarcinoma. During 3 years we have studied 208 patients with Human Dicrocoeliasis, 16 of these patients had disturbed liver functions and 10 patients had gall-bladder or biliary tree disease. Immunology and microbiology: GI infections in adults } "Parasitic Liver Disease"

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"P P 49 1188" P 49 1188 **Eliza in Diagnosis of Cryptosporidiosis S. El-Ghoneimy,**

\*M. El-Khashab, Aboul-Maged

Faculty of Medicine Zagazig University Egypt Many authors considered *Cryptosporidium* as one of the main causes of diarrhoea in man. In the present work stool analysis and ELISA test were performed to detect *Cryptosporidium* oocyst and antibody in the stool and sera respectively of 206 patients with acute diarrhoeal disease and 15 healthy individuals as a normal control group. It was found that *Cryptosporidium* oocysts were detected in 35 cases (16.9%). Most of them aged less than 10 years, with insignificant difference between male and females. Stool of *Cryptosporidium* infection was offensive, watery and yellowish. ELISA was positive in 32 out of 35 cases having *Cryptosporidium* oocyst with 91.4% sensitivity and was negative in 32 out of 40 negative cases by stool examination with 80% specificity. Thus *Cryptosporidium* oocyst should be looked for in routine examination of diarrhoeal stool especially of young patients. ELISA is a simple easily performed serological test with high sensitivity and specificity in detecting *Cryptosporidium* infection. Association of other parasitic infections with cryptosporidiosis did not affect the optical density (O.D.) reading of infected cases and to avoid cross reaction, fractionated oocyst antigen may improve the test specificity. Immunology and microbiology: GI infections in adults } "Eliza in Diagnosis of Cryptosporidiosis"

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"P P 49 1189" P 49 1189 ***Salmonella Typhimurium INV Mutants Invade Intestinal M Cells***

\*M.A. Clark, B.H. Hirst, M.A. Jepson

Department of Physiological Sciences, Medical School, University of Newcastle upon Tyne NE2 4HH, UK Invasion of intestinal epithelial cells is a crucial step in *Salmonella* pathogenesis. Recent studies employing ligated murine intestinal loops have demonstrated that the specialised antigen sampling intestinal M cells are the primary site of *Salmonella* invasion. While the precise mechanisms and genetic basis responsible for *Salmonella* invasion of epithelial cells remain obscure, mutagenesis studies have identified a number of genetic loci necessary for internalisation of *Salmonella* into cultured epithelial cells. The significance of these loci *in vivo* is, however, unclear. The aim of this study was to investigate the significance of one such locus, *inv*, during *Salmonella* invasion of M cells. *S. typhimurium invA* (SB111) and *invG* (mutant 83) mutants which are severely attenuated for invasion of cultured cells and their parental strains (SR11 and TNP-5, respectively) were incubated in Peyer's patch-containing ligated intestinal loops which had been created in anaesthetised mice. After incubation, the tissues were harvested, fixed and dual stained for bacteria and M cells. Examination by confocal laser scanning microscopy revealed that both parent and mutant strains readily adhered to and invaded M cells: no difference could be detected between parent and mutant strains in their interaction with these cells. Bacterial association with M cells was accompanied by a redistribution of *Ulex europaeus* I staining of M cells and by the formation, as detected by scanning electron microscopy, of M cell surface protrusions indistinguishable from the "membrane ruffles" previously described in association with other wild type *Salmonella*. These observations demonstrate that *Salmonella* invasion of murine M cells may proceed via mechanisms independent of the *inv* locus which is essential for invasion of cultured cells. The multifactorial nature of *Salmonella* invasion may account for the ability of many *Salmonella* to infect a range of hosts and to invade a variety of cell types. Immunology and microbiology: GI infections in adults } "Salmonella Typhimurium INV Mutants Invade Intestinal M Cells"

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"P P 49 1190" P 49 1190 **Organ Involvement in Hepatointestinal Schistosomiasis**

\*Z. Ghandour, A.E. Mohamed, M.A. Al Karawi, M.I. Yasawy

Armed Forces Hospital, Riyadh, Saudi Arabia The endoscopic, radiological and histological findings in several of our patients with schistosoma mansoni infection are described. Seventy two patients had hepatosplenic schistosomiasis. Endoscopic sclerotherapy was effective in 45 patients with bleeding varices. Ultrasound of the liver was suggestive of peri-portal fibrosis in 48 of these 72 patients and in 30 of whom liver biopsy demonstrated schistosoma granuloma or periportal fibrosis. Gastroscopy showed congestion erosions or ulcerations in the stomach in 40 of these patients and in 23 patients in the duodenum. Schistosoma ova with inflammatory changes were seen in endoscopic biopsies from the stomach in three out of twelve and five out of eight duodenal biopsies. The colonoscopic findings were suggestive of schistosomiasis. Eight patients had schistosomal polyps and one had colonic calcifications. Schistosoma ova were seen in surgical specimens from patients presenting with acute abdomen due to appendicitis in six, cholecystitis in three and mesenteric vein thrombosis in three, in one of which mesenteric angiogram showed a blocked inferior mesenteric vein by ova. Immunology and microbiology: GI infections in adults } "Organ Involvement in Hepatointestinal Schistosomiasis"

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## "P P 49 1191" P 49 1191 Intestinal Immune Cells in *S. Stercoralis* Infection

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Federal University of Rio de Janeiro, Brazil

<sup>1</sup> The Medical College of St. Bartholomew's Hospital, London, UK *Introduction:* *Strongyloides stercoralis* may cause a wide spectrum of disease in humans, ranging from a chronic asymptomatic infection to a hyperinfective, often fatal syndrome. In rodents, spontaneous expulsion of related parasites after experimental infection occurs. Mast cells, goblet cells and eosinophils have been identified as possible effectors of this expulsion. The aim of the present study was to assess the intestinal immune response in chronic mild strongyloidiasis. *Methods:* We performed a jejunal biopsy in 19 immunocompetent patients with at least one positive stool examination for *S. stercoralis* and few or no symptoms, and in 7 healthy controls. Specimens were processed for histopathological analysis and by the three-stage immunoperoxidase technique, using the following monoclonal antibodies: CD2, CD3, CD4, CD8, TcR- $\alpha/\beta$ , RFD1, RFD7 (macrophage markers), Ki67+ (proliferating) cells, HLA-DR and collagen IV. In addition, CD25+ cells, mast cells, IgE expressing cells, calprotectin-containing cells (Mac 387+) and neutrophil elastase+ cells were stained by the alkaline phosphatase method. Positive cells were counted using a Seescan Image Analyzer. *Results:* Jejunal morphology and the numbers of different T-cell subsets, mast cells, eosinophils and goblet cells were unaffected by *S. stercoralis* infection. Conversely, the number of mature macrophages and of dividing enterocytes in the crypts was reduced. Crypt enterocytes did not express HLA-DR in both groups. The expression of HLA-DR by villus enterocytes was similar in patients and controls. There were no activated (CD25+) cells in the mucosa of either patients or controls. *Conclusions:* Architectural damage to the mucosa and the resulting immune-mediated diarrhoea apparently do not develop due to the absence of an immune response against the parasite. On the other hand, the infection is allowed to persist for several years. Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation Immunology and microbiology: GI infections in adults } "Intestinal Immune Cells in *S. Stercoralis* Infection"

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## "P P 49 1192" P 49 1192 Does Serum Angiotensin Converting Enzyme Level Raise in Familial Mediterranean Fever?

\*H. Simsek, A. Kadayifci

Hacettepe University Medical School, Ankara, Turkey

The diagnosis of familial Mediterranean fever (FMF), which is a periodical disease of unknown origin, has usually been based on a knowledge of ethnic status, a positive family history, the exclusion of other disease entities, in addition to clinical findings of polyserositis and elevation of acute-phase reactants during periodic attacks. However, diagnosis of FMF is difficult for clinicians in some cases and there is no specific biological test for FMF. Angiotensin converting enzyme (ACE) is a carboxypeptidase that hydrolyses angiotensin I to angiotensin II and widely found in human tissues. ACE is also produced by sarcoid granulomata cells and elevated serum ACE level is a useful test in the diagnoses of sarcoidosis and monitoring the activity. Persistent raise of serum ACE level in FMF was claimed in a recent case report and FMF has been suggested another cause of raised serum ACE level. However, this claim has not been proved by another study up to now. In this study we aimed to investigate the serum ACE level in our FMF group and to clarify the idea whether ACE level may be a marker of disease or this relation was a fortuitous one. Fifteen patients (6 male and 9 female, with a median age of 27) followed at our center with a diagnoses of FMF were enrolled to the study. The serum sample was obtained in asymptomatic phase of disease in 13 patients and during an acute attack in 2 patients. Serum ACE level was measured by EIA and results expressed as U/L. The normal range of serum ACE level was 5–10 U/L and the minimum detection limit was 1 U/L in this method. The serum ACE level was found in a minimal level in all patients and no elevation was detected. *Conclusion:* This study clearly showed that serum ACE level has not been raised in FMF patients. It is well known that ACE production is increased in only sarcoidosis and certain other granulomatous diseases. Therefore, it seems that, there is no reason for the elevation of this enzyme level in FMF patients. Immunology and microbiology: Inflammation } "Does Serum Angiotensin Converting Enzyme Level Raise in Familial Mediterranean Fever?"

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"P P 49 1193" P 49 1193 **Study of Antigenic Sites on the Asialoglycoprotein Receptor Recognize by Autoantibodies**

\*O. Hajoui, F. Alvarez

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**Background & Aims:** Antibodies against the asialoglycoprotein receptor are frequently found in sera of patients with autoimmune hepatitis. The study was designed to identify the antigenic sites on the receptor recognized by specific anti-asialoglycoprotein receptor antibodies.

**Methods:** Isolated asialoglycoprotein receptor from normal human liver was used as an antigen in an ELISA test to detected specific antibodies in the sera of patients with autoimmune hepatitis. Positive sera were further tested against the same antigen by Slot blot, Western blot and immunoprecipitation. The mature, unglycosylated and partially glycosylated forms of the asialoglycoprotein receptor synthesized by HepG<sub>2</sub> cells were tested against positive patients' sera. The mature receptor in HepG<sub>2</sub> differs from the receptor in human normal liver by the H2 subunit sequence and the carbohydrate chains. The recognition by the same sera of the in vitro translated unglycosylated form of the H1 subunit of the receptor was also screened.

**Results:** Sera from patients with autoimmune hepatitis recognized the native form of the human mature receptor. No reactivity was found when these sera were tested against the denatured human protein. In addition, neither the unglycosylated H1 subunit nor any of HepG<sub>2</sub> synthesized asialoglycoprotein receptor forms bound to the antibodies.

**Conclusions:** Anti-asialoglycoprotein receptor antibodies in the sera of patients with autoimmune hepatitis are directed against conformational structures of the mature hetero-oligomeric form of the protein. The carbohydrates chain are probably part of the conformational antigenic sites. Liver and bile ducts, 1: Liver diseases, children Liver and bile ducts, 1: Chronic non viral hepatitis }

"Study of Antigenic Sites on the Asialoglycoprotein Receptor Recognize by Autoantibodies"

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"P P 49 1194" P 49 1194 **Interferon Induced Autoimmunity**

\*J. Graus, R. Bernalcena, V. Ureña, C. Caballero

Hospital Ramón y Cajal de Madrid, Spain *Purpose:* To study the role of alpha Interferon (IFN) in antibody production during chronic hepatitis C (CHC) treatment. *Methods:* We studied 54 CHC patients measuring thyroid stimulating antibody (TSAb), antinuclear cell (ICA), antiinsulin (Ai), antipituitary (Ap) and antiadrenal (Ad) antibody; 86 CHC patients measuring antimicrosomal (AM) and antithyroglobulin (AT) and 60 CHC patients obtaining antinuclear (ANA), antimitochondrial (AMA), antismooth muscle (SMA) and antiliver and kidney microsomes (LKM) antibodies every 3 months during IFN treatment. IFN dosage ranged 1 to 6 million units three times per week. *Results:* When ANA was investigated, 4 patients were found to develop it during treatment. None of the 6 patients showing ANA before treatment, did increase ANA titles with IFN. In one of these 6 patients, the antibody disappeared. No patient developed SMA during treatment. Seven patients were SMA+ before IFN treatment: titles increased in one of them while they became negative in 6 patients. Other studied antibodies (AMA, Ad, ICA, Ai, Ap, and TSAb) were not observed in any case. Six patients presented with AM and 3 with AT previously to IFN treatment showed a title increase during treatment. All of them also showed thyrotropin (TSH) changes. Six different cases develop AM and nine cases AT during IFN treatment. A coincidence was observed in two patients developing AM, AT and ANA. *Conclusions:* 1.- IFN is capable of inducing ANA frequently associated with AM and AT. 2.- IFN may drop previously positive ANA and SMA. 3.- IFN increase or develops AM and AT titles. 4.- AMA, Ad, ICA, Ai, Ap or TSAb are not observed during IFN treatment. Liver and bile ducts, 1: Hepatitis, viral, treatment Liver and bile ducts, 1: Hepatitis viral, diagnosis Immunology and microbiology: Host defense mechanisms } "Interferon Induced Autoimmunity"

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## "P P 49 1195" P 49 1195 **Glutamine Enriched Enteral Feeding Reduces Rat Plasma Nitrate Levels**

\*A.P.J. Houdijk, J.J. Visser, E.R. Rijnsburger, T. Teerlink<sup>1</sup>, P.A.M. van Leeuwen

Department of Surgery, Free University Hospital, Amsterdam, The Netherlands

<sup>1</sup> Clinical Chemistry, Free University Hospital, Amsterdam, The Netherlands Nitric oxide (NO) is a potent vasodilating and immune modulating agent that is produced in many cell types including endothelial cells and macrophages. It is a product of the enzymatic conversion of L-arginine (ARG) to L-citrulline (CIT) by NO-synthase. Nitrate is the stable endproduct of the NO-pathway. It has been shown that the *in vitro* production of NO in endothelial cells can be inhibited by L-glutamine (GLN). We hypothesized that GLN enriched feeding also inhibits NO production *in vivo*. To investigate this, nitrate measurements were performed in rats fed GLN enriched diets (6.25%, 12.5% and 25%) and compared to rats fed balanced control diets. The respective diets were fed for one or two weeks. Nitrate was measured in the diet, in plasma samples (day 7 and 14) and in samples of 24 hours urine collections. Plasma amino acids were determined weekly. **Results:** In a dose dependent manner GLN supplementation significantly increased plasma levels of GLN (from 630 to 1200  $\mu\text{Mol/L}$ ; 91%,  $p < 0.0001$ ), ARG (from 120 to 139  $\mu\text{Mol/L}$ , 17%,  $p < 0.001$ ) and CIT (from 50 to 75  $\mu\text{Mol/L}$ ; 54%,  $p < 0.0001$ ). Nitrate levels in the diets did not differ ( $\approx 1.70 \mu\text{Mol/g}$ ). Food intake ( $\approx 18.0 \text{ g}$ ) and nitrate intake ( $\approx 31 \mu\text{Mol/day}$ ) showed no differences between the groups. Glutamine supplementation resulted in significantly lower plasma nitrate levels ( $\approx 50\%$ ) in all GLN fed groups ( $\approx 15 \mu\text{Mol/L}$ ) compared to control groups ( $\approx 27 \mu\text{Mol/L}$ ,  $p < 0.0001$ ). No further reduction was observed after two weeks of feeding. Between 1 and 4  $\mu\text{mol}$  more nitrate was excreted compared to intake in all groups without any significant differences. **Conclusions:** The decrease in plasma nitrate levels by GLN enriched feedings indicates for the first time an inhibitory effect of GLN on NO production *in vivo*. This effect was not related to the amount of GLN supplementation. Lower nitrate levels was not due to a diminished availability of ARG as substrate for NO synthases, since plasma ARG levels were significantly increased by GLN feeding. Nutrition: Metabolism } "Glutamine Enriched Enteral Feeding Reduces Rat Plasma Nitrate Levels"

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## "P P 49 1196" P 49 1196 **Prophylaxis Against Pneumococcal Infection after Splenectomy**

\*P. Ejstrud, J.B. Hansen, D.A. Andreasen

Departments of Gastrointestinal Surgery and Clinical Chemistry, Aalborg Hospital, 9100 Aalborg, Denmark Splenectomy predisposes to serious infections from Streptococcus pneumoniae. The aims of the present study were to evaluate prophylaxis against pneumococcal infection after splenectomy. 561 patients splenectomised from 1984–1993 were identified and the hospital records were available for 555 patients. The hospital records and the discharge letters were searched for informations on splenectomy and information about pneumococcal vaccination. General practitioners of living, apparently unvaccinated patients were asked for evidence of vaccination. To study differences in relation to the operative indications for splenectomy, the patients were classified into 5 major groups: haematological, trauma, incidental, accidental and other. The total vaccination rate was 62%, but vaccination rates from 47% to 91% in five different groups of indications were observed. Patients undergoing splenectomy during gastrointestinal cancer surgery or because of inadvertent intra-operative trauma to the spleen were particularly at risk of not being vaccinated. 64% of the patients were vaccinated at an inappropriate time in relation to the splenectomy. Recording of splenectomy was missing in 10%, and vaccination status was mentioned in 35% of the discharge letters. The pneumococcal vaccination rates in patients after splenectomy were not satisfactory. The majority of patients were vaccinated at an inappropriate time in relation to the splenectomy. The discharge letters often lacked information concerning the patients' vaccination status. More effort is needed to reach an acceptable level with respect to prophylaxis against pneumococcal infection after splenectomy. Clinical practice: Quality assurance } "Prophylaxis Against Pneumococcal Infection after Splenectomy"

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## "P P 50 1207" P 50 1207 **Helicobacter Pylori: Is It a Risk Factor for Hepatic Encephalopathy in Cirrhotic Patients?**

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<sup>1</sup> Department of Biochemistry, Faculty of Medicine, Assiut University, Assiut, Egypt *Objective:* To determine whether *Helicobacter pylori* (Hp) infection is a risk factor for hepatic encephalopathy in patients (pts) with liver cirrhosis. *Methods:* 108 cirrhotic pts undergoing upper GI endoscopy for detection of oesophageal varices were included in this study: 34 pts Child-Pugh grade A, 60 pts grade B and 14 pts grade C. The aetiology of liver cirrhosis was either posthepatic or mixed; Bilharzial fibrosis and posthepatic cirrhosis. Diagnosis of Hp infection was done by histopathology using antral and fundal biopsies, hp fast test and serologically by estimating Hp IgG antibody titers by ELISA (more than 20 u/ml). Estimation of serum NH<sub>3</sub> using an enzymatic assay for all pts was done and the results were compared with that of 24 normal subjects as a control group. *Results:* Serum NH<sub>3</sub> is significantly higher in cirrhotics than in normal controls (P < 0.001) 86 cirrhotic pts with Hp +ve were similar to 22 Hp. { - }ve with regard to age, sex, aetiology of cirrhosis and Child score. Hp. +ve had significantly high NH<sub>3</sub> in comparison with Hp { - }ve pts (P < 0.01). Also significant high NH<sub>3</sub> in pts grade C compared with grade A (P < 0.01) and grade B (P < 0.01). Detection of Hp IgG antibodies by ELISA is a sensitive test as it was positive (more > 20 u/ml) in all pts with positive hp fast test and positive histopathology for Hp. There was a significant positive correlation between serum NH<sub>3</sub> levels and Hp IgG antibody titers in cirrhotic pts (r = 0.9, P < 0.001). *Conclusion:* Hp infection as ammonia producer can be considered as a risk factor for hepatic encephalopathy in cirrhotic patients and may warrants eradication. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Liver and bile ducts, 1: Cirrhosis: ascites, encephalopathy }" "*Helicobacter Pylori: Is It a Risk Factor for Hepatic Encephalopathy in Cirrhotic Patients?*"

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## "P P 50 1211" P 50 1211 Effects of Canrenoate Potassium on Portal Hemodynamics in Patients with Compensated Liver Cirrhosis

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*Aim:* Long-term administration of spironolactone is reported to reduce portal pressure in cirrhotic patients. We examined the effects of acute administration of canrenoate potassium, an aldosterone antagonist, on portal hemodynamics in compensated cirrhotic patients using noninvasive duplex Doppler ultrasonography. *Methods:* Baseline values were obtained in the fasting state, and then 200 mg of canrenoate potassium in 10 ml of saline solution was intravenously administered to 22 patients, whereas 10 ml of saline solution was administered as a placebo to 8 patients. *Results:* The portal cross-sectional area, portal blood velocity and portal blood flow decreased by 5.3 – 9.2, 10.4 – 8.7% and 13.0 – 12.4%, respectively at the nadir 60 min after administration and these decreases persisted until 120 min. Placebo did not affect these parameters of portal hemodynamics. Eleven responders who had a more than 10% fall in portal blood flow 60 min after administration had significantly higher levels of plasma aldosterone than 8 non responders who had less than 10% fall. The reduction rate of portal blood flow was closely correlated with plasma aldosterone level. *Conclusion:* These findings suggest that aldosterone antagonist directly causes a reduction in portal blood flow probably through inhibition of aldosterone-induced vasoconstrictive action. Liver and bile ducts, 1: Cirrhosis: portal hypertension Radiology and ultrasound: Therapy } "Effects of Canrenoate Potassium on Portal Hemodynamics in Patients with Compensated Liver Cirrhosis"

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## "P P 50 1212" P 50 1212 **Cytoprotective and Cytoinjurious Factors in Chronic Liver Diseases with Bleeding Gastro-Oesophageal Varices**

\*I. Mostafa, M. Hassan, F. Essawy, S. Omran

Theodor Bilharz Research Institute, 14 El-Nour Street, Dokki-Mehandeseen, Giza, Egypt Portal hypertension and subsequent bleeding gastro-oesophageal varices are frequent complications of chronic liver diseases. The pathogenesis of this bleeding is still unclear, many factors are known to be involved. The aim of this study was to evaluate the possible role of some factors in the pathogenesis of bleeding varices, in attempt to study the integrity of GIT mucosa which depends on cytoprotective and cytoinjurious factors. We measured epidermal growth factor (EGF), prostaglandinE2 (PGE2), thromboxane (TXB2), 6-ketoPGF1, leucotrienes LTC4, LTD4 and cyclic-AMP (c-AMP) in specimens from oesophageal, gastric and duodenal mucosa. This study included 10 healthy subjects (group I), 10 patients with portal hypertension without history of bleeding varices (group II) and 19 patients with portal hypertension and history of bleeding gastro-oesophageal varices (group III). Patients were classified according to Child-Pugh's system into Child A (7), Child B (11), Child C (11). Homogenization, extraction and purification of the mucosal specimens were done to allow measurement of PGE2, TXB2, 6-ketoPGF1 and LTC4, LTD4 using ELISA technique, EGF and c-AMP were assessed by RIA method. The data revealed that tissue levels (ng/mg protein) of PGE2, EGF in group I were significantly higher than those of group II ( $p < 0.05$ ) and III ( $p < 0.01$ ). On the other hand significant increase in TXB2, LTC4 & LTD4 in group II and III when compared to group I ( $p < 0.05, 0.01$ ) was detected in all different biopsies. However c-AMP (nmol/mg protein) and 6-ketoPGF1 showed significant reduction in group II and III when compared to group I ( $p < 0.05, 0.01$ ) in oesophageal biopsies only, this could explain the predominance of bleeding from oesophageal varices than gastric varices. It was concluded that there is an imbalance between prostaglandins and leucotrienes in patients with chronic liver diseases, this may be related to alteration of arachidonic acid metabolism causing mucosal damage and ulceration initiating variceal bleeding. The results may be of help in the effective intervention to control bleeding process, prevention of rebleeding and to choose the best line of treatment. Liver and bile ducts, 1: Cirrhosis: portal hypertension Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation }"  
"Cytoprotective and Cytoinjurious Factors in Chronic Liver Diseases with Bleeding Gastro-Oesophageal Varices"

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## "P P 50 1213" P 50 1213 Effects of Diltiazem in Low Flow Portal Arterialization for Liver Protection

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First Department of Surgery, Gifu University School of Medicine, Gifu, Japan Ischemia during hepatectomy and liver preservation of transplantation causes liver damages. We performed portal arterialization (PA) to prevent injuries caused by ischemia, and have reported energy metabolism was maintained in PA, the rate of which was 25% in total hepatic blood flow (THBF). The advantage of decreasing the flow of PA is to facilitate operative procedures and control of bleeding, but it may reduce protective effects. We studied effects of diltiazem in low flow PA for liver protection in mongrel dogs (12.2 – 2.8 kg). Portal venous flow (PVF) and hepatic arterial flow (HAF) were measured by transit-time flowmeter. THBF was calculated at sum of PVF and HAF. Low flow PA was at the rate of 15% in THBF. The portal vein was clamped and the hepatic arteries were ligated under portacaval shunt. Then PA was performed with a roller pump from the right femoral artery to the portal vein through a 6Fr. tube for 120 minutes. Dogs were divided into two groups. The diltiazem group (Group D, n = 4) was received with continuous administration at a dose of  $10^{-5}$  mg/kg/min of diltiazem intraportally from 30 minutes before PA, and control group (Group C, n = 7) with none. Aortic pressure (AoP), portal venous pressure (PVP) and hepatic venous pressure (HVP) were measured, and portal venous resistance (PVR) was calculated with them. Oxygen extraction of the liver was calculated with oxygen saturation and hemoglobin of arterial, portal venous and hepatic venous blood. Arterial ketone body ratio (AKBR), ATP and energy charge were indexed in energy metabolism. Histological findings after PA were examined in hematoxylin and eosin (HE), and thrombomodulin (TM) stain. After PA, AoP decreased, but PVP, PVR and oxygen extraction increased. No significant differences were observed in them between two groups. AKBR was 0.52 – 0.24 in Group D at 120 minutes of PA, which was significantly ( $p < 0.05$ ) higher than Group C (0.20 – 0.10). ATP and energy charge showed a tendency to be high in Group D. In histological findings, cytoplasm was maintained in Group D on HE stain, and sinusoid function also was preserved in Group D on TM stain. In conclusion, our results suggest that administration of diltiazem reduce liver damage due to ischemia in low flow PA. Liver and bile ducts, 1: Liver transplantation } "Effects of Diltiazem in Low Flow Portal Arterialization for Liver Protection"

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## "P P 50 1216" P 50 1216 Somatostatin Effectiveness in Serious Upper Gastrointestinal Hemorrhage

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Second Dept of Medicine, Hellenic Red Cross General Hospital, Athens, Greece *The aim* of this study was to estimate the effectiveness of intravenous infusion of somatostatin in patients with serious upper gastrointestinal hemorrhage (GH). *Methods:* The study included 40 patients, 24 men and 16 women with mean age 55.4 – 8.6 years, who were admitted to the hospital because of GH. Twelve of them suffered from gastric ulcer, 27 from duodenal ulcer and 1 had had erosive hemorrhagic gastritis. All the diagnoses had been proved endoscopically. They were divided randomly in two groups A and B. The group A received somatostatin 250 µg as bolus infusion initially, followed by 250 µg per hour for 5 days. The group B received cimetidine 200 mg intravenously every 4 hours for 5 days. Groups A and B were compared for a) the number of patients in whom the GH stopped with medical treatment b) the duration of hemorrhage c) the number of blood units transfused. Student t-test and  $\chi^2$  methods were used. *Results:* The GH stopped by medical treatment in 19 (95%) patients of group A and 14 (70%) patients of group B ( $p < 0.05$ ). One patient from group A (5%) and 6 (30%) from group B needed surgical treatment. The GH stopped in 4.3 – 0.89 hours in group A and 9.8 – 1.31 hours in group B ( $p < 0.05$ ). The patients of group A needed 2.65 – 0.73 blood units and those of group B 4.86 – 0.96 ( $p < 0.05$ ). *Conclusion:* Somatostatin administration reduced significantly the need of surgical treatment, the duration of hemorrhage and the number of blood units compared with those of cimetidine. *Clinical practice:* Management strategy Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Somatostatin Effectiveness in Serious Upper Gastrointestinal Hemorrhage"

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## "P P 50 1217" P 50 1217 Medical Treatment of Portal Hypertension Using Verapamil, Ketanserin and Propranolol Alone and in Combinations

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Department of Tropical Medicine, Faculty of Medicine, Cairo University and Theodor Bilharz Research Institute, Cairo, Egypt Bleeding from oesophagogastric varices and portal hypertensive gastropathy is a major cause of morbidity and mortality in patients with chronic liver disease. The aim of this study was to evaluate the potential synergistic effect of portal hypotensive agents with different modes of action, using combinations of ketanserin and verapamil or ketanserin and propranolol and to optimize the doses used for each drug to avoid the deleterious effects of these agents. Fifty patients with portal hypertension due to cirrhosis and/or hepatic schistosomiasis were randomly allocated into four groups. Group I (12 patients) treated with verapamil 80 mg t.d.s. Group II (10 patients) treated with ketanserin 20 mg b.i.d. Group III (15 patients) treated with combination of verapamil 80 mg b.i.d. and ketanserin 20 mg b.i.d. Group IV (13 patients) treated with propranolol 40 mg t.d.s. and ketanserin 20 mg b.i.d. Clinical and laboratory assessment, upper gastrointestinal endoscopy, liver biopsy and splenic pulp pressure (SPP) measurement were done before and after one month of treatment. It was found that verapamil has produced significant increase in SPP. While, ketanserin with or without propranolol has produced significant reduction of SPP. However, addition of propranolol to ketanserin allowed the use of smaller and fixed doses of both agents avoiding the production of serious side effects. It was concluded that verapamil has no benefit in the treatment of portal hypertension. Ketanserin, in smaller doses, produced nearly the same effect of reduction of portal pressure without producing major side effect. Combination of ketanserin and propranolol proved to be better than each agent alone, particularly in comparison with propranolol. This allowed the use of smaller and fixed dose of each agent which minimized the side effects. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Medical Treatment of Portal Hypertension Using Verapamil, Ketanserin and Propranolol Alone and in Combinations"

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**"P P 50 1219" P 50 1219 Effect of Verapamil on Portal and Splanchnic Hemodynamics in Patients with Advanced Posthepatic Cirrhosis Using Duplex Doppler Ultrasound H. Din\ 'e7,**

\*S. Kapicioglu, N. Cihanyurdu, G. \ 'c7an

Black Sea Technical University School of Medicine, Department of Internal Medicine and Radiology, Trabzon, Turkey *Purpose:* To assess the effect of verapamil (80 mg) oral administration on portal and splanchnic hemodynamics in patients with advanced posthepatic cirrhosis using duplex Doppler Ultrasound (US). *Methods:* Fourteen patients with posthepatic liver cirrhosis were included in the study. Duplex Doppler sonographic examinations were performed. Portal and splanchnic hemodynamics including vessel diameters (mm), mean flow velocities (cm/sec), blood flows (ml/min), Doppler indices such as pulsatility and resistive indices (PI and RI), were investigated before and after verapamil administration. *Results:* After verapamil administration; diameter of portal vein, splenic vein and superior mesenteric artery (SMA) showed increase of 8%, 10% and 7% ( $p < 0.05$  –  $p < 0.001$ ), respectively. Increases of 20%, 38% and 47% were found in blood flows ( $p < 0.5$  –  $p < 0.0001$ ) with respect to the above vessels. Decreases of 17%, 10%, 11% and 7% were found in SMA PI, splenic artery (SA) PI, and SA RI, respectively ( $p < 0.5$  –  $p < 0.0001$ ). *Conclusions:* Verapamil appears to have splanchnic, portal, splenic, portocollateral and probably intrahepatic vasodilator effect in patients with advanced posthepatic liver cirrhosis. Verapamil should be further investigated in the treatment of patients with advanced liver cirrhosis with prospective studies measuring portal and wedged hepatic pressure. Radiology and ultrasound: Diagnosis Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Effect of Verapamil on Portal and Splanchnic Hemodynamics in Patients with Advanced Posthepatic Cirrhosis Using Duplex Doppler Ultrasound"

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## "P P 50 1220" P 50 1220 Acute Portal Venous System Thrombosis. Systemic Treatment with Heparin and Recombinant Tissue Plasminogen Activator (rt-PA) or Heparin alone in 10 Patients

\*J.P. Lagasse, M.L. Bahallah, G. Debillon<sup>1</sup>, N. Salem, D. Labarri re, M.P. Serve, V. Advenier<sup>1</sup>, X. Causse, J.L. Legoux

<sup>1</sup> Dept. of Hepato-Gastroenterology, C.H.R., Orl ans, France

Dept. of Radiology, C.H.R., Orl ans, France Some authors have reported successful anticoagulation or thrombolytic therapy in some patients with acute splenoportal or mesenteric vein thrombosis. We report the efficacy of systemic rt-PA with heparin or heparin alone in the treatment of acute portal venous system thrombosis in 10 patients. *Methods:* 10 consecutive patients [9 men, 1 woman, mean age 51 years (27–71 years)] with acute extrahepatic portal vein thrombosis (5), left portal vein thrombosis (3) and superior mesenteric vein thrombosis (2) were studied. In all patients the ultrasonic diagnosis was based on the presence of an echogenic thrombus in the venous lumen. The cause of vein thrombosis was hepatic cirrhosis (4), pancreatitis (2), biliary tract infection (1), myeloproliferative disorders (1), protein C deficiency (2). Treatment with systemic infusion of rt-PA (100 mg over 2 h) with intravenous heparin were performed in 5 patients. The remaining 5 patients (asymptomatic or contraindication of rt-PA) were treated with continuous heparin systemic infusion only (2) or subcutaneous low molecular weight heparin twice daily (3). *Results:* In 3 of the 5 patients treated with rt-PA ultrasonography showed total resolution of the thrombus 7 days (1) and 15 days (2) later. The remaining 2 had partial resolution of the thrombus. In 4 of the 5 patients treated with heparin alone (in 3 of 3 with subcutaneous heparin) ultrasonography showed total resolution of the thrombus 7 days (1) and 30 days (3) later, and partial in 1. No bleeding occurred, one patient had heparin-associated-thrombocytopenia. Whereas total resolution of the thrombus was achieved, 3 patients with hepatic cirrhosis had bleeding from oesophageal varices 1 month, 6 months and 26 months later. *Conclusions:* The treatment with heparin can produce a complete recanalisation of acute portal venous system thrombosis. These data suggest that systemic rt-PA seems not increase the efficacy of heparin. A prospective study should be useful in order to confirm these results. Liver and bile ducts, 1: Cirrhosis: portal hypertension Intestinal disorders: Splanchnic circulation, ischemia Clinical practice: Management strategy } " Acute Portal Venous System Thrombosis. Systemic Treatment with Heparin and Recombinant Tissue Plasminogen Activator (rt-PA) or Heparin alone in 10 Patients"

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## "P P 50 1221" P 50 1221 Stapler Transsection of Oesophagus for Bleeding Varices

\*S. Malinger, M. Drews, T. Kosinski, J. Szmaja

Dept. of General Surgery University School of Medicine, Poznan, Poland This study was performed to assess the efficacy of stapler transections of the oesophagus to stem haemorrhage from ruptured oesophageal varices. *Patients and methods.* Between 1988 and 1995-25 patients (aged from 32 to 70 years) have been operated on. Hepatic cirrhosis was the main cause of variceal appearing. Child's hepatic failure evaluation showed stage A in 11 patients and stage B in 14 patients. According to the endoscopic variceal evaluation scale-stage I was observed in 2 patients stage II in 10 and stage III in 13 patients. Emergency indications for the surgical treatment were present in 3 patients, selective indications – in 22 patients. *The operation technique.* Consisted of introducing of a stapler device (ILS) by a gastrotomy to the subdiaphragmatic part of the oesophagus. Then a band was tied around the oesophageal wall upon opened stapler working head. Firing of the device formed a double layer end to end anastomosis transecting and ligating the submucosal varices. When the vagal trunks couldn't be saved a pyloromyotomy was performed. *Results.* There were 4 important rebleedings and 2 anastomotic leaks postoperatively. Five patients died, 3 of them were operated on in emergency during a massive haemorrhage. After one year 11 variceal relapses were observed. *Conclusions.* 1. Stapler transection of the oesophagus should be performed after the control of massive haemorrhage. 2. One half of the patients treated by this method has variceal reappearing during the first year. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Oesophagus } "Stapler Transsection of Oesophagus for Bleeding Varices"

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"P P 50 1222" P 50 1222 **Portal Hemodynamics and Portal Hypertensive Gastropathy in Liver Cirrhosis**

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<sup>1</sup> The Third Department of Internal Medicine, Saitama Medical School, Moroyama, Japan We evaluated the association between portal hypertensive gastropathy and portal hemodynamics. The subjects were 49 patients with liver cirrhosis complicated by esophageal varices in whom the clinical course were observed for 5 years. They were classified into the group who developed a spleno-renal shunt during the course (11 patients) and that who did not (38). They were not complicating with hepatocellular carcinoma and no treatment of esophageal varices. Furthermore, They had no collateral circulation of the portal system except gastroesophageal varices and spleno-renal shunt. Endoscopic findings of portal hypertensive gastropathy were divided into two criterias (mild and severe). Incidence of portal hypertensive gastropathy during the course, the spleno-renal shunt group (5/4) was lower than non-shunt group (18/27). Grade of portal hypertensive gastro-pathy (mild:severe) at the ending of observation were portal hypertensive gastropathy were the spleno-renal shunt group (3:1) and non-shunt group (14:15). Since no difference were observed in the size of spleen, the diameter of the main trunk of the portal vein, or blood biochemical findings between the two groups during the observation period. The development of the spleno-renal shunt, i.e., the state of the development of the collateral circulation seems to be involved in the development of portal hypertensive gastropathy. Liver and bile ducts, 1: Cirrhosis: portal hypertension Endoscopy, specific: Oesophagus Endoscopy, specific: Stomach, duodenum } "Portal Hemodynamics and Portal Hypertensive Gastropathy in Liver Cirrhosis"

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## "P P 50 1223" P 50 1223 **Clinical Outcome Two Years after Implantation of a Tips for Recurrent Variceal Bleeding**

\*M. Gschwantler, A. Gebauer, J. Vavrik, M. Rohrmoser, C. Schrutka-K\ 'f6lbl, E. Brownstone, D. Tscholakoff, W. Weiss

Department of Internal Medicine and Department of Radiology, KA Rudolfstiftung, Vienna, Austria *Objective:* At present there is only sparse data on midterm outcome after TIPS implantation. The role of TIPS in the management of portal hypertension thus remains controversial. The aim of this study was to assess clinical course 2 years after TIPS procedure. *Methods:* The study was designed as a prospective, uncontrolled cohort study. 46 patients who underwent successful TIPS implantation were followed prospectively by clinical examinations, duplex sonography and portal venography. Mean follow-up in surviving patients was 24.1 + 9.0 months. The Kaplan-Meier method was used to calculate cumulative rates of survival, variceal rebleeding, shunt stenosis or occlusion as well as rates of primary, primary-assisted and secondary patency over a 24-months period. Patients were stratified according to their CHILD-PUGH class. The Generalized Wilcoxon Test (Breslow) was performed to detect differences between strata. *Results:* The cumulative rate of survival was 80.4% at 1 year and 70.2% at 2 years. The cumulative rebleeding rate was 12.4% at 1 year and 21.3% at 2 years. The mortality rate of episodes of variceal rebleeding was 22.2%. Variceal rebleeding was associated with shunt abnormalities in all cases, and successful shunt revision resulted in control of the bleeding. The cumulative incidence of shunt stenosis or occlusion was 41.2% at 1 year and 54.9% at 2 years. 23.3% of patients without shunt abnormalities after 1 year developed shunt stenosis or occlusion during the second year after TIPS procedure. Shunt revision was successful in 96.6% of cases. Secondary patency rate was 88.1% after 2 years. The risk of variceal rebleeding and shunt stenosis did not differ significantly between CHILD-PUGH classes. *Conclusions:* Successful TIPS implantation results in a low rate of morbidity and mortality from variceal rebleeding over 2 years. TIPS creation in combination with careful follow-up examinations represents a safe and effective long-term treatment of recurrent variceal bleeding. Even in patients in whom no shunt abnormality was detected during the first year routine duplex follow-up examinations should be continued at 3-month intervals. Liver and bile ducts, 1: Cirrhosis: portal hypertension }" "Clinical Outcome Two Years after Implantation of a Tips for Recurrent Variceal Bleeding"

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## "P P 50 1224" P 50 1224 Artificial Neural Network Analysis of Prognostic Variables for Prediction of Early Mortality after TIPSS: Development and Validation

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<sup>5</sup> Department of Statistics Unit, Royal Infirmary Edinburgh, UK *Background and Aims:* TIPSS is followed by deterioration in liver function tests and early mortality in about 20–30% patients. The purpose of this study was to develop and validate a model based upon artificial neural network (ANN) analysis of prognostic variables and compare this with a model based upon logistic regression (MLR). *Methods:* 82 consecutive patients undergoing TIPSS for variceal haemorrhage were studied. They were divided into two groups. Group I (66 patients) comprised the patients that were used to train the ANNs and establish the model based upon the results MLR. Group II (16 patients) comprised the patients that were used in a blinded manner to assess the trained neural network and also the MLR. *ANN:* A feed-forward fully-connected ANN with 10 hidden neurons (DynaMind<sup>®</sup>) was trained with the 25 clinical variables related to clinical or biological data obtained from patients in Group I (input) to predict early mortality (output). *MLR:* Significant independent predictors (sodium;  $p < 0.001$  and Pugh score  $p < 0.001$ ) were combined using the formula:  $p = e^x / (1 + e^x)$ ; where  $p$  is the predicted probability of survival and  $x = 13.42 \{ - \} 0.1429 \times [\text{sodium}] + 0.445 \times [\text{Pugh score}]$ . This network and the MLR model were then applied to predict early mortality of patients in Group II. *Results:* Sensitivity and specificity for predicting early mortality were 100% and 87.5% for the ANN and 25% and 93.8% for the MLR. *Conclusions:* This study illustrates that ANN analysis can be useful in the prediction of early mortality before TIPSS is inserted, using routine clinical and biochemical parameters. Moving from the assessment of outcome by current methods towards ANN analysis will require similar comparisons, prospective evaluation and an open mind. Liver and bile ducts, 1: Cirrhosis: portal hypertension } "Artificial Neural Network Analysis of Prognostic Variables for Prediction of Early Mortality after TIPSS: Development and Validation"

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**"P P 50 1225" P 50 1225 Long Term Patency of Transjugular Intrahepatic Portosystemic Shunt (TIPS): A Surgical Prospective Experience D. Azoulay, D. Castaing, H. Bismuth**

Hepato-Biliary and Liver Transplantation Center, Paul Brousse Hospital, Villejuif, France Stent obstruction is the main argument against the use of transjugular intrahepatic portosystemic shunt (TIPS) for the long term management of portal hypertension. This prospective study analyses the impact of a stringent follow-up on the long term patency rate of TIPS performed by a surgical team. From November 1991 to December 1995, 122 attempts of TIPS placement were performed and successful in 115 cases (94%). Follow-up included Doppler ultrasonography at 15 days, 1 month, every 3 months and when patients (pts) developed recurrent complication. Transjugular venography was systematically performed at 1 and every six months, when Doppler ultrasonography was doubtful and when the pts developed recurrent complication. End points for follow-up were death, liver transplantation (LT) or survival with TIPS in place. Fifty nine pts (51%) had a follow-up below 6 months (27 deaths, 16 LT, 11 recent survivors with a TIPS in place, 5 pts lost for follow-up). Fifty-six pts (49%) have a complete follow-up of at least 6 months with a TIPS in place (mean 20 + 2 months, range 6 to 55 months) and are analysed here. The primary patency rate was 36/56 (64%) with a mean follow-up of 18.4 + 5 months. Twenty four episodes of TIPS obstruction occurred in 22 pts: 12 within 2 months, 4 between 2 and 6 months, 8 after 6 months. Obstruction was treated successfully by TIPS dilatation in 2 cases and coaxial TIPS deployment in 20 cases. Two cases of transjugular desobstruction failures were treated by portacaval shunt. Actuarial primary patency rate of TIPS was 77%, 70%, 60%, 56% at 6, 12, 24 and 36 months respectively. Assisted patency rate of TIPS was 96% at 6 months and at 2 years. Actuarial survival was 90% and 83% at 1 and 2 years. Provided TIPS is performed by trained operators and followed carefully, assisted patency rate comparable to portacaval shunt may be achieved. TIPS may be considered as a long term treatment of portal hypertension. }"  
"Long Term Patency of Transjugular Intrahepatic Portosystemic Shunt (TIPS): A Surgical Prospective Experience"

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## "P P 51 1239" P 51 1239 ERCP for Diagnosing Hemobilia and Hemosuccus Pancreaticus

\*J. Bauer, U. Erhard-Plate, H. Sch\`f6nek\`e4s, H.G. Schmidt

Klinikum N\`fcrnberg, N\`fcrnberg, Germany This retrospective study presents the findings made in 8 patients (P) with hemobilia (H) and 4 P with hemosuccus pancreaticus (HP), which were treated at our hospital from 1/88 to 4/96. *Results:* Hemobilia: Causes for H were hemangiosarcoma of the liver in 1 P, pseudo-aneurysm of the hepatic artery in 1 P, cholezystolithiasis in 3 P, liver biopsy in 3 P. All P showed colics, 6 P icterus, 1 P hematemesis and 3 P melena. Emergency endoscopy established hemorrhage from the papilla in 2 P with the front-view endoscope and in another 2 P with the lateral-view endoscope. Blood clots in the bile duct were observed in 5 P with ERCP. After EPT these were extracted from the bile duct with a Dormia-basket. Angiography produced evidence of hemobilia in 2 P. As for therapy, embolisation failed in 1 P with arrosion bleeding from the right hepatic artery due to cholezystolithiasis. Embolisation was successful in 1 P with pseudo-aneurysm of an intrahepatic liver artery. 3 P were operated on. H stopped spontaneously in 4 P (hemangiosarcoma 1 P, state after liver biopsy 3 P). Hemosuccus pancreaticus: 2 P showed chronic pancreatitis and 2 P a pancreas-ca. 4 P displayed melena, 2 P icterus and 1 P epigastric pain. Hemorrhage from the papilla was observed in 1 P with the front-view endoscope and in 4 P with the lateral-view endoscope. ERCP demonstrated blood clots in the pancreatic duct and bile duct in 1 P, blood clots in the pancreatic duct in 1 P and blood clots in the bile duct in 1 P. Angiography produced evidence of HP in 2 P. As for therapy embolisation was successful in 1 P with chronic pancreatitis, fibrin-adhesive was successfully applied via endoscopy in the pancreatic duct of 1 P with pancreas-ca., and 1 P with chronic pancreatitis was operated on. Hemorrhage stopped spontaneously in 1 P with pancreas-ca. *Summary:* 1. As for our patient group, the ERCP method for diagnosing hemobilia and hemosuccus pancreaticus ranked higher than angiography. 2. No patient died as a result of hemobilia or hemosuccus pancreaticus. Endoscopy, general: GI bleeding Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic }" "ERCP for Diagnosing Hemobilia and Hemosuccus Pancreaticus"

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## "P P 51 1258" P 51 1258 Management of Bile Duct Injuries of Laparoscopic Cholecystectomy with Endoscopic Sphincterotomy or Stenting: A Comparison

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Although laparoscopic cholecystectomy (LC) has several advantages over open cholecystectomy, the rate of bile duct injury is higher in the former. Several endoscopic retrograde techniques were advocated in management. We compared the efficacy of sphincterotomy with temporary stenting. The 31 patients, referred after LC with the clinical diagnosis of bile leak between Jan 94, and March 95 were studied. At endoscopic retrograde cholangiography (ERC), the patients without leak (2), with retained stones (5), with bilomas requiring percutaneous drainage (1), and with transection (2) were excluded. The remaining 21 (12 female, 9 male with median age of 51 and range 28–74) were randomized into two treatment arms: sphincterotomy or stenting. In 12/21, leak was from cystic duct remnant. Tannenbaum stents of 8.5 FR size (Wilson Cook Company, Winston-Salem, NC, USA) were used. A prior sphincterotomy was not performed. All the patients were followed up until the resolution of the symptoms and signs in the hospital. Stented patients were called for a second endoscopy, two weeks after the first one. For the first four stented patients, ERC was performed before stent removal, to confirm the resolution of the leak. For the remaining 7 patients, removal was without fluoroscopic guidance. Leaks eventually resolved in all. Symptoms resolved more rapidly in the stent group in comparison to sphincterotomy group: 1.9 – 8, 1–3 days (mean – SD, range) vs. 2.9 – 1.0, 2–5 days;  $p < 0.05$ . Mean hospital stay was also shorter in the stent group: 2.7 – 0, 1–4 days vs. 3.9 – 1.1, 2–6 days,  $p < 0.05$ . No procedure-related complication occurred. Our study suggests that for the patients with isolated common bile duct injury or cystic duct leak, temporary moderate size stent (8.5 FR) insertion, across the site of the leak without ES is as effective as sphincterotomy and it confers faster improvement. Advantages of this new type of stent without side holes and, possibly, shorter stented periods require more studies. Endoscopy, general: Instrumentation, therapy Endoscopy, specific: Biliary Laparoscopic surgery: Therapy }

"Management of Bile Duct Injuries of Laparoscopic Cholecystectomy with Endoscopic Sphincterotomy or Stenting: A Comparison"

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"P P 52 1259" P 52 1259 **Increasing Prevalence of Right-Sided Colonic Polyps**

\*A. Van Gossum, A. Mandieau, M. Adler, M. Cremer

Department of Gastroenterology, Erasme Hospital, ULB, Brussels, Belgium *Introduction:* Colorectal cancer is the second leading cause of cancer mortality in Europe. Actually, sigmoidoscopy is the most frequently used screening method. The aims of this study were 1. to determine in a large population the percentage of polyps which would be not detected by sigmoidoscopy; 2. to determine if there is an increasing prevalence of lesions isolally located in the right colon. *Material and methods:* All the protocols of total colonoscopy (13.500) performed at Erasme Hospital from 1983 to 1994 were retrospectively reviewed. For patients with polyps, the following parameters were recorded: age, sex, location of the polyps, size of the polyps. Patients were divided in two periods: a) from 1983 to 1989, b) from 1990 to 1994. *Results:* Polyps were detected in 1441 patients (period 1983–89) and in 1544 patients (period 1990–94). For the global population, the sex ratio male/female was 2/1 and the mean age was 61.9 y for males and 65.2 y for females, respectively. In the global series, 50.6% of patients had polyps located into the rectosigmoid (50 cm from the anal verge). The percentage of patients having polyps located only into the right colon or above the splenic flexure statistically increased between the 2 periods. Period 1983–89 Period 1990–94 (n = 1441) (1544) % of patients with polyps located only in: the right colon 8.6% 13%  $p < 0.0001$  Above the splenic flexure 12.9% 21.3%  $p < 0.000001$  Sizes of the polyps were similar in the different segments of the colon. *Conclusions:* The sensitivity of sigmoidoscopy for detecting patients with polyps is about 50%. Our data suggest a continuing trends in the prevalence of right-sided colonic polyps. That must be taken into account in evaluation of cost-effectiveness of screening endoscopic method. Endoscopy, specific: Colon, rectum Oncology, specific: Colon, rectum } "Increasing Prevalence of Right-Sided Colonic Polyps"

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## "P P 52 1262" P 52 1262 Colo-Rectal Adenomas and Flow Cytometric Analysis

\*S. Gasperoni, F. Monti, D. Tassinari, P. Rinaldi, R. Bronzetti, A. Ravaioli, A. Cardelli

Ospedale Infermi, Istituto Oncologico Romagnolo, Rimini, Italy Colorectal adenomas have a definite but unpredictable potential to become malignant. The currently accepted criteria are not sufficient to predict the transformation through the adenoma-carcinoma sequence. During this sequence the genetic instability of the epithelial cells increases resulting in structural and numerical chromosome aberrations (aneuploidy). Flow cytometry permits a measurement of DNA-ploidy and S-phase fraction; it has been suggested to use data from flow cytometry to further define biologic behaviour of colorectal adenomas. Aim of the present study was to evaluate prevalence of aneuploidy among polyps endoscopically removed and to relate DNA-index and S-phase fraction to size, histological type, dysplasia and site of polyps. Flow cytometric analysis was performed on 44 polyps of patients who underwent endoscopic polypectomy (32 M, 12 F; mean age 65, range 35–89). In our series, prevalence of DNA aneuploidy was 18.2%; in detail results are summarized in the following table. Size Histological type Dysplasia Site < 1 cm 1–2 > 2 cm tubul tub- vill low high rectum left right cm vill colon colon Diploid 17 9 10 19 10 7 31 5 7 25 4 (%) (94) (75) (71) (86) (77) (78) (82) (83) (58) (89) (100) Aneuploid 1 3 4 3 3 2 7 1 5 3 0 (%) (6) (25) (29) (14) (23) (22) (18) (17) (42)\* (11)\* (0)\* S-phase 7.7 6.7 5.4 7.6 7.0 4.0 6.8 6.1 4.5 7.4 8.3 m – SD – 4.8 – 5.2 – 3.1 – 5.2 – 3.7 – 2.2 – 4.7 – 3.2 – 2.7 – 5.0 – 2.9 \*p < 0.05 (chi-2) *Conclusions:* Our preliminary data show that the prevalence of aneuploidy is significantly higher in distal polyps. Size, histological type and grade of dysplasia of adenoma were not related to data from flow cytometry. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Colo-Rectal Adenomas and Flow Cytometric Analysis"

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## "P P 52 1265" P 52 1265 Concentration of Methane in Breath of Colonic Polyps Patients Measured with a New Technique

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Dpt Malattie Digestive & Nutrizionali Osp S Filippo Neri, Roma, Italy

<sup>1</sup> ENEA Inn-fiss Spet Frascati, Italy Much controversy exists regarding the role of methane (CH<sub>4</sub>) producing anaerobic bacteria in colonic carcinogenesis. According to some authors, the presence of CH<sub>4</sub> producing bacteria is correlated with colon cancer [1], whilst this finding was not confirmed by others [2,3]. The aim of our study was to evaluate the production of CH<sub>4</sub> by bacterial flora in the intestine of patients with colo-rectal adenomas and in normal subjects. Forty eight consecutive patients with an endoscopic diagnosis of colo-rectal polyps (44 adenomatous/villous polyps, 4 adenomas with cancer) and 65 normal subjects were included in the study. The concentration of CH<sub>4</sub> in breath was measured using a technique devised at ENEA in Frascati (Italy) based upon the absorption, by the CH<sub>4</sub> molecules, of a laser beam of known wavelength emitted by a diode. In patients with polyps, gaschromatography measurements were also made. The amount of CH<sub>4</sub> in breath was expressed in parts per million (ppm). Individuals presenting CH<sub>4</sub> concentration > 50% than CH<sub>4</sub> concentration in the surrounding air were considered CH<sub>4</sub> producers. Fifteen out of 48 patients (31%) and 35/65 controls (54%) were found to be CH<sub>4</sub> producers (p = 0.02). The amounts of CH<sub>4</sub> detected in breath of patients and controls are shown in the figure below. A close correlation was found between the two breath tests (laser diode and chromatography) (r = 0.72) even if the latter failed to detect 4/15 (27%) of the CH<sub>4</sub> producers revealed by the laser diode.

Data emerging from this study failed to demonstrate a higher frequency of CH<sub>4</sub> producers in the colonic polyps patients as compared to normal controls.

Reference: Pique J M et al Gastroenterology 1984. 87, 601–605.

Hoff G et al Scand J Gastroenterol 1986. 21, 193–198.

Siversten SM et al Scand J Gastroenterol 1992. 27, 25–28 Oncology, general: Screening, prevention } "Concentration of Methane in Breath of Colonic Polyps Patients Measured with a New Technique"

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"P P 52 1266" P 52 1266 **Colonic Glutathione Content and Glutathione S-Transferase Activity in Patients with X-Linked A-Gammaglobulinaemia and Patients with Adenomas** M.J.A.L. Grubben<sup>1</sup>, C.C.M. vd Braak<sup>1</sup>, W.H.M. Peters<sup>1</sup>, J.W.M. vd Meer<sup>2</sup>, F.M. Nagengast<sup>1</sup>

<sup>1</sup> Dept. of Gastroenterology, University Hospital Nijmegen, The Netherlands

<sup>2</sup> Dept. of Internal Medicine, University Hospital Nijmegen, The Netherlands X-linked agammaglobulinaemia (XLA) is a primary immunodeficiency disorder. Patients with XLA have a 30-fold greater incidence of rectal cancer compared to the normal population. Glutathione (GSH) and GSH-related enzymes are involved in the metabolism and detoxification of cytotoxic and carcinogenic compounds. The glutathione S-transferase (GST) activity in the mucosa along the gastrointestinal tract is reciprocal to tumour incidence in humans. *Aim and methods:* we investigated GSH content and GST activity in normal colonic mucosa at three levels (ascending colon, sigmoid and rectum) of XLA-patients (n = 8, mean age 34 – 2 yrs) and patients with colonic adenomas (n = 25, age 60 – 12 yrs) and in rectal mucosa of healthy controls (n = 10, age 24 – 3 yrs). Statistical analyses were assessed by Mann-Whitney U test. *Results:* values are given as means – SEM. Asc. colon Sigmoid Rectum GST (nmol/min/mg protein) XLA 237 – 17<sup>#,\*</sup> 222 – 19<sup>#,\*</sup> 143 – 17<sup>#</sup> Adenoma 333 – 23 316 – 27 285 – 19 Control ND ND 321 – 29<sup>&#</sup> p {\a3} 0.03 XLA versus adenoma. \*p {\a3} 0.02 versus XLA-rectum. &p {\a3} 0.01 control versus XLA. ND: not determined. GSH content did not differ between all study groups at all levels. *Conclusion:* XLA-patients have a lower GST-activity at all levels in the colon compared to patients with adenomas. The rectal GST activity in XLA-patients also differs from healthy controls. In XLA patients rectal GST activity is lower than the proximal GST activity. The increased risk of colorectal cancer in XLA-patients might partly be explained by a lower detoxification capacity in the mucosa. Oncology, general: Proliferation, carcinogenesis Oncology, general: Screening, prevention Oncology, specific: Colon, rectum } "Colonic Glutathione Content and Glutathione S-Transferase Activity in Patients with X-Linked A-Gammaglobulinaemia and Patients with Adenomas"

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"P P 54 1279" P 54 1279 **p53 and Proliferating Cell Nuclear Antigen as Prognostic Factors in Colorectal Cancer**

\*S. Knezevic-Usaj<sup>1</sup>, S. Cerovic<sup>1</sup>, Lj. Rabrenovic<sup>1</sup>, Z. Bogdanovic<sup>1</sup>, V. Cuk<sup>1</sup>, V. Todorovic<sup>2</sup>, A. Skaro-Milic<sup>1</sup>, J. Dimitrijevic<sup>1</sup>, V. Tatic<sup>1</sup>

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In light of the role of p53 in cell proliferation, we were interested in markers of the cell cycle whose expression might be correlated with p53 protein overexpression. Formalin -fixed paraffin embedded surgical specimens of 29 CC of different Dukes' stages were analysed. Nuclear p53 protein overexpression in tumor cells and proliferative activity of tumor by identifying proliferative cell nuclear antigen (PCNA) were detected by immunohistochemistry. p53 protein overexpression was identified in 48.2% CC and found to correlate with stage of disease (22.2, 40.0 and 80.0% in Dukes A, B and C stages respectively), site of tumor (52.38% p53 positive tumor in left colon versus 37.5% positive CC in right colon) and nonmucinous histological type (61.9% of p53 positive tumor in nonmucinous e.g. 25.0% in mucinous tumor). Nuclear immunoreactivity for PCNA to a varying degree was expressed in 93% of CC. High PCNA distribution score 3 (> 50% PCNA positive nucleus) was more frequently found in p53 positive CC (71.42%) and in Dukes' C stage of disease (all 10 cases) and the difference was statistically significant. Our results suggested that overexpression of p53 protein and higher PCNA score in later stages of CC indicate higher proliferative rate of tumor and therefore may have prognostic implications. Our results also indicate that mucinous differ from nonmucinous CC as well as proximal differ from distal CC in their genetic lesions. }" "p53 and Proliferating Cell Nuclear Antigen as Prognostic Factors in Colorectal Cancer"

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## "P P 54 1280" P 54 1280 Colorectal Cancer: Prognostic Factors and Chemotherapy

\*I. de Waziers<sup>1</sup>, L. Gervot<sup>1</sup>, A. Pfohl-Leszkwicz<sup>2</sup>, V. Carrière<sup>3</sup>, P.H. Cugnenc<sup>4</sup>, A. Berger<sup>4</sup>, F. Carnot<sup>4</sup>, P. Beaune<sup>1</sup>

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<sup>4</sup> Hospital La\ebnec, 75007 Paris, France Colorectal cancer is one of the most frequent causes of death by cancer in developed countries. Until now, few prognostic factors for colorectal cancer have been recognized and chemotherapeutic agents do not demonstrate much significant progress in the treatment of this disease. Epidemiological studies suggest that colorectal cancer can be attributed, at least in part, to carcinogens and mutagens present in diet and environment. The covalent binding of the xenobiotics or their reactive metabolites to DNA is believed to initiate chemical carcinogenesis. Using a <sup>32</sup>P-post labelling method, we investigated DNA adduct levels in control colons from patients without colorectal adenocarcinoma and in nontumoral and tumoral tissues from patients with colorectal adenocarcinoma. We showed that the DNA adduct level is significantly higher ( $p < 0.001$ ) in nontumoral than in control or tumoral colon samples. For the first time, we demonstrated in humans that the presence of numerous adducts in colonic mucosa is associated with colorectal cancer, a finding in agreement with the importance of chemical factors in causing this disease; therefore the measurement of DNA adduct level in colon samples could constitute a useful approach to the early detection of colorectal cancer. Since human colorectal tumors are insensitive to most chemotherapeutic agents there is a need for the discovery of new drugs that would show activity against this disease. We compared the drug-metabolizing enzyme expression in human tumors and in several differentiated populations isolated from the human colon carcinoma cell lines HT-29 and Caco-2. We showed that these cells could be used as models for candidate anticancer screening. Moreover, to increase the sensitivity of these cells to anticancer drugs for which the metabolism is known we began to transfect these cells with the cDNA of the P450 implicated in the formation of the antineoplastic metabolites. This strategy, if it appears efficient, could lead to possible gene therapy. Oncology, general: Screening, prevention Oncology, general: Therapy Oncology, specific: Colon, rectum } "Colorectal Cancer: Prognostic Factors and Chemotherapy"

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"P P 54 1281" P 54 1281 **Prognosis of Mucinous Colorectal Cancer** D. Lomanto, G. Dalsasso, A. De Luca, F. Giacobozzo, Meli E. Zarba, A. Salvio, L. De Angelis, G. Mennini, C. Tatarelli, V. Speranza

II Clinica Chirurgica-University of Rome "La Sapienza", Italy *Purpose of the Study* was to compare recurrence and survival rate of patients with adenocarcinoma (ADK) and mucinous carcinoma (MC) of colon rectum. *Methods.* We studied retrospectively 380 pts. operated for colorectal cancer. We classified the pts. in two groups: in the first 36 pts. (9.5%) with mucinous carcinoma (MC), defined as a neoplastic lesion of the mucosa with elevated present of mucin (60% of the volume), and in the second group 344 pts. (90.5%) with adenocarcinoma (ADK). We analyzed in these pts. the following parameters: age, sex, localization, stage, resectability, recurrence disease, prognosis and long term survival. Mean age was 54 yrs. in MC group and 63 yrs. in ADK group. *Results.* We observed more frequently rectal localization vs. other colonic sites in both groups (50% in MC group vs. 50.8% in ADK group). As for staging data, according to Duke's classification, in both groups we observed a lower rate of stage A in MC group than ADK group (10.5%) while we didn't observe any difference in pts. with stage B and D (MC: stage B 41%; stage D 19.5%) (ADK: stage B 48.8%; stage D 20%). Pts. with stage C showed a statistical significant difference with following results: 36.1% for MC group vs. 22.6% for ADK group ( $p < 0.05$ ). Among the pts. with recurrent disease (correcting the data for the perioperative mortality and excluding the pts. in stage D), we found that local recurrence rate was 72.7% in MC group and 46.6% in ADK group, the metastasis in MC group was 9% and 46.6% in ADK group, while the presence of both (metastasis + local recurrence) was 18.2% in MC group and 20% in ADK group. *Conclusion.* Our study show a different biological behaviour between MC and ADK especially for the local recurrence. This behaviour, for us and other Authors, is related to the presence of elevated quantity of mucin. Oncology, specific: Colon, rectum Oncology, general: Therapy } "Prognosis of Mucinous Colorectal Cancer"

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"P P 54 1282" P 54 1282 **Multivariate Analysis of Prognostic Factors in Resected Colorectal Cancer: A New Prognostic Index**. Guerra,

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<sup>1</sup> Dept. Pathology, H.V.C. y H.N., Pamplona, Spain *Aims:* The aims of the present study is to analyse different clinico-pathological variables of colorectal cancer to assess their prognostic value in order to elaborate a prognostic index helpful to select patients for adjuvant therapy. *Material and Methods:* 108 surgically treated patients of colorectal cancer with controlled 5-year survival were studied. Eighteen clinico-pathological variables and new biological parameters for image analysis (DNA or tumoral ploidy, proliferating cellular nuclear antigen PCNA and nucleolar organizing regions NORs) were analysed. *Statistical analysis:* Cox regression method. Prognostic index has been calculated as beta regression coefficients of independent variables. *Resultados: Final multivariate analysis model* (RR = relative risk) included: elevated CEA (RR 8.1) No CEA (RR 3.7) C<sub>1</sub>-C<sub>2</sub> stages (RR 2.4) D stage (RR 6.9) histological grade III (RR 3.9) lymphatic invasion (RR 4.7) Aneuploidy (RR 3.7). *Prognostic index (PI) scoring:* \* CEA postoperative: Normal = 0/No CEA = 2/CEA Elevated = 3 \* *Staging:* A-B<sub>1</sub>-B<sub>2</sub> = 0/C<sub>1</sub>-C<sub>2</sub> = 1/D = 3 \* *Ploidy:* diploid tumors = 0/aneuploids tumors = 2 \* *Histological grade:* I = 0/II = 0/III = 2 \* *Lymphatic invasion:* absent = 0/present = 2 *Risk groups:* Low (PI 0-5), Moderate (PI 6-8) y High (PI 9-12). After stratifying tumoral stages and grades according to PI different risk subgroups in B<sub>2</sub> and C<sub>1</sub>-C<sub>2</sub> stages and in the three differentiation grades could be established with significant differences concerning 5-year survival. *Conclusions:* 1.- The new prognostic index improves the prognostic information provided by conventional staging in B<sub>2</sub> and C<sub>1</sub>-C<sub>2</sub> stages due to the possibility of establishing subgroups of different risk and 5-year survival. 2.- Different risk subgroups are also determined in each histological grade according to PI with significantly different 5-year survival. Therefore this new index improves the prognostic significance of histological grade as an independent variable. 3.- This PI can be helpful to improve prognostic information and allows a better selection of patients for adjuvant therapy. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics }" "Multivariate Analysis of Prognostic Factors in Resected Colorectal Cancer: A New Prognostic Index"

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"P P 54 1283" P 54 1283 **Prognostic Value of Lymphocytic Infiltration and Tumoral Growing Margin in Surgically Treated Colorectal Cancer** A. Guerra, F.J. Jimenez,

\*F. Borda, B. Larrinaga, J.M. Martínez Peñuela, C. Jimenez

Hospital de Navarra, Pamplona, Spain Peritumoral lymphocytic infiltration and the type of tumoral growing margin have been considered of prognostic value by some authors in colorectal cancer, but results still remain controversial. The aim of the present study is to evaluate lymphocytic infiltration and tumoral growing margins in a series of colorectal adenocarcinomas, analysing possible influence upon 5 years survival. *Material and Methods:* 108 surgically treated colorectal adenocarcinomas were included in the study. Kaplan-Meier and Logrank tests were used for statistical analysis. *Results:* 5 years survival Lymph. infiltration No lymph. infiltration p(n = 86) (n = 22) Moderate 67.4 – 7.2% 45.4 – 10.6% N.S. Severe 64.7 – 7.8% 45.4 – 10.6% N.S. Expanding margin Infiltrating margin (n = 11) (n = 97) 100% 58.6 – 5.2% < 0.01 *Conclusions:* 1. Colorectal carcinoma 5 years survival rates are higher when lymphocytic infiltration is moderate or severe, but statistical significance is not reached. 2. Survival rate decreases with the presence of an infiltrating tumoral growing margin with statistical significance. 3. Evaluation of lymphocytic infiltration and tumoral growing margin supplies prognostic information in surgically treated colorectal carcinoma. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics } "Prognostic Value of Lymphocytic Infiltration and Tumoral Growing Margin in Surgically Treated Colorectal Cancer"

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"P P 54 1284" P 54 1284 **Peritoneal Carcinomatosis (PC) in Colorectal Cancer (CRC)  
Patients: Factors Influencing Survival**

\*V. Durand<sup>1</sup>, E.D. Dorval<sup>1</sup>, P. Bourlier<sup>2</sup>, C. Regimbeau<sup>1</sup>, Z. Benchellal<sup>2</sup>, J. Viguier<sup>1</sup>, P. Garraud, E.H. Metman<sup>1</sup>, G. Calais<sup>3</sup>

<sup>1</sup> Services de Gastroent\`e9rologie, CHU, F 37044 Tours

<sup>2</sup> Services de Chirurgie Visc\`e9rale et de, CHU, F 37044 Tours

<sup>3</sup> Services de Radioth\`e9rapie, CHU, F 37044 Tours PC associated with CRC is considered as a pejorative factor. *The purpose of this study* was to analyse the factors influencing survival of patients seen in our institution for PC with CRC. *Patients and methods:* 23 patients (15 men, 8 women) aged 64 years (extr: 24–83) were followed from November 1993 to January 1996. In all cases PC was diagnosed either macroscopically (clinical or CT scan assessment) or by biopsies during surgery. PC and CRC diagnosis were synchronous in 7 patients and metachronous in 16 with a mean delay between diagnosis of 14.9 months (extr: 0–137 months). CRC was located in the sigmoid colon in 13 patients, descending colon 2 patients, transverse colon 2 patients and right colon 6 patients. One patient had two synchronous CRC. Eight occlusions were diagnosed in 7 patients and required a surgical treatment in 3 cases. Survival, calculated since PC diagnosis, was analysed according to age, gender, OMS performance status, occlusion occurrence, CRC synchronism and resection, liver metastasis or ascitis presence or occurrence and PC treatment (chemotherapy N = 8, palliative surgery N = 9, corticosteroids N = 11, symptomatic treatment N = 4). *Results:* Overall survival was 26% and 7.8% at 1 and 2 years respectively and median survival was 5 months. Gender, age, presence of liver metastasis, CRC synchronism and resection and occlusion had no influence on survival. In contrast, a better survival was observed in patients without ascitis or good performance status and patients treated by chemotherapy or palliative surgery. 1 year survival 1 year survival p < Absence of ascitis 42% vs ascitis 9% 0.05 OMS 0–1 50% vs OMS 2–3 8% 0.05 Chemotherapy 64% vs corticosteroids 0% 0.01 Palliative surgery 56% vs corticosteroids 0% 0.01 *Conclusion:* PC from CRC origin has a poor prognosis however absence of ascitis and a good OMS performance status allowing chemotherapy or palliative surgery are associated with a significantly longer survival. Oncology, specific: Colon, rectum Clinical practice: Management strategy Oncology, general: Therapy }" "Peritoneal Carcinomatosis (PC) in Colorectal Cancer (CRC) Patients: Factors Influencing Survival"

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"P P 54 1285" P 54 1285 **Overexpression of p53 Protein in Colorectal Carcinoids**

\*Cheng Jhy-Young, Lin Jih-Chang

Division of Colorectal Surgery, Department of Surgery, Tri-Service of General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C. *Purpose:* The overexpression of p53 protein is considered to be a potential marker for the transition to advanced stages of tumor progression in many human cancers. The frequency and prognostic significance of such events in colorectal carcinoid tumors remain unknown. *Methods:* Thirty-one paraffin-embedded specimens of colorectal carcinoid tumor were studied by immunohistochemical staining. The association of p53 with tumor site, tumor size, invasion level, tumor stage, DNA pattern and patient survival were analyzed. *Results:* p53 protein was detected in 5 (16%) of 31 colorectal carcinoid tumors. There was a correlation between p53 expression and tumor site, tumor size, tumor stage and DNA ploidy ( $p < 0.05$ ). In addition, p53 overexpression indicated a poor prognosis in survival ( $p < 0.001$ ). *Conclusion:* Although the overexpression of p53 protein is uncommon in colorectal carcinoid, the expression has an association with clinicopathological criteria and may be used as an associated parameter to predict patient survival. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Overexpression of p53 Protein in Colorectal Carcinoids"

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"P P 54 1286" P 54 1286 **Prognostic Value of P-53 Protein in Surgically Treated Colorectal Carcinoma** A. Guerra, F.J. Jimenez-Perez,

\*F. Borda, B. Larrinaga, J.M. Martinez-Peñuela, C. Jimenez

Hospital de Navarra, Pamplona, Spain P.53 gene alteration with abnormal expression of P.53 protein has been reported in several malignant tumors. In some studies this abnormal expression has shown an independent prognostic value. The aim of the present study is to determine P.53 protein expression in a series of surgically treated colorectal carcinoma, analyzing its relation with overall 5 years survival and survival according to tumoral stage and differentiation grading. *Material and Methods:* 75 surgically treated colorectal adenocarcinomas were included in the study. Anti-P.53 antibody (Dako) was used for evaluation of P.53 protein expression. Kaplan Meier and Logrank tests were used for statistical analysis. *Results:* Overall 5 years survival was 63.12 – 4.8% for the whole series. Depending on P.53 protein expression, results were as follows: P.53+ P.53- p (n = 31/41%) (n = 44/59%) Overall 48.04 – 9.2% 64.2 – 7.3% < 0.1 Dukes A/B1/B2 62.8 – 12.7% 85.4 – 7.6% N.S. Dukes C1/C2/D 33.6 – 15.8% 42.9 – 11.4% N.S. Grade I–II 63.4 – 10.2% 66.6 – 8.2% N.S. Grade III 0% 55.5 – 18.5% < 0.05 *Conclusions:* 1. Colorectal adenocarcinomas with P.53 protein expression have poorer prognosis and lower 5 years survival than tumors without this protein, although statistical significance is not achieved. 2. In poorly differentiated tumors, 5 years survival is significantly lower when P.53 protein is present. 3. P.53 protein determination might be useful in colorectal cancer in order to improve prognostic information. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics } "Prognostic Value of P-53 Protein in Surgically Treated Colorectal Carcinoma"

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"P P 54 1287" P 54 1287 **Does Tumor Heterogeneity Influence the Staining for P53 in Colonic Adenocarcinomas and Their Lymph Node Metastases?** Ataoglu 'd6m'fcr, 'c7elik Bet'fcl, Kayhan Bur'e7ak,

\*G'f6rg'fclAhmet

G'dcTF, Ankara, T'fcrkiye A high percentage of colon carcinomas show positive staining for p53 immunohistochemically. Using a polyclonal antibody for p53 (CM1-Novacastra lab.) which is specific for wild and mutant forms, we investigated whether or not the tumor heterogeneity significantly affects the staining of the colonic adenocarcinomas and their lymph node metastasis with p53 antibody. In 40 colon specimens containing invasive colonic adenocarcinoma with lymph node metastases, positive staining was found in 37 carcinomas. Three cases (2 well-differentiated mucinous adenocarcinomas and 1 signet-ring cell carcinoma) showed no positive staining for p53. In these cases, the tumor positive lymph nodes also did not stain. One poorly differentiated adenocarcinoma showed positive staining for the tumor but the lymph node metastasis of the case was not positive for p53. The results show that the tumor heterogeneity does not significantly influence the staining of colonic adenocarcinomas and their positive lymph nodes, and p53 expression of the colonic adenocarcinomas is retained in their lymph node metastases. Oncology, specific: Colon, rectum }" "Does Tumor Heterogeneity Influence the Staining for P53 in Colonic Adenocarcinomas and Their Lymph Node Metastases?"

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"P P 54 1288" P 54 1288 **DNA Ploidy Pattern and P53 Expression in Some Colonic Lesions in Egypt** M.A. Madwar,

\*S.M. Kamal, M.A. Massoud, R.R. Kamel, S. Eissa, S. Ismail, N.H. Ismail, H. Shaker

Departments of Clinical Tropical Medicine, Surgery, Molecular Biology, Oncology and Pathology, Ain Shams and Cairo Universities, Cairo, Egypt *Background Aim:* The assessment of premalignancy and increased cancer risk is rather difficult. Ulcerative colitis and colorectal adenomas represent important premalignant conditions in the colon. The increasing incidence of colonic cancer in these patients made the search for detection of premalignancy of great value. This study was designed to determine DNA ploidy pattern and P53, the tumor suppressor gene, expression in some colonic lesions as ulcerative colitis, colorectal adenomas and colorectal carcinoma in Egypt. *Patients & Methods:* DNA ploidy and S phase fractions were assessed by flowcytometry together with detection of P53 by RT-PCR-SSCP method in colonic and rectal biopsies from 18 patients with ulcerative colitis, 8 patients with colorectal adenomas and 10 patients with colorectal carcinoma in addition to 20 patients with infective and nonspecific colitis as control group. *Results:* Diploid histograms were found in 12 ulcerative colitis cases, all colorectal adenoma cases and all control subjects. All colorectal cancer cases and 6 patients with ulcerative colitis exhibited DNA aneuploidy. Out of these 6 ulcerative colitis cases, four showed low grade dysplasia and two cases were indefinite for dysplasia. S phase fractions were highest in colorectal cancer (18.4 – 6.4%) followed by ulcerative colitis (17.4 – 5.0%) compared to colorectal adenoma (14.3 – 3.9%) and control subjects (13.8 – 2.1%) and a correlation was found between S phase fraction values and disease duration but not with disease activity in ulcerative colitis. P53 expression was detected in 6 (60%) of colorectal cancer and one case of ulcerative colitis all of which showed aneuploidy. Follow up of the 6 patients of ulcerative colitis showing aneuploidy without or with P53 expression (1993–1996) revealed early neoplastic transformation in one case. *Conclusion:* (1) DNA aneuploidy and P53 could be useful biomarkers of colorectal cancer risk and have a prognostic potential. (2) DNA aneuploidy and P53 can be valuable complement to endoscopy and histological examination in colonic cancer surveillance especially in high risk individuals. Oncology, specific: Colon, rectum Intestinal disorders: IBD diagnosis, monitoring Endoscopy, specific: Colon, rectum } "DNA Ploidy Pattern and P53 Expression in Some Colonic Lesions in Egypt"

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"P P 54 1289" P 54 1289 **Long-Term Outcome Following Surgery for Malignant Large Bowel Obstruction**

\*K. Yoshimura, M. Onda, N. Tanaka, H. Takasaki, K. Furukawa, K. Higuchi, T. Seya, S. Yokoyama, H. Kan, H. Maruyama, H. Sasabe, T. Yamada

First Dept. of Surg., Nippon Medical School, Tokyo, Japan This study determined the factors causing poor prognosis of patients with obstructing colorectal cancer. Seventy-six patients with bowel obstruction who had undergone curative surgery were studied in comparison with 1,039 patients of non-obstructive colon cancers (control cases) in the period from 1976 to 1994. Poor prognosis in survival was obtained after surgery for obstructing colorectal cancers ( $p = 0.025$ , log rank test). Tumour differentiations were not so poor in obstructing colorectal cancers ( $p = 0.181$ ), and outcome of poor prognosis after surgery for obstructing cancers was not related to tumour location, poor differentiation and vascular invasion. Tumour stage in Dukes' classification of obstructing colorectal cancer was more advanced than control cases ( $p = 0.004$ ). In the respect of tumour stage, there were no significant difference in survival between obstruction and control cases of stage A and B in Dukes' classification ( $p = 0.620$  and  $0.904$ , respectively). On the other hand the 5-year survival rate in stage C obstructing cancers was 37 per cent against 57 per cent of survival rate in stage C control cases ( $p = 0.065$ ). Thus it was suggested from these results that lymph nodes metastasis was most influential factor for poor prognosis in obstructing colorectal cancer. To dissect lymph nodes adequately, we attempt to remove intraoperatively feces in obstructing bowel by suction or lavage through colon with saline. These intraoperative procedure led to improve in survival compared with control ( $p = 0.886$ , log rank test). } "Long-Term Outcome Following Surgery for Malignant Large Bowel Obstruction"

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"P P 54 1291" P 54 1291 **CT Evaluation of the Resectability of Locally Advanced Rectal Cancer after Radiation and Chemotherapy**

\*N. Momot, J. Solovyova, V. Berejnoj

*Ukraine Purpose:* To determine accuracy of CT in evaluating the resectability of locally advanced rectal cancer in patients who underwent radiation and chemotherapy (5FU). *Materials and Methods:* 128 patients with locally advanced rectal cancer were studied by CT both before and after preoperative treatment. Optimal distention and better visualization of rectal wall were achieved by balloon dilatation of rectum with air insufflation. CT findings were compared with surgical and histopathological specimen. *Results:* Postoperative histology confirmed complete tumor disappearance in 26 patients, considerable reduction of tumor mass (more than 50% of initial size) – in 88 patients. 106 patients of the both group underwent sphincter-saving resection and 8 – abdomino-perineal resection. Remaining 14 patients had minimal or no effect and were identified as inoperable. CT results were correct in 105 cases (82%), equivocal – in 15 cases (12%) and incorrect – in 8 patients (6%). *Conclusion:* CT has a high diagnostic value in determining the efficacy of preoperative radiation and chemotherapy and evaluating subsequent resectability in patients with locally advanced rectal cancer. Oncology, specific: Colon, rectum Radiology and ultrasound: Diagnosis } "CT Evaluation of the Resectability of Locally Advanced Rectal Cancer after Radiation and Chemotherapy"

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"P P 54 1292" P 54 1292 **Safety of DVT-Prophylaxis with Enoxaparin Vs. Dextran-70 and Heparin in Digestive Surgery-Play-The-Winner Designed Studies**

\*G. Thorsen, T. Gerner, T. L'f8vig, R. St'f8rkson, P. Mowinckel, O. Reiertsen, S. Larsen

Harstad County Hospital, Norway *The aims* were to compare the safety of DVT-prophylaxis with enoxaparin vs. dextran-70 and unfractionated heparin in digestive surgery. *Materials:* In the first study comparing enoxaparin and dextran-70, 327 patients undergoing digestive surgery in two Norwegian hospitals were included. In the second study, comparing enoxaparin and heparin, 183 patients from two other hospitals were enrolled. *Methods:* In a Play-the-Winner (PTW) designed study the treatment of any next patient will depend on the outcome of the previous. If successful, the next patient receives the same treatment, if not, the comparative regimen will be given. Excessive bleeding according to specified criteria, severe adverse reaction, clinically detected DVT or pulmonary embolism (PE) were criteria for classification as "loser". The PTW-design will allocate most patient to the superior treatment. The main variable in PTW studies is the number of consecutive patients receiving the same treatment. *Results:* In the first study 200 patients were allocated to enoxaparin and 127 to dextran-70 ( $p < 0.01$ ). The rate of success was 83% in the enoxaparin group and 74.8% in the heparin group. The survival analysis confirmed superiority of enoxaparin ( $p < 0.01$ ). In the second study enoxaparin had a success rate of 80% and unfractionated heparin 81%. The survival analysis showed no significant difference between the groups. *Conclusion:* From a safety point of view DVT-prophylaxis with enoxaparin was found to be superior to dextran-70 and clinical equal to unfractionated heparin in digestive surgery. Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance }  
"Safety of DVT-Prophylaxis with Enoxaparin Vs. Dextran-70 and Heparin in Digestive Surgery-Play-The-Winner Designed Studies"

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"P P 54 1293" P 54 1293 **Intraluminal Prosthesis (SBS-Tube) Enhances Healing in One Layer Colon Anastomoses**

\*N. Buch, H. Glad, P. Svendsen, H.R.W. Oxlund, F. Gottrup, C.P. Hovendal

Dept. of Surgery A, Odense University Hospital, Denmark

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Copenhagen Wound Healing Center, Bispebjerg Hospital, Denmark  
In one layer colonic anastomoses the risk of anastomotic insufficiency is approximately 6.2% (Sarin S, Lightwood RG. Br J Surg 1989; 76: 493–5). Several factors impairs healing in anastomoses. Among these are local ischemia, infection, insufficient adaption of the cut ends and insufficient surgical technique. *Purpose:* To compare healing in one layer colonic anastomoses performed with or without a new intraluminal prosthesis (SBS-tube). *Method:* In 16 pigs the sigmoid colon was transected and an anastomosis was performed end-on with extramucosal continuous suturing. In the SBS-tube group (n = 8) the colon was slipped over the SBS-tube and the ends were approximated before suturing. The integrity and position of the SBS-tubes were examined post operatively by x-ray every second hour. After 96 hours the anastomoses were tested for leakage and breaking strength, and histology was performed. Measurements of tissue oxygen tension in the colonic wall at the anastomotic line, – 1 cm, and – 5 cm were performed after suturing and after 96 hours. *Results:* 75% of the tubes dissolved in less than 2 hours. Histology (see Figure): The SBS-tube group had a significantly better structure of layers (L) and mucosal epithelial covering (E). Similarly a tendency in favor of the SBS-tube group was found in tissue gap (A) and inflammation (I) but not in breaking strength (B) and amount of granulation tissue (G). Oxygen tension in the anastomotic line was also in favor of the SBS-tube group.

*Conclusion:* The SBS-tube facilitates the sewing of the anastomosis and seems to enhance healing parameters and restoring normal histology. This might be due to a better apposition of the cut ends and to a reduced suture tension. } "Intraluminal Prosthesis (SBS-Tube) Enhances Healing in One Layer Colon Anastomoses"

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"P P 55 1294" P 55 1294 **Analysis of Low Density Lipoprotein Receptor (LDLR) mRNA Expression by Polymerase Chain Reaction Assay in Colorectal Cancer** M. Notarnicola, M.G. Caruso, A. Cavallini, M. Bianco,

\*A. Di Leo

Lab. Biochemistry IRCSS "S. De Bellis" Castellana Grotte (Ba) Italy Proliferating tumour cells express increased numbers of LDLR molecules on their surface which enable them to bind and take up cholesterol-delivering LDL particles for growth and replication. Recently, the LDLR and its mRNA have been detected in 19 samples of human colon carcinoma [1]. On the contrary, in a previous study, we have demonstrated the presence of LDLR only in 17% of 53 specimens of human colorectal adenocarcinoma (CRA) [2]. *Aim* of this preliminary study was to verify whether the absence of LDLR in mostly neoplastic samples was due to the loss of its transcript. *Materials and Methods*: Twenty CRA neoplastic samples without LDLR protein, previously evaluated by ELISA method, were studied. LDLR mRNA expression was investigated by the reverse transcriptase polymerase chain reaction method (RT/PCR), and the relative PCR products by HPLC. *Results*: Both LDLR and LDLR mRNA were absent in 13 of 20 CRA samples, while LDLR mRNA (1.34 pg/<sup>5</sup>g total RNA), but not LDLR, was found in the remaining 7 CRA samples. *Conclusions*: The LDLR absence was due to the loss of its mRNA in 65% of cases (13/20). In the remaining 35% of cases (7/20), the absence of LDLR with high levels of LDLR mRNA may be due to a block of the translation process, with a subsequent store of mRNA within cells. Further studies will be required to detect the molecular events regulating the LDLR metabolism in neoplastic colorectal mucosa.

Reference: Int J Cancer 61: 461–464, 1995

Ital J Gastroenterol 25: 361–367, 1993. Hormones and receptors: Molecular biology Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Analysis of Low Density Lipoprotein Receptor (LDLR) mRNA Expression by Polymerase Chain Reaction Assay in Colorectal Cancer"

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"P P 55 1295" P 55 1295 **Polyamine Levels and Polyamine Oxidase Activity in Human Colorectal Cancer** M. Linsalata, B. D'Attoma,

\*A. Di Leo

Lab. Biochemistry, IRCCS "S. de Bellis" Spec. in Gastroenterologia Castellana G. (BA) Italy Polyamines (putrescine, spermidine and spermine) are low molecular weight amines required for normal cellular growth. Polyamine biosynthesis is known to increase with mitogenesis, and elevated polyamine concentrations are found in tumour tissue including gastrointestinal mucosa [1,2]. As regards the mechanisms maintaining cellular polyamine levels, the regulation of biosynthesis has been already clarified, but little is known about the regulation of their degradation pathway. During catabolism, N<sup>1</sup> acetylpolyamines are converted back to spermidine and putrescine by polyamine oxidase (PAO). Therefore, this enzyme seems to play an important role in modulating polyamine levels in the actively proliferating tissues such as neoplastic ones. In order to obtain more information about the metabolism of polyamines in human colorectal cancer, our *aim* was to evaluate polyamine levels and PAO activity in colorectal adenocarcinoma (CRA) and in surrounding mucosa. *Materials and Methods:* Twenty-five patients (18 males and 7 females; mean age 69 yrs, range 33–87) with CRA entered the study. Polyamine levels and PAO activity in neoplastic colorectal tissue and in surrounding uninvolved mucosa were analysed by HPLC [3,4]. Data were assessed by Student's t-test for paired data. *Results:* (polyamines are expressed as nmol/gr weight tissue, PAO activity is expressed as nmol of putrescine formed for 30 minutes for mg of tissue protein). M – \* p <0.01  
Put Spd Spm Total PAO  
Neoplastic tissue 32 – 31\* 297 – 170\* 531 – 353 859 – 533\* 1.3 – 0.6\*  
Normal mucosa 13 – 5.4 188 – 124 463 – 343 664 – 468 2.1 – 1.5  
*Conclusions:* Higher polyamine levels and a lower PAO activity were found in CRA samples than in normal mucosa. This suggests that PAO in neoplastic tissue is no more able to modulate polyamine levels and induces an abnormal polyamines accumulation.

Reference: Scand J Gastroenterol 1994, 29: 67–70.

J Gastroenterol 1995, 30: 705–709.

Dis Col Rec 1992, 35: 305–309.

J Chrom 1990, 533: 187–194. Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum } "Polyamine Levels and Polyamine Oxidase Activity in Human Colorectal Cancer"

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"P P 55 1296" P 55 1296 **Immunohistochemical Studies on the Histogenesis of Colorectal Carcinoma Induced by DMH**

\*T. Honjo, M. Onda, Y. Ozawa, T. Okuda, Y. Sumiyama

The Third Department of Surgery, School of Medicine, Toho University, Tokyo, Japan To elucidate the mechanism of the development in human colorectal carcinoma, we studied the kinetics of neuroendocrine cells in the tissue of experimentally-induced colorectal carcinoma in rats by DMH administration. *Materials & Methods:* Thirty six-week-old male rats (Donryu strain) were injected subcutaneously in the hip with DMH, at a dose of 20 mg/kg, once a week, 20 times continuously. *Results:* We sequentially observed the evolution of colorectal carcinoma by endoscopic examinations. The process of the evolution was classified into 4 types; small elevation type, flat elevation type, dome type, and elevation type with central depression. Neuroendocrine hormones such as endogenous peptides and biogenic monoamine as well as in normal colorectal mucosa were found in response to the tumor progression in each type. No physiological roles of these cells has been evidently known yet. *Conclusion:* It is highly suggested that trophic action of gastrointestinal hormones, which is known in normal gastrointestinal mucosa, possibly effects to the progression of the colonic carcinoma induced by DMH. Oncology, specific: Colon, rectum } "Immunohistochemical Studies on the Histogenesis of Colorectal Carcinoma Induced by DMH"

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"P P 55 1297" P 55 1297 **Immunohistochemical Study of Peptide and Amine Cells in Human Colorectal Cancer**

\*Y. Ozawa, M. Onda, T. Honjo, T. Okuda, Y. Sumiyama

Third Department of Surgery, School of Medicine, Toho University, Tokyo, Japan *Aim:* In order to clarify the histological occurrence, differentiation and development of colorectal cancer, the incidence and degree of peptide and amine cells in colorectal cancer tissue were studied relationship with its growth and progress. *Materials and Methods:* The subjects consisted of 220 cases colorectal cancer surgically removed in our department. Immunohistochemical activities were stained by streptavidin-biotin (SAB) technique using formalin-fixed, paraffin-embedded tissue sections Haematoxylin-eosin-stained specimens were used for histological classification. *Results:* In normal colorectal tissue, many peptideYY-, moderate numbered glucagon-, small numbered somatostatin-, immunoreactive cells were shown. On the other hand well- and moderately-differentiated adenocarcinoma tissue contained moderately numbered peptideYY- and many glucagon- immunoreactive cells. Tissue of poorly differentiated regions contained small numbered peptideYY- and many glucagon-immunoreactive cells. Peptide and amine cells were recognized significantly in the following cases: high blood vessel invasion, lymphatic invasion cases, high lymph node metastasis, positive cases of peritoneal dissemination and liver metastasis. Peptide cells appeared highly in a considerably deep focus infiltrating through the mucosa. *Conclusions:* Although the precise meaning of peptide cells in the focus of colorectal cancer has remained obscure, it is suggested that peptide and amine cells may be secreted from colorectal cancer tissue, and then has strongly inference on the differentiation and development of colorectal cancer. Oncology, specific: Colon, rectum } "Immunohistochemical Study of Peptide and Amine Cells in Human Colorectal Cancer"

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"P P 55 1298" P 55 1298 **Diagnostic and Prognostic Evaluation of Adenosine Deaminase Activity in Human Colorectal Tumors**

\*G. Kocic, D. Pavlovic, S. Nagorni, I. Stamenkovic, T. Cvetkovic, R. Kocic, S. Zivic

Institute of Biochemistry and Clinic for Gastroenterology University Nis, Yugoslavia  
Colorectal cancer is one of the most frequently occurring cancer in humans and there is an attempt to devise more selective novel tumor markers. High activity of adenosine deaminase (ADA) have been found during rapid growth state and/or after stimulation by growth factors. The study included patients with: colorectal carcinoma (10), polyps (8), resected colon carcinoma (4), patients without any pathological manifestation during colonoscopy (6). The ADA activity (IU/g prot.) was determined in endoscopic samples obtained from: carcinoma or polyp adjacent tissue, anastomoses after carcinoma resection and healthy tissue farther from lesion. The ADA activity was especially high in carcinoma adjacent tissue, i.e. endoscopically looking healthy (65.49 – 24.33 vs farther healthy 10.15 – 0.18;  $p < 0.001$ ). It means that ADA is important as early marker of abnormal proliferation, to discriminate normal and malignant colon epithelium and point to radical surgical resection. Estimating ADA activity from polyp adjacent tissue, the same trend was shown but significantly lower than in carcinoma (26.92 – 8.92 vs 14.28 – 5.87;  $p < 0.05$ ). The enzyme activity from anastomosis varied (from 13.38 to 40.60) with mean value 31.37 – 12.69. Obtained results could be useful in assessing prognosis and clinical outcome of the disease. The ADA activity in patients without pathological manifestations was 15.8 – 3.8. It confirms that ADA is included in growth control, progression and invasion of human colorectal cancer and could be used as simple routine test for monitoring tissue neoplastic transformation.  
Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum  
Endoscopy, specific: Colon, rectum } "Diagnostic and Prognostic Evaluation of Adenosine Deaminase Activity in Human Colorectal Tumors"

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"P P 55 1299" P 55 1299 **Effects of Pro-Oxidant Systems on the Lipid Peroxidation and Antioxidative Capacity in Human Colon Carcinoma and Polyps**

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Institute of Biochemistry & Clinic for Gastroenterology, University of Nis, Yugoslavia  
There is convincing evidence that cell prooxidant state can promote to neoplastic growth, and that antioxidants are antipromoters and anticarcinogens. The study included 8 patients with colon carcinoma and 6 with polyps. Biopsies were from tissue surrounding malignant lesion and polyp as well as from normal tissue farther from alternative spot. The level of lipid peroxidation products was examined in homogenates after exposing to suspensions of prooxidant system (ascorbate + iron) measuring MDA (nmol/mg prot.). Obtained results show that used prooxidant system was capable to produce much greater effects in control healthy tissue (MDA concentration 4.14 – 0.9 and 3.37 – 0.88) than in corresponding tissue surrounding carcinoma (2.19 – 0.45;  $p < 0.005$ ) or polyps (1.87 – 0.59;  $p < 0.01$ ). The antioxidative capacity of biopsy was tested using model of  $Fe^{++}$  induced generation of MDA in phospholipid liposome suspension and expressed as percent of the inhibition of MDA formation. The antioxidative capacity was increased from tissue surrounding carcinoma (72.2 – 11.5%) vs control healthy farther tissue (50.7 – 13.47%;  $p < 0.05$ ). However, there was not significant change in antioxidative capacity of polyps biopsy compared with normal mucosa. Decreased lipid peroxidation in tissue surrounding cancer and polyps is consistent with fact that transformation of normal into malignant tissue makes cells less peroxidisable. The increase of antioxidative capacity together with the decrease of lipid peroxidation in tissue surrounding carcinoma indicates that this change apparently occurs in early stage of complex sequences of malignant transformation. Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum  
Endoscopy, specific: Colon, rectum } "Effects of Pro-Oxidant Systems on the Lipid Peroxidation and Antioxidative Capacity in Human Colon Carcinoma and Polyps"

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"P P 55 1300" P 55 1300 **Dissimilar Activation Pattern of the Carcinogen Dimethylhydrazine (DMH) on Intracellular Polyamine Metabolism in Various Organs**

\*Chr. Löffler, F. Starp, U.R. Fölsch

I. Medical Department, Christian-Albrechts-University of Kiel, Germany Polyamines, and especially the key enzyme of polyamine de novo synthesis ornithine decarboxylase (ODC) are well known to play an important role in cell growth as well as tumour carcinogenesis. Weekly administration of the potent carcinogen dimethylhydrazine (DMH) is known to highly induce predominantly carcinoma of the colon after 6 months' treatment in rats. Simultaneous administration of the ODC inhibitor difluoromethylornithine (DFMO) highly significantly reduces DMH-induced carcinoma formation (Cancer Res 43: 1983; Anti Cancer Res 7: 1987). Furthermore, it is known that carcinogens have different activation patterns on polyamine metabolism in various organs (Löffler et al., Pancreas 10: 1995). *Methods:* Male Wistar rats (180 g) were s.c. injected with a single dose of DMH (20 mg/kg b.wt.) and 5–7 animals were killed 4, 8, 12, 24, 72, 120, 168, and 240 hours after DMH or saline injection, respectively. Polyamines, ODC, SAM-DC, SAT, organ weight, DNA polymerase, and DNA were analysed in distal colon, proximal colon, small intestine, liver, and pancreas. Additionally, 7 animals were simultaneously treated with DFMO (2% in drinking water plus 300 mg/kg b.wt. i.p. during daytime) and sacrificed 7 days after a single injection of DMH. *Results:* DMH treatment resulted in a significant increase in ODC activity and putrescine concentration in the proximal and distal colon after 7 days and DNA-polymerase after 10 days, while the other parameters were unchanged in the colon during the whole experiment. In small intestine ODC, SAM-DC, putrescine, and spermidine were in part significantly and prolonged increased between 8 and 168 hours. While in the liver SAT was significantly increased after 78 and 240 hours, no changes were found in the pancreas. DFMO treatment completely prevents DMH-induced activation of polyamine de novo synthesis in the gut. *Conclusions:* A single dosage of the potent colon carcinogen DMH resulted in dissimilar activation patterns in different organs: In the colon polyamine de novo synthesis is significantly induced after 7 days, in small intestine putrescine and spermidine de novo synthesis is increased between 8 and 168 hours, interconversion pathway is induced in liver, while no changes were found in the pancreas. Interestingly DMH activation of polyamine de novo synthesis appears late, which is different from findings in other carcinogens. These findings further contribute to a better understanding of carcinogen-induced complex intracellular biochemical mechanisms (DFG Lf6 459/2-1; AIR 569-92) Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Dissimilar Activation Pattern of the Carcinogen Dimethylhydrazine (DMH) on Intracellular Polyamine Metabolism in Various Organs"

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## "P P 55 1301" P 55 1301 **Telomerase Expression in Colorectal Cancer**

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Telomeres are DNA sequences found at the ends of all chromosomes. They have no synthetic function, but protect chromosomal ends during cell division. The telomeric sequence shortens with each cell division and when it reaches a critical length the cell dies (senesces). Telomerase is an enzyme not expressed by somatic tissues, but found in some tumours. It replaces lost telomeric sequences, preventing cell senescence and thus rendering the cell immortal. This immortalization may be an important step in the process of tumorigenesis. There has been little work on telomerase in colorectal cancer to date. We have studied 20 patients undergoing surgical resection of malignant colorectal tumours, as well as 8 patients with premalignant lesions. The cancers varied from Duke's stage A to advanced metastatic tumours. Mean age was 72, with a range of 51 to 80. Curative resections were carried out on 14 patients while 6 had palliative surgery. Enzyme activity was studied using a polymerase chain reaction (PCR) based method. Specific oligonucleotide primers are acted on by telomerase and telomeric sequences formed. These can then be separated and visualized by tel electrophoresis. Telomerase activity was detected in 19 of 20 (95%) primary tumours. All corresponding pieces of normal mucosa were negative. Of the adenomas 3 of 8 were positive. These results show that telomerase activation occurs in a high percentage of colorectal tumours and is an early feature of tumour progression. This sensitive technique for detecting telomerase activity could be a useful tool for early diagnosis and follow up of malignant disease in the future. Oncology, general: Molecular biology, genetics Oncology, specific: Colon, rectum } "Telomerase Expression in Colorectal Cancer"

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## "P P 55 1302" P 55 1302 The Value of Flow Cytometry in Colorectal Carcinoma

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<sup>1</sup> Dept. of Medical Oncology, Ankara University School of Medicine, Ankara, Turkey

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There has been a considerable number of conflicting reports on the role of DNA ploidy and S-phase fraction (SPF) as prognostic factors in colorectal carcinoma (CRC). Paraffin-embedded tumor specimens from 55 patients with operable CRC were studied by flow cytometry in order to determine the prognostic value of DNA ploidy and SPF. Twenty-two patients (40%) had aneuploid tumors and 33 (60%) had diploid ones. Mean SPF was calculated as 10.1% (range: 1.2%–34.8%) in all patients. There were no significant correlations between DNA ploidy and the other clinical and histological parameters used in the study. Twenty-two patients (40%) had aneuploid tumors and 33 (60%) had diploid ones. Mean SPF was calculated as 10.0% (range: 1.2%–34.8%) in all patients. There were no significant correlations between DNA ploidy and the other parameters used in this study, SPF was found to be significantly higher in aneuploid tumors and rectal tumors ( $p = 0.0002$  and  $p = 0.0397$ , respectively). Histologic grade, age and SPF were found to be significant factors for OAS in univariate analysis ( $p = 0.0225$ ,  $p = 0.0283$  and  $p = 0.0256$ , respectively). Adjuvant chemotherapy and age ( $\geq 60$  years) yielded better DFS rates in univariate analysis ( $p = 0.0493$  and  $p = 0.0074$ , respectively). While age and the histologic grade of the tumor were the independent significant factors for OAS ( $p = 0.033$  and  $p = 0.011$ , respectively), DNA ploidy and histologic grade of the tumor were found as independent prognostic factors for DFS ( $p = 0.0046$  and  $p = 0.0029$ , respectively). In conclusion, we can say that DNA ploidy status may be a weak prognostic factor for patients with CRC, whereas SPF seems to be a more important factor than DNA ploidy in the assessment of the prognosis.

Oncology, specific: Colon, rectum  
Oncology, general: Proliferation, carcinogenesis  
Clinical practice: Management strategy }

"The Value of Flow Cytometry in Colorectal Carcinoma"

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## "P P 55 1303" P 55 1303 **Dual Nature of Colorectal Cancer Mucin and Its Significance**

\*J.R. Jass, Y. Ajioka

University of Auckland, Auckland, New Zealand Mucin secretions within colorectal cancers appear to be of a dual nature. MUC2 codes for the protein component of secretory mucin produced by goblet cells. MUC1 codes for the protein component of glycolalyceal material produced normally by columnar cells and upregulated in cancers. The expression of MUC1 and MUC2 apomucins was studied in a series of colorectal cancers with the aim of distinguishing subtypes with differing histogenesis and prognosis. A series of 51 colorectal cancers was stained immunohistochemically with monoclonal antibodies to the mucin protein core structures MUC1 and MUC2. Four phenotypes were recognised: MUC2+/MUC1{ -}, MUC2+/MUC1+, MUC2{ -}/MUC1+ and MUC2{ -}/MUC1{ -}. The distribution of pathobiological and prognostic features within the four groups was studied. The phenotype MUC2+/MUC1{ -} was closest to normal large bowel mucosa. Cancers with this phenotype showed a negative correlation with lymph node metastases ( $p < 0.05$ ). MUC2+/MUC1+ cancers were associated with contiguous adenoma (villous and tubulovillous) and exhibited abundant mucin secretion ( $p < 0.05$ ). MUC2{ -}/MUC1+ cancers were frequently accompanied by a marked peritumoural lymphocyte reaction ( $p < 0.05$ ). Those with no lymphocyte reaction were associated with lymph node spread. MUC2{ -}/MUC1{ -} cancers were the most aggressive of the four phenotypes. The preceding data support the earlier suggestion that MUC2{ -} colorectal cancers may arise de novo and provide an approach to classification that cuts across traditional methods and may be highly relevant to aetiology, pathogenesis and prognosis. Oncology, specific: Colon, rectum Oncology, general: Proliferation, carcinogenesis } "Dual Nature of Colorectal Cancer Mucin and Its Significance"

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"P P 55 1304" P 55 1304 **Cathepsin B Like Activity in Colorectal Adenomas** M. Laiglesia,

\*F.J. Jimenez, I. Monreal<sup>1</sup>, P. Liso, F. Borda

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<sup>1</sup> CUN, Pamplona, Spain Cathepsin B is one of the proteinases that may play a key role in invasion and metastasis of colorectal cancer cells. It has been demonstrated that neoplastic cells possess cathepsin B at the plasma membrane whereas the enzyme is present only intracellularly in lysosomes of normal cells. Increased cathepsin B activity has also been reported in serum of patients with colorectal cancer. The aim of this study is to evaluate cathepsin B activity in serum of patients with colorectal adenomas. *Material and Methods:* 57 patients (39 males/18 females; mean age 63.4 yr) who underwent endoscopic resection of colorectal adenomas and had no other disease were included in the study. Patients were divided into three groups: I (n = 20) Tubular adenomas; II (n = 20) Villous adenomas; III (n = 17) High grade dysplasia adenomas. A control group of healthy donors (n = 20) was also evaluated. Cathepsin B activity was measured in serum using L-BAPNA as substrate, adding EDTA and DTT, at a reaction pH = 6. *Results:* Control: 0.163 – 0.03 U/l; I: 0.166 – 0.04 U/l; II: 0.168 – 0.05 U/l; III: 0.178 – 0.07 U/l. Statistical significance was found between the four groups (p < 0.01) and when comparing group III with the rest of groups (p < 0.05). *Conclusions:* 1. The increase in expression of cathepsin B activity may be a sensitive marker for progression from the premalignant to the malignant state in the development of colorectal cancer. 2. It might be questionable to consider a high grade dysplasia adenoma as a local lesion, when systemic biological modifications are found. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics } "Cathepsin B Like Activity in Colorectal Adenomas"

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## "P P 55 1306" P 55 1306 Effect of Radiotherapy on the Potential Doubling Time (Tpot) of Rectal Cancer

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*Aim:* The benefit of radiotherapy in adjuvant treatment of rectal cancer is demonstrated. However many questions remain about the modalities of this treatment which could be improved by a better understanding of the biological effects. We have evaluated the influence of radiation (34.5 Gy in 15 fractions and 3 weeks) on Tpot of rectal cancer. *Methods:* Four hours after infusion of 250 mg of bromodeoxyuridine (BrdU) endoscopic biopsies of the tumor were taken and we have studied the following kinetic parameters: labelling index (LI) of BrdU, duration of the S phase (Ts) and Tpot, with Begg's method. 36 measures have been done: 19 in patients with colonic cancers without prior chemotherapy or radiotherapy (group 1), 10 in patients with rectal cancers after radiotherapy (group 2) and 7 out of these 10 have been also investigated before radiotherapy (group 3). The means values of LI, Ts and Tpot were compared with Mann-Whitney's U test. *Results:* The LI, Ts and Tpot values (mean – SD) were: LI in % Ts in hours Tpot in days Group 1 11.7 – 6.0 14.3 – 4.4 5.1 – 2.7 Group 2 8.5 – 8.8 15.0 – 4.1 12.6 – 8.7 Group 3 10.3 – 5.2 13.1 – 4.2 5.5 – 3.3 The comparison between these groups suggests a decrease of Tpot value in the radiotherapy group (1 vs 2, p = 0.048) however no difference was shown neither between group 2 and 3 (p = 0.097) nor between colon and rectum cancers (p = 0.81). No difference were significant for LI and Ts. In the subgroup of diploid tumors a significant difference has been found for Tpot (1 vs 2 = 0.001; 2 vs 3 p = 0.008) and LI (1 vs 2 p = 0.008). *Conclusion:* These results suggest a decreased of kinetic activity of rectal cancer after radiotherapy, mainly in diploid tumors. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Effect of Radiotherapy on the Potential Doubling Time (Tpot) of Rectal Cancer"

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## "P P 55 1307" P 55 1307 Potential Doubling Time (Tpot) and Node Involvement of Colorectal Cancer

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*Aim:* In colorectal cancer (CRC) the node involvement determined by pathologic exam of surgical specimen is the main prognosis factor. Among new prognosis factors, the Tpot of CRC remains in evaluation. In this study we have studied relation between Tpot and node status of CRC.  
*Methods:* Four hours after infusion of 250 mg of bromodeoxyuridine (BrdU) endoscopic biopsies of the tumor were taken. We have studied the kinetic parameters: ploidy, labelling index (LI) of BrdU, duration of the S phase (Ts) and Tpot ( $Tpot = 1 LI/Ts$ ) with Begg's method. After surgical resection of the tumor, pathologic exam determined the node involvement (N+, N-). Means values of LI, Ts and Tpot were compared with Mann-Whitney's U test.  
*Results:* 19 ACR were studied. No difference was shown for kinetic parameters (ploidy, LI, Ts and Tpot) between N+ and N- groups. n LI (%) Ts (hour) Tpot (day) m – DS m – DS m – DS  
Diploid 8 5.8 – 3.0 9.7 – 2.6 6.5 – 3.4  
Aneuploid 11 13.1 – 3.0 10.7 – 3.0 2.9 – 1.2  
N+ 12 10.0 – 1.3 10.5 – 0.8 4.1 – 0.5  
N- 5 12.6 – 2.0 9.6 – 1.3 2.9 – 0.8  
LI was significantly lower in diploids tumors ( $p < 0.05$ ) and Tpot was shorter in aneuploids tumors ( $p < 0.05$ ). Ts values were not different between diploids and aneuploids tumors.  
*Conclusion:* The present results suggest that kinetic parameters of CRC are not linked to the node involvement. Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Colon, rectum } "Potential Doubling Time (Tpot) and Node Involvement of Colorectal Cancer"

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"P P 55 1308" P 55 1308 **Broad Bean Lectin Increases Morphological Differentiation and Inhibits Proliferation of Colon Carcinoma Cells** M. Jordinson, J. Calam,

\*M. Pignatelli<sup>1</sup>

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<sup>1</sup> Department of Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0NN, England *Purpose:* To investigate the effects of soya bean, peanut, mushroom, wheat germ and broad bean (BBL) lectins on the differentiation, proliferation and adhesion of colorectal carcinoma cell lines (SW1222, HT29, LS174T, S480, SW620). *Methods:* Cells were cultured in the presence or absence of each lectin at serial concentrations. Differentiation was determined in 3D-collagen gel, cell-cell adhesion by a homotypic cell aggregation assay and proliferation by tritiated thymidine incorporation and MTT assay. The role of molecules involved in cell-cell adhesion and epithelial differentiation was investigated using blocking antibodies to Epithelial cadherin (HECD-1), carcinoembryonic antigen (PR3B10) and EGP-40 (AUA1). *Results:* BBL which binds to mannose groups caused LS174T cells to differentiate markedly into organised glandular structures. Both gland formation and cell-cell adhesion induced by BBL was specifically inhibited by the monoclonal antibody AUA1. BBL also inhibited the proliferation of LS174T cells. *Conclusion:* BBL promotes differentiation and inhibits proliferation of LS174T cells and the adhesion molecule EGP-40 seems to be involved in this effect. These results point to a novel mechanism controlling the differentiation of colonic cancer cells. Oncology, specific: Colon, rectum Oncology, general: Proliferation, carcinogenesis Hormones and receptors: Growth factors } "Broad Bean Lectin Increases Morphological Differentiation and Inhibits Proliferation of Colon Carcinoma Cells"

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"P P 55 1309" P 55 1309 **Determination of the RER Status in Tumor Cells by a Single Microsatellite Genotyping** J.M. Hoang, P. Cottu, B. Thuille, S. Olschwang, R.J. Salmon, G. Thomas,

\*R. Hamelin

INSERM U434, G\ 'e9n\ 'e9tique des tumeurs, Institut Curie, Paris, France *Background and Aims.* Inactivation of mismatch repair (MMR) genes has been involved in tumorigenesis, leading to rapid accumulation of replication errors at microsatellite loci in tumor cells, called RER+. Microsatellite instability has been first described in colorectal tumors associated with hereditary non-polyposis colorectal cancer (HNPCC) syndrome. Somatic inactivation of MMR genes accounts for 15% of sporadic cases, that do not exhibit extended losses of heterozygosity, thus allowing to define two alternative pathways in colorectal carcinogenesis. Significant difference in prognosis has been shown between these two types of tumors, giving rise to a systematic determination of the RER status. *Methods.* 134 primary tumors and 27 cell lines derived from colorectal cancers were typed for at least 20 microsatellite loci. All but one were highly polymorphic dinucleotide repeats; the last one was a constant mononucleotide repeat. *Results.* 35 tumors exhibited instability at more than 50% of tested dinucleotide repeats loci and were thus classified RER+; 99 tumors did not show instability at more than 6% of the tested loci; 8 out of 27 cell lines were RER+. Genotyping of the mononucleotide repeat locus gave similar information for 160 out of the 161 samples. In RER{ - } samples, the size of the PCR product did not differ from that observed in normal matched DNA and in 70 DNAs of unrelated CEPH individuals. All but one RER+ samples were shown to carry an additional smaller allele, that could be resolved by non denaturing polyacrylamide gel electrophoresis and ethidium bromide staining. *Conclusion.* Genotyping of a single mononucleotide repeat microsatellite enables to unambiguously determine the RER status of colorectal tumor cells, even in the absence of matching normal DNA in the vast majority of cases. This simple, low-cost and rapid approach could be implemented in a routine hospital laboratory. Oncology, general: Molecular biology, genetics Oncology, general: Epidemiology Oncology, specific: Colon, rectum } "Determination of the RER Status in Tumor Cells by a Single Microsatellite Genotyping"

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"P P 55 1310" P 55 1310 **The Human Gastrin/Cholecystokinin Type B Receptor Gene: Study of Its Spliced Expression in Healthy and Tumoral Colon Samples, Associated Hepatic Metastases and Colonic Cell Lines**

\*Ph. Biagini<sup>1</sup>, D. Parriaux<sup>2</sup>, J.F. Cantaloube<sup>1</sup>, Ph. De Micco<sup>1</sup>, G. Monges<sup>2</sup>

<sup>1</sup> Regional Center for Blood Transfusion, Marseille, France

<sup>2</sup> Paoli Calmettes Institute, Marseille, France *Purpose* – The hypothesis that the growth of some gastro-intestinal cancers may be regulated by hormones requires the presence of receptors. The gastrin/cholecystokinin type B receptor (CCK-B receptor) are clearly recognized by gastrin, which is known to be involved in the development of some gastro-intestinal cancers. Variable splicing of exon 4 of the human receptor gene results in the presence of 2 different mRNA isoforms, the exact significance of which still remains to be elucidated. Here we investigated the expression of the 2 isoforms of the receptor on a series of healthy and tumoral colon samples, the associated hepatic metastases and four colonic cell lines. Gastrin mRNA expression was also investigated *Methods* – We performed reverse transcription-nested PCR using primers for the gastrin/CCK-B receptor; after Southern blotting, the long isoform was distinguished by hybridization with a specific probe and revealed by chemiluminescence. *Summary* – The short isoform was detected in all tumour and metastasis samples, in 8/10 normal colon and 3/4 colonic cell lines; whereas the long isoform, presumably functional, was expressed in 40% of the colon tumours, 43% of the hepatic metastasis, 50% of the normal colon samples, and 1 cell line (Sk-Co15). However, while gastrin transcript was detected in 90% of the tumours tested, only 30% also expressed the long isoform of the receptor. *Conclusions* – The implication of the gastrin/CCK-B receptor in an autocrine proliferative loop seems to be plausible in some colonic tumours and cell lines. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis } "The Human Gastrin/Cholecystokinin Type B Receptor Gene: Study of Its Spliced Expression in Healthy and Tumoral Colon Samples, Associated Hepatic Metastases and Colonic Cell Lines"

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## "P P 55 1311" P 55 1311 The Role of Transforming Growth Factor Alpha on Kinin Stimulated Ion Transport and Barrier Function in Human Colonic Epithelial Cells

\*J. Beltinger, W.A. Stack, C.J. Hawkey

Divison of Gastroenterology, University Hospital, Nottingham NG7 2UH, UK *Introduction:* Enhanced PG synthesis has recently been shown after activation of EGF receptors with TGF $\alpha$  on the basolateral cell surface of HCA-7 cells. Bradykinin has been shown to stimulate electrogenic chloride secretion both by a Ca<sup>2+</sup> dependent pathway and via eicosanoid production which can be attenuated by a cyclooxygenase inhibitor. We used the colonic epithelial cell line HCA-7, colony 29 to study the modulatory effect of TGF $\alpha$  on bradykinin induced chloride secretion and to show the possible interaction with local PG synthesis. *Methods:* HCA-7 cells were grown in DMEM (10% FCS), seeded on Snapwell filters and formed confluent monolayers within 10–12 days. Cells were either treated with TGF $\alpha$  (10 ng/ml) for 24 h in the presence or absence of NS398 (10<sup>-5</sup> M), a specific cyclooxygenase-2 (COX-2) inhibitor, added two hours before removing cells from the wells. The filters were placed into an Ussing chamber bathed in oxygenated Krebs-Henseleit solution and voltage clamped by continuous application of a short circuit current (SCC). Basal SCC (5A/cm<sup>2</sup>) and resistance (W/cm<sup>2</sup>) was measured and after an equilibration period bradykinin (BK) (10<sup>-6</sup> M) was added. All drugs were added to the basolateral side of the monolayer. Data are expressed as mean – SEM. *Results:* TGF $\alpha$  10 ng/ml significantly increased baseline resistance (control 138 – 9.9 vs TGF $\alpha$  169 – 16.2 W/cm<sup>2</sup>, n = 20, p = 0.03). The COX-2 inhibitor NS398 did not affect basal resistance of controls but enhanced resistance of TGF $\alpha$  pretreated monolayers (TGF $\alpha$  169 – 16.2 vs TGF $\alpha$ +NS398 178 – 17.2 W/cm<sup>2</sup>, n = 13, p = 0.03). SCC due to BK was attenuated by TGF $\alpha$  (control 13.3 – 2.7 vs 9.2 – 1.8 5A/cm<sup>2</sup>, n = 11, p = 0.03). SCC to BK was further reduced by NS398 in basal and TGF $\alpha$  pretreated cells (control vs control + NS398: 13.3 – 2.7 vs 6.6 – 1.4 5A/cm<sup>2</sup>, n = 6, p = 0.049; TGF $\alpha$  vs TGF $\alpha$ +NS398: 9.2 – 1.8 vs 4.4 – 1.3 5A/cm<sup>2</sup>, n = 6, p = 0.03). *Conclusion:* These data provide evidence of the regulatory role of growth factors on resistance and BK stimulated ion transport in intestinal epithelial cells with a central role of PG synthesis which may have important implications in pathogenic conditions such as inflammatory bowel disease. *Acknowledgment:* J Beltinger is supported by a grant from the Swiss National Foundation Hormones and receptors: Growth factors } "The Role of Transforming Growth Factor Alpha on Kinin Stimulated Ion Transport and Barrier Function in Human Colonic Epithelial Cells"

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## "P P 55 1312" P 55 1312 Nonsteroidal Anti-Inflammatory Drugs Inhibited Human Colonic Cancer Cell Migration in Culture

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Dept. of Gastroenterology, Juntendo Univ. School of Med. Tokyo, Japan Recently, it was reported that nonsteroidal anti-inflammatory drugs (NSAIDs) inhibited carcinogenesis in the colon, possibly inhibiting cyclooxygenase (COX). Intake of NSAIDs is believed to reduce the relative risk of colorectal cancer in human. The mechanism of reduction is not clear, but as NSAIDs are potent inhibitor of tumorigenesis in rodent models of colon cancer, inhibition of COX may be involved in the mechanism for its antitumor activity. Recently, we established a new, simple and convenient model to analyze the cancer cell migration using a human colonic cancer cell line. Using this model, we assessed the migration capacity of colonic cancer cell line (Human rectal adenocarcinoma: SW837) and assessed the effects of aspirin (ASA) and indomethacin (IND) treatment. *Method:* SW837 cells ( $3.5 \times 10^5$  cells) were inoculated into the round enclosed area (diameter, 15 mm) by silicon fence in a plastic culture dish and cultured in L-15 medium with 10% FBS. Inoculated cells formed round shaped cell sheet in 3 h and subsequently silicon fence was removed and then the cancer cell migration was monitored. The number of migrated cells from the cell sheet in a unit area of free space was counted after 48 h. The effects of ASA ( $0.1 \times 10^{-2}$ ,  $0.2 \times 10^{-2}$ ,  $0.3 \times 10^{-2}$  mM) and IND treatment (0.01, 0.03, 0.1 mM) were assessed. Cell growth of the controls, ASA and IND treatment groups were detected by using monoclonal anti-5-bromodeoxyuridine antibody (BrdU) and BrdU labeling index (BrdU positive cell number/total cell number  $\times 100$ ) were calculated randomly selected unite area. *Result:* After the removal of the fence, cancer cells started to migrate and spread to all directions from the edge of the cell sheet. The number of cancer cells migrated from the cell sheet 48 h after the start of migration was presented in a table. Data: mean – SD, \*  $p < 0.05$ , \*\*  $p < 0.01$ , n = 4, mm: distance from the edge of cell sheet. 0 – 5 mm 5 – 10 mm 10 – 15 mm Control 971 – 76 812 – 61 483 – 30 ASA  $0.1 \times 10^{-2}$  mM 781 – 68 707 – 52 419 – 190.2  $\times 10^{-2}$  mM 712 – 59\* 503 – 31\*\* 303 – 11\*\* 0.3  $\times 10^{-2}$  mM 520 – 41\*\* 276 – 21\*\* 178 – 12\*\* IND 0.01 mM 830 – 72 794 – 57 425 – 26\* 0.03 mM 688 – 62\*\* 589 – 50\* 388 – 32\* 0.1 mM 490 – 38\*\* 377 – 38\*\* 322 – 21\* The migrated cell number decreased in relation to ASA and IND dose. BrdU labeling index of ASA and IND treatment groups were lower than that of the control groups. *Conclusion:* Our data suggest that ASA and IND inhibit not only colon cancer cell growth but also cancer cell migration, thus possibly exhibiting the antitumor effects in the colon. Motility, specific: Colon, anorectum Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach } "Nonsteroidal Anti-Inflammatory Drugs Inhibited Human Colonic Cancer Cell Migration in Culture"

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"P P 55 1313" P 55 1313 **Regulation of RXR{  $\alpha$  } is not the Mechanism by which 9-*cis* Retinoic Acid Modulates Vitamin D Action in Two Human Colon Cancer Cell Lines**

\*K.F. Kane, E.A. Walker, G.R. Williams, M.J.S. Langman

The University of Birmingham, Birmingham, U.K. 1{  $\alpha$  }, 25(OH)<sub>2</sub> vitamin D<sub>3</sub> (D<sub>3</sub>) protects against colorectal cancer and has been proposed as a potential therapeutic agent in the treatment of this malignancy. D<sub>3</sub> action is mediated by a high affinity nuclear receptor (VDR) that regulates target gene transcription by binding to specific sequences of DNA known as D<sub>3</sub> response elements (VDREs). VDR may bind to VDREs as a homodimer or as a heterodimer with a retinoid X receptor (RXR). The ligand for RXR is 9-*cis* retinoic acid (9-*cis*RA) which has the potential to modify D<sub>3</sub> action. 9-*cis*RA has been proposed as a chemotherapeutic agent in its own right. We have previously demonstrated VDR and RXR{  $\alpha$  } and {  $\gamma$  } mRNA expression in both normal and malignant human colorectum and the presence of functional VDR in primary cultures. In addition, 9-*cis*RA differentially modifies D<sub>3</sub> action in two human colon cancer cell lines. The aim of the present studies was to determine the mechanisms by which 9-*cis*RA modifies D<sub>3</sub> action in HT-29 and Caco-2 cells. HT-29 and Caco-2 cells were treated with D<sub>3</sub> and 9-*cis*RA (10<sup>-8</sup> M) and RXR{  $\alpha$  } protein was assessed by Western analysis. Nuclear extracts from human tissues also underwent Western analysis. Caco-2 cells were transfected with reporter genes containing VDREs from two D<sub>3</sub> responsive genes (24-hydroxylase or calbindin D<sub>9K</sub>) and treated with D<sub>3</sub> or 9-*cis*RA. A 55 kDa RXR{  $\alpha$  } protein was expressed in both cell lines and was not regulated by either D<sub>3</sub> or 9-*cis*RA. RXR{  $\alpha$  } was also expressed in both normal mucosa and malignant tissue from 15 human specimens. In transfection studies, D<sub>3</sub> caused a modest activation of both VDRE constructs (- 1.5 fold) although this did not reach significance. Treatment with 9-*cis*RA resulted in a response of similar magnitude (- 1.4 fold activation, not significant). We demonstrate that RXR{  $\alpha$  } protein is present in malignant and normal human colorectum and two colonic carcinoma cell lines. Hormonal treatment did not alter RXR{  $\alpha$  } expression and regulation of RXR{  $\alpha$  } does not account for the differential responses of the two cell lines to 9-*cis*RA. Early transfection studies suggest that 9-*cis*RA may have a direct effect on the transcription of D<sub>3</sub> responsive genes but further investigations are necessary to elucidate these pathways. It is important to determine the action of 9-*cis*RA on D<sub>3</sub> signalling before it can be considered as an antiproliferative agent. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics Oncology, general: Therapy } "Regulation of RXR $\alpha$  is not the Mechanism by which 9-*cis* Retinoic Acid Modulates Vitamin D Action in Two Human Colon Cancer Cell Lines"

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"P P 55 1314" P 55 1314 **Establishment and Characterization of a New Human Rectal Neuroendocrine Carcinoma Cell Line**

\*T. Yamada, M. Onda, N. Tanaka, T. Seya, Y. Kanazawa, K. Furukawa, K. Higuchi, H. Takasaki, K. Yoshimura, S. Yokoyama, H. Kan, H. Maruyama, H. Sasabe

First Dept. of surg. Nippon medical school, Tokyo, Japan Human colorectal neuroendocrine carcinomas (NEC) are rare, and there are a few reports of NEC cell lines available for study. We have reported rectal NEC xenograft in nude mice at 4th UEGW (1995). This tumor derived from a metastatic inguinal lymph node of a 58-year old Japanese female. We succeeded in establishing of a human NEC cell line from this tumor. This cell line has been maintained in culture for more than 1 year. The cells grew in a monolayer, thereafter tended to pile up and formed a cluster. The doubling time was approximately 44 hours at the 10th generation. Immunohistochemical studies of these cells showed positive reactivity for somatostatin, chromograninA, NSE, S-100, gastrin, glucagon, pancreatic peptide, CEA, p53, and PCNA, although negative reactivity for serotonin and VIP. These results were similar to formalin-fixed, paraffin-embedded tissue samples of the original tumor and xenograft tumor. CEA p53 SS CgA NSE S-100 gas. glu. PP PCNA Ser. VIP Primary + + + + + + + + + { - } { - } Xenograft + + + + + + + + + { - } { - } Cell line + + + + + + + + + - { - } This cell line provides an excellent model to study the biological behavior of NEC, enabling future studies on treatment of the disease. Oncology, specific: Colon, rectum } "Establishment and Characterization of a New Human Rectal Neuroendocrine Carcinoma Cell Line"

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"P P 55 1315" P 55 1315 **Gastrointestinal Hormone mRNA Expression in Human Colonic Adenocarcinomas, Hepatic Metastases and Cell Lines**

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<sup>1</sup> Regional Center for Blood Transfusion, Marseille, France

<sup>2</sup> Paoli Calmettes Institute, Marseille, France *Purpose* – To investigate the expression of four main hormones of the digestive tract by performing reverse transcription polymerase chain reaction (RT-PCR) on a series of samples including both tumoral and healthy colonic tissues, hepatic metastases and colonic cell line samples, as well as to study the patterns of labelling obtained with serological and morphological markers. *Methods* – After extraction and reverse transcription, gastrin, somatostatin, cholecystokinin (CCK) and transforming growth factor alpha (TGF { a}) mRNA were detected by performing PCR and nested PCR using specific primers. Immunohistochemical assays against the corresponding proteins were also performed. *Summary* – The cell lines expressed all four mRNAs. Gastrin mRNA was present in most of the tumoral and metastatic samples, while the somatostatin transcript was detected in all the samples and was frequently over-expressed in the normal colon. TGF { a} mRNA was systematically expressed in tumours of the right and transverse colon, but not in those located in the left colon; the expression of CCK mRNA was systematically absent in the left colon. *Conclusions* – The data presented here shed some light on the transcriptional events involved in the production of the various hormones present in the gastrointestinal tract, in both healthy and tumoral tissue. The various mRNAs which are expressed in cell lines are therefore not systematically expressed in the human pathology. Oncology, specific: Colon, rectum Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis }" "Gastrointestinal Hormone mRNA Expression in Human Colonic Adenocarcinomas, Hepatic Metastases and Cell Lines"

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"P P 55 1316" P 55 1316 **The Distribution of *Kirsten-ras* Mutations within Early Colorectal Adenocarcinomas**

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<sup>3</sup> Dept of Histopathology, The Royal Marsden Hospital & Institute of Cancer Research, Sutton, Surrey, UK **Background:** We have previously shown that detection of mutations in codons 12 or 13 of *Ki-ras* in whole tissue samples from early colorectal adenocarcinomas do not predict relapse. However, tumours may not be homogeneous for *Ki-ras* genotype and a few mutated cells may be responsible for subsequent relapse. Therefore, would microdissection of specific areas of colorectal tumours increase the rate of detection of mutations and are there differences between regions within the tumour? **Methods:** Blocks were retrieved from patients who had undergone apparently curative resection for early colorectal adenocarcinoma but subsequently developed tumour recurrence. Blocks from patients with no relapse after more than 5 years follow up were also used. PCR amplification and direct sequencing to determine *Ki-ras* status was used firstly, in whole tissue samples, secondly, in microdissected samples prepared from the 1 mm leading edge of tumour and thirdly, in microdissected samples from the central tumour core at least 2 mm away from the leading edge. **Results:** Eighteen patients with relapse and 5 long term survivors were identified. Astler-Coller modification of Dukes staging was stage A in 2, B1 in 18 and B2 in 3 patients. A sequence was obtained in all 23 whole tissue samples, in 22 of the leading tumour edges and 20 of the tumour centres. The same genotype was always found in both microdissected samples from the same tumour. In 4 tumours these were mutated. No mutation was found in a microdissected sample which was not detected in the whole tissue sample. In 1 patient, a mutation was detected in the whole tissue sample, but not in the microdissected samples. It is likely that this mutation arose from the epithelium surrounding the tumour rather than from the tumour itself. **Conclusions:** These findings suggest that colorectal tumours are homogeneous for *Ki-ras* genotype and that using PCR amplification followed by direct sequencing of whole tissue samples is accurate, so microdissection of tumours is not necessary. These results also support the hypothesis that the *Ki-ras* status of a colorectal adenocarcinoma is determined early during it's development. (Dr. H.J.N. Andreyev is supported by the British Digestive Foundation) Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "The Distribution of *Kirsten-ras* Mutations within Early Colorectal Adenocarcinomas"

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"P P 55 1317" P 55 1317 **Colon Cancer and Gut Hormones**. J. Payer Jr., M. Huorka, I. & Dobrev;uris, P. Ondrejka, M. Ilkov'e1,

\*P. Hol'e9czy

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The etiopathogenesis of colon cancer (CC) seems to be multifactorial. Hormonal imbalance may be involved. Somatostatin (S) has an antiproliferative influence on mucosal cells. The main antimitogenic effect of S is the inhibition of cell proliferation via inhibition of phosphorylation. Gastrin (G) stimulates DNA synthesis in large bowel epithelial and tumorous cells. Cortisol (C) as a stress-catabolic hormone may be involved in development of some malignant diseases. In 11 patients suffering from CC S, G and C circadian rhythmicity was studied. Seven blood samples were withdrawn during 24 hours for RIA analysis, Fisher's periodogram and Halberg's cosinor analysis was applied for each individual set of measurement. A 24-hour endogenous circadian rhythm of S, G and C was confirmed. The results were compared to the circadian rhythm of the hormones observed in healthy subjects (N) (n-12), patients with ulcerative colitis (UC) (n-10), and colon polyps (P) (n-9). Higher 24 hours amplitude of S compared to N ( $p < 0.05$ ), higher mesor ( $p < 0.05$ ) of G compared to all other groups and lower 24 hours amplitude, ( $p < 0.01$ ) of C compared to all other groups were found. These findings may reflect the role of G in the etiopathogenesis of CC and results of C secretion could indicate a reduced responsiveness in patients with malignant diseases. S blood levels probably do not reflect its antitrophic effect at cellular and subcellular levels. } "Colon Cancer and Gut Hormones"

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"P P 55 1318" P 55 1318 **Edible Mushroom (*Agaricus Bisporus*) Lectin, a Cell Growth Inhibitor, Stops Growth of HT29 Colon Cancer Cells in G<sub>1</sub> and Decreases the Expression of *c-myc***

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<sup>2</sup> Department of Biochemistry, University of Liverpool, Liverpool, UK *Purpose:* The Thomsen-Friedenreich (TF) antigen (Gal{ b}1-3GalNAc{ a}{ -}) is a common onco-fetal carbohydrate antigen in intestinal epithelia. Our previous work has shown that the non-cytotoxic TF-binding lectin from the edible mushroom *Agaricus bisporus* (ABL) inhibits proliferation in a range of malignant and normal epithelial cells (Cancer Res. 1993; 53; 4627) and has to be internalized to produce its inhibitory effect (Gastro. 1995; 108 (4); A558). The present study was designed to assess the relationship of this inhibitory effect by ABL to cell cycle and the expression of protooncogenes *c-myc* and p53. *Methods:* 1) HT29 colon cancer cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) with 5% fetal calf serum (FCS). The cells were partially\_synchronized by culturing in 0.5% FCS for 2 days. ABL (80 \b5g/ml) or PBS (control) was added for 8 hours at 37\b0C. 4% FCS was added to stimulate cell growth. Cells were fixed at various times in ethanol and stained with propidium iodide. Total DNA content per cell was assessed using a flow cytometer. 2) Subconfluent HT29 cells were precultured in serum-free DMEM for 1 day before addition of ABL (30 \b5g/ml). RNA was extracted at different time by the guanidinium thiocyanate-phenol-chloroform method. Northern blots were probed with cDNA for *c-myc* or p53. *Results:* After 21 hours addition of FCS, the proportion of ABL treated cells in G<sub>1</sub> had increased from 81.1% to 90.6% compared with a decrease to 70.8% (n = 3) in control. The expression of *c-myc* mRNA was decreased by 48 – 7% (n = 3) in the presence of ABL and this effect on *c-myc* of ABL was abolished by coincubation with asialo fetuin which expresses GalGalNAc. No significant effect on p53 mRNA expression was found. *Conclusion:* Mushroom lectin inhibits proliferation by holding cells in G<sub>1</sub>. The decrease of *c-myc* mRNA expression may provide a partial explanation for the anti-inhibitory effect. Motility, specific: Colon, anorectum Hormones and receptors: Molecular biology Oncology, general: Proliferation, carcinogenesis }" "Edible Mushroom (*Agaricus Bisporus*) Lectin, a Cell Growth Inhibitor, Stops Growth of HT29 Colon Cancer Cells in G<sub>1</sub> and Decreases the Expression of *c-myc*"

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"P P 55 1319" P 55 1319 **Expression of the Transforming Growth Factor Alpha, Epidermal Growth Factor and Epidermal Growth Factor Receptor, in Colorectal Cancer and Its Liver Metastasis**

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<sup>2</sup> 2nd Dept. of Patho., Nippon Medical School, Tokyo, Japan Transforming growth factor { a } (TGF{ a }) which is structurally homologous to epidermal growth factor (EGF) binds to epidermal growth factor receptor (EGFR) and is implicated in the growth and proliferation of colorectal cancer. To evaluate the role of TGF{ a }, EGF and EGFR in colorectal cancer progression, we investigated their expression in colorectal cancer and its liver metastasis. *Materials and method:* Immunohistochemical staining was performed on paraffin-embedded specimens of 32 colorectal cancer and 40 liver metastasis. EGFR, EGF and TGF{ a } expression were evaluated semiquantatively. *Results:* Overall expression of TGF{ a }, EGF and EGFR in primary lesion were 40.6%, 75.2% and 78.3%, respectively. In metastatic liver lesion, a significantly higher rate of TGF{ a } and EGFR expression was found (77.5% and 87.5%), but there was no difference in the expression of EGF (67.5%). Synchronous expression of TGF{ a } and EGFR occurred in 52.5% in liver metastasis compared with 34.1% in primary lesion. And overexpression of TGF{ a } and EGFR in the hepatocytes surrounding metastatic cancer cells were observed. *Conclusions:* These results suggests that autocrine/paracrine interaction of TGF{ a } and EGFR play an important role in liver metastasis of colorectal cancer and hepatocytes are also involved in these interaction. Hormones and receptors: Growth factors Oncology, specific: Colon, rectum }" "Expression of the Transforming Growth Factor Alpha, Epidermal Growth Factor and Epidermal Growth Factor Receptor, in Colorectal Cancer and Its Liver Metastasis"

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"P P 56 1320" P 56 1320 **Role of Proximal Stomach and Pylorus on Gastric Emptying and Gastrointestinal Transit Delays Elicited by Acute Blood Volume Expansion in Awake Rats** M.C.V. Rêago, J.R.V. Graça, F.A.A. Gondim, R.B. de M. Gondim, R.P. Dantas,

\*F.H. Rola

Department of Physiology and Pharmacology, Federal University of Ceará, Brazil. Acute blood volume expansion delays gastric emptying (GE) and gastrointestinal (GI) transit rates of liquid in awake rats (Gondim, F. de A.A., *In VIII European Symposium on Gastrointestinal motility*, 1996). In this study, we investigated the proximal stomach and pyloric roles on the phenomenon. Male Wistar rats, 180–220 g were fasted for 16–24 h, with water *ad libitum*, anaesthetized with thiopental and a proximal gastrectomy (n = 22) or Heineke-Mikulicz pyloroplasty (n = 20) performed 7 days before GE and GI transit measurements. Blood volume expansion was performed by Ringer-Bicarbonate, i.v. infusion (1 ml/min up to 5% of body weight). Before the experiment, the animals were fasted for 24 h, with water *ad libitum* until 2 h before the intragastric intubation – 1.5 ml of a phenol red solution, 0.05 g/ml with 5% glucose. The animals were sacrificed by thiopental overdose 10 min or immediately after meal (standards). Data (mean – SEM) were analyzed by One-Way ANOVA and Student Newman-Keuls test. Analogous to intact controls GE and GI transit rates were decreased in SHAM operated (laparotomy) animals after 5% expansion (p < 0.05). Proximal gastrectomy increased both GE and GI transit rates (p < 0.05), blocked blood volume expansion effect on GE but not on GI transit rates. Pyloroplasty increased GE and GI transit rates, but did not block blood volume expansion effect. Subdiaphragmatic vagotomy blocked blood volume expansion effect on GE and GI transit of liquid in SHAM and animals submitted to pyloroplasty. Mean arterial pressure was not modified, but central venous pressure levels increased and haematocrit rates decreased (p > 0.05). Pyloroplasty did not block blood volume expansion effect on GE and GI transit. The proximal stomach plays a role on GE delays elicited by blood volume expansion. However, GI transit delays can be accomplished without its participation, probably by an increase on the intestinal resistances as part of the mechanisms that acutely balance blood volume excess. *Financial support*: CNPq, CAPES-PET, UFC e UNIMED-Ce. *Motility, specific: Stomach Motility, specific: Small bowel* } "Role of Proximal Stomach and Pylorus on Gastric Emptying and Gastrointestinal Transit Delays Elicited by Acute Blood Volume Expansion in Awake Rats"

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"P P 56 1321" P 56 1321 **Increased Gastric Emptying of Liquids in Rats Is Induced by "*H. helmanii*" Type I Infection**

\*I. Duval-Araujo, D.M.M. Queiroz, C.J.R. Simal, V.S.P. Marino, A.G.P. Magnago, S.D. Carvalho, L.A.S. Machado

Laboratory of Research in Bacteriology & Post-Graduate Surgery Laboratory, Faculdade de Medicina, UFMG, Brazil It has been demonstrated that *H. pylori* infection induces somatostatin and gastric secretion alterations, which could be associated to gastric motility alterations. However, this hypothesis has not yet been experimentally validated because of the lack of an appropriate animal model. It was recently demonstrated that "*H. helmanii*" type I (Hh), a spiral bacterium that infects the stomach of both humans and pig, easily colonizes and induces an inflammatory response in the gastric mucosa of rodents. Therefore, we aimed to study the relationship between gastric motility and gastrin and somatostatin levels in rats experimentally infected by Hh. Twenty Wistar female rats were included in this study. They were divided in two experimental groups: A, 10 non-infected animals (control group) and B, 10 animals inoculated *per os* with 0.2 ml of gastric mucus of a Hh positive swine. After 56 days of inoculation, the animals were anesthetized with ketamine chloride (50 mg/Kg body weight) and gastric emptying was studied by scintigraphy after oesophageal administration of 0.2 ml <sup>99m</sup>Tc-fitate diluted (1:1) in 2.5% peptone solution. After the scintigraphic study, blood samples were collected for serum gastrin contents measurement and fragments of the gastric antrum were obtained for somatostatin contents evaluation. Hh infection was confirmed by urease test and carbolfuchsin-stained smears examination. The results were analyzed by the Kruskal-Wallis test and the level of significance was set at  $p < 0.05$ . All animals of the group B were Hh-positive. There was an decrease in the gastric remnant in group B when compared to the group A (72.7 – 17.7% vs. 47.7 – 13.9%,  $p = 0.01$ ). Serum gastrin levels of the group B were higher than in the group A (7.7 – 5.7 pg/ml vs. 3.7 – 1.9 pg/ml,  $p = 0.03$ ), and gastric somatostatin levels were lower in the same group (1.3 – 0.2 ng/ml vs. 4.9 – 3.0 ng/ml,  $p = 0.01$ ). In conclusion, gastric motility is altered in rats infected by a gastric spiral bacterium. This abnormality could be related to the concurrent abnormalities of gastrin and somatostatin secretion. } "Increased Gastric Emptying of Liquids in Rats Is Induced by "*H. helmanii*" Type I Infection"

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"P P 56 1322" P 56 1322 **Gastric Emptying Rate of Solid Food in Relation to Body Mass Index: A Scintigraphic Evaluation** A. Brogna, R. Ferrara, A.M. Bucceri,

\*F. Catalano, V. Leocata, G. Natoli, A. Blasi

Istituto di Medicina Interna "A. Francaviglia" University of Catania, Catania, Italy It's known that different physiologic conditions including body size can modify gastric emptying. Few studies in the literature have compared gastric emptying to the Body Mass Index (BMI). We have evaluated gastric emptying rate of solid meal in volunteers of varying sizes to determine whether BMI and gastric emptying rate are correlated. Twelve healthy volunteers (males, mean age 42 – 12 (SD) yrs, age range 23-54 years) with different BMI (mean 26.6 – 4.2 (SD) kg/m<sup>2</sup>, range 18.5–31.8 kg/m<sup>2</sup>) were studied. All the subjects, after an overnight fast, ate a standard 750 kcal meal containing chicken liver prelabelled in vitro with 150 <sup>99m</sup>Tc sulphur colloid. Immediately after the meal, the subject was asked to lie supine for radioscanning with two scintillators placed opposite one another and connected to a computerized ratemeter to evaluate gastric radioactivity decrement. Results were expressed as emptying index at 120 min (E.I.) calculated by means of the following formula: E.I. = [(100{ - }RRt)/At] times; 100, where RRt = % residual radioactivity at time t; At = area under the emptying curve at time t (= 120 min). Results are shown in fig. They demonstrate an inverse linear relationship between gastric emptying rate and BMI. *Conclusion:* The variable of BMI must be taken in account when gastric emptying is evaluated.

Motility, specific: Stomach } "Gastric Emptying Rate of Solid Food in Relation to Body Mass Index: A Scintigraphic Evaluation"

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"P P 56 1323" P 56 1323 **Effects of Levosulpiride on Clinical Symptoms, Gastric Emptying and Orocaecal Transit Time in Functional Dyspepsia: A Randomised, Double-Blind Placebo-Controlled, Cross-Over Study**

\*M.P. Brunori, P. Bovo, M. Marcori, S. Brunelli, L. Rigo, B. Vaona, M. Filippini, G. Talamini, V. Di Francesco, L. Frulloni, A. Gaudio, A. Moi, G. Cavallini

Gastroenterological Unit, University of Verona, Italy Fifty percent of patients with functional dyspepsia present abnormal gastric emptying [1]. Levosulpiride is an orthopamidic drug which stimulates gastrointestinal motility. The aim of the study was to assess the efficacy of levosulpiride in speeding up gastric emptying and oro-caecal transit time and in relieving symptoms in patients with functional dyspepsia. The patients sample comprised 30 subjects (11 M, 19 F; mean age 37.63 – 12.21 years; range 22–65 years) suffering from functional dyspepsia. The patients were submitted to clinical assessment, blood-chemistry tests and instrumental investigations (US, EGDS, barium enema) to exclude the presence of organ disease and were then treated for two 3-week periods with levosulpiride (25 mg  $\times$  3/day) and placebo (according to a double-blind cross-over design) with a 2-week wash-out period between the two treatments. Prior to therapy and after each course of treatment, oro-caecal transit time was estimated (lactulose H<sub>2</sub> breath test) together with gastric emptying (ultrasonographical method), the latter after a standard balanced 700 cal meal. Subjective symptoms were assessed before and after treatment with scores from 0 to 3 for each symptom. Data were analyzed statistically by non-parametric multivariate analysis for repeated measures. *Results* 1) gastric emptying time was significantly reduced ( $p < 0.00001$ ) after levosulpiride (236.6 – 38.7) as compared to both baseline (295.50 – 32.3) and post-placebo (298.50 – 30.0) levels; 2) oro-caecal transit time was also reduced ( $p < 0.007$ ) after levosulpiride (66.00 – 25.09) as compared to both baseline (88.00 – 38.54) and post-placebo (84.0 – 36.01) levels; 3) symptoms, considered as a whole, were better relieved by levosulpiride therapy (6.90 – 6.01) ( $p < 0.0001$ ) than by placebo (13.8 – 7.33) ( $p < 0.0001$ ) as compared to baseline value (20.30 – 4.23). *Conclusions:* from both the clinical and instrumental points of view levosulpiride was found to be an effective drug in the treatment of functional dyspepsia.

Reference: Talley NJ. *Gastroent Int* 1991; 40: 145–60. Motility, specific: Stomach Motility, general: Functional GI disorders Motility, specific: Small bowel } "Effects of Levosulpiride on Clinical Symptoms, Gastric Emptying and Orocaecal Transit Time in Functional Dyspepsia: A Randomised, Double-Blind Placebo-Controlled, Cross-Over Study"

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"P P 56 1324" P 56 1324 **Effect of Cisapride Suppositories in Patients with Delayed Gastric Emptying. A Double-Blind Trial**

\*R.J.M. Brummer<sup>1</sup>, E.A.J.M. Schoenmakers<sup>2</sup>, G.A.K. Heidendal<sup>2</sup>, L.G.J.B. Engels<sup>3</sup>, C.T.B.M. van Deursen<sup>4</sup>, R.W. Stockbr\fcgger<sup>1</sup>

<sup>1</sup> Department of Gastroenterology, University Hospital Maastricht, The Netherlands

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<sup>3</sup> Internal Medicine, Maasland Hospital, Sittard, The Netherlands

<sup>4</sup> Internal Medicine, St. Gregorius Hospital, Brunssum, The Netherlands *Aim:* to determine whether a single dose of cisapride suppositories (60 mg) promotes gastric emptying in patients with demonstrated delayed gastric emptying. *Methods.* This was a randomized, double-blind, placebo-controlled, cross-over study. Patients with delayed gastric emptying received 2 suppositories (either 2 {b4} 30 mg of cisapride or placebo, interval 1 week). Gastric emptying (Tc-labelled solid meal) was determined during 3 hours by scintigraphy with an attenuation correction using a lateral scintigraphy. Of the 32 patients, 4 were excluded because of protocol deviations. An on-protocol analysis was applied (28 patients, 14 in each group, 13 women, 15 men). *Results.* The main results are presented in the table below. Cisapride Placebo Half emptying time (min) 76.2 \*\* 103.7 Normalized patients 25 (89%) 17 (61%) Remaining activity (2 hours) 19.2% \*\* 35.2% Patients with rectal complaints 7 2 Patients with adverse events 10 4 \*\* p < 0.001, Wilcoxon two-sample test Mainly mild or moderate gastrointestinal adverse events were found (cisapride 9, placebo 3). *Conclusions.* A single dose (60 mg) of cisapride suppositories promotes gastric emptying of a solid meal in patients with delayed gastric emptying: compared to placebo the half emptying time was reduced by 30 minutes. Overall, the treatment was well tolerated. Clinical practice: Management strategy Motility, general: Functional GI disorders Motility, specific: Stomach } "Effect of Cisapride Suppositories in Patients with Delayed Gastric Emptying. A Double-Blind Trial"

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## "P P 56 1325" P 56 1325 Gastric Emptying Time and CLO-Test in Patients with NUD: Effect of Cisapride

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<sup>3</sup> Chulalongkorn University Hospital, Bumrungrad Hospital, Bangkok This study was designed to compare the gastric half emptying time (GET 1/2) in patients with non-ulcer dyspepsia (NUD) and healthy controls, and to study the effect of cisapride on GET-1/2 in NUD patients. All NUD patients had normal ultrasound and normal upper endoscopy. Gastric biopsy was taken from the antrum for CLO-test. All underwent a solid gastric emptying test using a Technetium-99 labeled egg meal. NUD patients received oral cisapride 10 mg tid ac for 2 weeks and had a repeated gastric emptying test after treatment. Symptoms were scored before and after cisapride treatment. In total 35 patients with NUD and 22 healthy controls were studied. The pre-treatment GET-1/2 in NUD patients was 90.92 – 28.47 min. This value was significantly different from that of healthy controls who had a mean GET-1/2 of 77.64 – 14.23 min ( $p = 0.023$ ). CLO test was positive in 20/35 patients (57.1%). After 2 weeks of cisapride treatment, the GET-1/2 decreased significantly (90.92 – 28.47 min VS 73.59 – 21.63 min,  $P < 0.0001$ ) in the NUD group. Significant symptom improvement was obtained similarly in the CLO positive and CLO negative NUD patients. The GET-1/2 after cisapride treatment was reduced to the same extent in both CLO positive and CLO negative patients. This study suggested that cisapride can improve dyspeptic symptoms and shorten GET-1/2 in NUD patients regardless of their CLO status. Delayed gastric emptying may be one of the permissive factors in the pathogenesis of NUD and may account for the symptomatology in this group of patients. Motility, specific: Stomach/Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Gastric Emptying Time and CLO-Test in Patients with NUD: Effect of Cisapride"

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"P P 56 1326" P 56 1326 **The Effect of Phenytoin on Gastric Dysrhythmia in Diabetic Patients**  
**S. Unal, Z. Ozturk, I. Dogan**

Gazi University School of Medicine, Department of Gastroenterology, Ankara, Turkey Patients with diabetes frequently complain about gastrointestinal symptoms. Almost half of these patients have delayed gastric emptying. In EGG, the frequency of gastric dysrhythmia observed more frequently than normal population. It has been thought that at least in some diabetic patients gastric dysrhythmia might still be the probable causes of delayed gastric emptying. In this study, we examined 42 diabetic patients and 20 healthy controls. The diabetic patients consist of 33 female and 9 male, whereas the control group was 13 female and 7 male. The mean age was 52 – 12 for the diabetic patients and 34 – 12 for the controls. The average duration of diabetes was 7 – 5 years. EGG examinations were done after an overnight fasting period with cutaneous electrodes. The electrogastrograms were recorded for 30 minutes fasting period and 30 minutes postprandial period. Patients with abnormal EGG records were given 300 mg, 200 mg phenytoin P.O. at 7 p.m and 12 p.m., respectively. In the following morning EGG records were repeated. 52 percent of diabetic patients had peripheral neuropathy, 26 percent had autonomic neuropathy, and 59 percent had upper gastrointestinal symptoms. While 15 diabetics patients had abnormal EGG records, in controls only 2 were abnormal ( $p < 0.05$ ). Table 1: The effect of phenytoin on gastric dysrhythmia

	Before	After	p value
phenytoin	phenytoin	phenytoin	
Percentage of normal slow waves	49 – 13	70 – 11	$< 0.001$
Tachygastria percent	33 – 13	19 – 6	$< 0.001$
Percentage of bradygastria	17 – 11	10 – 7	$< 0.05$
Power ratio (postprandial/fasting)	1.38 – 1.02	1.97 – 0.78	$< 0.05$

In this study, it has been found that diabetics have more EGG abnormalities compared to normal subjects. Phenytoin reduces the gastric dysrhythmia in most of the patients. It is concluded that the therapeutic benefit of phenytoin is due to its effects on the activity of ectopic pacemaker foci in the antrum. Motility, specific: Stomach } "The Effect of Phenytoin on Gastric Dysrhythmia in Diabetic Patients"

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"P P 56 1327" P 56 1327 **Solid Meal Gastric Emptying in Hypothyreosis — A Prospective Clinical Study**

\*K. Jonderko, G. Jonderko, T. Golab, C. Marcisz

Dept. of Physiology, IOMEH Sosnowiec, IV. Chair and Dept. of Internal Medicine, SUSM Tychy, Poland

**Objective.** The study aimed at the evaluation of the gastric emptying (GE) kinetics of a solid meal in hypothyreotic patients before and after a substitutive treatment with L-thyroxin. **Methods.** Twelve female hypothyreotics (aged 45.3 – 8.7 years, mean – SD) and a control group of 12 healthy women (aged 34.5 – 8.1 years) were examined. The GE of a <sup>99m</sup>Tc-labelled solid meal was measured with the use of a gamma camera in every patient before the treatment, and in 10 of them a repeat GE examination was performed after the restoration of euthyreosis; the median duration of the treatment was 5.5 mo (range 2.5 to 12 mo). **Results.** The mean gastric transit time (MTT<sub>90</sub>) and the fraction of the test meal retained in the stomach after 90 min (F<sub>90</sub>) were statistically significantly greater in untreated hypothyreotics than in healthy controls (MTT<sub>90</sub>: 42.01 – 1.86 min patients vs 40.06 – 1.00 min controls, p = 0.0043; F<sub>90</sub>: 64.3 – 15.4% patients vs 50.8 – 8.2% controls, p = 0.0173). In ten patients in whom a second GE measurement was taken after the achievement of euthyreosis, a slight increase of the GE was observed (MTT<sub>90</sub>: 41.46 – 1.49 min before vs 41.04 – 1.81 min after the treatment, NS) which was then no longer statistically significantly different from that of the healthy controls. No relationship was found between the GE and the severity of clinical symptoms of hypothyroidism. GE remained, however, slowed in some patients despite the restoration of euthyreosis. **Conclusion.** We conclude that: (i) long-lasting hypothyreosis is accompanied by a slightly slowed GE of solids, and (ii) restoration of euthyreosis does not imply a parallel improvement of the hypothyroidism-associated delay in GE. Motility, specific: Stomach Motility, general: Functional GI disorders } "Solid Meal Gastric Emptying in Hypothyreosis / A Prospective Clinical Study"

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"P P 56 1328" P 56 1328 **Patterns of Solid Meal Gastric Emptying in Hyperthyreotic Patients-Effect of Pharmacological Management** G. Jonderko,

\*K. Jonderko, T. Golab, C. Marcisz

IV. Chair and Dept. of Internal Medicine, SUSM Tychy, Poland

Dept. of Physiology, IOMEH Sosnowiec, Poland *Objective.* The study aimed at the evaluation of the kinetics of gastric emptying (GE) of a solid meal in hyperthyreotic patients during a pharmacological treatment with thiamazole until the moment of euthyreosis restoration.

*Methods.* Fourteen female patients (33.4 – 2.6 y, mean – SE) with recently diagnosed hyperthyreosis took part in the study. Twelve age-matched healthy women (34.5 – 2.3 y) constituted a control group (C). Every patient underwent the GE examination before treatment (I). In 12 patients the GE was re-examined on the 3rd treatment week (II). After the achievement of euthyreosis, which happened after 4.5 mo (median; interquartile range 2.0 to 7.3 mo), a third GE measurement was taken in 13 patients (III). The GE of a <sup>99m</sup>Tc-labelled solid meal was measured with the use of a gamma camera. Time-activity curves from the gastric region of interest were used, after subjection to appropriate corrective procedures, to calculate the mean gastric transit time (MTT<sub>90</sub>) and the fraction of the test meal retained in the stomach after 90 min (F<sub>90</sub>). *Results.* Before the treatment and on the third week of management the GE of hyperthyreotics was not statistically significantly different from that of healthy controls (MTT<sub>90</sub>: 39.44 – 0.30 min [I], 39.31 – 0.64 min [II] and 40.06 – 0.29 [C]; F<sub>90</sub>: 46.6 – 1.9% [I], 47.9 – 3.7% [II] and 50.8 – 2.4% [C]). The restoration of euthyreosis was accompanied by a slight but statistically significant increase in the GE – p < 0.05 in the case of F<sub>90</sub> vs the pre-treatment situation. Also the patients' GE was found then to be slightly but statistically significantly faster than in healthy controls (MTT<sub>90</sub>: 38.72 – 0.39 min [III], and F<sub>90</sub>: 42.2 – 2.3% [III] – p < 0.05 vs C for both parameters). *Conclusion.* We conclude that in hyperthyreotic women the GE of solids does not differ significantly from age-matched healthy female controls and remains unchanged during a pharmacological treatment. After achievement of euthyreosis a slightly but statistically significantly faster GE is observed in the patients when compared to healthy controls. Motility, specific: Stomach Motility, general: Functional GI disorders }" "Patterns of Solid Meal Gastric Emptying in Hyperthyreotic Patients-Effect of Pharmacological Management"

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"P P 56 1329" P 56 1329 **Gastric Emptying of Fat Determines the Pattern of Postprandial Gallbladder Contraction in Humans**

\*A. Kasicka-Jonderko, K. Jonderko, Z.K. Sliwinski, A. Nowak

Dept. of Gastroenterology, SUSM Katowice, Poland

Dept. of Physiology, IOMEH Sosnowiec, Poland *The purpose* of this study was to determine factor(s) accounting for the functional relationship between the gallbladder (GBE) and gastric (GE) emptying. *Methods.* Two nearly isocaloric but differing with regard to their fat content semiliquid meals were used. A low-fat meal (LFM, 0.94 kcal/ml, 500 ml, 10.5 g fat) was consumed by 19 healthy subjects (8 M and 11 F, aged 27.8 – 1.7 years) on 19 occasions. A high-fat (HFM, 1.08 kcal/ml, 250 ml, 21.3 g fat) was eaten by 12 healthy subjects (8 M and 4 F, aged 33.8 – 3.0 years) on 22 occasions. Gallbladder volume and antral cross-sectional area was measured ultrasonographically before and at 10-min intervals for one hour after meal ingestion. Data are means – SE. *Results.* The two meals evoked different patterns of GE and GBE (Figure). At 60 min postprandially 154.7 – 17.0 kcal contained in 165 – 18 ml of the LFM left the stomach, whereas with HFM the corresponding values were 205.0 – 11.4 kcal in 190 – 11 ml. At that time, however, 3.5 – 0.4 g fat was evacuated from the stomach with LFM, as opposed to 16.2 – 0.9 g fat with HFM. Considering the fractional GBE as a dependent variable, whereas volume, energy, and fat emptied from the stomach as possible predictive factors, a forwardly prosecuted stepwise multiple linear regression revealed that only the GE of fat was a significant predictor of the postprandial GBE: multiple R = 0.8817, p = 0.00015. *Conclusion.* The gastric evacuation of fat appears to be a crucial factor determining the time-course of the GBE evoked by a semiliquid caloric meal.

Nutrition: Nutrients and gut function Motility, specific: Stomach } "Gastric Emptying of Fat Determines the Pattern of Postprandial Gallbladder Contraction in Humans"

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"P P 56 1330" P 56 1330 **An Experimental Stressor, Isometric Exercise, Affects the Intra-gastric Distribution of a Solid Meal in Humans**

\*A. Kasicka-Jonderko, K. Jonderko, J. Kolodziejczak, S. Nowak, A. Nowak

Dept. of Gastroenterology, and Dept. of Nuclear Medicine, SUSM Katowice, Poland

Dept. of Physiology, IOMEH Sosnowiec, Poland *Aim.* We investigated the effect of physical stress by handgrip isometric exercise on human solid meal gastric emptying (GE). *Methods.* Twelve healthy subjects (7 M and 5 F, aged 26.2 – 1.5 [SE] years) participated in the study. On separate days, after ingestion of a 300 kcal solid test meal they performed isometric exercise by squeezing a handgrip dynamometer for five three-minute periods separated by seven-minute intervals, *or* rested on the control day. The gastric emptying of a <sup>99m</sup>Tc-Amberlite-labelled meal was continuously surveyed for 120 min postprandially by means of a gamma camera. Systolic (SBP) and diastolic (DBP) arterial blood pressure, heart rate (HR) and skin resistance (SR) were monitored as indices of the cardiovascular response to stress. Data are means – SE. *Results.* Isometric exercise brought about a strong sympathetic excitation: { D } SBP +35.7 – 2.0 mmHg (p << 0.001); { D } DBP +29.5 – 2.2 mmHg (p << 0.001); { D } HR +16.0 – 1.7 beats { \d7 } min<sup>-1</sup> (p << 0.001); { D } SR = { - } 448 – 55 kohm (p << 0.001) ( { D } = mean difference stressor minus control). In every subject the repeated handgrip exercise caused transient retrograde shifts of the radiolabelled solid meal from the antral into the fundal stomach part. This phenomenon resulted in short-term periods of delayed emptying of the proximal stomach (ANOVA: p < 0.001 vs control) and antral filling (ANOVA: p < 0.005 vs control). The total stomach emptying of solids remained, however, unaffected during and after the stress period, although shortly after the termination of the stress exposure a negligible trend towards an increased GE was observed. *Conclusion.* Isometric exercise evokes bouts of a retrograde movement of solid food from the distal into the proximal stomach without, however, any significant effect on the overall GE of solids. Motility, specific: Stomach Hormones and receptors: Brain gut axis } "An Experimental Stressor, Isometric Exercise, Affects the Intra-gastric Distribution of a Solid Meal in Humans"

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## "P P 56 1331" P 56 1331 The Effect of Cisapride on Gastric Emptying in the Critically Ill Patient

\*D. Heyland, G. Tougas, D.J. Cook, G.H. Guyatt

McMaster University Medical Centre, Hamilton, Canada *Background:* Early administration of enteral nutrition to critically ill patients is associated with improved clinical outcome including reduced sepsis, improved wound healing, maintenance of intestinal mucosal integrity, and decreased mortality. In critically ill patients, gastric emptying is often markedly delayed and precludes enteral nutrition. The efficacy of prokinetic therapy in improving gastric emptying has not been demonstrated in critically ill patients. *Objective:* To evaluate the effects of cisapride, a gastrointestinal motility agent, on gastric emptying on critically ill patients. *Methods:* In a randomized, double-blind, placebo-controlled study, we recruited mechanically ventilated patients expected to remain the ICU for more than 48 hours. We enrolled 72 patients; male (61%), age 54.0 (+19.1), 47% were post-operative, 83% were receiving narcotics and the mean SAP Score was 9.5 ( { - } 2.9). As acetaminophen is only absorbed in the small bowel, acetaminophen absorption rate can be used as an index of gastric emptying. 1.6 g of acetaminophen suspension was administered via a nasogastric tube into the stomach (day 1). Blood samples were drawn at t = 0, 30, 60, 90, 120, and 180 minutes for measurement of plasma acetaminophen levels determined by the enzymatic degradation method. We measured the maximum plasma concentration ( $C_{max}$ , umol/L), time to reach  $C_{max}$  (min.) and area under the plasma concentration-time curve t = 180 ( $AUC_{180}$ , umol/min/L). The following morning (day 2), patients were randomized to receive either 20 mg of cisapride suspension or placebo and gastric emptying was repeated. *Results:* The difference (day 2 { - } day 1) in  $C_{max}$  was 49.1 umol/L in the cisapride group compared to 12.3 umol/L in the placebo group (p = 0.005). The time reach to reach  $C_{max}$  was also significantly shorter in the cisapride group ( { - } 40.8 minutes vs. { - } 4.2 minutes, p = 0.02). The difference in the area under the time-acetaminophen concentration curve was also greater in the cisapride group (5534 vs 2832, p = 0.09). *Conclusions:* Cisapride enhances gastric emptying in critically ill patients. Since intolerance to enteral feedings is associated with increased morbidity, improved gastric emptying with cisapride may improve mortality and morbidity in this patient population. Studies to specifically examine the effects of Cisapride on tolerance of enteral nutrition and infectious morbidity are needed. Supported by the Janssen Research Foundation. Motility, specific: Stomach Nutrition: Nutrients and gut function } "The Effect of Cisapride on Gastric Emptying in the Critically Ill Patient"

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## "P P 56 1332" P 56 1332 Intra-gastric Distribution and Gastric Emptying Estimated by 3D-Ultrasonography

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**Aims:** To investigate the accuracy and applicability of a magnetic position sensor system for acquisition of 3D ultrasound images for the purpose of determining gastric emptying rates and intra-gastric distribution of a meal. **Methods:** A system for position and orientation measurement based on magnetometry was interfaced to an ultrasound scanner with a 5–3 MHz phased array transducer. After calibration, in vitro accuracy was evaluated by scanning a porcine stomach. Thereafter, fourteen male volunteers, median age 35 years, were included and examined in the morning after ingestion of a 500 ml soup meal (20 kcal). One subject was scanned on 6 consecutive days. Scanning was performed fasting, and up to 35 min postcibally by conventional 2D scanning of the antrum and 3D ultrasound of the total stomach. Volume estimation and reconstruction of the stomach in 3 dimensions were performed after manual tracing on a Unix workstation. **Results:** This 3D system yielded a strong correlation ( $r = 0.997$ ) between true and estimated volumes in vitro. The limits of agreement were  $\{-9.1; 70.1\}$  ml in the volume range 1200–1900 ml. The mean error was  $2.1 - 1.1\%$  (SD) in vitro. The intersubject variability of the total gastric volumes ranged from 12.5% to 46.0%, less than for antral area variability. The average half emptying time in healthy subjects was  $22.1 - 3.8$  min. Intra-gastric distribution of the meal, expressed as Proximal/Distal volume, varied on average from  $3.6 - 2.1$  (5 min pc) to  $2.7 - 1.9$  (30 min pc). **Conclusions:** This 3D ultrasound system using magnetic scanhead tracking demonstrated high in vitro accuracy, calculated gastric emptying rates more precisely than 2D ultrasound, and enabled estimation of intra-gastric distribution of a soup meal in healthy subjects. **Motility, specific: Stomach Motility, general: Functional GI disorders Radiology and ultrasound: Diagnosis }** "Intra-gastric Distribution and Gastric Emptying Estimated by 3D-Ultrasonography"

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"P P 56 1333" P 56 1333 **Accommodation of the Proximal Stomach is Fat Dependent in Functional Dyspepsia**

\*O.H. Gilja, T. Hausken, S. \d8degaard, A. Berstad

Medical Department A, Haukeland Hospital, University of Bergen, Bergen, Norway *Aims:* Patients with functional dyspepsia seem to have impaired accommodation of the proximal stomach to a meal. The objective of this study was to examine whether the amount of fat in the soup influenced gastric accommodation in functional dyspepsia. *Methods:* 11 patients, 9 females and 2 males, median age 40 years (range 21–52 years), were scanned fasting in a sitting position after ingestion of 500 ml meat soup (Toro<sup>®</sup>). On two separate days, the patients randomly ingested either 2 or 17 g of bovine fat in the meal (20 vs. 170 kcal). An ultrasound scanner, CFM 750 Vingmed Sound, with a 3.25 MHz transducer was used to obtain images 10 min after a 4 min ingestion period. Two sonographic sections, a sagittal area and an oblique frontal diameter were applied on the proximal stomach. 3D ultrasound with a tilting device for acquisition was used to scan the distal stomach. Volumes of the gastric antrum were estimated on a Unix workstation after scanconversion and manual contour indication using software from Advanced Visual Systems<sup>®</sup>. All subjects were asked to score total symptoms (1–9) provoked by the meal. Statistical differences were analyzed using Wilcoxon signed ranks test. *Results:* The size (mean – SD) of the proximal stomach was larger after high fat compared with low fat content, both in the sagittal (22.1 – 3.4 cm<sup>2</sup> vs 15.5 – 4.4 cm<sup>2</sup>, p = 0.01) and the frontal section (6.8 – 0.8 cm vs 6.0 – 0.8 cm, p = 0.01). Volumes of the antrum were 28.7 – 13.8 ml and 27.7 – 10.4 ml after high fat and low fat (p = 0.86, NS), respectively. Symptom score was 2.18 – 2.04 after high fat and 1.09 – 1.22 after low fat (p = 0.12, NS). *Conclusions:* In patients with functional dyspepsia, volumes of the antrum did not change significantly with increasing fat content of the meal whereas accommodation of the proximal stomach seemed to be dependent on the fat content. Motility, specific: Stomach Motility, general: Functional GI disorders Radiology and ultrasound: Diagnosis }

"Accommodation of the Proximal Stomach is Fat Dependent in Functional Dyspepsia"

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"P P 56 1334" P 56 1334 **Effects of Medium-Chain and Long-Chain Triglycerides on Antroduodenal Motility**

\*M. Verkijk, J. Vecht, H. Gielkens, I. Biemond, C. Lamers, A. Masclee

Dept. of Gastroenterology, University Hospital Leiden, The Netherlands

The use of medium-chain triglycerides (MCT) as additional caloric source in diets is limited by the frequent occurrence of abdominal symptoms. Recently we have shown that MCT accelerates intestinal transit but little is known on the effect of MCT on gastrointestinal motility. Therefore, we have investigated the effects of both equimolaric and equicaloric amounts of MCT and long-chain triglycerides (LCT) on antroduodenal motility, duodenocecal transit time (DCTT; lactulose H<sub>2</sub> breath test) and CCK release (RIA). Eight healthy subjects (age 19–28 yr) were studied on 4 separate occasions, after spontaneous occurrence of duodenal phase III, in random order during continuous intraduodenal administration of: (a) saline (control), (b) MCT 15 mmol/h, 67 kcal/h (MCT-1), (c) MCT 30 mmol/h, 135 kcal/h (MCT-2) or (d) LCT 15 mmol/h, 135 kcal/h, each for 360 min. *Results:* Both doses of MCT resulted in a sign. faster reoccurrence of phase III (MCT-1, 75 – 7 min,  $p < 0.05$ ; MCT-2, 58 – 13 min,  $p < 0.05$ ) compared to saline (151 – 18 min). LCT, on the other hand, sign. ( $p < 0.05$ ) delayed reoccurrence of phase III compared to saline (290 – 30 versus 151 – 18 min), and induced a fed motor pattern. MCT at both doses did not interrupt interdigestive motility. Migrating motor complex (MMC) cycle length was sign. ( $p < 0.05$ ) shorter during MCT (MCT-1, 65 – 7 min; MCT-2, 53 – 6 min) compared to saline (127 – 14 min) resulting from a sign. ( $p < 0.05$ ) shorter duration of phase II. Phase III amplitude and velocity were sign. ( $p < 0.05$ ) reduced during MCT. Infusion of LCT did not affect DCTT (105 – 13 min) compared to saline (101 – 9 min), whereas DCTT was sign. ( $p < 0.05$ ) accelerated during MCT (MCT-1 56 – 6 min and MCT-2 69 – 9 min). DCTT was positively correlated with MMC length ( $r = 0.42$ ;  $p = 0.05$ ). LCT but not MCT sign. ( $p < 0.05$ ) increased plasma CCK levels. *Conclusions:* LCT induces a fed motor pattern, whereas MCT maintains interdigestive antroduodenal motility with shorter MMC cycle length resulting from shorter duration of phase II. MCT accelerates intestinal transit. The effect of MCT is independent of CCK. Nutrition: Nutrients and gut function Motility, specific: Small bowel } "Effects of Medium-Chain and Long-Chain Triglycerides on Antroduodenal Motility"

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"P P 56 1336" P 56 1336 **Interdigestive Antroduodenal Motility and Gastric Acid Secretion. Effect of Acid Inhibition**

\*H.A.J. Gielkens, A. Nieuwenhuizen, I. Biemond, C.B.H.W. Lamers, A.A.M. Masclee

Dept. of Gastroenterology, University Hospital Leiden, The Netherlands In man interdigestive acid secretion and antroduodenal motility are closely related with cyclic variations in acid secretion synchronous with the various phases of the migrating motor complex (MMC). Duodenal acidification inhibits antral motility but little is known on the effect of acute acid inhibition on antroduodenal motility. We have simultaneously studied antroduodenal motility (perfusion manometry) and gastric acid secretion (continuous aspiration in 10 min portions using phenol red as recovery marker) in 9 healthy subjects (age 20–31 yr). Each subject was studied twice in random order during 1) saline i.v. (control) for 1–2 complete MMC cycles and 2) during acute acid inhibition with famotidine i.v. (bolus 20 mg, continuous infusion 4 mg/h) for 1–2 complete MMC cycles. Plasma gastrin and pancreatic polypeptide (PP) levels were determined (RIA). *Results:* In the control study acid output in phase III (2.1 – 0.3 mmol/10 min) and late phase II (1.7 – 0.2 mmol/10 min) was significantly ( $p < 0.05$ ) increased over early phase II and phase I (1.2 – 0.2 and 1.2 – 0.2 mmol/10 min resp.). Famotidine increased gastric pH to  $> 6$  within 30 min. After acid inhibition duration of MMC cycle during famotidine (106 – 8 min) was reduced but not significantly different from the control experiment (133 – 14 min). Phase distribution of the MMC cycle was not significantly different between famotidine (I, II and III: 12 – 3%, 83 – 2% and 5 – 1% resp.) and control (I, II and III: 14 – 3%, 82 – 3% and 4 – 1% resp.). Plasma PP levels fluctuated synchronous with phase I (25 – 3 pM), phase II (32 – 3 pM;  $p < 0.05$ ) and phase III (40 – 3 pM;  $p < 0.01$ ) independent of acid secretion. No cyclic alterations in serum gastrin levels were observed. *Conclusions:* Gastric acid secretion varies cyclically with interdigestive antroduodenal motility. Acute acid inhibition with famotidine i.v. does not significantly affect interdigestive antroduodenal motility and PP secretion. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Motility, specific: Stomach } "

"Interdigestive Antroduodenal Motility and Gastric Acid Secretion. Effect of Acid Inhibition"

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"P P 56 1337" P 56 1337 **Glyceryl Trinitrate Improves Intra-gastric Meal Distribution and Prevents Meal-Induced Discomfort in Patients with Type I Diabetes Mellitus**

\*K.A. Undeland, O.H. Gilja, T. Hausken, A. Berstad

Division of Gastroenterology, Medical Department A, N-5021 Haukeland University Hospital, Bergen, Norway *Purpose:* Impaired accommodation reflex of the proximal stomach is often seen in patients with diabetes. Nitrogen monoxide (NO) serves as a neurotransmitter in this reflex, and we hypothesised that glyceryl trinitrate (GTN), an exogenous donor of NO, could improve accommodation and intra-gastric meal distribution in patients with diabetes. *Methods:* A double blind, placebo-controlled, cross-over study was designed in twenty patients with type 1 diabetes (DM) and twenty healthy controls (HC). All received GTN or PLC in random order five minutes prior to a 500 ml soup meal. Two proximal sections, a sagittal area (sA) and a frontal diameter (fD), and an antral area (aA) was outlined by ultrasound. Symptom score was assessed by visual analogue scales. *Results:* GTN had no significant effect on the sagittal area (sA) or on the frontal diameter (fD). An estimated volume (eV) based on these measures ( $eV = sA \cdot fD$ ) was neither significantly different with GTN compared to PLC. GTN decreased significantly ( $p = 0.05$ ) antral area (aA) 5 min after soup in patients with diabetes ( $16.1 \text{ cm}^2 - 4.3$  with PLC vs.  $13.5 \text{ cm}^2 - 4.5$  with GTN). This effect was consistent throughout the investigation period in DM. In HC, there was a similar tendency ( $p = 0.14$ ) 5 min after soup ( $16.4 \text{ cm}^2 - 6.6$  vs.  $13.2 \text{ cm}^2 - 5.6$ ). GTN had a significant ( $p = 0.04$ ) effect on the intra-gastric meal distribution in DM, increasing eV/aA -ratio from  $9.1 - 4.0$  to  $11.9 - 6.4$ . GTN also prevented meal-induced symptoms in patients with diabetes. *Conclusion:* GTN improves intra-gastric meal distribution and prevents postprandial symptoms in patients with type 1 diabetes mellitus. Motility, general: Functional GI disorders Motility, specific: Stomach Oncology, general: Therapy } "Glyceryl Trinitrate Improves Intra-gastric Meal Distribution and Prevents Meal-Induced Discomfort in Patients with Type I Diabetes Mellitus"

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"P P 56 1338" P 56 1338 **Relationship between Early Postprandial Symptoms and Transpyloric Flow**

\*T. Hausken, K.A. Undeland, A. Berstad

Div. of Gastroenterology, Med. Dept., Haukeland University Hospital, Bergen

Norway *Background:* Patients with functional dyspepsia (FD) exhibit increased sensitivity to gastric distension (mechanoreceptors) and to meals rich in fat (duodenal chemoreceptors). *Aim:* to relate initial transpyloric emptying and antral motility to early postprandial symptoms in FD using duplex sonography. *Methods:* Twelve patients with FD were investigated during 3 min of fasting, during 3 min of ingesting 500 ml of a meat soup and during the first 10 min postprandially. *Results:* Transpyloric forward flow commenced on average 52 sec and propulsive transpyloric flow (generated by propulsive antral contractions) 115 sec after start of drinking the soup. Initial nonpropulsive transpyloric flow (i.e., pendulating, transpyloric flow not generated by antral contractions) lasted 58 sec. Postprandial symptoms occurred in all patients and commenced on average 142 sec after start of ingestion. In all subjects symptoms appeared after commencement of transpyloric emptying. A negative correlation was found between intensity of fullness and time duration between start of emptying and start of symptoms. No correlation was found between antral distension and symptoms. *Conclusion:* The inverse relationship between symptom intensity and duration of the emptying period before symptoms suggests that meal related symptoms in FD patients are mainly due to gastric mechanoreceptors. Motility, specific: Stomach Motility, general: Functional GI disorders Hormones and receptors: Clinical disorders }  
"Relationship between Early Postprandial Symptoms and Transpyloric Flow"

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"P P 56 1339" P 56 1339 **Duodeno-jejunal Postprandial Motility in Severe Chronic Idiopathic Dyspepsia: Comparison with Motor Patterns of Healthy Volunteers and Relationship with Results of Radionuclide Gastric Emptying**

\*O. Lalaude, C. Maillot, G. Riachi, A. Zalar, F. Ducrot, P. Ducrot, P. Denis

GBPDN Hospital Charles Nicolle, 76031 ROUEN Cedex Our aim was to describe the duodeno-jejunal postprandial motility in dyspeptic patients having an objective delay at radionuclide gastric emptying. *Methods:* Ten patients, 5 men and 5 women, (median age: 52 years; range 34–76), with daily symptoms were studied. Gastric emptying of solids was delayed in all patients: lag phase > 60 mn (N < 40) (n = 6), decreased evacuation slope (N > 0.25) (n = 6). Liquid emptying was also impaired in 6 cases with an half emptying time > 113 mn. A four port recording device registered duodenojejunal motility during three hours after a 750 kcal-meal (carbohydrates: 50%, lipids: 30%, proteins: 20%). The duodenal and jejunal areas under curves (AUC) were calculated by a validated software on the whole 3 hours and on each of the 6 half-hours of the postprandial period. Manometric results in dyspeptics were compared to those of 20 healthy volunteers, 10 men and 10 women, median age 30 years (range 21–46) studied in the same conditions. *Results:* a) In volunteers, postprandial motility was characterised, at each level of recording, by a maximal motor activity during the first half hour, followed by a significant decrease with time ( $p < 0.003$ ). In every volunteer, jejunal post-prandial motor activity was always higher than the duodenal one ( $p < 0.01$ ). b) The global overall AUC and the AUC on each of the successive half hours were not different between dyspeptics and volunteers. c) in all dyspeptic patients, duodenal and jejunal AUCs failed to decrease with time. d) Duodenal activity was greater than the jejunal one in 6 cases. d) Lag phase duration was correlated with the duodenal AUC in the first hour ( $r: 0.85$ ;  $p < 0.01$ ). No other correlation was found between duodenal or jejunal motor parameters and results of radionuclide gastric emptying for solids or liquids. *Conclusion:* In severe dyspepsia with a gastric emptying objectively delayed, the kinetics of the duodeno-jejunal postprandial motility was always different from that observed in volunteers. The correlation between lag phase and duodenal motor index suggests that duodenum could act as a brake in some dyspeptic patients. Motility, general: Functional GI disorders Motility, specific: Stomach Motility, specific: Small bowel } "Duodeno-jejunal Postprandial Motility in Severe Chronic Idiopathic Dyspepsia: Comparison with Motor Patterns of Healthy Volunteers and Relationship with Results of Radionuclide Gastric Emptying"

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**"P P 56 1340" P 56 1340 Gastric and Gallbladder Emptying after a Mixed Meal are not Coordinated in Liver Cirrhosis: An Ultrasound Monitoring**

\*Monica Acalovschi, Dan L. Dumitrascu, Ildiko Csakany

3rd Medical Clinic, University of Medicine and Pharmacy, Cluj-Napoca, Romania An impaired contractility has been suggested as a contributing factor to the increased incidence of gallstones in liver cirrhosis, but the few studies on gallbladder emptying in cirrhotics offered contradictory results. Ingestion of a meal triggers the physiological pathway of gallbladder emptying, therefore it seems very important to assess simultaneously the rates of gastric and gallbladder emptying in analyzing postprandial kinetics. Gastric and gallbladder emptying were measured using ultrasound techniques after a solid-liquid meal (14 g fat, 465 kcal) in 24 patients with liver cirrhosis and in 12 controls. None of the subjects had gallbladder disease. Sequential changes in cross-sectional area of the gastric antrum and in gallbladder volume were represented as a monoexponential process after the test meal. Cirrhotic patients were analyzed according to the severity of disease (Child classes). The presence of portal gastropathy was assessed by endoscopy. Differences between groups were analyzed using the two-tailed Student's t test for unpaired observations and the correlations by linear regression (Pearson's coefficient). We found all parameters of gastric emptying following the solid-liquid meal similar in patients and controls. On the contrary, gallbladder emptying was significantly diminished in cirrhotic patients: the area under curve was reduced in Child A ( $p = 0.01$ ), Child B ( $p = 0.04$ ) and Child C ( $p = 0.014$ ) cirrhotics. No correlation was found between the parameters of gastric and gallbladder emptying. Gallbladder refilling began earlier in cirrhotics than in controls, before completion of gastric emptying. Our results indicate the lack of a quantitative coordination between gastric and gallbladder emptying in liver cirrhosis. They also support the hypothesis that diminished gallbladder contractility could contribute to the increased gallstone formation in liver cirrhosis. Motility, specific: Stomach Liver and bile ducts, 1: Cirrhosis: portal hypertension Liver and bile ducts, 2: Gallstones, formation, treatment } "Gastric and Gallbladder Emptying after a Mixed Meal are not Coordinated in Liver Cirrhosis: An Ultrasound Monitoring"

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"P P 56 1341" P 56 1341 **Effect of Intraduodenal Application of Acid and Lipids on Gastric Tone in Healthy Subjects**

\*J.E. Domínguez-Muñoz, G. Manes, A. Leodolter, P. Malfertheiner

Department of Gastroenterology, University of Magdeburg, Germany Gastric emptying of fat leads to inhibition of antral motility and relaxation of the proximal stomach, which are likely mediated by neural duodenogastric reflexes. An acidic intraduodenal pH also induces an inhibition of the antral motility, but the effect on the tone of the proximal stomach is unknown. Aim of this study was to compare the relaxation of the proximal stomach after intraduodenal perfusion of different doses of a citric acid solution (pH = 2.2) and of a fat solution (Intralipid 20%) in healthy subjects. *Methods.* 6 healthy males, age 24–28 years, were studied. After an overnight fast a duodenal tube was placed through the nose with a side hole in duodenal bulb. A second tube with a 1200 ml balloon at the tip was placed in the proximal stomach and connected to a barostat. After a 30 min accommodation period, the balloon was inflated at a pressure of 1 mmHg above the minimal distending pressure of the stomach and volume was continuously recorded. A citric acid solution was infused into the duodenal bulb at rates of 1, 5 and 10 ml/min, each one for one minute. After each infusion the maximal volume of the proximal stomach and the slope (velocity of relaxation, ml/sec) from onset to maximal relaxation were recorded. Each following infusion was given after gastric volume had returned to basal value. The same procedure and the same infusion rates were repeated with Intralipid. Results are expressed as median. *Results.* The basal volume of the proximal stomach was 48 ml. A similar relaxation was obtained with both citric acid and lipids from the lowest infusion rate (gastric volume 139 ml after 1 ml citric acid and 182 ml after 1 ml intralipid, n.s.), and no further volume increase was achieved with higher doses (max. gastric volume 167 ml after 10 ml citric acid and 187 ml after 10 ml intralipid; n.s. compared to values after 1 ml). The velocity of gastric relaxation (slope) was similar with both citric acid (2.9 ml/sec) and lipids (3.6 ml/sec). *Conclusions.* Intraduodenal acid and fat infusions exert a similar dose-independent relaxation of the proximal stomach. This relaxation occurs at a similar velocity, which supports a common reflex mechanism for acid and fat. Motility, specific: Stomach } "Effect of Intraduodenal Application of Acid and Lipids on Gastric Tone in Healthy Subjects"

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"P P 56 1342" P 56 1342 **Comparison of Radiologic and Isotopic Measurement of Gastric Emptying**  
**A. Giguère,**

\*P. Poitras, R. D'ery, M. Picard, M. Boivin

Hospital Saint-Luc, University de Montréal, Montréal, Canada

Scintigraphic measurement of isotopes labelled nutrients is currently the gold standard technique for the evaluation of gastric emptying function. However, its availability is often limited. Radiologic gastric emptying of radioopaque markers could constitute a cost effective and easily available procedure but it remains unknown to many practitioners. We conducted a 5 yr retrospective study with 46 patients suspected of gastroparesis and submitted to both radiologic and isotopic gastric emptying tests, to verify if the radiologic emptying correlated with the isotopic one, and if the former could be an alternative to evaluate gastric emptying in the clinical setting. *Methods:* the gastric emptying of a meal containing Tc-99 beef liver was measured in the nuclear medicine laboratory, and was considered as our reference standard. The radiologic test required patients to ingest 10 radioopaque markers (consisting of 5 mm pieces of a 12 Fr radioopaque feeding tube) swallowed with 240 ml of 7-UP and a bun. Abdominal X-Rays (PA) were obtained 2, 4 and 6 hrs later, and the number of residual markers in the stomach was counted at each time point. *Results:* a) significant relationship ( $r = 0.66$ ;  $p < 0.00001$ ) was found between the emptying time of isotopes and pellets. b) isotopic emptying was considered abnormal in 24/46 patients. In these patients with identified gastroparesis, the number of pellets remaining in the stomach after 6 hrs was significantly higher than in those with normal isotopic emptying ( $5.1 - 1$  vs  $2.2 - 0.6$ ;  $p < 0.01$ ). c) both tests correlated perfectly in 85% subjects: both tests were normal in 21/46 and abnormal in 15/46 patients. d) three patients showed normal pellets emptying but had a slight delay in isotopic transit ( $T_{1/2} = 160, 160, 190$  min;  $n = < 150$  min). Seven patients with normal isotopic transit showed a delayed pellet emptying; 6 of these 7 patients were diabetics clinically suffering of gastroparesis. *Conclusion:* X-Ray determination of residual markers in the stomach 6 hrs after their ingestion seems to correlate with isotopic evaluation of the gastric emptying rate. In some circumstances, the radiologic test appeared even superior than the isotopic one to identify gastroparesis. The marker test is easy to realize in any clinical set up and appears to be a cost effective tool for the clinician. Clinical practice: Management strategy Motility, general: Functional GI disorders Motility, specific: Stomach } "Comparison of Radiologic and Isotopic Measurement of Gastric Emptying"

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"P P 56 1343" P 56 1343 **Treatment of Diabetic Gastroparesis with Cisapride** H. Hasche

Diabetes Zentrum, Ambulant Praxis, D-97688 Bad Kissingen, Germany Studies in gastroparesis mostly focus on gastric emptying in a limited patient (pt) sample. We evaluated the effects of cisapride (CIS) on symptoms and glucose control in pts with diabetic autonomic neuropathy. *Method.* Patients (pts) with a history of insulin-dependent diabetes mellitus  $\geq 5$  yrs, under medical control  $\geq 3$  months and with chronic abdominal symptoms, suggestive of delayed gastric emptying due to autonomic neuropathy, were eligible. They received CIS 10 mg qid. Patients were evaluated at start and after each month during a 3 month period. Several dyspeptic symptoms and hypoglycemia were scored as absent, mild, moderate, severe, very severe. HbA1c was also measured. Dose changes, daily insulin-intake and glucose control (unsatisfactory, satisfactory, good and very good) were documented. *Results.* 544 pts (55 – 13 yrs, 331 females, 174 with diabetic nephropathy, 294 with retinopathy and 316 with sensory neuropathy) participated. After 8 and 12 wks of treatment, 86% and 90% of pts had no or only mild symptoms. Before study, 65.2% of pts had no symptoms of hypoglycemia, 83% at end of the study. Only 4% still had mainly moderate symptoms of hypoglycemia. Glucose control was evaluated as good or very good in 31% of pts prior to study, 54% and 62% after 8 and 12 wks of treatment. After 12 weeks, the HbA1c-value indicated a better diabetic control in 386 (71%) of pts. CIS was well tolerated. Dose increase was not required, while a decrease occurred in a few pts only. *Conclusions.* These data support that CIS relieves dyspeptic symptoms and may have a beneficial effect on glucose control in diabetic neuropathy, indicating that the difficult diabetic control in these pts may be related to disordered gastric emptying. There was no evidence for tachyphylaxis over this 3-month study period. Nutrition: Nutrients and gut function Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Management strategy } "Treatment of Diabetic Gastroparesis with Cisapride"

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## "P P 56 1344" P 56 1344 **Overlapping Irritable Bowel Syndrome and Delayed Gastric Emptying Identify Different Subgroups among Patients with Functional Dyspepsia**

\*C. Tosetti, V. Stanghellini, A. Paternic\2, G. Barbara, B. Salvioli, R. Cogliandro, C. Berti Ceroni, M. Levorato, M. Marengo, R. Corinaldesi

Departments of Internal Medicine, Gastroenterology and Nuclear Medicine, University of Bologna; Italy Classifications based on non-quantitative symptom questionnaires failed to recognise, among patients with chronic functional dyspepsia (FD), distinct subpopulations characterized by different pathophysiological patterns. We evaluated if dyspepsia subgroups identified by a questionnaire quantitating (0–3) the influence of dyspeptic symptoms (epigastric pain, postprandial fullness, nausea, vomiting) on usual activities present different clinical and gastric motor patterns. A large group of strictly selected consecutive FD pts (total score {\b3} 3, with at least one symptom {\b3} 2) in the absence of organic, systemic, metabolic diseases were included in the study. The presence of at least 3 of Manning's criteria was required to diagnose irritable bowel syndrome (IBS). Prevalent pain (epigastric pain {\b3} 2 with any other symptoms {\a3} 1) was present in 84 pts (17%); prevalent discomfort (postprandial fullness and/or nausea and/or vomiting {\b3} 2 with pain {\a3} 1) was present in 222 pts (46%); the remaining 177 cases (= 37%) resulted unclassifiable. Results of scintigraphic GE of solids (638 kcal; <sup>99m</sup>Tc-chicken liver) were expressed as GE rates (%emptied/h). Fifty healthy volunteers served as controls (HC; GE rates: 40 – 11%/h). prevalent prevalent unclassifiable pain discomfort Males/females (%) 61/39% 40/60% # 40/60% # Age (yrs) 41 – 13 39 – 12 39 – 13 Overlapping IBS 12% 30% # 28% # GE rates (%/h) 39 – 13 28 – 13 \*#{\a5} 30 – 14 \*# Delayed GE (%) 11% 42% #{\a5} 30% # m – SD; \*p < 0.001 vs HC, #p < 0.005 vs prevalent pain, {\a5} p < 0.05 vs unclassifiable; X<sup>2</sup>, ANCOVA adjusted for sex and age. *Conclusions:* Patients with prevalent pain and patients with prevalent discomfort represent two distinct FD subgroups, respectively characterized by: 1) prevalent male gender, lower frequency of associated IBS, normal gastric emptying; 2) prevalent female gender, higher frequency of associated IBS, delayed gastric emptying. Motility, general: Functional GI disorders Motility, specific: Stomach Clinical practice: Management strategy }" "Overlapping Irritable Bowel Syndrome and Delayed Gastric Emptying Identify Different Subgroups among Patients with Functional Dyspepsia"

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"P P 56 1345" P 56 1345 **Identification of Gastric Contraction by Surface Electrogastrography**

\*C.I. Sohn, P.L. Rhee, J. Kim, K.C. Koh, S.W. Paik, J.C. Rhee, W.T. Han<sup>1</sup>, I.Y. Kim<sup>1</sup>

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<sup>1</sup> Samsung Biomedical Research Institute, Seoul, Korea *Purpose:* The aim of this study is to identify gastric contraction by surface electrogastrography (EGG). *Method:* Simultaneous recording of antro-pyloro-duodenal manometry and EGG was made in 10 functional dyspeptic patients during an hour fasting period. For EGG signal acquisition, high cutoff frequency was set 10 Hz and signal sampling frequency was 16 Hz. *Result:* During motor quiescence period, the EGG showed normal smooth sine wave form. On time domain frequency analysis, there was only single dominant frequency of three cycles per minute, namely first harmonic. During antral contraction, the slow wave showed configurational change resulting in a late peak on its wave form. On time domain frequency analysis, there was marked increase in second harmonic during contraction. When the power of second harmonic was compared to the manometric peaks, the increase in second harmonic was well matched with each group of gastric contractions.

*Conclusion:* Each group of gastric contractions could be identified by surface EGG. But 1:1 correlation between individual gastric contraction and EGG is not yet possible. Motility, general: Functional GI disorders Motility, specific: Colon, anorectum } "Identification of Gastric Contraction by Surface Electrogastrography"

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"P P 56 1346" P 56 1346 **Changes of Motility in the Stomach Transplant Implanted to the Small Intestine**

\*T.S. Popova, T.Sh. Tamazashvili, N.S. Tropkaya, G.A. Platonova, A.E. Shestopalov

Sklifosovsky Institute for Emergency Medicine, Moscow, Russia The objective was to study the morphofunctional restructuring of the stomach tissue implanted to the small intestine. A tubular transplant on vascular pedicle was formed on the greater curvature of the stomach in 6 dogs. It was implanted into the initial portion of the small intestine. We studied the electrophysiologic parameters and the morphology of the stomach stump, the transplant, the adducting and abducting portions of the small intestine. We used the computer-assisted method of processing electric myogram data taken from implanted electrodes, impedancemetry, histologic and histochemical methods. Observation period was 1.5–3 years. The obtained results indicate that from the first hours of transplantation in the transplant, besides the basic spectrum maximum located in the frequency range typical for basal stomach motility rate (0.05–0.10 Hz), there were noted additional maxima in the range of jejunum frequencies (0.27–0.29 Hz) and ileum frequencies (0.20–0.23 Hz). It is necessary to mention that the power of the basic maximum in the transplant was 6 fold higher than in the stomach stump. Within the further observation we found the restoration of the adhesive activity in the transplant. The impedancegraphy findings confirmed the transplant contractions with the frequency of the stomach basal electric rate and the intestine basal electric rate. The dystrophic abnormalities found in the smooth muscular tissue were probably related with the adaptation of transplant muscular fibers to bowel peristalsis. Motility, specific: Stomach Motility, specific: Small bowel } "Changes of Motility in the Stomach Transplant Implanted to the Small Intestine"

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"P P 56 1347" P 56 1347 **Simultaneous Validation of the Ultrasonographic Method and the Sulfasalazine Salivary Test for Gastric Emptying, Oro-Cecal and Duodeno-Cecal Transit Time Assessment — Comparison with the Isotopic Technique**

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*Aims:* To validate echographic gastric emptying after ingestion of a dyspeptic test meal and sulfasalazine (SAZ) salivary test in order to determine oro-cecal (OCTT) and duodeno-cecal transit time (DCTT) in comparison with the isotopic technique. *Methods:* Twelve healthy male volunteers were enrolled. In *phase 1*, after fasting for twelve hours, each volunteer consumed a dyspeptic meal (1020 kcal) labelled with Indium 111-DTPA (11.1 MBq) and SAZ (2 gm). Gastric emptying time was assessed simultaneously by ultrasound and scintiscans. Salivary samples were collected from the 4th to the 14th hour and the first detection of sulfapyridine (SP) in saliva allowed the determination of OCTT. In *phase 2*, measurements of saliva appearance time were realized after administration of SAZ (2 gm) and Indium 111-DTPA (11.1 MBq) into the duodenum through a nasogastric tube. DCTT was assessed using the same method as OCTT. In both periods, scintiscans were taken until the visualization of the cecum. *Results:* The correlation between the two methods in the assessment of GE time was strong (110 – 22 min and 72 – 25 min;  $r = 0.70$ ;  $p = 0.02$ ). OCTT assessed by both methods was respectively 506 – 83 min and 276 – 56 min ( $r = 0.63$ ;  $p = 0.07$ ). The correlation between the two methods in the evaluation of DCTT was highly significant (232 – 74 min and 178 – 38 min;  $r = 0.83$ ,  $p = 0.002$ ). *Conclusion:* This study validates echographic gastric emptying measurement in dyspeptic conditions. SAZ salivary test is a simple, non invasive and validated method for the evaluation of intestinal transit time useful in clinical pharmacology studies. It's possible to study simultaneously gastric emptying time by ultrasound and OCTT by SAZ test. DCTT can be measured by the SAZ test but it requires nasogastric intubation. Motility, general: Functional GI disorders Motility, specific: Stomach Motility, specific: Small bowel } "Simultaneous Validation of the Ultrasonographic Method and the Sulfasalazine Salivary Test for Gastric Emptying, Oro-Cecal and Duodeno-Cecal Transit Time Assessment / Comparison with the Isotopic Tech"

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"P P 57 1348" P 57 1348 **Polymerase Chain Reaction: A New Golden Standard for Diagnosis of Helicobacter Pylori Infection?** P. Rossi, O.A. Paoluzi, S. Bernardi<sup>1</sup>, O.P. Marchione<sup>1</sup>, E. Carnieri<sup>1</sup>, I. Luzi<sup>2</sup>, F. Nardi<sup>3</sup>, P. Paoluzi

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Polymerase chain reaction (PCR) has been recently proposed as a more reliable diagnostic tool for the identification of HP [1]. Aim of the present study was to compare diagnostic accuracy of this test in respect to rapid urease test (RT), histology (HI) and culture (CO). *Patients & Methods:* 43 pts (22 males and 21 females), with a mean age (SD) of 50 yrs (SD 14), undergoing upper GI endoscopy for ulcer-like dyspepsia were enrolled. During endoscopy five antral biopsies were collected to evaluate HP infection which was assessed by RT (1 biopsy), HI (2 biopsies, Giemsa), CO (1 biopsy) and PCR for ureA gene (1 biopsy). Endoscope and biopsy forceps were disinfected with glutaraldehyde 2%, and specimens for each test were collected with different forceps. Moreover, a "wash-out" test (search of HP DNA by PCR in 10 ml of sterile saline solution collected after lavage of biopsy channel) was performed. *Results:* HP infection was detected in 35/43 pts (81%) by PCR, in 26/43 pts (60%) by RT, in 24/43 pts (56%) by HI and in 18/40 pts (45%) by CO. In three pts culture was not reliable for contamination of grown plates. No wash-out test was positive. *Conclusions:* PCR seems to be the most accurate method to detect HP infection in the present series. Higher accuracy of PCR seems to be particularly useful to assess the presence of HP in coccoid form, such as after antibiotic or antisecretory therapies, or in pts with low bacterial charge, such as dyspeptic pts.

Reference: Gut 1994; 35: 905–908 Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Polymerase Chain Reaction: A New Golden Standard for Diagnosis of Helicobacter Pylori Infection?"

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"P P 57 1349" P 57 1349 **Is *Helicobacter Pylori* Serology on Plasma Accurate?**

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<sup>1</sup> Centre for Digestive Diseases and Academic Unit of Medicine, UK

General Infirmary at Leeds, UK **Introduction:** Serology is an important epidemiological research tool for investigating *H pylori*. Serology is conventionally performed on serum but in a retrospective survey that we wished to perform the only sample available was plasma. We aimed to validate a commercial *H pylori* serology kit (Shield Diagnostics) in plasma against a gold standard and against serum from the same patient. **Methods:** Patients attending the endoscopy unit were enrolled into the study and *H pylori* status was determined by histology, rapid urease test, culture and <sup>13</sup>C-urea breath test. Patients were defined as *H pylori* positive if two or more tests were positive and negative if all tests were negative. *H pylori* status was indeterminate if only one test gave a positive result. 10 ml of serum and plasma was obtained from each patient and anti-*H pylori* IgG was measured by ELISA with a value of > 10 IU/l defined as positive. **Results:** 96 patients were enrolled (mean age 47.7 – 14.4 years, 50 male), 42 were gold standard *H pylori* negative and 52 *H pylori* positive with 2 having indeterminate status. Serology on serum was 91% sensitive (5 false negatives) and 90% specific (4 false positives). Serology on plasma was 92% sensitive (4 false negatives) and 83% specific (7 false positives). Increasing the cut-off to > 13 IU/l increased specificity to 90% but reduced sensitivity to 85%. **Conclusions:** Serology on plasma is of similar accuracy to serum although there may be a small reduction in specificity at the manufacturers recommended cut-off point. **Clinical practice:** Quality assurance Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "Is *Helicobacter Pylori* Serology on Plasma Accurate?"

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## "P P 57 1350" P 57 1350 **B-Cell Clonality in Gastric Mucosa: The Significance of H. Pylori Infection**

\*D. Sorrentino, G.F. Ferraccioli, S. DeVita, A. Labombarda, C. Avellini, C.A. Beltrami, M. Boiocchi, E. Bartoli

Departments of Internal Medicine and Pathology, University of Udine and 1st Division Experimental Oncology, CRO Aviano, Italy Data from our group (Gut, 1996 in press) indicate that gastric B-cell clonality is much more frequent than MALT (Mucosa Associated Lymphoid Tissue) lymphoma of which it is considered a precursor lesion. In addition, despite the reported association between MALT lymphoma and H. pylori infection the latter was not associated with B-cell clonality in several cases suggesting that other factors can play a role in its pathogenesis. Aims of the present study were to evaluate the behavior of clonality in patients with and without H. pylori infection after eradication. *Methods:* We followed for up to twenty-six months fourteen H. pylori positive and one H. pylori negative patients initially subjected to upper endoscopy and tested for B-cell clonality. H. pylori infection was treated by a standard regimen including omeprazole bid or tid plus amoxicillin bid or tid. In case of lack of eradication amoxicillin was substituted by clarithromycin. B-cell clonality was tested by VDJ-PCR using two protocols (Fr1 and Fr2) and running in parallel agarose and acrilamide gels, the latter known to increase the resolution of the technique. *Results:* The H. pylori negative patient, initially VDJ negative, became VDJ positive at the second biopsy (at 20 months). Of 11 H. pylori positive-VDJ positive patients nine were H. pylori eradicated: seven of these remained VDJ positive after a follow-up of 9–26 months while two of them became VDJ negative after 5 and 24 months. Of those who were not H. pylori eradicated one became VDJ negative after three months and one remained VDJ positive. Of three H. pylori positive/VDJ negative patients, two became VDJ positive 3 and 5 months after H. pylori was eradicated while one remained H. pylori positive and became VDJ positive after seven months. In three patients in whom VDJ positivity persisted the pattern of positivity changed from protocol Fr1 to Fr2 or vice versa. Finally, while a given sample displayed just one band in agarose gel, the same sample showed a few bands in acrilamide gel. *Conclusions:* B-cell proliferation detected in gastric mucosa of patients without clinical or histologic criteria of a pre-lymphomatous lesion is often oligoclonal and not truly monoclonal. Its prognostic value is unknown. As assessed by this follow-up study, B-cell clonality appears and disappears independently of H. pylori infection. Hence, other factors may play a role in the pathogenesis of B-cell clonality and by inference gastric MALT lymphoma. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Screening, prevention Oncology, general: Proliferation, carcinogenesis } "B-Cell Clonality in Gastric Mucosa: The Significance of H. Pylori Infection"

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## "P P 57 1351" P 57 1351 Sensivity and Specificity of <sup>14</sup>C Urea Breath Test for Helicobacter Pylori Infection Diagnosis in Patients with Florid Duodenal Ulcer

\*M. Di Silvio<sup>1</sup>, J. Larish<sup>2</sup>, B. Vega<sup>2</sup>, M. Dehesa<sup>2</sup>, M. Dibildox<sup>1</sup>, F. Amigo<sup>3</sup>, L. Rodr\edguez<sup>2</sup>, I. Almaguer<sup>1</sup>, J. Torres<sup>2</sup>

<sup>1</sup> Clinical Research Byk Gulden M\exico

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<sup>2</sup> Centro M\edico Nacional Siglo XXI IMSS, M\exico *Objective:* The aim of this preliminary report is to compare the sensitivity and specificity, in an ongoing clinical trial, of <sup>14</sup>C urea breath test (UBT) versus rapid urease test (CLOtest), microbiology and histology, in order to evaluate H. pylori infection diagnosis in patients with florid duodenal ulcer. *Methods:* 36 patients (23 male) mean age 51 with no prior proton pump inhibitors or antibiotics intake 30 days before the study or history of gastric surgery were included. Fasted patients swallowed 1 gealtin capsule with 200 mg of sugar beads containing one microcurie of <sup>14</sup>C-labeled urea, after 15 minutes a breath sample was collected in a balloon, the isotope linked to scintillation fluid was quantified by beta-counter. At endoscopy several samples were taken from antrum and corpus and used for CLOtest, histology and microbiology which was performed in selective and non-selective media. *Results:* 34/36 (94%) patients with endoscopically demonstrated florid duodenal ulcer had positive CLOtest, positive in histology (Giemsa, H&E) and positive cultures for H. pylori. In this patients <sup>14</sup>C-UBT readings showed an average of 1768 DPM, max 4061 min 117, (positive cut-off value > 100 DPM). 2 patients with negative CLOtest, histology and culture showed also very low <sup>14</sup>C-UBT readings (6 and 4 DPM respectively). In this study <sup>14</sup>C-UBT, as a tool for gastric H. pylori infection diagnosis, had sensitivity and specificity of 100% *Conclusions:* Non-invasive <sup>14</sup>C-UBT is an excellent method for H. pylori infection diagnosis, easy to perform and timeless, with accuracy and reproducibility comparable to gold standard methods. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic }" "Sensivity and Specificity of 14C Urea Breath Test for Helicobacter Pylori Infection Diagnosis in Patients with Florid Duodenal Ulcer"

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"P P 57 1352" P 57 1352 **Detection of Helicobacter Pylori in Post-Treatment Gastric Biopsy: Comparison between Classic Histology, CLO Test and H.P.-DNA PCR. Pedrana<sup>1</sup>, P. Locicero<sup>1</sup>, M. Fay<sup>2</sup>, A. Naves<sup>2</sup>, M. Sylvestre Begnis<sup>2</sup>, C. Banchio<sup>3</sup>, H. Gramajo<sup>3</sup>, F. Fay<sup>3</sup>**

<sup>1</sup> Centro de Gastroenterologia, Rosario, Argentina

<sup>2</sup> Instituto de Histopatologia, Rosario, Argentina

<sup>3</sup> Bios Rosario, Rosario, Argentina *Background/Aims:* a sensitive and specific methodology is necessary for detection of H.P. in gastric biopsy to evaluate post-treatment microorganism presence. This would allow to differentiate recrudescence from reinfections. The aim of this study was to compare the sensitivity of gastric biopsy, Clo test and H.P.-DNA PCR for the detection of H.P. in a group of recently treated patients (6–8 weeks after treatment). *Patients and Methods:* H.P.-DNA PCR was performed gastric biopsies from 50 treated patients (33 males and 17 females) (age: 48 – 12 years), in whom success of treatment was defined only by histological means and Clo test. Therapeutic schemes were as follows: Treatment 1: (11 patients) Amoxiciline 500 mg b.i.d. during plus Metronidazol 500 mg b.i.d. plus Dicitrato Bismuth Tripotasic 120 mg q.i.d. during 14 days. Treatment 2: (19 patients) Omeprazole 20 mg b.i.d. plus Zitromicine 250 mg b.i.d. during 3 days. Treatment 3: (20 patients) Amoxiciline 1 gr b.i.d. plus Lanzoprasole 20 mg/day. H.P. eradication was defined on histological grounds (gastric histology: 10% buffered formol fixation; paraffin inclusion; Giemsa and HE staining), Clo test (Delta West Pty. Ltd. Bentley, Australia) and by the absence of H.P.-DNA by PCR (amplification of a 296 bp of the species-specific antigen of H.P. and visualization of the amplified product in agarose gel with Ethidium Bromide and U.V. light), all of them performed within 6 to 8 weeks after the end of treatment. *Results:* Histology & Clo Test PCR Positive Negative Positive Negative 0 50 6 44 1 out of 6 (16.7%) reinfected patients received treatment 1, 3 of them (50%) treatment 2 and the other 2 (33.3%) treatment 3. *Conclusions:* H.P.-DNA PCR is more sensitive than conventional accepted methods for assessing H.P. presence in the immediate post-treatment period, as it was able to detect a 12% false negatives by traditional methods. This would allow discriminate between residual replication and true reinfection of H.P. on a long term follow up basis of these patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Detection of Helicobacter Pylori in Post-Treatment Gastric Biopsy: Comparison between Classic Histology, CLO Test and H.P.-DNA PCR"

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"P P 57 1353" P 57 1353 **The Occurrence of IgG Antibodies to High Molecular Weight Proteins of H. Pylori Antigen among Duodenal Ulcer Patients and Practically Healthy Persons in Lithuania** T. Wadstrom<sup>1</sup>, J. Miciuleviciene<sup>2</sup>,

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Department of Gastroenterology, Kaunas Medical Academy, Kaunas, Lithuania *Aim of the study* – to assess in duodenal ulcer (DU) patients and practically healthy persons the presence of high molecular weight (85 and 120 kDa) IgG antibodies to H. pylori (HP). *Material and Methods:* The sera of 22 consecutive patients with DU and 18 practically healthy medical students were analysed for IgG antibodies in ELISA and immunoblot using glycine extracted proteins of HP (NCTC 11637) as antigen. ELISA results were expressed as relative antibody activity (positive > = 35). Presence of high molecular weight IgG antibodies to HP by western blotting method were assessed semiquantatively. *Results:* In ELISA, IgG antibodies to HP were found in 18/22 DU and in 15/18 controls. In the sera of DU ulcer patients, antibodies to 120 kDa protein were expressed in 21/22 cases and to 85 kDa – in 18/22 samples. In control group sera reactivity to 120 kDa protein was found in 13/18 cases and to 85 kDa antigen in 12/18 samples. The frequency and expression of 120 kDa antigen in DU patients were significantly higher ( $p < 0.001$  according to the  $\chi^2$  test) in comparison with the control group. No statistically significant differences in frequency of 85 kDa antigen were revealed between the groups. *Conclusion:* Our pilot study showed high frequency of 120 kDa antigen among Lithuanian DU patients (95.6%) as well as the control group of practically healthy persons (73.2%). The prevalence of virulence factors of HP infection (especially CagA – cytotoxin-associated protein closely related to 120 kDa protein) could likely explain high peptic ulcer morbidity and complication rate as well as high gastric cancer rate in Lithuania. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "The Occurrence of IgG Antibodies to High Molecular Weight Proteins of H. Pylori Antigen among Duodenal Ulcer Patients and Practically Healthy Persons in Lithuania"

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## "Plasma Nitrate/Nitrite Level is Higher in Patients with Peptic Ulcer Disease and Chronic Gastritis — The Increase is Independent of Helicobacter Pylori Status or Eradication"

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<sup>1</sup> Department of Physiology, Tokai University, School of Medicine, Isehara, Japan  
Plasma nitrate/nitrite level reflects the endogenous nitric oxide production in fasting human. Both elevated and unaltered nitric oxide synthase activity in the gastric mucosa, and in contrast, low nitrate/nitrite level in the stomach and in the plasma have been reported in patients with peptic ulcer disease. Helicobacter pylori (H. pylori) infection has been shown to induce nitric oxide synthesis in the gastric mucosa in vitro, but no data is available about the in vivo conditions. To answer the questions whether 1) nitric oxide synthesis is enhanced in peptic ulcer disease, 2) the increase is disease specific, and 3) whether it has any correlation with H. pylori infection; we measured plasma nitrate/nitrite levels in 50 patients (mean age 50 – 15 y.o.) with upper gastrointestinal symptoms. We also studied the effect of H. pylori eradication on plasma nitrate/nitrite levels in these patients. Blood was obtained from patients with upper gastrointestinal symptoms immediately after gastroscopy, and was repeated at 4 weeks after successful H. pylori eradication. Plasma nitrate/nitrite was measured by HPLC at 550 nm using a cadmium column for nitrate reduction. Plasma nitrate/nitrite level was significantly higher both in patients with peptic ulcer disease ( $87 \pm 48 \mu\text{M}$ ,  $n = 12$ ) and chronic gastritis ( $47 \pm 18 \mu\text{M}$ ,  $n = 23$ ), when compared with that in patients with reflux oesophagitis ( $33 \pm 5 \mu\text{M}$ ,  $n = 6$ ) or dyspepsia symptoms ( $28 \pm 3 \mu\text{M}$ ,  $n = 9$ ). When compared with histology grading, plasma nitrate/nitrite level increased significantly as the severity of chronic gastritis progressed (grade I =  $44 \pm 14 \mu\text{M}$ , grade II =  $49 \pm 21 \mu\text{M}$ , grade III =  $113 \pm 56 \mu\text{M}$ ). There was no difference in plasma nitrate/nitrite levels between H. pylori positive ( $n = 32$ ) and negative ( $n = 18$ ) patients ( $61 \pm 39 \mu\text{M}$  vs.  $42 \pm 18 \mu\text{M}$ ). Successful eradication of H. pylori did not alter the elevated plasma nitrate/nitrite levels (data not shown). Based on the elevated plasma nitrate/nitrite levels observed, nitric oxide synthase activity of gastric mucosa is enhanced in patients with peptic ulcer disease. This increase, however, is specific neither for peptic ulcer disease nor for H. pylori infection, since it can also be observed in patients with chronic gastritis and after the successful eradication of H. pylori.  
Oesophageal gastric duodenal disorders: Helicobacter Pylori  
Oesophageal gastric duodenal disorders: GD disorders, acid peptic  
Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation }  
"Plasma Nitrate/Nitrite Level is Higher in Patients with Peptic Ulcer Disease and Chronic Gastritis / The Increase is Independent of Helicobacter Pylori Status or Eradication"

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"P P 57 1356" P 57 1356 **Screening for IgG Antibodies Against Helicobacter Pylori** B.F.M. Werdmuller, A.B.M.M. v/der Putten,

\*R.J.L.F. Loffeld

Department of Internal Medicine, Ziekenhuis De Heel Zaandam, The Netherlands Screening for IgG antibodies against HP can be used for omitting endoscopy in selected cases. The present study was done in order to assess the best screening strategy. The population consisted of non selected consecutive patients referred for endoscopy from 3/1994 till 3/1995. A serum sample was taken. IgG antibodies against HP were detected using a home-made ELISA technique. During the study period 1527 patients underwent upper GI endoscopy. In 233 cases endoscopy was done because of follow-up or serum from the patient was not available. Hence 1293 serum samples were available. IgG antibodies were present in 622 patients (48%) (303 ♂ 319 ♀, mean age 57 years, range 17–87), the remainder, 671 (52%) (316 ♂, 355 ♀, mean age 52 years, range 13–84) was negative. The following abnormalities were present in the seropositive group: oesophagitis 10%, hiatal hernia 12%, oesophageal cancer 0.5%, Barrett 3.4%, varices 1.9%, candida 1.9%, gastritis 8.5%, GU 3.8%, gastric cancer 1.6%, DU 6.4%, and bulbitis 8.3%. And in the seronegative group: oesophagitis 15%, hiatal hernia 15.4%, oesophageal cancer 0.3%, Barrett 4.3%, varices 1%, candida 1.3%, gastritis 10.6%, GU 1.8%, gastric cancer 0.1%, DU 1.6%, and bulbitis 5.5%. The following abnormalities were present in the seropositives below the age of 45 years: oesophagitis 6.8%, hiatal hernia 8%, Barrett 1.3%, varices 1.3%, candida 0.65%, gastritis 6.8%, GU 0.6%, DU 14.5%, and bulbitis 6.8%. And in the seronegatives: oesophagitis 12%, hiatal hernia 6%, Barrett 1.7%, varices 0.4%, gastritis 7.3%, DU 2.6%, and bulbitis 4.7%. If screening would have been applied on the total group of seronegatives than 318 patient would undergo endoscopy and 353 (27.3%) endoscopies could have been saved. Omitting endoscopy in seronegative cases below the age of 45 years would result in 182 (14%) endoscopies saved. If this strategy again is applied on the total group of seropositives than 188 patients still would undergo endoscopy and 434 endoscopies (34%) would have been saved. Omitting endoscopy in seropositive cases below the age of 45 years would save 119 (9%) endoscopies. It is concluded that endoscopy can be safely omitted in seropositive cases. Endoscopy in seronegatives will reveal more reflux oesophagitis. In addition, in oesophagitis helicobacter infection needs treatment since long term acid suppressive therapy will increase the development of atrophic gastritis. After eradication therapy oesophagitis complaints are likely to return and endoscopy will be done. Many patients with functional dyspepsia will benefit from this therapy and the number of recurrent complaints will be low. This study indicates that omitting endoscopy in seropositive cases, regardless of age, reduces the workload more than omitting endoscopy in seronegative cases, 34% fewer endoscopies versus 27%. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Epidemiology (non cancer) } "Screening for IgG Antibodies Against Helicobacter Pylori"

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## "P P 57 1357" P 57 1357 **Detection of Helicobacter Pylori in Faeces by PCR Assay**

\*M. Notarnicola, F. Russo, A. Cavallini, M. Bianco, G. Di Matteo, A. Di Leo

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Italy Helicobacter pylori (Hp) is the major cause of chronic gastritis and has been associated with gastric cancer [1]. There are some evidences for a faecal-oral transmission, even if few data are available about Hp detection in faeces. Recently, Hp genome has been detected by PCR in faeces from patients with gastritis [2]. Notwithstanding, faecal samples can easily give false-negative results because different chemicals present in faeces, such as polysaccharides, inhibit PCR [3]. *Aims* of our study were: 1) to remove the possible inhibitors present in faeces and 2) to detect by PCR the presence of Hp in faecal samples of symptomatic patients undergoing endoscopy in our Institute. *Patients and Methods*: Fifty consecutive patients (28 males, mean age 51.8 – 10.4, and 22 females, mean age 46 – 12.8) entered the study. Faecal samples were suspended in phosphate buffered saline pH 7.4. The mixture was filtered by polypropylene filter (mesh opening 149 µm) in order to remove PCR inhibitors. DNA was extracted from faeces by Tri-Reagent (Mol. Res. Center Inc. Cincinnati, OH, USA), and subsequently amplified by the primers taken from urease gene A. PCR products were separated and identified by electrophoresis on 2% agarose gel. *Results*: Warthin Starry PCR Positive Negative Hp positive 34 30 4 Hp negative 16 0 16 Hp specific DNA was detected in 88% of faecal samples with a specificity of 100%. *Conclusions*: The present findings suggest a faecal oral route of Hp transmission. Nevertheless, an unequivocal pattern of Hp spread cannot be established. The presence of Hp DNA in our samples may be due to DNA from non viable or viable cells present in faeces. Finally, since Hp detection in faeces by PCR is a non-invasive method, it may represent a useful tool for the follow-up after eradicating therapy.

Reference: J Gastroenterol 1995, 30: 689–695.

Lancet 1993, 341: 447.

BioTechniques 1994, 17: 274–276. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oncology, general: Molecular biology, genetics } " "Detection of Helicobacter Pylori in Faeces by PCR Assay"

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"P P 57 1358" P 57 1358 **Determination of the Antibodies Raised against *H. Pylori* (*Hp*) by a Western Blot Method in 136 Patients with Gastroduodenal Ulcer, Gastric Malt Lymphoma**

\*D. Lamarque<sup>1</sup>, F. Roudot-Thoraval<sup>1</sup>, T. Gilbert<sup>1</sup>, L. Deforges<sup>1</sup>, R. Ferrero<sup>2</sup>, A. Labigne<sup>2</sup>, J.C. Delchier<sup>1</sup>

<sup>1</sup> CHU H. Mondor, Créteil, Paris

<sup>2</sup> INSERM U389, Institut Pasteur, Paris Different gastroduodenal diseases could be related to a particular antigenic profiles of *Hp* strains. The aim of this study was to compare, by using *Hp* serological test by Western Blot (Helico Blot 2.0, Genelabs), the different antibodies present in patients with gastric (GU) or duodenal ulcer (DU), gastric MALT lymphoma or non ulcer dyspepsia. Fifty-one patients with DU, 21 with GU, 17 with gastric MALT lymphoma and 35 with dyspepsia and normal gastro-duodenal endoscopy were selected by a positive *Hp* Elisa serological test (Enzygnost, Berhing). By using Western Blot serology, the presence of antibodies against different molecular weight antigens (19.5, 26.5, 30 or 35 kD) or against VacA (89 kD) and CagA (116 kD) was compared in the different groups. Results are shown in the table (percent of patients with antigen):

Antigens	19.5 kD	26.5 kD	30 kD	35 kD	89 kD	116 kD	VacA	CagA
ADU	51	88	73	75	45	86	*	GU
	52	86	62	62	62	76	MALT	35
	94	53	53	35	76	Dyspepsia	40	83
	43	46	37	43	*	P < 0.01	as compared with the group with dyspepsia.	The serology by Western Blot confirms the strong prevalence of CagA in patients with DU but is not able to distinguish a particular pattern in patients with GU or gastric MALT lymphoma.

Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Determination of the Antibodies Raised against *H. Pylori* (*Hp*) by a Western Blot Method in 136 Patients with Gastroduodenal Ulcer, Gastric Malt Lymphoma"

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"P P 57 1359" P 57 1359 **A Simplified 10 Minutes 14C Urea Breath Test for Diagnosis of H. Pylori Infection and the Impact of Acid Suppressive Treatment on Test Results** F. Lerang<sup>1</sup>, J.B. Haug<sup>2</sup>,

\*B. Moum<sup>1</sup>, A. Bjørneklepp<sup>3</sup>, O. Fausa<sup>3</sup>

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<sup>2</sup> Dept. of Microb., Østfold Central Hospital, Fredrikstad, Oslo, Norway

<sup>3</sup> Dept. of Med. Rikshospitalet, Oslo, Norway *Objectives:* To determine optimal cut-off value and sensitivity (SN), specificity (SP), negative (NPV) and positive (PPV) predictive value of a simplified 14C urea breath test (UBT) for diagnosis of H. pylori (Hp), and examine the impact of prior acid suppressive therapy (H2RA). *Methods:* From January to December 1995 350 dyspeptic patients (245 peptic ulcer disease, 74 NUD, 31 miscellaneous; mean age 58 yrs., 202 M/148 F, 144 H2RA usage prior to testing) were examined for Hp infection. The amount of excreted 14CO2 in percentage of ingested 14C was estimated 10 minutes after administration of 185 kBq of 14C labeled urea dissolved in 50 ml tap water. Hp infection was defined by a minimum of two of the comparative tests positive: serology (Orion Diagnostica Pyloriset New EIA-G), rapid urease test (RUT), culture, microscopy (acridine orange stain) and laboratory urease test (LUT). *Results:* SN, SP, NPV and PPV of UBT were calculated stepwise for cut-off values 0.6–1.2% and the optimal cut-off value was 1.0%. By stratification to prior H2RA usage the results at this cut-off value were: SN (%) SP (%) NPV (%) PPV (%) All 95 95 91 97 H2RA { - } 97 97 97 97 H2RA+ 92 90 75 97 *Conclusion:* This simplified C14 UBT for diagnosis of H. pylori infection seems to achieve excellent over all sensitivity and specificity, but the accuracy is reduced in patients on H2RA therapy. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "A Simplified 10 Minutes 14C Urea Breath Test for Diagnosis of H. Pylori Infection and the Impact of Acid Suppressive Treatment on Test Results"

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"P P 57 1360" P 57 1360 **A Comparison of <sup>13</sup>C Urea-Breath Test (UBT) with and without a Citric Acid Test Meal for Helicobacter Pylori (HP) in Adults and Children**

\*A. Al'ec, V. Stanghellini, D. Vaira, S. Salardi, M. Menegatti, N. Figura, F. Stella, F. Landi, C. Ricci, F. Mucci, V. Cuccaro, R. Corinaldesi, M. Miglioli, E. Cacciari

Dept of Int Med & Dept of Pediatrics, Bologna

Dept of Int Med, Siena, Cortex, Italia *Purpose:* to evaluate the reliability of UBT MAT (Cortex Italia) with and without an acidic test meal in adults and children. *Subjects:* In 8 consecutive endoscoped adults (M/F: 4/4, age range: 22–54 yrs) with idiopathic dyspepsia (ID) biopsies (culture/urease/histology) & IgG to HP were performed. Patients were considered HP+ve if 3/4 tests were +ve. In 36 children (M/F: 19/17; age range: 4–16 yrs) IgG and Western Blotting were performed for HP status determination (+ve if both tests +ve). *UBT:* Each test was carried out in two separate occasions, at least 5 days apart. A double base line breath sample (T<sub>0I</sub>, T<sub>0II</sub>) was collected immediately after ingestion of half a 200 mls test water solution with or without 1.5 g of citric acid according to a randomized protocol. Subjects then ingested the remaining test solution plus 75 mg of <sup>13</sup>C-urea dissolved in 50 mls of water. A 2nd double sample breath was collected after 30 min (T<sub>30I</sub>, T<sub>30II</sub>). The <sup>13</sup>CO<sub>2</sub>/<sup>12</sup>CO<sub>2</sub> ratio in the T30 sample compared with a standard, times; 1000 minus base line value was calculated (positive being > 5 per mil.) <sup>13</sup>C UBT 2+ve 12{ - }ve 18+ve 18{ - }vedelta/1000 ID ID children children+ Citric acid: T<sub>0I</sub>/T<sub>30I</sub> 31.95 0.39 36.42 0.56 T<sub>0II</sub>/T<sub>30II</sub> 31.88 0.47 36.99 0.50 No citric acid: T<sub>0I</sub>/T<sub>30I</sub> 13.18 0.32 17.12 0.84 T<sub>0II</sub>/T<sub>30II</sub> 12.98 0.46 17.48 0.61 *Conclusion:* <sup>13</sup>C-UBT with and without citric acid is effective and reproducible to identify HP status both in adults and children. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "A Comparison of <sup>13</sup>C Urea-Breath Test (UBT) with and without a Citric Acid Test Meal for Helicobacter Pylori (HP) in Adults and Children"

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"P P 57 1361" P 57 1361 **Sensitivity and Specificity of a Rapid Whole Blood Test for "In Office" Diagnosis of Helicobacter Pylori**

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Ist Medical Clinic, University of Bologna, Italy

Dept. of Microbiology University College, London, UK *Purpose:* to evaluate sensitivity and specificity of a new commercially available whole blood test for "in office" evaluation of Helicobacter pylori (H pylori) status (Medcard, Medimar, Milano Italy). *Methods:* Dyspeptics patients with no previous intake of drugs acting on H pylori underwent upper GI endoscopy with biopsies for culture, urease test and histology (Haematoxylin & Eosin, Giemsa). Before endoscopy, each patient was evaluated for IgG to H pylori by an "in house" ELISA assay (previously validated: sensitivity and specificity 94%) and by Medcard. Patients were considered H pylori+ve if two biopsy tests (Giemsa and/or culture/urease) and/or ELISA serology tested +ve. *Results:* 94 patients (M/F: 55/39, age: range 20–81, mean 43.1 yrs) have been evaluated; 55/94 (58.5%) tested HP +ve. Tab. 1: Giemsa/urease/culture/ELISA and Medcard H pylori positivity according to endoscopic findings (N = macroscopically normal, G/D = gastritis/duodenitis, PU = peptic ulcer, GC = gastric cancer, O = other). N G/D PU GC  
OGiemsa/Urease/culture/ELISA+ 42% 63% 73% 100% 33% Medcard+ 37% 59% 73% 100% –  
Total 19 59 11 2 3 Tab. 2: H pylori status according to Giemsa/Urease and Medcard.  
Giemsa/urease + { - } Medcard + 47 4 { - } 8 34 *Conclusion:* Medcard showed high sensitivity (85.4%) and specificity (90%) both overall and among the different endoscopic findings and could be safely used "in office" to predict H pylori status. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Sensitivity and Specificity of a Rapid Whole Blood Test for "In Office" Diagnosis of Helicobacter Pylori"

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"P P 57 1362" P 57 1362 **How Do Two Diagnostic Tests for *H. Pylori* at 1 Month Compare to Two <sup>13</sup>C-Urea Breath Tests (UBT) in Assessment of Eradication?** P.G. Johnson<sup>1</sup>, A.E. Duggan<sup>2</sup>, C. Olson<sup>3</sup>

<sup>1</sup> BSIA Ltd., U.K.

<sup>2</sup> Glaxo Wellcome R & D, U.K.

<sup>3</sup> Abbott Laboratories, Illinois, USA *Introduction:* To evaluate the eradication of *H. pylori* it has been suggested that either 2 diagnostic techniques might be used 1 month (m) post-treatment, or that UBT alone might be performed at both 1 and 3 m post-treatment. Data from 7 multinational studies conducted to the standards of Good Clinical and Laboratory Practice are presented for a series of time points. *Methods:* Patients who had an active DU and positive CLOtest™ pre-treatment, were evaluated post-treatment. *H. pylori* was assessed by UBT (excess 3.5 <sup>13</sup>CO<sub>2</sub> per mil = positive) and at least 1 other test, [CLOtest, histology (Hx), or culture (Cx)], before and 1, 3, 6, or 12 m post-treatment, dependent on study. UBT, Hx and Cx (antral and corpus biopsies) were processed by central laboratories. *H. pylori* status assigned from the pooled result of UBT at 1 and either 3, 6 or 12 m was compared with the pooled result of two diagnostic tests at 1 m, and also the UBT alone at 1 m, in the same subset of patients. *Results:* UBT (1 m + 3 m) (1 m + 6 m) (1 m + 12 m) % *Hp* { - }ve % *Hp* { - }ve % *Hp* { - }ve (n = 277) (n = 477) (n = 69) Pooled UBT 59.9 50.3 49.3 Two tests 1 m 62.1 54.7 50.7 UBT alone 1 m 64.3 56.0 50.7 *Conclusions:* 2 diagnostic tests at 1 m post-treatment or the pooled result from 2 consecutive breath tests provide satisfactory alternatives in the definitive assessment of *H. pylori* eradication. UBT alone at 1 m gives a slightly raised estimate of eradication, but on balance compares favourably for clinical practice by not requiring endoscopy whilst giving a rapid answer. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "How Do Two Diagnostic Tests for H. Pylori at 1 Month Compare to Two <sup>13</sup>C-Urea Breath Tests (UBT) in Assessment of Eradication?"

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## "P P 57 1363" P 57 1363 **Current Use of Helicobacter Serology for Pre-Endoscopy Screening in the UK**

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Considerable savings have been reported using *Helicobacter pylori* (HP) serology as a pre-endoscopy screening test for young dyspeptics although the extent of these savings and the efficacy of various clinical strategies have been disputed. We conducted a survey amongst UK hospital gastroenterologists and general practitioners with an interest in gastroenterology to establish current practice in the management of dyspeptics under the age of 45 years. Postal questionnaires were sent to 536 members of the British Society of Gastroenterology and 164 members of the Primary Care Society in Gastroenterology. The response rate was 66%. HP serology is currently used by 25% of general practitioners and 17% of gastroenterologists. Following screening, most general practitioners would eradicate infection prior to endoscopy (92.4%) whilst most gastroenterologists (74.5%) would endoscope patients before treatment. 70% of gastroenterologists would endoscope sero-positives but 30% would endoscope sero-negatives. Of those not currently using serology, 78% would use it as a pre-endoscopy test if it were available. 106 different drug regimens were used by respondents as first line HP treatment. 83.4% used triple therapy and the most popular combination was that of omeprazole, amoxicillin and metronidazole (38.2%). Following treatment 57% of respondents re-tested selected patients, 29% re-tested all patients and 14% never re-tested. Our survey shows that in the UK, HP serology is being used as a pre-endoscopy screening test for young dyspeptics by only a fifth of gastroenterologists. There was wide variation in strategies preferred by hospital gastroenterologists and by general practitioners. Trials comparing symptomatic outcome and economic consequences of different HP serology based clinical strategies are needed. Clinical practice: Management strategy Oesophageal gastric duodenal disorders: *Helicobacter Pylori* }

"Current Use of Helicobacter Serology for Pre-Endoscopy Screening in the UK"

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## "P P 57 1364" P 57 1364 Helisal Rapid Whole Blood Test for the Diagnosis of Helicobacter Pylori

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Diagnosis of *Helicobacter pylori* by histopathology, culture, urea breath tests or serology using enzyme linked immunosorbent assay (ELISA) are relatively time consuming. A test kit for diagnosing *H. pylori* using diluted whole blood has become commercially available (Helisal<sup>tm</sup> – Cortecs Ltd). This test is easy to perform, requires no laboratory equipment. Our aim was to independently assess its diagnostic accuracy. Dyspeptic patients referred for investigation at our hospital were invited to participate. Patients who had received proton pump inhibitors over the preceding month or had previously received *H. pylori* eradication therapy were excluded. <sup>13</sup>C urea breath test was used as the gold standard for *H. pylori* status. All urea breath tests and rapid whole blood tests were performed by a single investigator. 92 patients were recruited in this study (median age 52.5, range 10–72 years, 51 males). All rapid whole blood tests were completed within ten minutes. Of the 59 patients *H. pylori* positive by urea breath test, 4 were false negative by rapid whole blood test. Of the 33 patients *H. pylori* negative by urea breath test, 11 were false positive by rapid whole blood test. The sensitivity and specificity of the kits for *H. pylori* were 93% of 67% respectively. The Helisal rapid whole blood test was quick and easy to perform. In our hands, its sensitivity was good but its specificity was less impressive. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Helisal Rapid Whole Blood Test for the Diagnosis of Helicobacter Pylori"

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## "P P 57 1365" P 57 1365 Intra gastric Urease Activity in Helicobacter Pylori (H.p.) Infection after Urea Application

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<sup>3</sup> Biochemical Diagnostics, Department, Medical Academy, Bialystok, Poland  
*The purpose* of the study was to evaluate whether intra gastric ammonia production with exogenous urea as substrate by bacterial urease could be a criterion of severity H.p. infection and efficacy of therapy.  
*Methods.* In 31 patients (pts), (23 F, 19–68 yrs, and 8 M, 23–61 yrs) with peptic ulcer (6 pts) or gastritis (25 pts) and H.p. infection (in 14 severe), the ammonia output (mg/h) in basal (BAO) and pentagastrin (6 \b5g/kg s.c.) stimulated gastric juice (MAO<sub>1</sub>), was estimated. In 15 pts MAO<sub>2</sub> after repeated stimulation during i.g. infusion of urea solution (7.5 g/60 ml H<sub>2</sub>O {\b4} h<sup>-1</sup>) was collected. This test was repeated after treatment with triple or bismuth salt therapy when indicated.  
*Results.* The ammonia output (A.O.) in MAO<sub>2</sub> before treatment was almost twice higher than in MAO<sub>1</sub> (20.9 – 12.5 vs 10.9 – 4.8, p < 0.01). After effective treatment (8/15 pts) it decreased by 40% in BAO, 57% in MAO<sub>1</sub> and 42% in MAO<sub>2</sub> (p < 0.05). Ineffective therapy (3/15 pts) did not affect the ammonia output significantly. The ratio of A.O. in MAO<sub>2</sub>/BAO was markedly higher then in MAO<sub>1</sub>/BAO and MAO<sub>2</sub>/MAO<sub>1</sub> before treatment (3.86 – 2.99 vs 2.16 – 1.41; p < 0.01 and vs 1.93 – 0.93; p < 0.01). After effective therapy MAO<sub>2</sub>/BAO decreased by 37% and MAO<sub>2</sub>/MAO<sub>1</sub> by 30% (p < 0.05), what was not the case after ineffective therapy. MAO<sub>1</sub>/BAO ratio of A.O. after single stimulation was also reduced (1.45 – 0.35 vs 2.98 – 2.47) after effective treatment (p < 0.05).  
*Conclusion.* The ammonia output in the pentagastrin stimulated gastric juice secretion could be simple and nonexpensive test of total gastric Helicobacter pylori infection and effectivity of therapy, especially when performed after application of exogenous substrate: urea for bacterial urease. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic disorders: Helicobacter Pylori

"Intra gastric Urease Activity in Helicobacter Pylori (H.p.) Infection after Urea Application"

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"P P 57 1366" P 57 1366 **Does a Second Biopsy Specimen Increase Clo-Test Accuracy for Helicobacter Pylori (HP) Detection after Eradication Treatment in Duodenal Ulcer (DU) Patients?**

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Rapid urease test is considered as a reliable and inexpensive method for HP detection. Histology (HIS) is the reference method although misdiagnosis is possible when HP density is low. It is suggested that the positivity of CLO-test is related to the HP burden. Translocation of HP to the fundus after anti-secretory treatment has been reported. The *aim of our study* was to evaluate the diagnostic accuracy of CLO-test'-(Delta west Pty Ltd) in DU patients after HP eradication treatment, correlate CLO results with HP density and assess possible benefits by adding a fundic (F) or antral (A) biopsy specimen. *Patients and methods:* 123 patients (81 men), with DU had 2A + 2F biopsies for HIS [modified Giemsa, Warthin Starry] and immunohistochemical (IHC) [Rabbit anti HP antibodies DAKO: B 471] analysis, 4–6 weeks after the end of eradication therapy. All patients had a CLO-test with one A biopsy (CLO1). 63 patients had a second one (CLO2f) with one A and one F biopsy together while 60 patients had also a second one with two A biopsies together (CLO2a). *Stat:* t-test, x2-test, Bartholomew test. *Results:* There was no difference between CLO1 and CLO2f or CLO2a concerning the qualitative results. The time for the test to become positive was significantly shortened only when a second A biopsy was added (1.98 – 0.28 vs. 1.09 – 0.75 h)  $p < 0.001$ . CLO-test compared to HIS has 58% Se, 100% Sp, 100% ppv and 69% npv while compared to IHC has 77% Se, 100% Sp, 100% ppv and 86% npv. CLO positivity was strongly correlated to HP density ( $p < 0.01$ ). *Conclusions:* 1) The specificity of CLO-test is excellent for detection of HP after eradication treatment for DU patients, while its sensitivity is mediocre compared to IHC (77%) and poor compared to histology (58%) 2) The addition of a second biopsy specimen either A or F in the CLO-test does not improve its diagnostic value and 3) The disagreement between IHC and HIS (15/123 patients) needs further evaluation in order to avoid HP overdiagnosis. Clinical practice: Management strategy Clinical practice: Quality assurance Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Does a Second Biopsy Specimen Increase Clo-Test Accuracy for Helicobacter Pylori (HP) Detection after Eradication Treatment in Duodenal Ulcer (DU) Patients?"

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## "P P 57 1367" P 57 1367 **13C-Urea Breath Test and the Density of Helicobacter Pylori in Gastric Mucosa — Study of the Patients with Functional Dyspepsia**

\*J. Koskenpato, M. F\`e4rkkil\`e4

Helsinki University Central Hospital, Department of gastroenterology, Helsinki, Finland The studies of influence of *Helicobacter pylori* gastritis on symptoms of functional dyspepsia has produced inconclusive results. The 13C-urea breath test is a noninvasive method to detect the presence of *H. pylori* infection. The relationship between the results of 13C-UBT and the density of *H. pylori* in histologic samples is not established. The aims of our study were: 1. to analyse the relationship between the results of 13C-urea breath test and the density of *H. pylori* in histology and 2. to analyse the association between the symptoms of functional dyspepsia and the density of *H. pylori* in gastric mucosa. **Material and methods:** 29 patients with functional dyspepsia were evaluated by gastroscopy and ultrasonography of upper abdomen. Every patient had a nonerosive *H. pylori* positive chronic gastritis without any other macroscopic abnormality. Biopsies from duodenum, antrum and corpus were taken for histological examination. - The scores of the density of *H. pylori* were graded on a scale ranging from 0 to 6 (antrum 0–3, corpus 0–3). The dyspepsia symptom scores (range 0 to 12) were recorded by a standardized questionnaire. All patients received the 13C-UBT and the 13C-enrichment was analyzed by isotope ratio mass spectrometry. Statistical analysis was made by using simple linear regression analysis. **Results:** The mean delta-value of 13C-UBT was 43.0 – 21.1 ‰, the mean dyspepsia score was 4.2 – 2.4 and the mean value of the density of *H. pylori* was 3.6 – 1.4. There was a statistically significant association between the density of *H. pylori* in histological examination and the delta-value of 13C-UBT ( $p = 0.01$ ,  $\text{pearsonr} = 0.46$ ). There was no association between the symptoms of functional dyspepsia and the delta-value of 13C-UBT ( $p = 0.55$ ,  $\text{pearsonr} = -0.12$ ). **Conclusions:** These data suggest that the delta-value of 13C-UBT is associated with the density of *H. pylori* in gastric mucosa. The severity of symptoms caused by functional dyspepsia are not associated with the density of *H. pylori* in gastric mucosa. Oesophageal gastric duodenal disorders: Helicobacter Pylori Motility, general: Functional GI disorders } "13C-Urea Breath Test and the Density of Helicobacter Pylori in Gastric Mucosa / Study of the Patients with Functional Dyspepsia"

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"P P 57 1368" P 57 1368 **Diagnostic Value of a Commercial IgG Enzyme-Linked Immunosorbent Assay (Elisa) Kit for *Helicobacter Pylori* Infection Diagnosis**

\*C. Mart\edn de Argila, D. Boixeda, N. Valdezate, S. Mir, I. Garc\eda, J.P. Gisbert, R. Canton, A. Garc\eda Plaza

Gastroenterology and Microbiology Departments, "Ram\fn y Cajal" Hospital, Madrid, Spain Enzyme-linked immunosorbent assays (ELISAs) are considered good non-invasive methods to diagnose *H. pylori* infection. The aim of this study was to evaluate the clinical usefulness of a commercial IgG *H. pylori* antibody test kit. **Methods:** A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. *H. pylori* was diagnosed if culture was positive in at least one of the biopsy samples obtained. Ten milliliters of venous blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for *H. pylori* by a quantitative commercial IgG ELISA, based on an acid glycine extract: Helico G, Porton, Cambridge, UK. The test was performed in duplicate according to the manufacturer's instructions and by the same person. Results were evaluated on the basis of different cut-off values. **Results:** In the study population, 89.8% of the patients were *H. pylori* positive (by culture). The serology results were as follows: Cut-off Sensitivity (%) Specificity (%) PPV (%) NPV (%) LR8 U/ml 98.3 53.7 94.9 78.6 2.110 U/ml 97.2 85.4 98.3 77.8 6.611 U/ml 94.7 85.4 98.3 64.8 6.4 PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio. The area under the receiver operator characteristic (ROC) curve was 0.96. **Conclusions:** This study confirms the diagnostic efficiency of this IgG commercial ELISA in detecting *H. pylori* infection. According to the manufacturer, 10 U/ml is the most appropriate cut-off value. The competitive cost of this technique and the fact that it is non-invasive render this method an optimum tool to study *H. pylori* infection in large population groups. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Diagnostic Value of a Commercial IgG Enzyme-Linked Immunosorbent Assay (Elisa) Kit for Helicobacter Pylori Infection Diagnosis"

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"P P 57 1369" P 57 1369 **Measurement of Helicobacter Pylori Antibodies in Saliva: A Non Invasive in Comparison with 13C-UREA Breath Test and Serology** R. G<sup>a</sup> Valriberas, J.A. Correa Est<sup>a</sup>l, C. Hermida, Y. Jimenez, J.M. Pajares G<sup>a</sup>

Dept. of Gastroenterology, Hospital La Princesa, Madrid, Spain *Background & Aim:* Numerous serological Kits are available to provide cheaper, non invasive and more rapid diagnosis of the Helicobacter Pylori (Hp) infection. These study evaluated the accuracy of the determination of Ig G antibodies in saliva for detection of Hp status using 13C-Urea Breath Test (UBT) as gold standar. *Patients & Methods:* 24 patients (mean age 50, sex: 10 F, 14 M) presenting bleeding peptic ulcer endoscopically documented with two antral biopsies and rapid ureasa test (RTU) and 24 controls (mean age 23, sex: 4 F, 21 M) without peptic disease were studied. We realized to all the patients venous puncture for serology tests (Helico-G), collection of saliva using OMNI-Sal collection device (SDS), and 13C-UBT. We exclude those patients in treatment with omeprazol, antibiotics or eradication therapy in the previous four weeks. The cut-off of salivary antibody was established between 0.8–1 U/ml and for serum Ig G titers in 10. *Results:* Cases 24 Controls 24 Patients 15/24 3/24 6/24 8/24 1/24 7/24 2/24 Saliva antibodies + { - } ++ { - } + { - } + Serum serology + { - } ++ { - } ++ { - } UBT + { - } { - } + { - } { - } + { - } *In cases:* 6 patients were UBT negative, being positive both serologies. In the biopsies and RTU all except one, were negative for Hp infection. We review the results and we found that all these patients had taken antibiotics for urinary infection during the hospitalization. We repeat the UBT 3–4 weeks later and 4 were positive and 2 continue negative. The control group had false positives due to low sensibility, spontaneous eradication or urea-producers pathogens. *Conclusions:* The determination of specific Hp antibodies could be a valid method for determinate Hp infection in patients with peptic disease but isn't good for screening test. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Measurement of Helicobacter Pylori Antibodies in Saliva: A Non Invasive in Comparison with 13C-UREA Breath Test and Serology"

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"P P 57 1370" P 57 1370 **<sup>14</sup>C-Urea Breath Test in Detection of *Helicobacter Pylori*-Associated Gastric Diseases**

\*W. Bielanski, J. Dobrzanska, A. Kaminska, J. Pytko-Polonczyk, S.J. Konturek, E. Sito

Inst. Physiol., Univ. Sch. Med., Krakow, Poland *Purpose:* High urease activity of *Helicobacter pylori* (Hp) is used to detect this bacterium by non-invasive urea breath test (UBT). We employed the microdose version of the test in which 37 kBq of <sup>14</sup>C urea is given orally in capsule. The objectives of the study were: 1. to evaluate a microdose (37 kBq) <sup>14</sup>C-urea enclosed in a quick dissolve capsule; 2. to assess whether the fasting period is required before the procedure of <sup>14</sup>C-UBT; 3. to determine whether breath test results are changed when they are mailed to a remote site for analysis; 4. to define the diagnostic ranges of <sup>14</sup>C-UBT for Hp-positive and Hp-negative patients. *Methods:* In the study we breath tested 239 consenting patients (18–75 yr old) without previous antibiotic or antiulcer therapy or gastric surgery. The breath samples were collected and analyzed before (at basal state) and at 10 min intervals after the ingestion of 37 kBq <sup>14</sup>C-urea by patients prior to their endoscopy. With the cut-off value > 100 DPM as positive, UBT results correlated highly significant with combined results of invasive gold standards i.e. CLO-test + histology score. *Results:* The breath test performed locally were almost identical with those read at remote laboratory. The data found for fasting and fed states of subjects agreed in 87%. When <sup>14</sup>C-urea was dissolved in water and confined for 5 min in the mouth (without swallowing), both 30 Hp positive and 30 HP negative patients with gastric UBT showed the presence of urease activity in the mouth. *Conclusions:* 1. <sup>14</sup>C-urea in quick dissolved capsule is a convenient, non-invasive test for detection of gastric Hp with accuracy and reproducibility equal to those of gold standards; 2. feeding does not affect the accuracy of the test; 3. the results can be analyzed within 10–15 min locally or at a remote site; 4. orally applied liquid <sup>14</sup>C-urea may lead to false positive results due to oral urease activity. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } " <sup>14</sup>C-Urea Breath Test in Detection of *Helicobacter Pylori*-Associated Gastric Diseases"

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"P P 57 1371" P 57 1371 **Antibody Response to Helicobacter Pylori Antigens: Sensitivity and Specificity of IGG-ELISA and an H. Pylori Specific Immuno-Blot System** U. Schmidt-Wittig, U. Platzer, G. Illies, M. Nilius, A. Hackelsberger, P. Malfertheiner

Dept. Gastroenterology, Hepatology and Infect. Diseases Otto-von-Guericke-University Magdeburg, Germany *Background:* H. pylori infection is either detected by invasive means using the urease test (HUT), histology, culture or noninvasively by <sup>13</sup>C-urease breath test or serology. Antibody response may be determined either by ELISA or by immunoblot technique. Aim of our study was to investigate the sensitivity and specificity of a new immunoblot system in comparison to other methods. *Methods:* 66 patients with chronic gastritis (CG), 29 with gastric (GU) and 25 patients with duodenal (DU) ulcer were tested for presence of H. pylori infection by HUT, histology, IgG-ELISA (Biorad, Germany) and a new commercially available immunoblot system (BAG-Pylori-Blot, BAG Germany) based upon H. pylori specific antigens. For evaluation of IgG-ELISA and immunoblot 66 patients with positive and 43 patients with negative HUT and histology served as reference for sensitivity and specificity, respectively, as well as for positive (PPV) and negative (NPV) predicted value. *Results:* Both methods showed highest sensitivity in DU sera, while specificity was best in CG patients. In most of the calculated parameters immunoblot results exceed all those of IgG-ELISA. ELISA Sensitivity Specificity PPV NPV CG 77% 68% 70% 56% GU 76% 38% 76% 37.5% DU 94% 14% 74% 50% Blot Sensitivity Specificity PPV NPV CG 81% 68% 71% 58% GU 81% 38% 77% 43% DU 94% 28% 77% 66% *Conclusion:* Tested immunoblot-system represents a suitable alternative for IgG-ELISA with even higher sensitivity and specificity and implies the possibility of screening for specific antigens of infecting H. pylori strains in patients. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Antibody Response to Helicobacter Pylori Antigens: Sensitivity and Specificity of IGG-ELISA and an H. Pylori Specific Immuno-Blot System"

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"P P 57 1372" P 57 1372 **Fibrinogen and *H. Pylori* in Asymptomatic Post MI Patients and Healthy Controls**. J. Rajput-Williams<sup>1</sup>, N.R. Williams<sup>1</sup>, P.G. Johnson<sup>2</sup>, R.J. Dickinson<sup>3</sup>

<sup>1</sup> Papworth Hospital, Cambridge, UK

<sup>2</sup> BSIA, Brentford, UK

<sup>3</sup> Hinchingsbrooke Hospital, Huntingdon, UK A link between *H. pylori* seropositivity and coronary heart disease *via* plasma fibrinogen has been suggested, although this has been disputed. Fibrinogen (and Factor VII) were measured in non-smoking men who recently had a myocardial infarction (MI; n = 35) and healthy controls (n = 27) with known *H. pylori* status (assessed by <sup>13</sup>C-urea breath test, BSIA, UK). Results are presented below. Table. Plasma fibrinogen. Results are mean (95% confidence interval). Statistical significance was assessed by t-test. Pairs of comparisons are marked a, b and c. *H. pylori* n Fibrinogen (g/l) Control negative 20 2.68 (2.48–2.88) a, b, c Control positive 7 3.07 (2.85–3.30) a Post-MI negative 27 3.04 (2.82–3.26) b Post-MI positive 8 3.26 (2.64–3.89) ca, P = 0.044; b, P = 0.026; c, P = 0.010 There were no significant differences in Factor VII (data not shown). In conclusion, this data supports the hypothesis of an association between *H. pylori* status and fibrinogen. Oesophageal gastric duodenal disorders: Helicobacter Pylori } "Fibrinogen and H. Pylori in Asymptomatic Post MI Patients and Healthy Controls"

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## Is There Any Correlation between <sup>13</sup>C-UREA Breath Test Values and Response to *H. Pylori* Eradication Therapy?

\*J.P. Gisbert, D. Boixeda, Mart\edn C. de Argila, F. Bermejo, T. P\e9rez, I. Jim\e9nez<sup>1</sup>, J.M. Pajares<sup>1</sup>

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<sup>1</sup> ""la Princesa"" Hospitals, Madrid, Spain  
*Purpose:* To study whether there is a correlation between urea breath test values prior to treatment and the response to *H. pylori* eradication therapy in patients with duodenal ulcer.  
*Methods:* Two-hundred and one patients with duodenal ulcer were retrospectively studied (mean age: 47 – 13 years; 69% males). Initially, an endoscopy with biopsy samples (H&E stain) taken from antrum and body and a <sup>13</sup>C-urea breath test (according to the European standard protocol, measuring <sup>13</sup>C difference: { d }<sup>13</sup>CO<sub>2</sub>) were performed. Both procedures were repeated one month after completing therapy: ""classic"" triple therapy (n = 29), omeprazole or lansoprazole plus amoxicillin (n = 58), and omeprazol plus two of the following antibiotics: amoxicillin, clarithromycin, metronidazole (n = 114).  
*Results:* Overall, eradication was achieved in 66% (n = 132). The corresponding rates for the therapy groups were: ""classic"" triple therapy: 64%; omeprazole or lansoprazole plus amoxicillin: 33%; omeprazol plus two antibiotics: 83%. Mean { d }<sup>13</sup>CO<sub>2</sub> level was { - }31.5 – 23. There were no differences when comparing values of patients with therapy success (33 – 24) and failure (30 – 20). No differences were observed when considering therapies separately and comparing eradication rates depending upon breath test levels prior to therapy. Breath test values did not influence the eradication in the logistic regression model. Mean { d }<sup>13</sup>CO<sub>2</sub> values after therapy in patients with eradication failure ran in parallel with initial values.  
*Conclusion:* No correlation was observed between urea breath test values before treatment and the response to *H. pylori* eradication therapy in patients with duodenal ulcer. Thus, we conclude that quantitation of this diagnostic method is not useful to predict the success or failure of eradication therapy.  
Oesophageal gastric duodenal disorders: Helicobacter Pylori  
Oesophageal gastric duodenal disorders: GD disorders, acid peptic } ""Is There Any Correlation between 13C-UREA Breath Test Values and Response to H. Pylori Eradication Therapy?""

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## Breath Test for the Diagnosis of *H. Pylori* Infection: Concordance with Histologic Methods and Correlation with Histologic Lesions of Gastric Mucosa

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**Purpose:** To study the concordance between <sup>13</sup>C-urea breath test and histology in the diagnosis of *H. pylori* infection, and to evaluate whether there is a correlation between breath test values and histologic lesions of gastric mucosa.  
**Methods:** One-hundred and sixty-one patients with duodenal ulcer were prospectively studied. An endoscopy with biopsy samples (H&E stain) taken from antrum and body was performed, and a <sup>13</sup>C-urea breath test (according to the European standard protocol, measuring <sup>13</sup>C difference: { d }<sup>13</sup>CO<sub>2</sub>) was also performed at initial moment. Both procedures were repeated one month after completing therapy: "classic" triple therapy, omeprazole or lansoprazole plus one antibiotic, or omeprazole plus two antibiotics (amoxicillin, clarithromycin, metronidazole). Eradication was defined as the absence of *H. pylori* both by histologic and breath test methods.  
**Results:** At initial moment; 95.6% of patients (n = 153) were *H. pylori* positive by histologic methods, and 97.5% (n = 156) were positive by breath test (proportion of positive agreement = 0.98). Kappa for *H. pylori* diagnosis after therapy was 0.88 (EE: 0.08). A correlation between { d }<sup>13</sup>CO<sub>2</sub> and histologic lesions at initial moment was observed, both at the antrum (r = 0.23; p < 0.01) and body (r = 0.27; p < 0.01). Similarly, a correlation after therapy in both gastric antrum (0.55; p < 0.001) and body (0.3; p < 0.001) was demonstrated. A significant difference was observed when comparing mean { d }<sup>13</sup>CO<sub>2</sub> in patients with different degrees of histologic gastritis, both at initial moment (antrum: W Kruskal-Wallis = 9; p = 0.05; body: W = 12, p < 0.05) and after therapy (antrum: W = 60, p < 0.001; body: W = 23, p < 0.001).  
**Conclusion:** A high concordance was observed between <sup>13</sup>C- urea breath test and histology in the diagnosis of *H. pylori* infection. A correlation exists between breath test values and histologic lesions of gastric mucosa.  
Oesophageal gastric duodenal disorders: Helicobacter Pylori  
Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Breath Test for the Diagnosis of H. Pylori Infection: Concordance with Histologic Methods and Correlation with Histologic Lesions of Gastric Mucosa"

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## Usefulness of the Combined Use of IgG and IgA ELISA Methods for Diagnosing *Helicobacter Pylori* Infection

\*C. Martín de Argila, D. Boixeda, R. Cantón, N. Mir, S. Valdezate, F. Bermejo, J.P. Gisbert, A.L. San Roman

Gastroenterology and Microbiology Departments, "Ramón y Cajal" Hospital, Madrid, Spain  
**Aim:** To determine the diagnostic value of the combined use of IgG and IgA ELISA methods to diagnose *H. pylori* infection.  
**Methods:** A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. *H. pylori* was diagnosed if culture was positive in at least one of the biopsy samples obtained. Ten milliliters of venous blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for *H. pylori* by a commercial IgA ELISA (G.A.P. Test IgA. Bio-Rad, Italy) and a commercial IgG ELISA (HelicoG, Porton, Cambridge, UK). The tests were performed in duplicate according to the manufacturer's instructions and by the same person. Two interpretations were possible: 1) Assumption 1: a serological result was considered positive for *H. pylori* when both methods (IgG and IgA) were positive, and negative when at least one of them was negative; 2) Assumption 2: a serological result was considered positive when at least one of the methods was positive, and negative when both methods were negative. Titres higher than 10 U/ml were considered positive (following manufacturer's recommendations) for both tests.  
**Results:** In the study population, 89.8% of the patients were *H. pylori* positive (by culture). The serology results were as follows: Cut-off IgG/IgA Sensitivity (%) Specificity (%) PPV (%) NPV (%) LR10/10 U/ml\* 94.1 85.3 98.2 62.5 6.2610/10 U/ml\*\* 99 80 97 94 4.95  
PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio; \*Assumption 1; \*\* Assumption 2.  
**Conclusions:** 1) The combined use of both serological methods provided more useful information compared with single IgG or IgA determinations. 2) The high specificity and PPV for assumption 1 render both determinations very useful when the clinician wishes to accurately know the "true" infection *H. pylori* status. 3) The extremely high sensitivity obtained with the assumption 2 renders this method very useful for screening large population groups. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic }  
"Usefulness of the Combined Use of IgG and IgA ELISA Methods for Diagnosing Helicobacter Pylori Infection"

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"P P 57 1376" P 57 1376 **Diagnostic Value of a Commercial IgA Enzyme-Linked Immunosorbent Assay (ELISA) Kit for *Helicobacter Pylori* Infection Diagnosis**

\*C. Mart\edn de Argila, D. Boixeda, N. Mir, S. Valdezate, J.P. Gisbert, L. de Rafael, R. Cant\3n

Gastroenterology and Microbiology Departments, "Ram\3n y Cajal" Hospital, Madrid, Spain Enzyme-linked IgG immunosorbent assays (ELISAs) are good non-invasive methods to diagnose *H. pylori* infection, but scarce information are available on IgA ELISAs. The aim of this study was to evaluate the clinical usefulness of a commercial IgA *H. pylori* antibody test kit. **Methods:** A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. *H. pylori* was diagnosed if culture was positive in at least one of the biopsy samples obtained. Ten milliliters of venous blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for *H. pylori* by a semiquantitative commercial IgA ELISA, based on purified specific antigens: G.A.P. Test IgA. Bio-Rad, Italy. The test was performed in duplicate according to the manufacturer's instructions and by the same person. Results were evaluated on the basis of different cut-off values. **Results:** In the study population, 89.8% of the patients were *H. pylori* positive (by culture). The serology results were as follows: Cut-off Sensitivity (%) Specificity (%) PPV (%) NPV (%) LR8 U/ml 98.3 34.1 92.9 70 1.510 U/ml 96.4 80.5 97.7 71.7 4.911 U/ml 94.2 80.5 97.7 61.1 4.8 PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio. The area under the receiver operator characteristic (ROC) curve was 0.9. **Conclusions:** This study confirms the usefulness of this IgA commercial ELISA in detecting *H. pylori* infection. According to the manufacturer, 10 U/ml is the most appropriate cut-off value. The high sensitivity and positive predictive values render this method very useful for screening large populations groups. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Diagnostic Value of a Commercial IgA Enzyme-Linked Immunosorbent Assay (ELISA) Kit for Helicobacter Pylori Infection Diagnosis"

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## "P P 57 1377" P 57 1377 **Blind Gastric Biopsy in the Diagnosis of Helicobacter Pylori Infection**

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<sup>1</sup> Department of Internal Medicine, Istanbul, Turkey

<sup>2</sup> Department of Pathology of Cerrahpasa Medical Faculty of University of Istanbul, Istanbul, Turkey Gastric mucosal tissue is usually required for the diagnosis of helicobacter pylori (HP) infection. Serology, though a reliable method in initial diagnosis, is useless in assessing the response to the treatment. Breath test, on the other hand, is not widely available. We performed gastric mucosal biopsies through open ended 18 FR naso-gastric tube (NGT)s with Olympus FB-25 KR rotatable forcepses (Olympus, Japan) in 33 patients (19 female, 14 male, median age 38 ys; range 21–72) with dyspeptic symptoms. The average distance between the end of NGT and nasal insertion site was 50–55 cm. Four specimens obtained from each patient. Blind gastric biopsy (BGB) was repeated in 15 HP +ve patients one month after completion of treatment with 500 mg tid clarithromycin, 14 days, and omeprazole 20 mg bid, 28 days. Upper GI endoscopy was performed using a Fujinon FG7-CT2 panendoscope (Fujinon, Japan), immediately after BGB. The sites of biopsies were noted and four other specimens, two from corpus, and two from antrum, were obtained with the same type of forceps. Serological testing was performed from sera of 29/33 patients. All of the biopsies were evaluated by the same pathologist with hematoxylin-eosin staining in blinded fashion. 31/33 of initial biopsies obtained by endoscopic biopsy (EB) were +ve for HP. BGB was +ve in 30/31 of EB +ves. After treatment 13/15 (87%) were -ve for HP in both EB and BGB specimens and 2/15 (13%) were still +ve. All but one of the BGB specimens were from corpus. In 47/48 (98%), BGB were in accordance with EB. The only BGB sample with discordant result with EB was from distal esophagus, one of the first experiences. Serology was in accordance with biopsy results in all but one who was +ve by histology and -ve by serology. BGB was performed without anesthesia and tolerated well. We concluded that BGB is an easy, safe, reliable and cheap method in obtaining gastric mucosal tissue for HP evaluation. Its clinical value awaits further studies. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Instrumentation, diagnosis } "Blind Gastric Biopsy in the Diagnosis of Helicobacter Pylori Infection"

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## "P P 57 1378" P 57 1378 IgA Values and Gastroduodenal Diagnosis of *Helicobacter Pylori* Infection

\*C. Mart\edn de Argila, D. Boixeda, L. de Rafael, R. Canton, N. Mir, J.P. Gisbert, A. Garc\eda Plaza

Gastroenterology and Microbiology Departments. "Ram\fn y Cajal" Hospital, Madrid, Spain  
*Aim:* Given the close association between *H. pylori* infection and different gastroduodenal conditions we undertook a study to assess whether IgA antibody mean values to *H. pylori* can discern the gastroduodenal condition among patients.  
*Methods:* A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from duodenal bulb, gastric antrum, gastric body, and gastric fundus were obtained for histology and *H. pylori* culture. In patients who had undergone Billroth-II surgery biopsies were obtained from efferent loop, surgical stoma and gastric fundus. *H. pylori* infection was diagnosed if culture was positive in at least one of the biopsy samples obtained. In all patients IgA specific antibodies against *H. pylori* infection were determined. A semiquantitative commercial IgA ELISA based on purified specific antigens (G.A.P. Test IgA. Bio-Rad, Italy) was used.  
*Results:* Mean values of IgA specific antibodies and patients with positive culture for *H. pylori*: Endoscopic diagnosis IgA (U/ml) Normal 18.9 – 12.3<sup>0~</sup>⊙ Gastritis: Antrum 21.9 – 15.4<sup>b,\*</sup> Total 28.2 – 14.8 Duodenal ulcer 30 – 35.7<sup>0~.b.♥</sup> Gastric ulcer 50.9 – 64.7<sup>⊙.b4,\*♥</sup> Pyloric channel ulcer 19.5 – 2.1 Gastric cancer 32.7 – 29.7 Gastric surgery: Billroth I 32.6 – 30.8 Billroth II 37.9 – 63.1 Bulb duodenitis: With erosions 21.7 – 11.3 Without erosions 33.7 – 33.2<sup>b4</sup> Different symbols = p < 0.05. In the remaining comparisons between different groups: p > 0.05.  
*Conclusions:* The highest values of IgA specific antibodies to *H. pylori* corresponded to gastric ulcer, gastric cancer, Billroth-II gastric surgery and bulb duodenitis with erosions, but but the small statistically significant differences between these diagnostics limit the usefulness of these findings. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "IgA Values and Gastroduodenal Diagnosis of Helicobacter Pylori Infection"

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## "P P 57 1379" P 57 1379 IgG Values and Gastroduodenal Diagnosis of *Helicobacter Pylori* Infection

\*C. Mart\edn de Argila, D. Boixeda, R. Cant\ f3n, S. Valdezate, C. de la Serna, J.P. Gisbert, L. de Rafael

Gastroenterology and Microbiology Departments, ""Ram\ f3n y Cajal"" Hospital, Madrid, Spain  
**Aim:** Given the close association between *H. pylori* infection and different gastroduodenal conditions we undertook a study to assess wheter IgG antibody mean values to *H. pylori* can discern the gastroduodenal condition among patients.  
**Methods:** A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from duodenal bulb, gastric antrum, gastric body, and gastric fundus were obtained for histology and *H. pylori* culture. In patients who had undergone Billroth-II surgery biopsies were obtained from efferent loop, surgical stoma and gastric fundus. *H. pylori* infection was diagnosed if culture was positive in at least one of the biopsy samples obtained. In all patients IgG specific antibodies against *H. pylori* infection were determined. A quantitative commercial IgG ELISA based on an acid glycine extract (Helico G, Porton, Cambridge, UK) was used.  
**Results:** Mean values of IgG specific antibodies and patients with positive culture for *H. pylori*: Endoscopic diagnosis IgG (U/ml) Normal 77.7 – 49.3 Gastritis: Antrum 85.5 – 38\* Total 95.3 – 50.3 Duodenal ulcer 80.4 – 38.4# Gastric ulcer 90.2 – 33.1@ Pyloric channel ulcer 110 – 0 Gastric cancer 96.4 – 28.1 Gastric surgery: Billroth I 87 – 37 Billroth II 88.1 – 47 Bulb duodenitis: With erosions 105.5 – 47 Without erosions 110 – 0\*#.@ Different symbols = p < 0.05. In the remaining comparisons between different groups: p > 0.05.  
**Conclusions:** The highest values of IgG specific antibodies to *H. pylori* corresponded to bulb duodenitis, pyloric channel ulcers, pangastritis and gastric cancer, but the small statistically significant differences between these diagnostics limit the usefulness of these findings.  
Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "IgG Values and Gastroduodenal Diagnosis of *Helicobacter Pylori* Infection"

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"P P 58 1380" P 58 1380 **Prescribing Patterns for Dyspepsia in Primary Care**

\*K. Bodger, M.J. Daly, R.V. Heatley

Division of Medicine, St. James's University Hospital, Leeds, England

Department of Pharmacy, St. James's University Hospital, Leeds, England *Background*

Expenditure on drugs for dyspepsia in primary care remains high, yet there are few published studies on the indications currently used by general practitioners (GPs) for prescribing different classes of drugs. We report a prospective observational study of prescribing patterns in our area. *Methods* GPs were recruited from 5 local multi-partner surgeries, representing a cross-section of doctors with respect to list size, fundholding status and prescribing expenditure. Each GP prospectively recorded details of all consultations for dyspepsia over a 4 month period. *Results* 257 consecutive consultations were recorded. Percentages of patients in specified dyspepsia sub-groups receiving each class of drug are summarised in the table: [Nil = No prescription, Ant = antacid, Mot = motility agent, H2A = H2- antagonist, PPI = proton pump inhibitor, HpE = *H. pylori* eradication]

Subgroup N Nil Ant Mot H2A PPI HpE Never investigated 144 9% 32% 8% 33% 16% 1% – new 59 8% 44% 5% 31% 12% 0% – consulted before 85 9% 24% 11% 35% 19% 2% – ulcer-like dyspepsia 22 18% 9% 0% 68% 5% 0% – reflux-like dyspepsia 50 8% 40% 2% 16% 30% 4% – non-specific dyspepsia 72 7% 35% 15% 33% 10% 0% Previously investigated 113 5% 9% 5% 35% 31% 14% – normal investigations 27 11% 19% 7% 37% 19% 7% – minor disease only 39 5% 10% 10% 33% 31% 10% – peptic ulcer disease 30 3% 3% 0% 43% 20% 30% – reflux oesophagitis 17 0% 0% 6% 18% 70% 6%

*Conclusions* A wide range of agents were prescribed for dyspepsia, with considerable variation in drug choice for defined dyspepsia sub-groups. Management guidelines may help to reduce undue variation in practice, encourage more selective use of newer (more expensive) therapies, and thereby promote more cost-effective prescribing for dyspepsia in primary care.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Management strategy Clinical practice: Quality assurance } "Prescribing Patterns for Dyspepsia in Primary Care"

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"P P 58 1381" P 58 1381 **Evaluation of Duodenogastric Reflux and Antral Motility by Color Doppler Sonography in Patients Underwent Cholecystectomy**

\*J.R. Ladny, J. Laszkiewicz, J. Polak, Z. Puchalski

Departments of General Surgery and Radiology, Medical University of Bialystok, Poland *Purpose:* to evaluate duodenogastric reflux, along with antral motility and gastric emptying of a liquid meal in patients underwent open and laparoscopic cholecystectomy. *Material and methods:* 53 patients (15 male and 38 female), aged 35–56 years, previously underwent open or laparoscopic cholecystectomy, underwent color Doppler sonography (CDS). Duodenogastric reflux, antral motility, and gastric emptying of 400 ml liquid meal were evaluated. As a control group served 23 asymptomatic healthy volunteers. *Results:* this approach was feasible in 51 (96.2%) of the 53 subjects studied. Duodenogastric reflux was demonstrated in 16 (59.3%) of the 27 patients underwent open cholecystectomy and in 22 (84.6%) of the 26 patients after laparoscopic procedures and only in 3 (13%) of the healthy volunteers. The frequency of the duodenogastric reflux and the reflux index were significantly increased in patients after laparoscopic cholecystectomy as compared with open cholecystectomy and asymptomatic volunteers groups. Gastric emptying and the motility index of antral contractions were significantly decreased in these patients. *Conclusions:* color Doppler sonography is useful for evaluating of gastroduodenal, especially in patients underwent laparoscopic cholecystectomy. These simple, noninvasive method can be used to understand the pathogenesis of such disorders. Motility, general: Functional GI disorders Motility, specific: Stomach Radiology and ultrasound: Diagnosis } "Evaluation of Duodenogastric Reflux and Antral Motility by Color Doppler Sonography in Patients Underwent Cholecystectomy"

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"P P 58 1382" P 58 1382 **Prognosis of Dyspepsia among Patients in General Practice. Dyspepsia Subgroups and Patient Characteristics**

\*V. Meineche-Schmidt, T. Jørgensen

Dept. of General Practice, The Panum Institute and Surgical Dept. K, Bispebjerg Hospital, University of Copenhagen, Denmark *Aim:* To assess the courses of different subgroups in dyspepsia. *Methods:* In 1991 to 1993 all patients consulting 93 general practitioners (GPs) because of dyspepsia (N = 7270) had a structured interview, covering 18 dyspepsia symptoms. The patients were classified in dysmotility-like (*dys*), reflux-like (*refl*) ulcer-like (*ulc*) or uncharacteristic (*unch*) dyspepsia. Patients with two or more presentations to the GP were classified as relapsing (*relap*) dyspepsia. A random sample of 300 patients with *dys*, *refl* and *ulc* and all patients with *unch* (n = 114) and *relap* (n = 212) were contacted after an average of 37 months (range: 17–53) through the GP. Both GPs and patients were asked to fill in a questionnaire. Information on consultation habits, upper endoscopy, dyspepsia symptoms and medication within the latest year were recorded. All deaths were recorded. *Results:* Among eligible patients, 98% of the doctors and 85% of the patients returned the questionnaires. Frequencies of various end-points according to the dyspepsia subgroups are shown in the table. End-point: 

	Ulc %	Refl %	Dys %	Unch %	Relap %
Symptoms disappeared	8	10	19	28	1
Dyspepsia subgroup unchanged	46	32	35	27	-
Further consultations	66	57	59	53	48
Dyspepsia medication	65	53	33	23	63
Upper endoscopy	10	7	4	1	3

 Patients with *ulc* dyspepsia had the highest frequencies of consultation, endoscopies, medication and unchanged symptoms, whereas patients with *unch* dyspepsia had the lowest frequencies. *Relap* dyspepsia seldom disappeared. Among the 67 deaths 24% were due to gastrointestinal disorders. *Conclusions:* A classification of dyspepsia patients in general practice reveals differences in course, consultations, investigations performed, and medication given. The classification could be a useful tool in decision making. Clinical practice: Management strategy }" "Prognosis of Dyspepsia among Patients in General Practice. Dyspepsia Subgroups and Patient Characteristics"

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"P P 58 1383" P 58 1383 **Demographic, Socio-Economic and Stress Factors in Patients with Upper Gastrointestinal Symptoms (Dyspepsia) Who Seek Medical Help: Impact on the Therapeutic Response to Cisapride** A. Andrade<sup>1</sup>, C. Arrozo<sup>1</sup>, T. Bacalhau<sup>1</sup>, F. Cardoso<sup>1</sup>, I. Carra<sup>1</sup>, A.P. Granadeiro<sup>1</sup>,

\*J.J. Mendonça<sup>1</sup>, T. Moy<sup>1</sup>, E. Neves<sup>1</sup>, D. Pires<sup>1</sup>, A. Rio<sup>1</sup>, M.V. Gomes<sup>2</sup>

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<sup>2</sup> Pharmaceutical Physician, Medical Director Janssen-Cilag Farmacêutica, Portugal

Stress factors and personality traits seem to influence the appearance and symptomatology of non ulcer dyspepsia and other related conditions. In order to assess the prevalence of economic, socio-demographic and stress factors in dyspeptic patients, as well as to determine whether an influence exists on the initial symptom score and the response to treatment with cisapride, an open multicentric study was carried out in a Portuguese population of dyspeptic patients. 96 ambulatory patients with dyspeptic symptoms since at least four weeks were studied. Patients with history, symptoms or signs of organic underlying diseases were excluded. At selection upper gastrointestinal symptoms were assessed and patients were asked to complete a stress questionnaire giving details of socio-economic situation, health, living habits and stress factors according to the Holmes and Rahe scale. Patients were treated with cisapride 5 mg t.i.d. for 4 weeks and their symptoms were reassessed at the end of treatment. It was possible to establish a relationship between some stress factors and the severity of initial symptoms and their response to treatment. Independence at work, regularity of the meals, number of medical visits and non gastrointestinal symptoms were all correlated to the severity of the initial symptoms. The response to the treatment was good in the vast majority of patients ( $p < 0.0001$ ) and also influenced by the independence at work, the regularity of meals and their smoking habits. The other 17 stress factors evaluated were not significantly correlated with the patient symptomatology either before or after treatment. In conclusion in this patient population only 4 out of 20 stress factors were correlated with dyspeptic symptoms and its treatment. This lack of correlation for the majority of stress factors is perhaps due to the number of patients and the big variability in this population and their response.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Psychosomatics Clinical practice: Management strategy } "Demographic, Socio-Economic and Stress Factors in Patients with Upper Gastrointestinal Symptoms (Dyspepsia) Who Seek Medical Help: Impact on the Therapeutic Response to Cisapride"

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## "P P 58 1384" P 58 1384 Symptom Profile of Dyspepsia in Latin America: A Multicentric Study

\*L.M. Bustoz Fern\ 'e1ndez<sup>1</sup>, General Trial Coordinator, and Dyspepsia Study Group

<sup>1</sup> Instituto de Gastroenterología Dr Bustos Fern\ 'e1ndez, 1428 Buenos Aires, Argentina  
Dyspepsia is a broad symptom complex, overlapping with the irritable bowel syndrome (IBS). Studies often focus on epigastric pain. We studied the symptom profile in dyspeptic patients (pts) in Latin American populations and the response to cisapride (CIS). *Method: Phase 1:* 713 GPs, in coordination with local gastroenterologists, from Argentina, Bolivia, Paraguay, Uruguay and Venezuela enrolled 4020 pts with dyspepsia (4 weeks). Pts were evaluated for demographic and disease characteristics, as well as symptoms, and classified into dysmotility-like (DL), ulcer-like (UL), reflux-like (RL) or non-specific (NS) dyspepsia. *Phase 2:* Pts were treated with CIS 10 mg t.i.d. for 4–8 weeks; pts with alarm symptoms, UL symptoms or history of ulcer/GORD, or receiving medication for GI symptoms or regular NSAIDs were excluded. *Results.* 3744 cases (47.8 – 15.3 (18–92) yrs, 38.7/61.3 M/F) were eligible for analysis: 47.3% had DL dyspepsia, 12.1% UL, 13.1% RL and 3.2% NS. Mixed types of dyspepsia were: 3.6% DL + UL, 12.2% DL + RL, 2.2% UL + RL and 6.5% DL + UL + RL. Concomitant disease was present in 50% of pts, history of previous ulcer and oesophagitis in 7.2% and 16% resp. Excessive use of alcohol, coffee or smoking was found in 20%, 53% and 28% resp. The most common symptoms were: postprandial fullness (in 83%), epigastric bloating (83%), belching (72%), postprandial nausea (66%), diffuse epigastric pain (64%), early satiety (62%), fat intolerance (58%) and heartburn (53%). Localized epigastric pain was present in 49%, nocturnal pain in 19%, periodic discomfort or pain in 46% and relief by meals or antacids in 32%. 55% had concomitant symptoms of IBS (37% in RL, 74% in the mixed group DL + UL + RL). Of the 2965 pts treated with CIS, 67% and 21.6% had excellent and good responses resp.; 6.7% experienced adverse events (leading to discontinuation of treatment in 23 pts only). *Conclusions.* DL symptoms prevail among the Latin American dyspeptic population. Overlap with IBS is very common. Pts (after exclusion of significant UL or alarm symptoms) respond well to CIS. Clinical practice: Epidemiology (non cancer) Clinical practice: Management strategy Motility, general: Functional GI disorders } "Symptom Profile of Dyspepsia in Latin America: A Multicentric Study"

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"P P 58 1385" P 58 1385 **An International Survey Reveals Marked Differences between Countries in the Incidence, Diagnosis and Management of Upper Gastrointestinal (GI) Disease in Primary Care** J. Brun, S.A. Brunton, F. Carelli, H. Haslbauer, P. Heyse, H. Maurer, P. O'Connor, W. Peterz, K. R\fcy,

\*M.J. Whitaker

International Gastro Primary Care Group The International Gastro Primary Care Group (IGPCG) is a group of primary care physicians with representatives from different countries formed to improve the understanding and management of upper GI disease in primary care. This group conducted an international survey to examine differences between countries in the incidence and management of upper GI disease in primary care. A comprehensive questionnaire on upper GI disease was completed by 542 doctors from 11 countries. Key questions were asked concerning the number of patients with upper GI symptoms seen by doctors per week, the association of predominant symptoms with the diagnosis of upper GI disorders and the choices made regarding clinical investigations and drug therapy. The results revealed some interesting variations between countries in the incidence of upper GI disease. Of the doctors participating in the survey, 51% reported seeing 50 to 150 patients per week and 62% saw 11 to 25 patients with upper GI complaints. In Japan, 57% of responding doctors saw more than 300 patients per week and 62% detected 21 to 25 patients a week with upper GI symptoms. Although the high number of patients seen per week by doctors in Japan must increase detection rates of upper GI disease, the data does suggest a higher incidence of these disorders when compared to other countries in the survey. Sweden had the lowest incidence with 80% of GPs seeing 10 or less patients per week with upper GI symptoms. Clear differences were observed in the responses of doctors from different countries to H. pylori (Hp) eradication programs. In those patients testing positive for Hp, eradication was considered logical by over 50% of doctors in 4 countries and by under 50% of doctors in the remaining 7 countries. The percentage of doctors agreeing that patients with duodenal ulcer history need further investigation prior to Hp treatment, varied from 42% to 79%. In summary, this IGPCG international survey demonstrates the different approaches taken by the participating countries in the management of upper GI disorders and highlights the fact that any conclusions drawn from limited data (from one or a few countries) may not apply on a worldwide basis. Clinical practice: Management strategy } "An International Survey Reveals Marked Differences between Countries in the Incidence, Diagnosis and Management of Upper Gastrointestinal (GI) Disease in Primary Care"

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## "P P 58 1386" P 58 1386 The Clinical Presentation of Peptic Ulcer Disease

\*R.J.L.F. Loffeld, B.F.M. Werdmuller, A.B.M.M. van der Putten

Department of Internal Medicine, Ziekenhuis De Heel Zaandam, The Netherlands According to the literature the discriminative value of the classical ulcer symptoms is rather poor. A prospective study was done in order to assess the presentation of peptic ulcer. Consecutive patients undergoing upper GI endoscopy received a questionnaire consisting of 82 different questions, 23 questions were related to the upper abdomen. Eleven questions were scored on a linear scale, a symptom score was calculated (minimum score 2, maximum score 55). In addition the reason for doing the endoscopy, the duration of complaints, the medical history, smoking habits, alcohol use, and use of anti-ulcer drugs were noted. Patients with a gastric (GU) or duodenal (DU) ulcer were included. Patients with concomitant abnormalities like gastric carcinoma or reflux oesophagitis were excluded. As a control group patients, in whom endoscopy did not reveal abnormalities were included. This group, for the sake of the study designated as functional dyspepsia (FD), was subdivided pending on whether their history was positive (FD+) or negative (FD{-}) for peptic ulcer. GU was diagnosed in 43 patients (♂ 19, ♀ 24, mean age 67), DU in 60 (♂ 37, ♀ 27, mean age 50), FD+ in 94 (♂ 49, ♀ 45, mean age 52), and FD{-} in 382 (♂ 148, ♀ 134, mean age 47). Patients with GU were significantly older ( $p < 0.0001$ ) than the other groups; while FD{-} patients were the youngest. DU was more often diagnosed in men, while FD{-} was present more often in women. Patients with DU and FD+ were significantly more often treated with anti-ulcer drugs prior to endoscopy ( $p < 0.001$ ). The symptom score was 14 in GU, 16.6 in DU, 19.5 in FD+, and 16.7 on FD{-}. Patients with FD+ had significantly higher symptom score than the other groups. The mean number of complaints present was 8.1 in GU, 9.2 in DU, 9.8 in FD+, and 9.2 in FD{-}. No statistical differences were present. If all ulcer patients (amalgamation of DU, GU and FD+) were compared with FD{-} a prior history of complaints or peptic ulcer (sens 64%, spec 56%, ppv 44%, npv 74%); pain waning after a meal (sens 35%, spec 70%, ppv 51%, npv 70%); and smoking (sens 38%, spec 74%, ppv 44%, npv 69%) were the only features linked to peptic ulcer. On the other hand, post prandial pain (sens 31%, spec 58%, ppv 28%, npv 61%); food intolerance (sens 43%, spec 47%, ppv 31%, npv 60%); nausea (sens 49%, spec 38%, ppv 30%, npv 58%); and alcohol use (sens 39%, spec 51%, ppv 30%, npv 61%) have a negative prediction and plead more for the presence of FD. It can be concluded that the symptoms score in peptic ulcer disease is rather low, this cannot be explained by prior use of anti-ulcer agents. It is not possible to distinguish peptic ulcer patients from FD{-} patients on basis of clinical presentation. Further investigations are inevitable. Whether serological testing for *Helicobacter pylori* in combination with a simple and reliable questionnaire can increase the prediction of outcome of endoscopy is yet to be studied.

Oesophageal gastric duodenal disorders: GD disorders, acid peptic Clinical practice: Epidemiology (non cancer) } "The Clinical Presentation of Peptic Ulcer Disease"

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"P P 58 1387" P 58 1387 **Measurement of Quality of Life (QoL) with QPD32, a New Specific Questionnaire for Italian Peptic Patients (Pts)** A. Olivieri,

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<sup>1</sup> Glaxo Wellcome S.p.A. Research and Development, Verona, Italy

<sup>2</sup> Italy

University of Plymouth, UK Measurement of QoL is become important since therapies are not only aimed at an increase of quantity of life, but also at an improvement in its quality. Despite the number of Italian peptic pts and their social and economical importance, no specific QoL questionnaire was available up to 1994, when we developed a specific tool. It was validated in a multicentre trial on a 1774 pts sample. Validation reduced the 48 original items to 30, which increased to 32 after the inclusion of an item on the severity of pain and the Personality Inventory Scale, that allows us to detect differences in individual QoL due to psychological characteristics. The validated questionnaire was called QPD32. During 1995, QPD32 was administered to 2155 pts suffering from gastric or duodenal ulcer or reflux oesophagitis by 222 gastroenterologists and endoscopists of Italian scientific societies. Pts suffering from other acute and severe diseases or experiencing recent psychosocial trauma (loss of job, death of spouse etc) were excluded. Most of pts were male (62.6%), with a mean age of 49.2 y., suffering from duodenal ulcer (53.8%), oesophagitis (18.4%) gastric ulcer (10.6%), other upper gastrointestinal complaints (16.0%). The latter group was submitted to analysis because of its size, in spite of the protocol's violation. The mean total score of QPD32 was similar in pts who filled in the questionnaire before (61.25, sd 11.9), just after (60.0, sd 11.4) or few days after endoscopy (60.5, sd 11.2). Mean score in different diseases was like (range 59.8–60.2), and the score of each domains of QPD32 (pain, symptoms and physical) did not differ significantly among diagnoses. In conclusion, pts with different upper gastrointestinal diseases have the same perception of their illness; moreover, thanks to its specificity, our questionnaire could be administered indifferently before or after an upper digestive tract endoscopy. } "Measurement of Quality of Life (QoL) with QPD32, a New Specific Questionnaire for Italian Peptic Patients (Pts)"

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"P P 58 1388" P 58 1388 **Role of Peptides in Hydrochloric Acid Secretion Regulation of Patients Sick of Duodenal Ulcer before and after Surgical Treatment**

\*L.I. Vinnitsky, M.V. Poroykova

Research Center of Surgery of the A.M.S. of Russia, Moscow, Russia  
The acid creation regulation mechanisms in duodenal ulcer were studied. We determined contents of gastrin (G), somatostatin (S) and glucagon (Glu) of patients with hydrochloric acid hyposecretion and hypersecretion in case of duodenal ulcer (20 persons – 1a group and 25 persons – 1b group accordingly), in case of duodenal ulcer complicated by reflux esophagitis (6 persons – 2a group and 11 persons – 2b group accordingly) and in case of duodenal ulcer complicated by pylorostenosis (9 persons – 3a group and 7 persons – 3b group accordingly) before and after different surgical operation (in 3 weeks). 20 practically healthy persons were examined. Contents of G in all groups of patients (exclude 3b) exceeded the normal meanings. In hyposecretion groups G concentration before the operation was higher than in hypersecretion groups. After the operation G concentration in hyposecretion groups was the same, but in hypersecretion groups G concentration increased. Contents of S in all groups exceeded normal meanings. In groups 1 and 3 contents of S before the operation in case of hyposecretion was higher than in hypersecretion, and in group 2 vice versa. After the operation the contents of S in groups 1 and 2 was the same, in group 3a and 3b the contents of S in increased. Blood Glu level in all groups before the operation was less than normal meanings. In groups 2 and 3 in hyposecretion Glu concentration was less than in hypersecretion. After the operation content of glucagon in groups 1a, 1b, 2b and 3b was the same, in groups 2a and 3a content of Glu increased. In group 3a content of Glu increased up to normal meanings. Complex examination exposed compensating lowering G levels and prevailing of S and Glu contents in all groups of patients sick of duodenal ulcer with hypersecretion. The results of examination allow to assume that patients with duodenal ulcer have different status to receptor apparatus for G, S and Glu. Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Hormones and receptors: Clinical disorders } "Role of Peptides in Hydrochloric Acid Secretion Regulation of Patients Sick of Duodenal Ulcer before and after Surgical Treatment"

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"P P 58 1389" P 58 1389 **Peptic Ulcer in Rural Residents with Abdominal Complaints**

\*T. Litvinenko, P. Varmann, V. Bushina, N. Elshtein, E. Lond

Department of Gastroenterology, Institute of Experimental & Clinical Medicine, Tallinn, Estonia  
The aim of the present study was to evaluate the prevalence of peptic ulcer in rural residents with abdominal complaints. We interviewed 2304 subjects above 15 years of age, which was 74.6% of the population of a rural district of Estonia. The interview was based on a questionnaire compiled to screen out persons with abdominal complaints. All 854 subjects with abdominal complaints were offered upper endoscopy, 575 (67.3%, 374 female, 194 male) agreed to be investigated. Peptic ulcer disease was defined as an active peptic ulcer, a scar or a deformed duodenal bulb. Peptic ulcer was diagnosed in 71 cases (50 male, 21 female), the overall prevalence being 12.3%. The prevalence increased with age, reaching the peak in the 4th life decade in males and in the 5th life decade in females. Duodenal ulcer occurred 2.2 times more frequently than gastric ulcer. In 23 cases (32.4%) the diagnosis of the peptic ulcer was made for the first time. The prevalence of peptic ulcer in rural residents with abdominal complaints was 12.3%, the proportion of newly diagnosed cases being extremely high. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Peptic Ulcer in Rural Residents with Abdominal Complaints"

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"P P 58 1390" P 58 1390 **Monthly Variations of Symptomatic Duodenal Ulcer Activity in Taiwan: a Comparison Between Subjects with and without Hemorrhage** Chung-Jyi Tsai

Chi Mei Foundation Hospital, Yung Kang City, Tainan, Taiwan

The occurrence of peptic ulcer has geographic, temporal, socioeconomic and ethnic variations. Controversy exists regarding duodenal ulcer (DU) seasonality. We have observed that patients with DU may be divided into those whose ulcers repeatedly bleed as distinct from those whose ulcers repeatedly cause pain. It is still not known which or when DU patients would bleed. The purposes of the present study are, therefore, 1) to investigate the seasonal incidence of DU activity in a developed subtropical country, 2) to compare the seasonality of DU patients with pain and that of those with hemorrhage, and 3) to clarify the roles of sex and age factors play.

*Methods:* All of the reports of endoscopic examination of the upper gastrointestinal tract performed from April 1, 1989 to March 31, 1995, were reviewed to identify patients with DU disease. Active bleeding due to DU was confirmed when a definite bleeding site or visible vessel or a blood clot within an open crater in the mucosa of the duodenum was identified. Excluded were all patients who had any extrinsic factors that might influence the exacerbation of DU disease. In the same study period, hepatoma and colorectal adenocarcinoma were used as the control diagnoses. The 12 months of the year were divided according to the climate in Taiwan into four seasonal periods, viz. Dec.–Feb., Mar.–May, Jun.–Aug., Sep.–Nov. Statistical analysis with  $\chi^2$  test, linear regression with Pearson correlation, and ANOVA with post hoc comparisons were used as appropriate.

*Results:* During the years of the study, 10331 DUs were diagnosed. Among these, 2088 patients presented with hemorrhage, and 8243 patients with pain. The monthly distribution of total DU patients revealed a trend toward more occurrence from Nov. to Mar. ( $p < 0.001$ ). In the patients with DU hemorrhage, the peak incidence was in the months from Nov. to Mar. ( $p < 0.001$ ). There was significant seasonal variation ( $p = 0.03$ ), the peak was in the winter (Dec. through Feb.). In the DU patients with pain, the peak months were from Dec. to Feb. ( $p < 0.001$ ). Significant seasonal variation, peaked in winter, was also observed ( $p = 0.04$ ). In both groups, the monthly and seasonal variations were unaffected by age or sex. There were no significant monthly variations of control diagnosis for hepatoma ( $p = 0.94$ ) or colorectal adenocarcinoma ( $p = 0.79$ ).

*Conclusions:* Both groups of DU patients presenting with hemorrhage and those with pain demonstrated similar monthly and seasonal fluctuations, the incidence being significantly greater during the cold season. These data suggest that climatic changes may influence pain and hemorrhage in the DU patients, which brings important etiological and therapeutic implications.

*Clinical practice:* Epidemiology (non cancer) Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: Instrumentation, diagnosis }

"Monthly Variations of Symptomatic Duodenal Ulcer Activity in Taiwan: a Comparison Between Subjects with and without Hemorrhage"

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## "P P 58 1391" P 58 1391 Helicobacter Pylori Infection and Chronic Antral Gastritis in Patients with Non-Ulcer Dyspepsia

\*S. Grgov, M. Stefanovic, J. Dimitrijevic, P. Stamenkovic

Internal department, Health centre, Leskovac, Yugoslavia We made a prospective study on 66 patients, averaged 46.6, with the symptoms of non-ulcer dyspepsia and histological findings of chronic superficial (21 or 31.8%) and atrophic (45 or 68.2%) antral gastritis. Helicobacter pylori (Hp) has been proved in bioptic sample of antral mucosa by urease test and histological check-up of preparations coloured with hematoxylin-eosin. Endoscopically, diffuse erythema was found in 31.2% of Hp positive patients and polychority of antrum with bizzarre reddish-pale zones in 38.9%, but without statistically significant difference with regard to Hp negative patients ( $p > 0.05$ ). Chronic mucous erosions were present in 87.5% Hp positive and 12.5% Hp negative patients, which is statistically significant difference ( $p < 0.05$ ). Hp infection existed in 47.6% chronic superficial gastritis and 46.7% chronic atrophic antrum gastritis. In the group of active superficial gastritis there were 90.9% with Hp infection. The group with active atrophic gastritis comprised 87% of Hp positive and 13% Hp negative patients which is statistically significant difference ( $p < 0.01$ ). At low degree of chronic gastritis atrophy Hp was positive in 46.7% of patients, at medium degree in 38.5% and in high degree of atrophic gastritis in 52.9%, but differences are not statistically significant with regard to Hp negative ( $p > 0.05$ ). Intestinal metaplasia was found in 18 (40%) patients with atrophic gastritis, but without statistically significant difference between Hp positive and Hp negative patients ( $p > 0.05$ ). Our research shows that endoscopically seen chronic mucous erosions of antrum in the majority of cases indicate Hp infection, which is an important factor of chronic antral gastritis activity. Although the presence of Hp infection doesn't correlate with the degree of gravity of chronic atrophic antral gastritis, it is one of the possible factors of the development of intestinal metaplasia and dysplasia as precancerous lesions. Oesophageal gastric duodenal disorders: Helicobacter Pylori Endoscopy, general: Instrumentation, diagnosis Endoscopy, specific: Stomach, duodenum } "Helicobacter Pylori Infection and Chronic Antral Gastritis in Patients with Non-Ulcer Dyspepsia"

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"P P 58 1392" P 58 1392 **Colonization of Human Achloridric Stomach by Bifidobacteria**

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<sup>2</sup> Istituto di Microbiologia Agraria e Tecnica, Bologna University, Italy Aim of the study was to ascertain whether and which populations of bifidobacteria are able to colonize the stomach of subjects with achloridria induced either by autoimmune atrophic gastritis (CAG), or by omeprazole (Ome) treatment (20 mg/day for 1 month) for reflux oesophagitis. The isolation of bifidobacteria was carried out on samples of gastric juice and homogenates of biopsies (4 for the antrum and 4 for the corpus) of 14 subjects (6 CAG: mean age 39 yrs; 8 Ome: mean age 48 yrs) by using BHA and TPY added with propionic acid. The mean pH value of the juice 7.3 in CAG subjects and 6.8 in Ome-treated ones. In order to assign the isolates to the genus *Bifidobacterium*, we took into consideration morphology, Gram staining, fermentation products and the presence of the fructose-6-phosphate phosphoketolase enzyme. Fifty-five strains of bifidobacteria isolated from 10 subjects over 14 examined have been grouped by cell protein electrophoresis. They were characterized through the following determinations: G-C% of DNA, fermentations of 49 complex carbohydrates, DNA-DNA hybridization. Fifty-two strains can be subdivided in different groups which differ to the typical species of the oral cavity: *B. denticolens*, *B. inpinatum* (two new species recently isolated from human dental caries) and *B. dentium*. The remaining 3 strains (all from the same subject), which were recognized as a single group, do not hybridize with any species of the genus *Bifidobacterium* or with *Gardnerella vaginalis*. We were unable to isolate similar strains from the oral cavity of this subject. Our results suggest that the three strains belong to a new species (description in preparation). The achloridric stomach represents a suitable habitat for the colonization of bifidobacteria mainly belonging to the oral cavity rather than to the intestinal tracts. The probiotic potential of the isolates, demonstrable through clinical and nutritional studies, makes promising and desirable further experimentation in this area. Oesophageal gastric duodenal disorders: EG Reflux Oesophageal gastric duodenal disorders: Oesophageal disorders, non reflux Immunology and microbiology: GI infections in adults } "Colonization of Human Achloridric Stomach by Bifidobacteria"

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"P P 58 1393" P 58 1393 **Long Term Follow-Up of Fedotozine Treatment in a Cohort of Dyspeptics in Current Medical Practice**. J. Salducci, J.-C. Grimaud, J.-L. Abitbol<sup>1</sup>, C. de Meynard<sup>1</sup>,

\*B. Fraitag<sup>1</sup>

Hospital Nord, 13015 Marseille, France

<sup>1</sup> Institut de Recherche Jouveinal, 94265 Fresnes, France The efficacy of fedotozine (F) administered for 6 weeks had already been demonstrated in functional gastrointestinal disorders, both in functional dyspepsia [1] (FD) and irritable bowel syndrome [2] (IBS). However, the chronic course of these diseases can justify long-term treatment. *Methods.* During an open, prospective, uncontrolled, multicenter study in France, we evaluated the safety of prolonged administration of F (30 mg tid for one year) in dyspeptic outpatients seeking medical advice (diagnostic criteria of FD left to the investigator, concomitant treatments allowed). The course of symptoms and their impact on the quality of life (QoL) were secondary criteria. Safety was evaluated every 3 months by monitoring adverse events (AE), standard blood tests, ECG and EEG (2 subgroups). The overall therapeutic result was evaluated every 3 months and QoL every 6 months (SQLP questionnaire [3]). Statistical analysis was purely descriptive. *Results.* 165 centers (28% gastroenterologists, 72% general practitioners) treated 624 patients with FD, most often associated with IBS (64%) or gastro-oesophageal reflux (19%). The study was completed by 66% of patients. The mean duration of exposure to treatment was 296 days (range 1 to 483), corresponding to 506 patient years. AE were recorded in 246 patients and were potentially treatment-related in 178. The most frequent were constipation, abdominal pain, headache, and nausea (5.5 to 2.1%). There were 30 serious AE, of which 6 were potentially treatment-related and which mainly concerned the GI tract. Laboratory tests showed the absence of any abnormal trend or specific abnormality. ECG and EEG further demonstrated the safety of F. Improvement or resolution of symptoms according to the patient and the investigator was reported in 84 and 87% of cases respectively. Efficacy was maintained over time. Patients noted an improvement in QoL for health-related items (digestion, pain, state of health, general form, diet). *Conclusion.* This study carried out in a large number of patients (equivalent to 506 patients followed-up for 1 year) demonstrated the very good clinical, ECG/EEG, biochemical and haematological safety of F (30 mg tid) administered for a long period. Good efficacy results, stable over time, and improvement in QoL were further obtained. This research was funded by Institut de Recherche Jouveinal, Fresnes, France.

Reference: Effects of fedotozine in FD. Fraitag B et al. Dig. Dis. Sci., 39 1072–1077, 1994

Effects of fedotozine in IBS. Dapoigny M et al. Dig. Dis. Sci. In press

QoL assessment in therapeutic trials. G\ 'e9rin P et al. Fundam. Clin. Pharmacol., 6, 263–276, 1992 Motility, general: Functional GI disorders } "Long Term Follow-Up of Fedotozine Treatment in a Cohort of Dyspeptics in Current Medical Practice"

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## "P P 58 1394" P 58 1394 Efficacy of Fedotozine in Functional Dyspepsia: A Meta-Analysis of Individual Data from Randomized, Placebo-Controlled Studies

\*J.-L. Abitbol, B. Scherrer, C. de Meynard, G. M'eric, B. Fraitag

Institut de Recherche Jouveinal, 94265 Fresnes, France A meta-analysis of the therapeutic efficacy of fedotozine (FZ) in functional dyspepsia was carried out on all the individual data from the phase IIb and III randomized, double-blind studies comparing a placebo group (PL) with a group receiving FZ 30 mg t.i.d. *Methods.* Since the study designs were identical (a one to two week run-in period followed by six weeks treatment in parallel groups), meta-analysis of 3 multicentre studies carried out in France and the UK was justified. Inclusion and evaluation criteria were similar for the 3 studies. Therapeutic efficacy was evaluated on the mean overall score of the intensity of the 5 dyspeptic symptoms assessed daily by the patient. The mean treatment effect (T) for the 6 weeks, the study effect (S), and the TxS interaction were tested by intent to treat ANCOVA with adjustment for the means at run-in. The difference between FZ and PL at each of the 6 treatment weeks was assessed by ANOVA. *Results.* 658 patients (FZ: 331, PL: 327; M: 39%, F: 61%) with a mean age ( $\pm$  SD) of 44 – 15 years were randomized in these 3 studies. The percentage of withdrawals was higher in the PL group (PL: 22.6%, FZ: 15.7%,  $p < 0.05$ ). The effect of FZ on the overall dyspepsia intensity score was greater than that of PL ( $p = 0.002$ ) with no significant difference in the magnitude of treatment effect between the studies (interaction TxS not significant), which justifies generalization of results. The PL overall score improved from 12% (week 1) to 29% (week 6) compared to run-in. The FZ overall score improved from 18% (week 1,  $p = 0.036$  vs PL) to 36% (week 6,  $p = 0.001$  vs PL). Moreover, the effect of FZ was significantly greater than that of PL for 4 dyspeptic symptoms out of 5: bloating/epigastric distension ( $p < 0.01$ ), epigastric pain ( $p < 0.01$ ), slow digestion ( $p < 0.057$ ), and nausea/vomiting ( $p < 0.05$ ), early satiety was NS. When meta-analysis was carried out on the 2 phase III studies alone, FZ was again more effective than PL and to a similar extent. There was no evidence of any effect due to patient characteristics (age, body mass index, sex) or to pre-inclusion gastroenterological or psychotropic treatments on the therapeutic effect of FZ. *Conclusion.* This meta-analysis allowed a comprehensive assessment of all available efficacy data from phase IIb and III studies. Fedotozine proved significantly more effective than placebo on both the overall dyspepsia intensity score and on 4 of the 5 dyspeptic symptoms. Motility, general: Functional GI disorders Clinical practice: Management strategy } "Efficacy of Fedotozine in Functional Dyspepsia: A Meta-Analysis of Individual Data from Randomized, Placebo-Controlled Studies"

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"P P 58 1395" P 58 1395 **Evaluation of the Quality of Life in Functional Gastrointestinal Disorders. Results of a 6-Month Study of Fedotozine Versus Usual Treatments.** J.L. M'erot,

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The objective of this general practice study was to evaluate the effects of functional gastrointestinal disorders on the quality of life (QoL) as well as changes in QoL during treatment. *Methods.* An open, prospective, randomized, six-month pharmacoeconomic study with 252 patients (irritable bowel syndrome: 74%; dyspepsia: 26%) compared fedotozine 30 mg per os tid. (n = 141, group F) with treatments usually prescribed by the investigator (n = 111, group T). The Functional Status Questionnaire was used to evaluate the 3 main dimensions of QoL: (i) physical, (ii) psychological, and (iii) social, as well as several sub-dimensions including overall satisfaction with general well being. The questionnaire was filled in by the patients at D0, D45, and D180. QoL scores vary in a range of 0 (worst QoL) to 100 (best QoL). *Results.* The reliability of the questionnaire was satisfactory with Cronbach { a } coefficients ranging from 0.69 to 0.88. At D0, scores were comparable between the two groups. The psychological dimension was the most altered (52.7 in the two groups), followed by the social dimension (74.6 F and 73.6 T), and the physical dimension (89.8 F; 90.0 T). Overall assessment of general well being was very perturbed at D0 (41.9 F and 49.4 T). Intragroup analysis showed a significant improvement at D45 and D180 for the two groups for the physical ( $p \{ \backslash \} a3 \} 0.05$ ) and psychological ( $p \{ \backslash \} a3 \} 0.05$ ) dimensions. The sub-dimensions social relations and general well being improved significantly at D45 and D180 only for group F ( $p \{ \backslash \} a3 \} 0.05$  and  $p \{ \backslash \} a3 \} 0.001$ ). Intergroup analysis showed that the improvement in the overall general well being score was significantly greater for group F at D45 (10.3 F versus 3.3 T;  $p = 0.02$ ) as well as at D180 (24 F versus 5.8 T;  $p = 0.03$ ). These results correspond to improvements compared to inclusion scores for F and T of 11% and 6% at D45, and 46% and 20% at D180, respectively. *Conclusion.* Functional gastrointestinal disorders affected the psychological and social dimensions of the QoL as well as the overall satisfaction of patients with their general well being. From D45 to D180 both fedotozine and the usual treatments had a beneficial effect on QoL. Only the fedotozine group showed significant improvement in general well being of the patient and from D45 to D180 the improvement was significantly greater in group F than in group T. Motility, general: Functional GI disorders Clinical practice: Management strategy }

"Evaluation of the Quality of Life in Functional Gastrointestinal Disorders. Results of a 6-Month Study of Fedotozine Versus Usual Treatments"

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"P P 58 1397" P 58 1397 **Bilitec 2000 Study in Evaluation of Duodenogastric Biliary Reflux Following Conventional and Laparoscopic Cholecystectomy** R.M. Herman, T. Popiela,

\*W. Kawiorski, P. Walega

1st Dept. of General and GI Surgery, Collegium Medicum Jagiellonian University, Cracow, Poland Several clinical studies showed that episodes of the duodenogastric biliary reflux (DGR) increased following cholecystectomy. The *aim* of present study was to evaluate the incidence of gastric biliary reflux following conventional (CCh) and laparoscopic cholecystectomy (LCh). Twenty patients with cholelithiasis were ambulatory studied before and 3 months following cholecystectomy – 10 patients after CCh (Group I) and 10 after LCh (group II). Gastroduodenoscopy and 24-hour gastric spectrophotometry monitoring technique using Synectics BILITEC 2000 were performed in each patients. The results were computer analyzed using Gastrosoft, Synectics Medical program. *Results:* There were no symptoms of DGR during gastrofiberoscopy, not the increasing incidence of reflux (above 0.14%) episodes and its duration before surgery and all bilirubin concentration results ranged within the normal values. In the 1st group (following CCh) the presence of biliary reflux was noted during gastroscopy in 50% of patients versus 36% of patients following LCh. Significant increase of incidence of bilirubin reflux episodes was observed in 8 patients (80%) of 1st group and only 5 patients (50%) of 2nd group, during 24-hour Bilitec studies. *Conclusion:* The incidence of DGR and total exposure of gastric mucosa to biliary contents increased both following classical and laparoscopic cholecystectomy, but significantly higher after CCh. Motility, specific: Stomach } "Bilitec 2000 Study in Evaluation of Duodenogastric Biliary Reflux Following Conventional and Laparoscopic Cholecystectomy"

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"P P 58 1398" P 58 1398 **Reflux Gastritis in Children with Giardiasis**

\*P. Grigorescu-Sido, M. Grigorescu, I. Trif

1st Pediatric Clinic, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj, Romania

*The purpose of the study.* Considering that giardiasis, a frequent parasitic disease in children can generate pyloric incompetence with jejuno-duodeno-gastric reflux (JDGR) and that epigastralgia is a common symptom in school age children infested with lamblia, the authors have studied the role of JDGR as a possible factor generating gastritis in these children. *Patients and methods.* Two groups of patients were studied: group I (20 children) aged 7–17 years with giardiasis) and group II – controls (10 healthy children). The methods used included: a) tests for the support of the diagnosis of gastritis (barium meal and/or gastroscopy with gastric mucosa biopsy) in group I and b) detection of JDGR by the determination in the gastric aspirate of: total bile acids (spectrophotometry); sodium (flame photometry) and pH in both groups. *Results:* a) statistically significant increased levels of the bile acids in the gastric aspirate in children with parasitosis as compared with the controls:  $\bar{x}_I = 1.84 - 0.71 \text{ } \mu\text{mol/l}$ ;  $\bar{x}_{II} = 0.42 - 0.4 \text{ } \mu\text{mol/l}$ ;  $P < 0.001$ ; b) a 90% incidence of the cases with high levels of bile acids in children with giardiasis; c) the presence in these children of endoscopic and histopathologic changes of the gastric mucosa, interpreted as reflux gastritis and d) the absence of statistical significance between the values of sodium and pH in the gastric aspirate in the two groups. Association of drugs regulating digestive motility with the etiologic treatment clearly improved the course of these cases. *Conclusion.* The study indicates the presence of reflux gastritis in 90% of the investigated children with giardiasis and recommends the determination of the bile acids in the gastric aspirate as a sensitive test for the detection of JDGR. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Reflux Gastritis in Children with Giardiasis"

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"P P 58 1399" P 58 1399 **The Houston Classification (HC) of Gastritis Applied in the "Real World"**

\*C. Ricci, N. Salfi, M. Menegatti, P. Bacchini, B. Massardi, F. Landi, A. Al'ec, F. Mucci, S. Farinelli, G. Martinelli, M. Miglioli, D. Vaira

Ist Medical Clinic & Histopathology Department, University of Bologna, Bologna, Italy *Purpose:* To assess the usability of the HC in the day by day practice. *Methods:* During a 3 months period, 113 patients with upper gastrointestinal symptoms (M/F 55/58; range 19–87; mean 49.7 yrs), underwent endoscopy. According to HC, 5 biopsies were obtained: antrum (A) = 2; corpus (C) = 2; angulus (AN) = 1. In addition 2 antral biopsies were taken for *Helicobacter pylori* (HP) culture and urease testing. The specimens were histologically assessed and scored according to the HC guidelines. Serum IgG to HP were assessed by a previously validated ELISA (sensitivity and specificity of 94%). 3/4 techniques testing positive gave H pylori status (gold standard). *Results:* A total of 68/113 (60%) patients were HP+ve (histology/urease test/culture/serology). The endoscopic findings were: macroscopically normal (n = 26; HP+ 50%), antral gastritis (n = 59, HP + 54%), erosive duodenitis (n = 12, HP + 67%), gastric ulcer (n = 5, HP + 80%) and duodenal ulcer (n = 11, HP + 100%). Sensitivity and specificity of samples taken compared to the gold standard were (%): A C AN A + AN A + C AN + C Sensitivity 91 89 89 98 97 97 Specificity 87 84 84 98 95 95 The biopsies from the angulus revealed 15 cases of atrophy (moderate 1 and mild 14) that would otherwise not have been detected. *Conclusions:* 1. The combination of antral and angulus biopsies showed the highest rate of HP detection, 2. The additional biopsy specimen from the angulus added little to the diagnosis. However, in geographic areas with high prevalence of gastric carcinoma it may help detect early pre-neoplastic lesion. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* } "The Houston Classification (HC) of Gastritis Applied in the "Real World"

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"P P 58 1400" P 58 1400 **Nuclear Volume of Type I Gastric Intestinal Metaplasia** D. Mihailovic, B. Mladenovic, M. Ilic, V. Mihailovic

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The three-dimensional nuclear size may be viewed as a dynamic reflection of the metabolic state of the nucleus and as a physical correlate of its total content of biochemical constituents. Among these were histone and nonhistone proteins, inorganic materials, water, RNA and DNA. Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type. It has been postulated that intestinal metaplasia of gastric mucosa, characterized by incomplete differentiation and by sulphomucin secretion (type III intestinal metaplasia), is closely related to intestinal type gastric carcinoma, whereas other non-sulphomucin-secreting types (types I and II) are predominant in situations where the risk of cancer is relatively low (gastric cancer and chronic gastritis). The aim of this study was to estimate the mean volume-weighted nuclear volume of epithelial cells in type I intestinal metaplasia in various pathological states of gastric mucosa. *Material and Methods.* Endoscopic mucosal biopsies from gastric cancer (n = 25), gastric ulcer (n = 32), and chronic gastritis (n = 40) patients were analyzed. After standard fixation, embedding, sectioning, routine HE and AB-PAS (pH 1.0 and 2.5) staining, the mean point sampled nuclear intercept was estimated by the original test system and objective x100, at total magnification of x1200. To obtain the mean nuclear volume, the cubed nuclear intercept was multiplied by  $\{ p \} / 3$ . In each case a hundred epithelial cell nuclei were analyzed. For the statistical analysis Student's two tail t-test was used. *Results.* In type I intestinal metaplasia found in gastric carcinoma patients there is significantly greater nuclear volume ( $118.34 - 10.32 \mu\text{m}^3$ ) than in type I intestinal metaplasia in other pathological states of gastric mucosa ( $77.72 - 8.58 \mu\text{m}^3$ ). *Discussion.* The sampling of intercepts by points is a mathematical necessity to ensure an unbiased estimation. Our results suggest that nuclear volume may be used in early detection of precancerous states of gastric mucosa. } "Nuclear Volume of Type I Gastric Intestinal Metaplasia"

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## "P P 58 1401" P 58 1401A Flow Cytometric Study of Gastric Nuclear DNA Ploidy in Gastritis

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**Purpose:** This study aimed to assess the gastric nuclear DNA ploidy pattern and correlate it with the clinicopathologic findings in gastritis.

**Patients & Methods:** Forty patients (32 males and 8 females; mean age 42 – 5.8 yr) with endoscopic evidence of gastritis were enrolled in the study in addition to 20 patients not showing endoscopic evidence of gastritis as control group. Endoscopic assessment was done to every patient and at least two biopsies were taken from the site of lesion, close to each other, one for histopathological examination and Giemsa staining for *Helicobacter pylori* and the other biopsy for determination of DNA content (ploidy) and S phase fractions by Flowcytometry.

**Results:** Whereas only diploid DNA histograms were found in control subjects, patients with gastritis showed diploid histograms in 34 (85%) cases while 6 (15%) specimen exhibited DNA aneuploidy. S phase fractions were higher in gastritis than control cases and showed significant direct correlation with age and duration of complains but not with activity of gastritis. All the six lesions showing DNA aneuploidy were antral lesions and were positive for *Helicobacter pylori*. Their histopathological examination revealed atrophic gastritis in the 6 cases with intestinal metaplasia in 4 (66.7%) of these cases and low grade dysplasia in 2 (33.3%).

**Conclusion:** (1) This study suggests that determination of gastric nuclear DNA content (ploidy) may help to identify individuals with increased cancer risk as aneuploid histograms were found in non dysplastic mucosa. (2) Thus combination of endoscopy, histology and flowcytometry can be integrated surveillance procedures for follow up of patients with gastritis for early detection of malignant transformation.

Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Endoscopy, specific: Stomach, duodenum } "A Flow Cytometric Study of Gastric Nuclear DNA Ploidy in Gastritis"

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## "P P 58 1402" P 58 1402 Neural Networks in the Investigation of Gastric Lesions

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<sup>4</sup> Department of Pathology, Medical School, Athens University, Athens, Greece *Objective:* To compare the accuracy of two different artificial neural networks (ANN), for the discrimination of benign and malignant gastric lesions using morphometric and textural data of the nucleus. *Study Design:* This study was carried out on 39 cancer cases, 34 cases of gastritis and 83 cases of ulcer. In each case 100 cells were measured from gastric smears stained by the Papanicolaou technique using a custom image analysis system. As a training set 30% of the cells were used and the remaining cells were used as a test set using two different neural net architectures: Back propagation (BP) and learning vector quantizer (LVQ). *Results:* The application of BP and LVQ established correct classification of more than 97% of the benign cells and more than 95% of the malignant cells, obtaining an overall accuracy of 97% at cellular level and 99.1% at patient level in both neural networks. *Conclusion:* This study indicates that the use of ANNs and image morphometry may offer useful information on the potential of malignancy of gastric cells and may improve the accuracy of cytological diagnosis. Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Neural Networks in the Investigation of Gastric Lesions"

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"P P 58 1404" P 58 1404 **Do Dyspeptic Patients under the Age of 45 Need to be Investigated?**

\*H. Kolk, H.-I. Maaros

Department of Family Medicine, University of Tartu, Tartu, Estonia Age under 45 years and negative non-invasive tests for detection of *Helicobacter pylori* (Hp) infection are the most often recommended criteria to avoid unnecessary endoscopy in dyspeptic patients without obvious clinical signs of organic diseases. *Aim:* To evaluate the diagnostic field of open access upper gastrointestinal endoscopy in relation to the age and Hp status of the patient. *Methods:* 135 consecutive dyspeptic patients aged 18 years and over referred for upper endoscopy by their GPs were included. Patients' Hp status was evaluated by histology (2 antral, 2 corpus, 2 duodenal biopsies). Gastritis was scored according to the Sydney classification. *Results:* Diagnostic category No (%) Sex Age Hp posit/ M/F < 45/ 45 yrs Hp negat Duodenal ulcer 44 (33%) 30/14 34/10 41/3 Gastric ulcer 10 (7%) 4/6 1/9 9/1 Gastric carcinoma 1 (1%) 0/1 1/0 1/0 Gastric erosions 21 (16%) 12/9 14/7 17/4 Chronic gastritis 63 (47%) 42/21 39/24 61/2 Other diseases 7 (5%) 3/4 4/3 6/1 Normal findings 12 (9%) 7/5 12/0 0/12 Total 135 63/72 88/47 112/23 There is an overlap between duodenal ulcer and gastric erosions in 4 cases and between chronic gastritis and gastric erosions in 20 cases. The only case of gastric cancer was 36 years old female. Only 9% of all patients have normal endoscopic and histological findings. *Conclusions:* Among populations with high prevalence of Hp infection more than half of dyspeptic patients have clinically relevant disease at the age under 45 years. Presence of Hp infection is important predictor for organic disease. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, specific: Stomach, duodenum } "Do Dyspeptic Patients under the Age of 45 Need to be Investigated?"

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## "P P 58 1406" P 58 1406 Gastric Duplications: Diagnosis and Management

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*Purpose:* Intestinal duplications are a rare congenital disease. They appear in the whole gastrointestinal tract, especially in the ileum. In the literature 112 cases of gastric duplications are described, 80 of them in children. Here we describe two cases of gastric duplication cysts in adults. Diagnostic findings and surgical therapy are discussed.

*Patients:* a.) A 23 year old patient had pain in the right upper abdomen, nausea, vomiting and attacks of fever. No pathological findings were described in endoscopy. CT-scan showed a fluid filled structure with obstruction of the duodenum. A duodenal duplication or choledochus cyst was discussed.

b.) A 59 year old patient with pain in the left upper abdomen since one year was admitted to our department. She had no fever or vomiting, no weight loss. CT-scan and sonography presented a big cyst (14 × 13.5 × 9 cm) in the left upper abdomen close to the pancreas body, probably a pancreas pseudocyst. In ERCP were no pathological findings. Sonography was normal.

*Methods:* Both patients had a diagnostic laparotomy. At the first patient a subtotal gastrectomy (Billroth I) was accomplished. For the second patient a tangential resection with a small wall of gastric mucosa was performed.

*Results:* There were no perioperative problems. At the first patient an early dumping syndrome was successfully treated conservatively. The second patient had a good recovery without complications.

*Conclusion:* Gastric duplications in adults are extremely rare. Diagnosis is often missed. Symptoms are unspecified pain in the upper abdomen, vomiting and fever. Some patients have weight loss. Complications are rare. Chronic infections and ruptures are described. For diagnosis, CT-scan with oral contrast should be preferred. Endoscopy is negative in most cases. Therapy is surgical. Local excisions with a small wall of gastric mucosa in most cases is sufficient. Sometimes, a subtotal gastrectomy is necessary.

*Clinical practice: Management strategy* Motility, general: Functional GI disorders Radiology and ultrasound: Diagnosis }

"Gastric Duplications: Diagnosis and Management"

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"P P 59 1407" P 59 1407 **Pharmaceutical Versus Non-Pharmaceutical Acute Upper Gastrointestinal Bleeding**

\*V. Nikolopoulou, K. Thomopoulos, E. Katsakoulis, B. Margaritis, K. Mimidis, A. Panagaris, C. Vagianos

Division of Gastroenterology and Department of Surgery, University Hospital, Patras, Greece This is a prospective study comparing the outcome between pharmaceutical and non pharmaceutical upper gastrointestinal bleeding (GI) due to benign peptic ulcer. *Methods:* A total of 907 patients were studied prospectively. They were suffering from acute upper GI bleeding due to endoscopically and histologically identified benign peptic ulcer. The patients were divided in two groups. *Group A* included 506 patients who had received ulcerogenic drugs (either aspirin or NSAID's) and *Group B*, 401 patients with no history of drug consumption. The two groups were comparable in all clinical and endoscopic parameters which are known to influence prognosis: age, sex, history of previous GI bleeding, associated disease, shock on admission, endoscopic stigmata and location of ulcer, need for haemostasis, rebleeding, need for transfusion and duration of hospital stay. *Results:* Emergency surgical intervention for persistent or recurrent bleeding was required in 38 patients (7.5%) in Group A and in 42 (10.5%) in group B ( $p = 0.148$ ). The overall mortality was 2.95% for Group A and 1.2% for group B. Endoscopic stigmata, median transfusion requirements, median duration of hospital stay, endoscopic haemostasis did not differ significantly. There were differences in sex distribution (more women than men), age, history of previous GI bleeding, associated disease, shock on admission ( $p = 0.073$ ) and gastric ulcer ( $p = 0.002$ ). Interestingly in Group A patients rebleeding rate was significantly less. *Conclusions:* Despite clinical presentation pharmaceutical haemorrhage do not seem to differ in mortality, morbidity and hospital stay than non pharmaceutical. Endoscopy, general: GI bleeding Endoscopy, specific: Stomach, duodenum } "Pharmaceutical Versus Non-Pharmaceutical Acute Upper Gastrointestinal Bleeding"

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"P P 59 1408" P 59 1408 **Helicobacter Pylori Infection Increases the Risk of Peptic Ulcer Bleeding — A Case-Control Study** H. K. Fahl, F. Leverkus, J. Labenz

Elisabeth Hospital Essen, Germany *Purpose:* The study was designed to evaluate the role of *H. pylori* infection in the pathogenesis of peptic ulcer bleeding. *Methods:* 128 patients presenting with upper GI bleeding and 128 matched controls (age and gender) were studied prospectively. In all patients and controls a standardized questionnaire was performed. Patients were investigated endoscopically with assessment of *H. pylori* infection by a rapid urease test, culture and histology. In controls, the current *H. pylori* status was determined using a <sup>13</sup>C-urea breath test. Statistics included the Cochran-Mantel-Haenszel test and a conditional multiple logistic regression analysis (CMLR). *Results:* 72 patients had peptic ulcer bleeding (gastric ulcer (GU): n = 39; duodenal ulcer (DU): n = 33) and 56 patients bled from other sources. *H. pylori* infection was more frequently detected in ulcer patients than in controls (GU: OR 4.3 95%-CI 1.6–11.5, p = 0.005; DU: OR 3.3 95%-CI 1.1–9.4, p < 0.03), while the infection was not related to non-ulcer bleeding (OR 1.2 95%-CI 0.6–2.5, p = 0.59). NSAID use was associated with an increased risk of gastric ulcer bleeding (OR 4.5 95%-CI 1.1–18.2, p = 0.035). CMLR suggested that *H. pylori* infection is an independent risk factor for peptic ulcer bleeding (OR 3.3 95%-CI 1.5–7.0), p = 0.002). No interactions could be detected between the infection and NSAID use. *Conclusions:* *H. pylori* infection increases independently the risk of peptic ulcer bleeding. Thus, cure of the infection will lead to a decreased incidence of ulcer bleeding. However, it cannot be expected that curing *H. pylori* infection in NSAID users will substantially diminish the risk of ulcer complications. Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "Helicobacter Pylori Infection Increases the Risk of Peptic Ulcer Bleeding / A Case-Control Study"

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"P P 59 1410" P 59 1410 **Clinical Investigation of Bleeding Peptic Ulcer in the Elderly**

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<sup>2</sup> Department of Internal Medicine, Kitasato University, Sagamihara, Kanagawa, Japan  
*Introduction:* The rapid increase in the elderly population of Japan has led to an increased number of elderly patients with bleeding peptic ulcer. *Objectives:* We compared the clinical characteristics of bleeding peptic ulcer in patients over 70 years of age or older in whom hemostasis was performed by heater probe treatment (elderly group) with those less than 70 in whom similar treatment was performed (younger group). *Methods:* Over a period of 9 years, 274 patients were enrolled, 48 in the elderly group and 226 in the younger group. *Results:* The incidence of concomitant disease was significantly higher in the elderly group (83.3%) than in the younger group (33.3%) ( $p < 0.01$ ). The incidence of emergency surgery (younger group 5.8% vs. elderly group 6.3%) and the rate of mortality due to hemorrhage (2.2% vs. 2.1%, respectively) were similar in the two groups. *Conclusion:* Bleeding peptic ulcer in elderly patients was thus characterized by a high incidence of concurrent disease. Despite this, the results of the present study indicate that the rates of mortality and emergency surgery in elderly patients with bleeding peptic ulcer who undergo heater probe treatment are comparable to those in younger patients, provided that their general condition is monitored carefully and that endoscopic hemostatic procedures. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding } "Clinical Investigation of Bleeding Peptic Ulcer in the Elderly"

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## "P P 59 1411" P 59 1411 Fifty Years of Upper Gastrointestinal Haemorrhage in NE Scotland

\*J. Masson, P. Bramley, G. McKnight, A. Fraser, N.A.G. Mowat

Gasrointestinal Unit, Aberdeen Royal Infirmary, Aberdeen, UK The mortality associated with acute Upper Gastrointestinal Haemorrhage (UGIH) has not generally reflected the major improvements in patient care introduced over the past 50 years and this has been confirmed by the recent Royal College of Physicians' Audit with a mortality of 14%. The factors that influence the outcome of UGIH have been the subject of many studies, but no study has addressed the impact of changes in medical practice and demographic characteristics in a single community. There have been three whole-community studies over 5 decades which provide data on the management and outcome of upper gastrointestinal bleeding in NE Scotland and these studies provide an exceptional record of the changing patterns of UGIH in a single community. There has been an increase in age (in 1950 1.5% and 1990's 18.5% of patients admitted were over 80 years of age), the use of ulcerogenic drugs and co-morbid disease in patients presenting with UGIH. However, the incidence of UGIH has remained static (117,000 admissions per adult population per year) over the last 25 years and at present is similar to other recent large studies. Endoscopy has replaced barium meal as the investigation of choice and with the introduction of powerful anti-ulcer drugs semi-elective surgery for ulcer prevention has disappeared. The proportion of gastric ulcer, oesophagitis and Mallory-Weiss tear have increased, whereas the proportion of duodenal ulcer and undiagnosed patients has declined. These changes in the diagnostic mix may reflect more accurate diagnosis or a true change in the incidence of certain diagnoses. During the same period outcome was improved with surgical mortality falling from 25% to 8% and overall mortality from 13.7% to 3.9%. The factors determining outcome in UGIH are constantly changing and this review clearly demonstrates this within a single community. Despite an increasing aged population with its associated co-morbid disease we have shown that by optimising patient care the mortality rate for UGIH can be reduced. Endoscopy, general: GI bleeding Clinical practice: Epidemiology (non cancer) } "Fifty Years of Upper Gastrointestinal Haemorrhage in NE Scotland"

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## "P P 59 1412" P 59 1412 High Prevalence of Upper GI Tract Asymptomatic Diseases as Causes of Micro and Macrocytic Anemia in Adults

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Oxyntic mucosa through acid and intrinsic factor secretions determines the availability for absorption of alimentary iron and vitamin B12 that are crucial in the haemoglobin synthesis. Furthermore duodenal mucosa is the main site for the absorption of reduced iron. The functional and structural integrity of gastric and duodenal mucosa is crucial since some diseases in which this integrity is lost, could result in anemia e.g. peptic ulcer disease (PUD), corporal atrophic gastritis (CAG), celiac disease (CD). Aim of study was to investigate in a consecutive anemic outpatients population referring to our Hematology Dept., the role played by gastric and duodenal mucosa integrity as possible cause of anemia. During a three-month period, 266 anemic consecutive outpatients (213 microcytic, 53 macro) were observed. Obvious blood loss causes, active gastrointestinal haemorrhage, fecal occult blood positivity, and all haematological and GI malignancy constituted exclusion criteria for this study. 80 anemic patients (age 20–76; M 24, F 56) 36 macrocytic, 44 microcytic, without GI complaints, resulted eligible and were investigated with a screening procedure consisting in the serological determinations of gastrin, IgG anti H pylori, antiendomysial IgA antibodies (EMA). Positivity of at least one of these determinations was further investigated with upper GI endoscopy with multiple antral (n = 2), fundic (n = 4) and duodenal (n = 2) biopsies. Patients negative to the screening also underwent gastroscopy. *Results* Gastrin was found increased in 35 pts, IgG Hp in 37 pts and EMA 16 pts. 6 patients refused further control. Endoscopy/histology

Microcytic	Macrocytic	Normal
22 (29.7%)	14 (8.1%)	4 (28.4%)
8 (13%)	13 (17.5%)	7 (6%)

(pernicious anemia) Adult CD 12 (16.2%) 10 (29.7%) Hp+ antral gastritis 13 (17.5%) 7 (6%)

*Conclusion:* This study in a consecutive asymptomatic anemic population enabled us to identify 39 out of 74 pts (52.7%) in whom upper GI diseases were the cause of anemia. The occurrence of both types of anemia is similarly distributed in PUD and CAG. Only 29.7% of anemic screened patients had no alteration of gastric and duodenal mucosa. Evaluation of unexplained anemia in adults should include a thorough investigation of upper GI tract. Clinical practice: Management strategy

Oesophageal gastric duodenal disorders: GD disorders, acid peptic Intestinal disorders, absorption: Gluten enteropathy } "High Prevalence of Upper GI Tract Asymptomatic Diseases as Causes of Micro and Macrocytic Anemia in Adults"

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"P P 59 1414" P 59 1414 **Incidence of Gastro-Intestinal Haemorrhagic Complications during Anticoagulant Therapy in a Danish Population-Based Cohort** F.H. Steffensen, K. Kristensen<sup>2</sup>, E. Ejlersen<sup>3</sup>,

\*J. Møller-Petersen<sup>2</sup>, H.T. Sørensen<sup>1</sup>

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<sup>2</sup> Department of Medicine V, Aarhus University Hospital, Aarhus, Denmark

<sup>3</sup> Department of Medicine M, Aalborg Hospital, Denmark *Background* – Recent clinical trials has established new indications for oral anticoagulation with warfarin; the efficacy was achieved with a low incidence of bleeding complications which may not be reproduced in clinical practice. Gastro-intestinal bleeding is the most frequent type of major bleeding and the objective of this study was to estimate the incidence of major gastro-intestinal bleeding requiring hospitalization among unselected outpatients treated with oral anticoagulants. *Design* – Through The Drug Prescription Register we identified a cohort of the 684 people commencing oral anticoagulant therapy in 1992 in the County of North Jutland. All discharge diagnoses for hospitalizations in this cohort from 1992 to October 1994 were reviewed for potentially bleeding complications followed by patient record review; death certificates were studied for deaths during follow-up. *Results* – The 684 patients represented 754 years at risk. There were 20 major gastro-intestinal bleeding events (2.7 per 100 treatment-years) in 19 patients of which none were fatal. Nearly all events were severe; requiring transfusion of two units of blood or more. Ten patients required four units of blood or more. *Conclusion* – The rates of major gastro-intestinal haemorrhages in this inception cohort was two to four times as high as in recent prospective trials and illustrates the continuous difficulties in translating the efficacy of oral anticoagulation in trials into effectiveness in clinical practice. Clinical practice: Epidemiology (non cancer) Clinical practice: Quality assurance Endoscopy, general: GI bleeding } "Incidence of Gastro-Intestinal Haemorrhagic Complications during Anticoagulant Therapy in a Danish Population-Based Cohort"

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"P P 59 1416" P 59 1416 **Upper Gastrointestinal Bleeding Today. A Prospective Analysis of 1350 Cases** K. Thomopoulos,

\*V. Nikolopoulou, K. Mimidis, E. Katsakoulis, A. Panagaris, C. Vagianos

Department of Internal Medicine, Division of Gastroenterology and Department of Surgery, University Hospital, Patras, Greece Upper gastrointestinal bleeding continues to be a serious and common clinical problem. In the last decades considerable improvement has been achieved concerning diagnostic and therapeutic approach to these patients. We present our data accumulated prospectively on 1350 patients admitted in our hospital over a 4 year period with upper gastrointestinal bleeding. During the last 4 years 1350 patients (14–96 years) admitted in our hospital with upper gastrointestinal bleeding (UGIB) or presented UGIB while were inpatient for any other reason. No exclusion have been made for age or comorbid disease. Emergency endoscopy was performed during the first 24 hours after admission or immediately after resuscitation in patients with massive bleeding. All patients have been managed by a team of gastroenterologists and surgeons in close cooperation. In all peptic ulcer, patients with active spurting or oozing bleeding, or a non bleeding visible vessel, endoscopic injection hemostasis with adrenaline diluted 1:10.000 in saline 0.9% (A/S) was performed during emergency endoscopy. Variceal bleeding was managed with octreotide, Sengstaken tube and emergency sclerotherapy. Peptic ulcer remains the main cause of UGIB (68.3%) following by gastroduodenal erosions (12.6%). We observed an increase in the incidence of peptic ulcer with a simultaneous decrease in the incidence of gastroduodenitis as a cause of UGIB in comparison to the previous decade. In patients with peptic ulcer the operation rate was 8.7%. Overall mortality was 2.5% and in patients with peptic ulcer as a cause of bleeding 2.2%. All patients who died had serious comorbid disease and 73.5% were over 65 years old. In conclusion peptic ulcer remains the main cause of upper gastrointestinal bleeding. Close cooperation between surgeons and gastroenterologists and endoscopic therapy has improved clinical outcome in patients with UGIB and reduced mortality. Endoscopy, general: GI bleeding } "Upper Gastrointestinal Bleeding Today. A Prospective Analysis of 1350 Cases"

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"P P 59 1417" P 59 1417 **NSAID Utilization and Frequency of NSAID Induced Gastrointestinal Bleeding** A. Jelenkovic

Department of Pharmacology and Toxicology, Faculty of Medicine, Nis, Serbia, Yugoslavia

Estimation of frequency of adverse drug reactions (ADR) is usually based on drug utilization expressed in the number of packages, number of prescriptions, single drug units. But, differences in drugs formulations (tablets, capsules, suppositories, solutions), weight of the active substance in drug packages and weight of every single unit in the package are neglected. Because of that, estimation of drug utilization is not precise enough, comparisons of different studies can not be made, and therefore neither can estimations of ADR. An internationally accepted statistical unit for drug utilization which takes into account all the parameters mentioned above is a defined daily dose (DDD). It is by agreement established drug quantity most frequently used for most frequent indications. In this study utilization of NSAIDs prescribed to outpatients of the Nis region (320190 inhabitants) in 1995 expressed in DDDs and the number of DDDs leading to one hospitalized hematemesis and/or melena (HM) induced by NSAIDs are analyzed. The number of HM (endoscopically found gastric or/and bulbar lesions) is already known. The utilization of acetylsalicylic acid (ASA) was 409172.4 DDDs. One HM appeared on every 7868.7 DDDs or more (as there is no evidence of sold unprescribed drugs, they could not be taken into account). The DDD for orally (O) or rectally (R) applied ASA is 3000 mg, so appearance of one HM can not be expected below 23606.1 g of ASA taken. One HM can not be expected below 46679.9 DDDs of ibuprofen (O the DDD is 1200 mg), 189450.2 DDDs for diclofenac (O, parenterally-P, R the DDD is 100 mg) and for piroxicam (O, P, R the DDD is 20 mg) 160174 DDDs. Because of the said advantages, introduction of DDDs in ADR research can lead to easier and more precise estimation of ADR frequency. The DDDs are also a good tool for further investigations in the ADR field, including ADR in the digestive system, too. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: GD disorders, acid peptic } "NSAID Utilization and Frequency of NSAID Induced Gastrointestinal Bleeding"

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## "P P 59 1418" P 59 1418 The Influence of Daily Dose on the Outcome of Aspirin-Induced Acute Upper Gastrointestinal Bleeding

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**Aim:** To examine the effect of prior use of aspirin on the clinical course of acute upper gastrointestinal bleeding (UGIB) regarding the daily dose.

**Methods:** We studied 345 patients admitted over a one-year period with UGIB and significant endoscopic findings. History of aspirin intake during the week preceding the onset of bleeding was positive in 59 cases (mean age 63, SD 16.6; 45 males, 14 females). These patients were included into two groups regarding daily dose aspirin: *Group 1*) with low-dose (< 325 mg) for prevention of arterial occlusive events, and *Group 2*) with high doses of aspirin (analgesic/antiphlogistic doses). In each patient information was collected on prior history of ulcer, gastroprotective agent use, comorbid conditions, mode of presentation, endoscopic findings and clinical course. Statistical analysis was performed using Student's t and Chi-square tests.

**Results:** Data Group 1 Group 2 p Difference n = 19 n = 40 (CI 95%) Age (mean – SD) 74.4 – 11 58 – 16 < 0.001 16 (9–24) Males 89.5% 70% NS Prior ulcer 36.8% 32.5% NS Protective agents 15.8% 12.5% NS Intake < 7 days 15.8% 72.5% < 0.001 56.3 (34.5–78.1) Co-morbidity 94.7% 45% < 0.001 49.7 (18.9–68.6) Transfusion 42.1% 45% NS Sclerosis 5.3% 15% NS Surgery 0% 2.5% NS Mortality 0% 0% NS Gastric ulcers 31.6% 45% NS

**Conclusions:** 1) A substantial proportion of UGIB is associated to aspirin intake in the week before the onset of bleeding; low-doses were responsible of over a third of bleeding episodes related to this drug. 2) The "low-dose aspirin" group was older, with longer intake and more comorbid conditions than the "high-dose aspirin" group. 3) In both groups gastric ulcer was the most common source of bleeding. 4) Clinical course of UGIB was similar in patients treated with low-dose aspirin as in patients with analgesic-anti-inflammatory doses. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding }

"The Influence of Daily Dose on the Outcome of Aspirin-Induced Acute Upper Gastrointestinal Bleeding"

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## "P P 59 1419" P 59 1419 Nonsteroid Anti-Inflammatory Drug-Associated Acute Nonvariceal Gastrointestinal Bleeding in the Elderly: Incident Cases and Morbimortality

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*Aim:* To determine the incidence of nonsteroid anti-inflammatory drugs (NSAIDs)-associated acute upper gastrointestinal bleeding (UGIB) and the impact of these drugs on the clinical course in elderly patients. *Methods:* We conducted a prospective study on 142 consecutive patients aged 65 years or older (mean age 76, SD 7; 97 males, 45 females) admitted with UGIB diagnosed endoscopically over a one-year period. These patients were divided into two groups: *Group A*) with use of NSAIDs in the week before admission and *Group B*) without NSAIDs. Data collected: Age and sex, prior ulcer disease and therapy, symptomatology prior to bleeding, mode of presentation, endoscopic findings, transfusion requirements, need for urgent endoscopic and/or surgical treatment, duration of hospital stay and mortality. Incidence rates of UGIB were estimated on a general adult population of 142.776 (elderly population 14%). Statistical analysis was performed using Student's t and Chi-square tests. *Results:* Variables Group A Group B p Difference n = 58 n = 84 (CI 95%) Age (mean – SD) 75.4 – 7.3 77.2 – 7.3 NS Males 62% 72% NS Prior ulcer 27.6% 43% 0.06 Protective agents 15.5% 31.3% < 0.05 15.8 (2.2–29.4) Transfusion 41.4% 51.2% NS Sclerosis 10.3% 15.5% NS Surgery 3.4% 3.6% NS Mortality 1.7% 4.8% NS Gastric ulcers 41.4% 21.4% < 0.01 20 (4.6–35.4) UGIB incidence for adult younger population: 172 per 100.000 UGIB incidence for elderly population: 560 per 100.000 Rate Ratio = 3.28; CI 95% (2.6–4.1) *Conclusions:* 1) In our community the incidence of UGIB for elderly is high, and a relevant number of cases (40.8%) is associated with NSAIDs exposure in the week before admission. 2) Elderly patients with NSAID-UGIB differ in the source of bleeding and prior history of peptic ulcer disease. 3) NSAID treatment is not an adverse prognostic factor in acute UGIB in the elderly. Clinical practice: Epidemiology (non cancer) Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding } "Nonsteroid Anti-Inflammatory Drug-Associated Acute Nonvariceal Gastrointestinal Bleeding in the Elderly: Incident Cases and Morbimortality"

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"P P 59 1423" P 59 1423 **Schönlein-Henoch Purpura in Adults (Gastrointestinal Manifestation and Endoscopy)** J. Novák

Department of Gastroenterology, Pécs County Hospital, Gyula, Hungary During a 10 years period 62 adult patients were admitted with diagnosis of Schönlein-Henoch purpura in our hospital. 25 female and 37 male patients ranging from 30 to 87 years (mean: 59.5 year) and presenting with cutaneous, joint, renal and particularly abdominal involvement were investigated retrospectively. During the course of the disease, all patients developed purpuric rash (100%), 14 (22.5%) patients had joint symptoms and renal involvement occurred in 12 (19.3%) patients. In this study, we discuss 15 (24%) patients with gastrointestinal symptoms appearing in Henoch's purpura. Analysis of the gastrointestinal clinical features revealed: abdominal pain 13 (86%), massive colorectal bleeding 3 (20%), occult blood loss 10 (66%) vomiting 6 (40%) and diarrhoea in 3 (20%) patients. Surgical consultation was obtained for 4 of the 15 patients and laparotomy was performed in 2 patients. All the patients underwent lower and upper endoscopic examination, in 3 cases the authors saw purpuric mucosal lesions in duodenum and in 8 patients were also found coin-like elevated lesions in colon, additionally, biopsy from colonic lesions showed leukocytoclastic vasculitis. It is concluded that endoscopy can be helpful in the diagnosis and treatment of Schönlein-Henoch purpura, especially is in those without typical skin rash. Endoscopy, general: Instrumentation, diagnosis Endoscopy, general: GI bleeding } "Schönlein-Henoch Purpura in Adults (Gastrointestinal Manifestation and Endoscopy)"

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"P P 60 1432" P 60 1432 **Clinical Uniformity of Inflammatory Bowel Disease at Presentation in the North and South of Europe** J.E. Lennard-Jones,

\*S. Shivananda, EC-IBD study group

University Hospital Maastricht, The Netherlands *Background:* A prospective epidemiological survey conducted by The European Collaborative Study Group on IBD (EC-IBD) has assessed the incidence of non-specific inflammatory bowel disease (IBD) in the North and South of Europe. The protocol was also designed to study whether the clinical features of IBD are different in these two areas, because of genetic or environmental factors. Twenty European centres participated in the study, 8 were from the North and 12 from the South. *Methods:* All centres used uniform criteria of disease definition in ulcerative colitis (UC) and Crohn's disease (CD) and a common protocol for recording clinical and epidemiological data. *Findings:* Altogether 2201 patients with IBD aged 15 years or more were identified. Of the 1379 with UC 869 were from the North and 510 from the South. Of the 706 with CD, 477 were from the North and 229 from the South. An analysis of the diagnostic measures used in making the initial diagnosis of UC or CD in the North and South showed that every patient with colitis had an endoscopy and that a biopsy or operation specimen was available for pathological examination in most cases. For CD over 80% of cases had an X-ray and tissue was available for pathological examination in 87–92% of cases. There was no difference in the proportion of cases investigated by each means in the North and South of Europe, except that radiology was used a little more often in the South. The analysis of duration and nature of presenting symptoms and site and extent of disease showed no evidence that the initial clinical features of disease vary from Iceland in the North to mediterranean countries in the South. *Conclusion:* This study provides evidence that modern methods of investigation of IBD are available both in the North and South of Europe, definitions of disease are uniform, clinical presentation of IBD is similar, and therapeutic management during the first year of disease follows a common pattern in most centres. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy }" "Clinical Uniformity of Inflammatory Bowel Disease at Presentation in the North and South of Europe"

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"P P 60 1433" P 60 1433 **Is Intestinal Permeability Really Increased in Patients with Inflammatory Bowel Disease?**

\*B.J. Geerling, M.A. v. Nieuwenhoven, R.W. Stockbrügger, R.-J.M. Brummer

Dept. of Gastroenterology, university hospital Maastricht, The Netherlands *Introduction.* During the last years there is much interest in the intestinal permeability of patients with Inflammatory Bowel Disease (IBD) as this may play a role in the pathogenesis of IBD. However, methods used to measure the urinary sugar concentrations show lack of reproducibility and results are often conflicting. The aim of this study was to evaluate intestinal permeability in patients with IBD (Crohn's disease (CD) and ulcerative colitis (UC) versus controls, using a validated, newly developed analysis method. *Methods.* After an overnight fast, 27 patients with IBD (8 CD, 19 UC) at time of diagnosis (IBD-new), 23 patients with long-standing CD > 10 years, but during an inactive period (CD-long) and 39 controls, ingested a solution consisting of 10 gram lactulose (L) and 1 gram rhamnose (R) in 65 ml of water. Urine was collected for 5 hours and urine L and R excretion was measured using a validated, newly developed fluorescent detection HPLC [1]. Results are expressed as mean – SEM. Statistical analysis was performed by one-way ANOVA. *Results.* The L/R ratio for IBD patients (IBD-new: 0.01 – 0.002; CD-long: 0.02 – 0.006) was not significantly different compared to controls (0.01 – 0.002). However, the % recovery of R was significantly decreased for CD-long patients, compared to controls ( $p < 0.001$ ). No significant correlations were observed between either disease activity indices (albumin, ESR, CRP or CDAI) and L/R ratio or disease activity indices and % recovery of the sugars. *Conclusions.* The L/R ratio was not increased in patients with IBD. The excretion of the monosaccharide rhamnose was decreased for patients with long-standing CD. Whether this observation is related to malabsorption and reduced absorptive capacity of the small intestine of patients with long-standing CD remains to be established.

Reference: Rooyackers, D. J. of Chromatography A, 1996; 730: 99–105. Intestinal disorders, absorption: Epithelial transport Nutrition: Nutrients and gut function Intestinal disorders: IBD, basic } "Is Intestinal Permeability Really Increased in Patients with Inflammatory Bowel Disease?"

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"P P 60 1434" P 60 1434 **Decreased Trace Element Status in Patients with Inflammatory Bowel Disease**

\*B.J. Geerling, R.-J.M. Brummer, R.W. Stockbr\fcgger

Dept. of Gastroenterology, university hospital Maastricht, The Netherlands *Introduction.* Trace element deficiency is described in patients with Inflammatory Bowel Disease (IBD), mainly in active Crohn's disease (CD). Those trace elements, which are anti-oxidants, may play an important role in the pathophysiology of IBD as scavengers of free radicals. The aim of this study was to evaluate trace element status in various groups of IBD patients (CD and ulcerative colitis (UC)). *Methods.* In 27 IBD patients at time of diagnosis (IBD-new: 8 CD, 19 UC) and in 31 patients with long-standing, but recently inactive CD (> 10 years with one or several small bowel resections; CD-long) and in 15 controls, trace element status was assessed by serum values of selenium (Se), zinc (Zn), magnesium (Mg), copper (Cu) and whole blood glutathion peroxidase (GPx). Statistical analysis was performed by ANOVA. *Results.* Trace element values were not significantly decreased for IBD-new patients versus controls. However, compared to controls, Se, Mg, Zn, Cu, GPx of CD-long patients were significantly lower (86.5%, 90.4%, 93.8%, 76.7% and 82.7% of control values, respectively;  $p < 0.05$ ). There were no correlations between trace element values and disease activity indices (albumin, ESR, CRP, CDAI or Truelove Witts index). We observed a significant correlation between Se and GPx in patients with IBD (IBD-new and CD-long:  $r = 0.37$ ;  $p < 0.05$ ), however, not in controls. *Conclusion.* Selenium requirement for GPx activity was met in controls, but not in patients with IBD. Patients with long-standing, but recently inactive CD, have significantly lower serum trace element values compared to controls. For IBD patients at time of diagnosis a similar, but not yet significant, trend was observed. This may indicate a poor anti-oxidant status with negative implications on the course of the disease. Nutrition: Nutrients and gut function Intestinal disorders: IBD diagnosis, monitoring } "Decreased Trace Element Status in Patients with Inflammatory Bowel Disease"

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"P P 60 1435" P 60 1435 **Serum Levels of Eosinophil Cationic Protein (ECP),  
""Neurotoxin"" (EPX) and Myeloperoxidase (MPO) as Markers of Clinical Activity in  
Inflammatory Bowel Disease (IBD)**

\*F. De Lazzari, A. D'Odorico, E.A. Galliani, E. Guido, P. Ravagnan, D. Faggian<sup>1</sup>, R. D'Inc\ 'e0,  
G.C. Sturniolo, M. Plebani<sup>1</sup>, F. Pozzato, R. Naccarato

Gastroenterology Dpt., University of Padua, Italy

<sup>1</sup> Medicine Laboratory Dpt., University of Padua, Italy Eosinophils may be the predominant cell type in the inflamed intestinal mucosa of IBD pts. Immunoallergic reactions have been postulated to be involved in the pathogenesis of IBD. *Aim:* to evaluate if serum levels of protein released by eosinophils (ECP and EPX) and neutrophils (MPO) were related to clinical activity and/or allergic features in IBD pts. *Methods:* 104 consecutive out-patients affected by ulcerative colitis (UC: n. 60; mean age: 40 yrs; range: 17–74 yrs) or Crohn's disease (CD: n. 44; mean age 41 yrs; range 15–76 yrs) were included in the study. Pts on steroids or other immunosuppressive agents, were not included. Pts were submitted to prick-by-prick tests for food allergens (milk, apple pear, celery, parsley, onion, garlic, tomato, capsicum, walnut, peanut, banana, flour) and prick test for common inhalants (Dermatophagoides D.F, D.PT, Graminaceae, Candida Albicans, Compositae, Betulaceae, Parietaria). Serum ECP, EPX and MPO levels were tested by commercial kits (Pharmacia; Uppsala, Sweden). *Results:* 34% of pts have positive prick test irrespective of the type of disease. 55–70% of positive tests were found in pts in remission, but no statistically difference was found with disease clinical activity. Pts with positive allergic tests have ECP, EPX and MPO serum levels similar to those with negative prick tests (p: n.s.). MPO serum levels are related to clinical activity in IBD pts especially in UC pts (P < 0.02 t: 2.28). A significant correlation was found between serum levels of ECP with MPO (r = 0.537; p < 0.0001) and EPX with MPO (r = 0.517; p < 0.001). *Conclusions:* MPO serum levels are related to clinical activity in IBD pts with a positive correlation with serum ECP and EPX levels. 34% of our pts had a positive reaction to food and/or inhalant allergens. These data indicate that PMN neutrophils might trigger eosinophils which contribute to tissue damage by releasing their active proteins. Intestinal disorders: IBD diagnosis, monitoring } "Serum Levels of Eosinophil Cationic Protein (ECP), ""Neurotoxin"" (EPX) and Myeloperoxidase (MPO) as Markers of Clinical Activity in Inflammatory Bowel Disease (IBD)"

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"P P 60 1436" P 60 1436 **Humoral Immune Response to Human Stress (Heat Shock) Proteins in Inflammatory Bowel Disease** G. Pedersen, P.N. Schmidt, J. Hendel, T. Saermark,

\*J. Brynskov

Dept. Medical Gastroenterology C, Herlev University Hospital, DK-2730 Denmark *Purpose:* Human Stress Proteins (HSP) is a large group of intracellular proteins expressed when cells are exposed to different kinds of stress. They appear to have a cytoprotective function which diminish cellular damage. HSP's are believed to be involved in the pathogenesis of IBD, supported by the finding of enhanced mucosal expression of the stress proteins HSP 60 and HSP 70 in IBD. The level of autoantibodies to HSPs seems to be elevated in other autoimmune diseases. In this study the presence of circulating autoantibodies to HSP 60 and 70 was compared to the expression of mRNA for the proteins in colon mucosal biopsies from a series of IBD patients. *Methods:* Sera from IBD patients and controls were tested for autoantibodies by an ELISA based on HSP 60 and 70 from recombinant sources as the primary layers. Endoscopic colorectal biopsies were tested by PCR for the expression of HSP 60 and HSP 70 mRNA. *Results:* Autoantibodies against HSP 60 were found in all patients with IBD, and no difference was found in titre level between patients with IBD and healthy controls. Autoantibodies to HSP 70 were not found. Using PCR to detect expression of HSP 60 and 70 it was found that both were expressed in both healthy subjects and patients with IBD. The sequence specificity excluded bacterial expression as a false positive signal. *Conclusion:* It has been found previously that patients with Ulcerative Colitis have elevated levels of autoantibodies to HSP 70. This could not be reproduced although it was found that both healthy subjects and patients with IBD expressed HSP 70. This and the finding of circulating autoantibodies to HSP 60 suggest that the circulating antibody response to these two proteins is without importance in IBD. HSPs could still be involved in the pathogenesis of IBD acting as a local immunological mediator induced by inflammation. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation }" "Humoral Immune Response to Human Stress (Heat Shock) Proteins in Inflammatory Bowel Disease"

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## "P P 60 1437" P 60 1437 **Hepatobiliary and Coexisting Pancreatic Duct Abnormalities in Patients with Inflammatory Bowel Disease**

\*B. Heikius<sup>1</sup>, S. Niemelä<sup>1</sup>, J. Lehtola<sup>1</sup>, S. Lehto<sup>2</sup>, T. Karttunen<sup>3</sup>

<sup>1</sup> Dept. of Internal Medicine, University Hospital of Oulu, Finland

<sup>2</sup> Dept. of Diagnostic Radiology, University Hospital of Oulu, Finland

<sup>3</sup> Dept. of Pathology, University of Oulu, Finland *Background:* We performed a cross-sectional study to evaluate the prevalence of hepatobiliary disease in unselected patients with inflammatory bowel disease (IBD) and to estimate the frequency of coexisting cholangiographic and pancreatographic duct abnormalities and to correlate the findings with clinical, endoscopic and histologic variables. *Methods:* 237 IBD patients were screened for increased liver function tests. Further hepatobiliary evaluation consisted of transabdominal ultrasonography, endoscopic retrograde cholangio-pancreatography (ERCP) and a liver biopsy. In addition, we evaluated the ERCP findings in patients with abnormal pancreatic screening tests (pancreatic enzymes or PABA excretion). *Results:* Laboratory signs of hepatobiliary disease were found in 37 (16%) of our IBD patients. Those abnormal liver tests were more common in patients with Crohn's disease (CD) than in patients with ulcerative colitis (UC) (30.4% vs 11.2%,  $p < 0.05$ ) and a similar trend was observed in the frequency of primary sclerosing cholangitis (PSC) in the respective groups of IBD patients. When combining ERCP findings with liver histology 26 (11% of the whole study group) patients with PSC were found, small duct disease included. In 23 (10% of the whole study group) patients definite cholangiographic changes consistent with PSC were found. In 11 (48%) of these there were coexisting pancreatic duct abnormalities. The prevalence of coexisting cholangiographic and pancreatographic duct changes in the whole study group was 4.6%. *Conclusion:* Hepatobiliary disease is at least equally common both in patients with UC and CD. Coexisting cholangiographic and pancreatographic duct abnormalities in patients with IBD are not occurring infrequently and they are considered extraintestinal manifestations of IBD. Endoscopy, specific: Biliary Endoscopy, specific: Pancreatic Pancreas: Pancreatitis, chronic }" "Hepatobiliary and Coexisting Pancreatic Duct Abnormalities in Patients with Inflammatory Bowel Disease"

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"P P 60 1438" P 60 1438 **Prevalence of ANCA and sANGA in Inflammatory Bowel Disease with Extra-Intestinal Manifestations**

\*K. Koss, K. Adrych, A. Kryszewski

Gastroenterology Clinic, Medical University of Gdansk, Poland The significance of anti-neutrophil cytoplasmic antibodies (ANCA) and other specific antibodies to neutrophil granules (sANGA) in ulcerative colitis (UC) and Crohn's Disease (CD) is unclear. We investigated the prevalence, antigen specificity and relative amounts of both ANCA and sANGA in sera of 45 UC patients. ten had extra-intestinal manifestations (EIM) such as arthritis, sacroiliitis, ankylosing spondylitis, pericholangitis, sclerosing cholangitis, uveitis, conjunctivitis. All sera (plus 50 controls) were tested by indirect immunofluorescence for the prevalence of ANCA and by ELISA for antibodies (ab) against the following highly purified enzymes of human neutrophil granules: myeloperoxidase (MPO), elastase (E), cathepsin G (CG) from primary granules, lactoferrin (LF) from secondary granules and lysozyme (LY) derived from primary and secondary granules. ANCA were more common in UC patients with EIM (&%) than in those without (30%). the prevalence of sANGA in UC patients with EIM (group A) and without EIM (group B) were: Group A: anti-MPO ab 60%, anti-E ab 80%, anti-CG ab 80%, anti-LF ab 70%, anti-LY ab 80%. Group B: anti-MPO ab 14%, anti-E ab 40%, anti-CG ab 38%, anti-LF ab 32%, anti-LY ab 49%. Titres of ANCA, anti-CG ab and anti-LF ab were significantly higher ( $p < 0.05$ ) in group A. Venn diagrams shown limited overlap between presence of ANCA and antibodies in the sANGA group. Considerable overlap was however observed within the sANGA group. Both ANCA and sANGA occurred more frequently in UC patients with EIM suggesting they role in pathogenesis. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Prevalence of ANCA and sANGA in Inflammatory Bowel Disease with Extra-Intestinal Manifestations"

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## "P P 60 1439" P 60 1439 Test of Renal Function in Patients with IBD: Effects of 5-ASA Treatment

\*M. Luk<sup>1</sup>, M. Bortl<sup>1</sup>, J. Kvasnicka, J. Fialov<sup>1</sup>

Internal Medical Department Charles University, Prague, Czech Republic It has been shown that long term therapy of inflammatory bowel diseases (IBD) with 5-aminosalicylic acid (5-ASA) preparations is potentially nephrotoxic in susceptible patients (pts). *Aim of the study:* 1. to establish frequency of impairment of renal function in pts with IBD, 2. to compare the dosage of 5-ASA in patients with normal and impaired renal function, 3. to find correlation between markers of renal (tubular and glomerular) damage and degree of IBD activity. *Patients and methods:* We have evaluated the renal function in 41 pts with Crohn's Disease (CD) and Ulcerative Colitis (UC). Activity of IBD pts was estimated according clinical, endoscopical and laboratory findings. Mean dosage of 5-ASA was known in all pts during last 6 months. Renal function was assessed by: creatinine clearance, the urinary excretion for two markers of tubular toxicity (2-microglobulin, 1-microglobulin) and microalbuminuria. The urinary markers of tubular damage, microalbuminuria, renal function and mean dosage of 5-ASA was compared in pts with active and inactive IBD. *Results:* 1. Microalbuminuria didn't correlate with activity of disease (12.5 mg/min in active group, 13.5 mg/min in inactive group  $p > 0.7$ ), 1-microglobulinuria was significantly higher in pts with active disease (53.9 mg/l vs 11.6 mg/l,  $p < 0.04$ ). 2. In pts with mean dosage of 5-ASA higher than 2 g/day was urinary excretion of 1-microglobulin significantly increased (43.7 mg/l vs. 8.6 mg/l,  $p < 0.1$ ). 3. We didn't find significant difference of mean dosage of 5-ASA in patients with normal vs. pathological urinary excretion of 2-microglobulin, 1-microglobulin and microalbumin. *Conclusions:* 1. According to the results of this study microalbuminuria isn't reliable marker of IBD activity. 2. We didn't find any correlation between the markers of tubular damage and mean dosage of 5-ASA. 3. It isn't clear, if higher urinary excretion of 1-mikroglobulin is consequence of disease activity or administration of 5-ASA. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy } "Test of Renal Function in Patients with IBD: Effects of 5-ASA Treatment"

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"P P 60 1440" P 60 1440 **Acute Pancreatitis in Patients with Chronic Inflammatory Bowel Disease**

\*H.H. Rasmussen, K. Fonager, H.T. Sørensen, J. Møller-Petersen

Dept. of Med. Gastroenterology M, Aalborg Hospital, Dept. of Medicine V, and the Danish Epidemiology Science Center, Aarhus University Hospital, Denmark

Several case reports on co-existence of pancreatic dysfunction and chronic inflammatory bowel disease, especially Crohn's disease, have been published during the past few years. However, only few studies have estimated the risk of acute pancreatitis in patients with chronic inflammatory bowel disease. *Aim:* To estimate the risk of acute pancreatitis in patients with chronic inflammatory bowel disease in the Danish population. *Methods:* The study included all patients discharged from Danish hospitals with a diagnose of chronic inflammatory bowel disease and acute pancreatitis, registered in the Danish National Registry of Patients in the period from 1977 to 1992. Age- and sex specific incidence discharge rates for acute pancreatitis in patients with chronic inflammatory bowel disease and the background population were calculated. The expected numbers of acute pancreatitis were calculated and divided into groups according to sex, age and calendar-time in three age-groups. *Results:* Overall, 2 patients were discharged and followed for 93774 person-years yielding an average follow-up of 7.7 years for Crohn's disease and 8.6 years for ulcerative colitis. The incidence discharge rate ratio (IRR) for acute pancreatitis was increased in both patients with Crohn's disease (IRR = 3.0, 95% CL: 2.0–4.3) and in patients with ulcerative colitis (IRR = 1.5, 95% CL: 1.1–2.0), especially in the age-group from 15–64 years. No patients < 15 years had acute pancreatitis. *Conclusion:* Patients with chronic inflammatory bowel disease are at an increased risk for acute pancreatitis. **Pancreas: Pancreatitis, acute** **Intestinal disorders: IBD, basic** **Clinical practice: Epidemiology (non cancer) }** "Acute Pancreatitis in Patients with Chronic Inflammatory Bowel Disease"

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"P P 60 1441" P 60 1441 **HLA Class II DRB1\*0301 or DRB3\*0301 Gene Involvement in Genetic Susceptibility to Inflammatory Bowel Disease (IBD)?** D. Heresbach, M. Alizadeh, M. Pagenault, J.F. Colombel, F. Quillivic, P.M. Danze, A. Gauthier, M. Gosselin, B. Genetet, A. Cortot, G. Semana, J.F. Bretagne

Department of Gastroenterology and University Laboratory of Immunology, 59000 Lille & 35033 Rennes

Recent european studies of HLA class II genes involvement in IBD genetic susceptibility have shown a negative association of HLA DRB1\*0301 with IBD as well as with Crohn's disease (CD) than with ulcerative colitis (UC). HLA DRB1\*03 allele and DRB1\*11, 12, 13 and 14 alleles are associated with an allele HLA DRB3 polymorphic locus (at least 4 alleles described). Recently a north american study have showed an increased risk of CD in individuals who inherit HLA DRB3\*0301 allele. *The aim* of the present study was to analyze the relationship between HLA DRB1 and DRB3 locus in the susceptibility to IBD. *Patients and methods:* One hundred thirty one UC and 157 CD patients were included in this study and compared with 200 ethnically matched controls. HLA DRB1 and DRB3 class II alleles were determined by PCR-SSO and if necessary by Reverse Dot Blot (Innolipa, kits from Innogenetics). *Results:* DRB1\*0301 and DRB3\*01, 02, 03 allelic distribution was analysed in patients groups and controls. A decrease frequency of DRB1\*0301 allele was observed in patients (respectively 4% and 7% in UC and CD) versus 15% in controls ( $p < 0.001$ ). Considering the DRB3 locus, a non significant increase frequency of DRB3\*03 allele characterize CD patients (8.6% versus 4.0% in UC and 4.5% in controls). Finally, the analysis of DRB3 alleles subtypes (165, 113 and 86 DRB3 alleles in controls, CD and UC respectively) shows that the DRB3\*03 allele is more represented in CD patients (23.8% vs 10.9% in controls and 12.8% in UC). *Conclusion:* The DRB3 locus is not involved in the protective effect conferred by the MHC class II DRB1\*0301 allele. We cannot confirm the strongly association of HLA DRB3\*0301 allele with CD in an european population of CD patients.

Intestinal disorders: IBD, etiology and genetics } "HLA Class II DRB1\*0301 or DRB3\*0301 Gene Involvement in Genetic Susceptibility to Inflammatory Bowel Disease (IBD)?"

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"P P 60 1442" P 60 1442 **Ultrasound Bone (US) Densitometry in Patients with Inflammatory Bowel Disease (IBD) — A Comparison with Conventional Double X-Ray Densitometry (DXA)** M. Dinca, W. Fries, G. Luisetto<sup>1</sup>, F. Peccolo<sup>1</sup>, F. Bottega<sup>1</sup>, A. Martin

Gastroenterologia, Universit'e0 di Padova; Italy

<sup>1</sup> Ist. di Semeiotica, Universit'e0 di Padova; Italy Patients with IBD are frequently found to have osteoporosis. Bone densitometric measurements are routinely carried out with instruments employing X-rays or radionuclides as energy-sources which imply exposure to radiation. Thus repeated measurements within a short period of time may be harmful. US measurements on the other hand are easy to perform and do not have such side effects. *Aim:* of the study was to compare the new methodology of US of the os calcis with the conventional DXA of the lumbar spine. *Methods:* Bone mineral density (BMD) was measured in 36 IBD patients considered at risk for osteoporosis due to persistent disease activity and/or prolonged steroid intake (24 with Crohn's disease and 12 with ulcerative colitis (aged 24 to 65 years). We performed DXA at the lumbar spine and US of the left os calcis, both examinations within the same day. DXA measurements were expressed as g/cm<sup>2</sup>, US measurements as speed of sound (SOS; m/sec), considered to represent density and elasticity, and attenuation of US (BUA: dB/MHz) indicating bone density and trabecular structure. *Results:* in our hands short term precision of DXA was 0.8%, that of US 1.1% for BUA and 1.8% for SOS. DXA and SOS values are closely correlated ( $r^2 = 0.669$ ,  $p < 0.00001$ ), whereas BUA showed a weaker but still significant correlation with DXA-values ( $r^2 = 0.414$ ,  $p < 0.01$ ). *Comments:* 1) Both indices, SOS and BUA, correlate with measurements obtained by conventional DXA of the lumbar spine; 2) US densitometric measurements have an acceptable reproducibility; 3) in IBD patients US may contribute to detect short-term variations due to disease activity, bed rest, or treatment influences (steroids or cyclosporin) and, thus, give new insights in pathophysiology of IBD-associated bone disease. Intestinal disorders: IBD diagnosis, monitoring }" "Ultrasound Bone (US) Densitometry in Patients with Inflammatory Bowel Disease (IBD) / A Comparison with Conventional Double X-Ray Densitometry (DXA)"

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"P P 60 1443" P 60 1443 **Familial Prevalence of Inflammatory Bowel Disease in Relatives of Finnish Patients with Crohn's Disease or Ulcerative Colitis**

\*T. Heliö<sup>1</sup>, M. Färkkilä<sup>1</sup>, L. Halme<sup>2</sup>, U. Turunen<sup>3</sup>, H. Järvinen<sup>2</sup>, K. Kainulainen<sup>1</sup>, A. Palotie<sup>2</sup>, K. Kontula<sup>1</sup>

<sup>1</sup> Helsinki University Central Hospital, Dpt of Internal Medicine, Haartmaninkatu 4, 00290 Helsinki

<sup>2</sup> Helsinki University Central Hospital

<sup>3</sup> Maria Hospital, Helsinki In order to evaluate the extent of the genetic component underlying inflammatory bowel disease (IBD) 880 Finnish subjects suffering from ulcerative colitis (UC) or Crohn's disease (CD) were asked to complete a questionnaire addressing to the occurrence of IBD in their first-degree relatives. The questionnaire was completed by 570 patients (65%), of whom 554 individuals (276 men and 278 women) were unrelated. UC was present in 290 (52%) and CD in 226 (41%) subjects; in 38 subjects (7%) the exact nature of the disease was indeterminate. 13 (5.7%) CD patients and 21 (7.2%) of those with UC had at least one sibling with IBD. Five subjects with CD (2.2%) and 12 (4.1%) with CU had a parent suffering from IBD. Five (2.2%) CD patients and 7 (2.4%) UC patients had at least one affected child. There was a tendency towards genetic anticipation (earlier onset of IBD in successive generations) in both UC and CD. Thus in four families with CD the mean difference between ages at diagnosis in the first and second generation was 20 years and in five UC families 17 years. In conclusion, at least one affected first-degree relative was detected in 13.1% of UC patients and in 10.2% of CD patients. Intestinal disorders: IBD, basic } "Familial Prevalence of Inflammatory Bowel Disease in Relatives of Finnish Patients with Crohn's Disease or Ulcerative Colitis"

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## "P P 60 1444" P 60 1444 **Thrombophilia in Inflammatory Bowel Disease**

\*A.G. Lim, L. Jones, S.R. Gould

Department of Medicine, Epsom General Hospital, Epsom, UK Thrombo-embolic complications are important in inflammatory bowel disease (IBD). Thrombophilia may contribute to this thrombotic tendency. It is unclear whether patients with IBD and a previous history of thrombo-embolic complications form a specific subgroup. The aim of our study was to determine the frequency of a range of thrombophilic abnormalities in patients with IBD and in the subgroup of patients who have also suffered from thrombo-embolic problems. Serum levels of antithrombin III, protein C, protein S and lupus anticoagulant and the presence or absence of activated protein C resistance was assessed as a thrombophilia screen. All tests were performed in the absence of anticoagulant therapy. 18 patients were studied. 11 had IBD alone (age range 27–78, 5 male) and 7 had BD and previous thrombo-embolic complications (age range 22–76, 3 male). Thrombo-embolic problems included 5 deep vein thromboses, 2 pulmonary emboli and 1 axillary vein thrombosis. The ratio of ulcerative colitis to Crohn's disease and active to inactive patients in the two groups were similar. Of those with IBD alone, thrombophilic abnormalities were detected in 6/11 patients. one patient had both antithrombin III and protein S deficiency, one had had both antithrombin III deficiency and lupus anticoagulant and one had activated protein C resistance. Borderline abnormalities in protein S deficiency and lupus anticoagulant were detected in three other patients. Of those with IBD and previous thrombo-embolic problems, one had activated protein C resistance, one had antithrombin III deficiency, one had protein C deficiency and one was borderline positive for lupus anticoagulant. In summary, the incidence of heterogeneous thrombophilic abnormalities is high (approx 60%) in IBD. Patients who have suffered from thrombo-embolic complications are not more likely to have thrombophilia. IBD patients requiring bedrest in hospital may need low dose heparin prophylaxis. Those with documented thrombophilia may need longterm anticoagulation. Intestinal disorders: IBD, basic }  
"Thrombophilia in Inflammatory Bowel Disease"

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"P P 60 1445" P 60 1445 **Adhesive *E. coli* in Inflammatory Bowel Disease**

\*B.J. Rembacken, J. Rothwell, A.M. Snelling<sup>1</sup>, E. Ellis<sup>1</sup>, L.C.F. Hibbert-Rogers<sup>1</sup>, A.T.R. Axon, P.M. Hawkey<sup>1</sup>

Centre for Digestive Diseases, The General Infirmary, Leeds, UK

<sup>1</sup> Dept of Microbiology, The General Infirmary, Leeds, UK *Escherichia coli* (*E. coli*) have been implicated in the aetiology of inflammatory bowel disease (IBD) as patients with active ulcerative colitis (UC) are more likely to carry strains adhesive to buccal epithelial cells. No previous study has investigated the coliform flora in patients with IBD and healthy controls over a prolonged period. Four faecal samples were collected over a 12 months period from 13 patients with UC, 8 with CD and 12 healthy volunteers. 10 *E. coli* colonies were isolated from each sample and typed by REP-PCR. The adhesiveness of each *E. coli* subtype was assessed by the buccal epithelial adhesive assay. Our adhesive standard *E. coli* strain (E851) had a mean buccal epithelial adhesive index (BECAI) of 15% and the non-adhesive standard (SC13), a mean of 0. The Mann-Whitney, Fisher's exact and Kruskal-Wallis tests were used in the analysis. Patients with IBD carried significantly more adhesive *E. coli* than healthy controls (UC; median BECAI 6, P = 0.007, CD median 8, P = 0.03, Controls median 0). This association did not change over time as more healthy controls carried non-adhesive *E. coli* (BECAI < 5) at most of the four collection times than patients with UC (9/12 and 2/12 respectively, P = 0.08). There was an association between adhesiveness and site of disease as patients with proctitis and extensive colitis were more likely to carry adhesive strains than patients with left colonic or small bowel disease (p = 0.02). Eight percent of *E. coli* strains followed for one year changed adhesiveness without changing REP-PCR pattern suggesting that the gene for adhesiveness is situated on a plasmid. In conclusion, we can confirm that not only patients with UC but also those with CD are more likely to harbour adhesive *E. coli* than healthy volunteers. The carriage of adhesive *E. coli* may be more related to site of inflammation than type of IBD. }" "Adhesive E Coli in Inflammatory Bowel Disease"

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"P P 60 1446" P 60 1446 **Immunoquantitation of a Novel Endothelial Cell-Specific Surface Antigen in Inflammatory Bowel Disease**

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Department of Medicine B, University of Münster, Münster, Germany

The aim of the present study was to investigate in detail the immunohistochemical properties of the two endothelial specific markers 1F10 (continuous endothelia) and MS-1 (discontinuous endothelia) in bowel tissues of patients suffering from chronic inflammatory bowel disease (IBD). Immunohistochemical techniques were employed to study the morphology and phenotypic expression of these two proteins in routinely processed bowel tissues from 27 patients with Crohn's disease (CD), 18 patients with ulcerative colitis (UC), and from 20 normal controls. All patients with IBD and controls showed a low to moderate 1F10 immunohistochemical staining restricted to the lamina propria and submucosa. In contrast to UC patients and healthy controls, 1F10 immunoreactivity was strongly *de novo* expressed in the muscularis propria of the small and large bowel in CD patients regardless of the histological severity of the inflammatory process. Neither in Crohn's disease nor in ulcerative colitis we observed immunoreactivity for MS-1 on endothelia surfaces. From this we conclude that endothelia in patients with IBD do not undergo metaplasia. The high immunoreactivity of 1F10 antigen in the muscularis propria in CD indicates a state of topical immunological activation and may be important in the maintenance of chronic inflammation by facilitating leukocyte migration into sites of Crohn's disease involvement. Further studies of the factors controlling endothelial cell differentiation in the bowel of CD patients may help to explain the features observed in this study. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } "Immunoquantitation of a Novel Endothelial Cell-Specific Surface Antigen in Inflammatory Bowel Disease"

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"P P 60 1447" P 60 1447 **Prothrombotic State in Inflammatory Bowel Disease (IBD)** G. Ciancio<sup>1</sup>, B. Mallardi<sup>1</sup>, G. Macri<sup>1</sup>, E. Surrenti<sup>1</sup>, M.T. Passaleva<sup>1</sup>, E. Chiarantini<sup>2</sup>, R. Abate<sup>2</sup>, G. Salvadori<sup>1</sup>, C. Surrenti<sup>1</sup>

Gastroenterology Unit, Institute of Internal Medicine and Cardiology, University of Florence, Florence, Italy Patients with Crohn's disease (CD) and Ulcerative Colitis (UC) show an increased risk of thromboembolic events. *Aims* were to investigate parameters of hemostatic function and the positivity of antiphospholipid antibodies (aPL) in IBD patients. *Patients and methods*: 22 consecutive patients affected by UC (13 M., 9 F; mean age 43.50) and 12 affected by CD (5 M, 7 F; mean age 49.59) were studied and compared with 20 healthy control subjects. In UC patients the disease activity was evaluated by Rachmilewitz index and in CD patients by Crohn's disease activity index (CDAI). In all patients platelet count (PLT), PT, aPTT, Fibrinogen (FBG), antithrombin (AT), protein C (PC), Protein S (PS), factor XIII (FXIII), plasminogen activator inhibitor (PAI), spontaneous platelet aggregation in platelet-rich plasma (PRP-SPA) and in whole blood (WS-SPA) and aPL were evaluated. The parameters of hemostatic function were analyzed by analysis of variance and the frequency of aPL by Fisher exact test. *Results*: In both UC and CD patients PLT, FBG were significantly increased ( $p < 0.05$ ), FXIII was significantly decreased ( $p < 0.05$ ) compared with controls. UC patients showed a higher aPL positivity ( $p < 0.05$ ) than CD patients in comparison to control group. The increase of PLT and FBG was related to the activity of disease; on the other hand the decrease of FXIII and the positivity of aPL was not related to the disease activity or to the site of lesions. In IBD patients, PAI, PRP-SPA, WS-SPA, PC, PS and AT didn't show a significant difference vs. the control group. For what concerns hemostatic parameters were not statistically significant differences in UC and CD. *Conclusion*: Our data suggest that 1) In both UC and CD patients, the only alteration of hemostatic function was a decrease of FXIII levels. 2) In all patients there was no significant relationship between hemostatic parameters and disease activity. 3) aPL were significantly increased in UC in comparison with CD. } "Prothrombotic State in Inflammatory Bowel Disease (IBD)"

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"P P 60 1448" P 60 1448 **ANCA in Ulcerative Colitis (UC): Comparison between ANCA + and ANCA { - } Patients and Longitudinal Follow Up**

\*E. Louis, S. Demoulin, A. Lamproye, D. Franchimont, J. Salmon, P. Mahieu, J. Belaiche

Departments of Gastroenterology and Immunology, CHU Sart Tilman, 4000 Liège, Belgium Positivity for ANCA has been described in about 65% patients with UC. The significance of this positivity is still unknown. The aim of our study was first to compare ANCA + and ANCA { - } UC patients on the basis of clinical characteristics and second to follow longitudinally the patients to assess the reproductibility of the results over time. *Patients and methods:* Forty seven consecutive UC patients, with ANCA determination, were included in the study. ANCA positivity was determined using an immunohistochemical method. *Results:* There were 24 ANCA { - } and 23 ANCA + patients. There was no significant difference between these 2 groups in duration of the disease or in smoking. The comparison between these 2 groups showed no significant difference in location and evolutivity (assessed by need for surgery and immuno-suppressive treatment) of the disease. The frequency of extraintestinal manifestations was however significantly higher in the ANCA + group (35% – including 8.5% of sclerosing cholangitis- vs 8%;  $p < 0.05$ ). Twenty out of the 47 patients had several successive tests for ANCA. Five of them showed a change in their ANCA status. These changes were not consistently associated with a modification in location, systemic manifestation, activity or treatment of the disease. *In conclusion,* 1) The ANCA status may determine subgroups of the disease with different risk of systemic manifestations 2) some patients (25%) had a change in ANCA status over time, but this was not associated with any clinical feature. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "ANCA in Ulcerative Colitis (UC): Comparison between ANCA + and ANCA – Patients and Longitudinal Follow Up"

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"P P 60 1449" P 60 1449 **IgM Specific Anti-Measles Antibodies in Patients with Inflammatory Bowel Disease (IBD)**

\*C. Goumas, A. Georgouli<sup>1</sup>, C. Nasopoulos, A. Zacharopoulos, D. Soutos, P. Golemati<sup>1</sup>, D. Katsaros

Gastroenterology Dept, Red Cross Hospital, Athens, Greece

<sup>1</sup> Microbiology Lab., "Saint Sabbas" Hospital, Athens, Greece IgM specific anti-measles antibodies were found significantly increased in patients with IBD, especially in Crohn's disease (CD). A persistent measles infection has been implicated in the pathogenesis of Crohn's disease, via a chronic granulomatous vasculitis process, but data from other studies are not consistent with this hypothesis. *The aim* of this prospective study was to assess a possible causal relationship between measles infection and IBD, by titrating serum IgM specific anti-measles antibodies in patients with exacerbated IBD. *Materials-Methods:* Sixty nine (69) patients (40 males and 29 females, mean age 48.7 years) with exacerbated IBD were included in this study. Forty four (44) patients suffered from ulcerative colitis (UC) and 25 from Crohn's disease. The diagnosis of the exacerbated IBD had been established by endoscopy, X-ray, histology and determination of UCAI (> 20) and CDAI (> 150). The control group comprised of 60 healthy blood donors. Sera of all patients and controls were examined for the presence of IgM and IgG specific anti-measles antibodies. The indirect immunofluorescent method was used for antibody detection. Titers of IgM antibodies in excess of 1:80 were considered indicative of persistent measles infection. *Results:* High IgM antibody titers (> 1:80) were detected in none of our patients and controls. IgG antibodies in titer greater than 1:80 were detected in 81.8% (36/44) of UC, 88.0% (22/25) of CD patients and 85.0% (51/60) of controls (p > 0.10; NS). *Conclusion:* High titers of IgM specific anti-measles antibodies were not detected in patients with exacerbated UC or CD. A causal relationship between persistent measles infection and IBD is not likely. Intestinal disorders: IBD, etiology and genetics Immunology and microbiology: GI infections in adults } "IgM Specific Anti-Measles Antibodies in Patients with Inflammatory Bowel Disease (IBD)"

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## "P P 60 1450" P 60 1450 **Faecal Calprotectin Concentration as a Marker of Disease Activity in Inflammatory Bowel Disease**

\*S.K. Bunn, A. Sim, D.E. Goudie, P. Clohessy, W.M. Bisset, B.E. Golden

Department of Child Health, University of Aberdeen, United Kingdom A non-invasive test to quantify bowel inflammation is greatly needed in the management of Inflammatory Bowel Disease (IBD). Calprotectin is an abundant neutrophil protein, which is very stable in faeces and is significantly increased in adults with IBD [1]. The aim of this study was to investigate whether faecal calprotectin is raised in children with IBD and to determine its usefulness as a marker of disease activity. Faecal calprotectin was estimated in 45 spot samples of faeces, collected from 29 children receiving treatment for IBD, (5.0 to 15.2 years) and was compared to a group of 25 children and 31 adult controls. The level of disease activity was scored by the clinician who was blind to the calprotectin results. Faecal calprotectin concentration was determined by an ELISA. The data was expressed as mean – SD, the disease groups were compared using an unpaired T test. In children with Ulcerative Colitis (8992 – 5591 ug/l,  $p = 0.001$ ) and Crohn's disease (10499 – 6746 ug/l,  $p < 0.001$ ) the stool calprotectin concentration was significantly increased over control range (3056 – 2303 ug/L). The mean faecal calprotectin level rose significantly with increasing severity of disease ( $p = 0.027$ ). In children felt clinically to be in remission, 40% with ulcerative colitis (UC) and 58% with Crohn's disease had stool calprotectin concentrations > 95th centile of the control range. Additionally, one newly presented child with UC had eight spot stool samples collected longitudinally. His faecal calprotectin concentration decreased from 500,000 ug/L before treatment to 6846 ug/L when clinically in remission two months later (within control range). The elevated faecal calprotectin in patients with IBD is likely to reflect the severity of disease activity and indicates that many children have active disease even when free of symptoms. Although further investigation is required, these preliminary studies illustrate the potential of this test for the screening and monitoring of IBD.

Reference: Fagerhol et al. Scand J Gastroent 1992, 27, 793–8 Intestinal disorders: IBD diagnosis, monitoring } "Faecal Calprotectin Concentration as a Marker of Disease Activity in Inflammatory Bowel Disease"

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"P P 60 1451" P 60 1451 **Antineutrophil Cytoplasmic Antibodies in Estonian Patients with Inflammatory Bowel Disease**

\*K. Kull, R. Salupere, R. Uibo, V. Salupere

Department of Internal Medicine, University of Tartu, Estonia

Department of Immunology, University of Tartu, Estonia Antineutrophil cytoplasmic antibodies (ANCA), originally found to be associated with vasculitis, have been reported to be present in inflammatory bowel disease (IBD). The ANCA staining pattern in IBD is most often perinuclear (p-ANCA). The presence of ANCA might prove the evidence of possible involvement of autoimmune mechanisms. However, the antigen to which those antibodies are reactive is not yet known. The aim of the study was to determine the prevalence and pattern of ANCA in patients with inflammatory bowel disease in Estonia. Enzyme-linked immunosorbent assay (ELISA), using myeloperoxidase, proteinase-3 and lactoferrin as antigens, was performed to characterize the antigen specificity. 64 sera of the patients with ulcerative colitis (UC), 16 with Crohn's disease (CD), 23 with irritable bowel syndrome and 87 healthy persons have been studied. Sera were analyzed for the presence of ANCA by the indirect immunofluorescence on ethanol-fixed neutrophils using fluorescein labelled anti-IgG. ELISA for specific ANCA was performed using antigens mentioned. ANCA were detected in 31/64 (48%) patients with UC, 3/16 (19%) patients with CD and 4/110 (4%) in controls. The immunofluorescence staining were mostly perinuclear (p-ANCA), but at the same time, ANCA with cytoplasmic pattern (c-ANCA) were also revealed. There was no correlation between ANCA and the duration or extent of the ulcerative colitis and Crohn's disease. In ELISA with purified proteinase-3, lactoferrin and myeloperoxidase only a few sera elicited binding above the normal range. Although, the prevalence of UC and CD in Estonia is much lower than in Scandinavia and Northern Europe, there seem to be no differences in immunological features. ANCA occur significantly more often in ulcerative colitis than in Crohn's disease. The ANCA pattern is predominantly perinuclear. The antigenic target for ANCA needs to be determined in further studies. Intestinal disorders: IBD, basic Immunology and microbiology: Host defense mechanisms } "Antineutrophil Cytoplasmic Antibodies in Estonian Patients with Inflammatory Bowel Disease"

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"P P 60 1452" P 60 1452 **Epidemiology of Inflammatory Bowel Disease (IBD) in the Province of Liege: Study of Subjects Older Than 60 Years** O. Plomteux,

\*D. Franchimont, E. Louis, P. Latour, J. Belaiche

CHU of Liège IBD unusually may occur in subjects older than 60 years. The aim of this work was first to determine the incidence of Crohn's disease (CD) and ulcerative colitis (UC) in a population older than 60 years (group 1), and second, to compare their clinical features to the ones in a population younger than 60 (group 2), with IBD occurring during the same period. *Patients and methods:* Prospective study of the new IBD cases occurring in the province of Liège between 1/6/93 and 31/5/94. Incidence in groups 1 and 2 were calculated from the whole population for the considered age. *Statistical analysis:* Chi<sup>2</sup> test *Results:* 104 new cases of IBD were recorded during the study. In group 1, there were 25 new cases (24%), including 10 CD (40%), 11 UC (44%) and 4 undetermined colitis (18%). In group 2, there were 79 (76%) new cases, including 46 CD (58%), 25 UC (32%), and 8 undetermined colitis (10%). In group 1, mean age at onset was 67 years for CD and 67.5 for UC. The incidences were 4.5 and 5 over 10<sup>5</sup> for CD and UC respectively. This was different from group 2, where the incidence of CD was significantly higher than the one of UC: 5.8 and 3.2 over 10<sup>5</sup> respectively ( $p < 0.02$ ). Sex ratio (F/H) was 1.7 and 1.5 for CD, and 0.6 and 1.2 for UC, in group 1 and 2 respectively. There was no significant difference in the clinical features (symptoms, location, systemic manifestations) at onset for both diseases. *In conclusion,* In the province of Liège, 1) the incidence of IBD is as high after 60 years of age as in younger subjects; 2) these 2 groups do not have different clinical features at onset. *Clinical practice:* Epidemiology (non cancer) Intestinal disorders: IBD, etiology and genetics } "Epidemiology of Inflammatory Bowel Disease (IBD) in the Province of Liege: Study of Subjects Older Than 60 Years"

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## "P P 60 1453" P 60 1453 Value of Pathological Examination of the Colectomy Specimen to Predict the Outcome of Patients with IBD Limited to the Colon

\*M. L'e9mann, A. S'e9n'e9joux, A. Lavergne, P. Valleur, E. Sarfati, A. Galian, P. Bertheau, J.C. Rambaud, R. Modigliani

St-Louis and St-Lazare Hospitals, Paris, France In patients (pts) with IBD limited to the colon who need colectomy, distinction between Crohn's disease (CD) and ulcerative colitis (UC) may be of great importance before deciding the restorative procedure, especially ileo-anal anastomosis. Our aim was to study whether gross and microscopic findings on the colectomy specimen may predict the final outcome of the disease. *Methods.* From 1978 to 1993, 147 pts with IBD had total colectomy in our hospitals. Pts with extracolonic involvement before surgery were excluded (n = 46). The remaining 101 pts were followed after operation for a median of 5.3 yrs (3 mo to 15 yr). Pathological reports of colectomy specimens were reviewed and 12 histological criteria were analyzed in order to classify the pts as CD (when typical granuloma was found), probable CD, probable UC or indeterminate colitis (IC). Final diagnosis CD was based on the occurrence of extracolonic involvement (small bowel or anus) during the post-operative follow-up. *Results.* 22 out of the 101 pts were definitely classified as CD because of the occurrence of typical small bowel involvement (n = 8), anal lesions (n = 8), or both (n = 6). Extracolonic CD involvement occurred more frequently in pts with granuloma (7/10) compared with the other pts (15/91; P < 0.001); in contrast, the risk of extracolonic involvement was not significantly different between pts classified as probable CD (9/43), probable UC (3/33) and IC (3/15). Among the 12 histological criteria, only 2 were found, using a multivariate analysis (Cox model), to be significantly associated with a higher risk of extracolonic CD involvement: granuloma (RR = 4) and focal inflammation with intervals of normal mucosa (RR = 1.8). *Conclusion.* In pts without granuloma, the occurrence of extracolonic CD involvement after surgery is poorly predicted by the pathological examination of the colectomy specimen. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy } "Value of Pathological Examination of the Colectomy Specimen to Predict the Outcome of Patients with IBD Limited to the Colon"

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"P P 60 1454" P 60 1454 **Phosphoprotein Patterns of Intestinal Mucosa in Chronic Inflammatory Bowel Diseases** B. Schnabl,

\*C. Heilmann, C. Spamer

Dept. of Gastroenterology, Medical Centre, University of Freiburg, D-79106 Freiburg, Germany Protein phosphorylations/dephosphorylations play a fundamental and almost universal role in the regulation of cellular functions. Consequently, defective protein phosphorylation/dephosphorylation can give rise to a variety of disease states. This aspect has not yet been investigated in chronic inflammatory bowel diseases (IBD). Here we demonstrate and compare phosphoprotein patterns in normal and chronically inflamed intestinal mucosa of patients with ulcerative colitis (UC) or Crohn's disease (CD). *Methods:* Samples of colonic mucosa were obtained by endoscopic forceps biopsy from patients with normal mucosa (n = 11), UC (n = 9) or CD (n = 9). Homogenized tissue was incubated with [ $\gamma$ - $^{32}$ P]ATP under conditions allowing for endogenous Mg-dependent protein phosphorylation. Endogenous phosphatases were inhibited with microcystin-LR. Following second dimensional electrophoresis (SDE, isoelectric focusing followed by SDS-PAGE) phosphoprotein patterns were analysed with a PDI-Scanner or with PD QUEST image master software, following auto-radiography. *Results:* A total of 45 – 8 distinct phosphoproteins were detected in normal mucosa as compared to 42 – 5 in UC and 36 – 3 in CD. UC and CD mucosa differed in 35 and 28 phosphoproteins, respectively, from normal mucosa. Importantly, UC and CD mucosa differed in 35 phosphoproteins. Major differences were detected in phosphoproteins in the range of 120 to 70 kDa and 32.5 to 23 kDa at isoelectric points between pH 5.4 to 7.9. The nature and function of the various phosphoproteins and related protein kinases is unclear at present. *Conclusions:* The incubation of intestinal mucosa with [ $\gamma$ - $^{32}$ P]ATP resulted in endogenous phosphorylation of numerous proteins that could be detected in characteristic and reproducible patterns by second dimensional electrophoresis. The phosphoprotein patterns of normal, UC and CD mucosa exhibited extensive and characteristic differences, potentially providing a new diagnostic tool in the distinction of IBD. The potential role of impaired protein phosphorylation/dephosphorylation in the etiopathogenesis of IBD merits further investigations. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, basic } "Phosphoprotein Patterns of Intestinal Mucosa in Chronic Inflammatory Bowel Diseases"

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"P P 60 1455" P 60 1455 **Incidence of Inflammatory Bowel Disease (IBD) in the Puy-De-Dome Department of France in 1993–94**

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*Background:* The aim of this prospective epidemiologic study was to investigate the incidence of Crohn's disease (CD) and ulcerative colitis (UC) in this county, using the same methodology as the Nord-Pas de Calais region and to determinate whether a North-South gradient of IBD in France is real. *Methods:* From 01/01/93 to 31/12/94, each Gastroenterologist collected patients consulting for the first time with clinical symptoms compatible with IBD. Data were reported on a questionnaire by an interviewer practitioner. The final diagnosis of CD, UC was made in a blind manner by two expert Gastroenterologists and recorded as definite, probable, or possible diagnosis. *Results:* 197 new cases were identified: 135 (68.5%) IBD with 100 (74.1%) CD, 31 (23.0%) UC, 4 (2.9%) unclassifiable chronic colitis and 51 (25.9%) acute colitis; 11 (5.6%) cases were unclassified. The annual incidence rate per 10<sup>5</sup> was 8.35 for CD (9.6 for men and 7.1 for women) and 2.5 for UC (2.4 and 2.7). The highest age-specific incidence rate for CD was between 40–49 ans (15.3) and for UC between 80–89 ans (6.8). The sex-ratio F/M was 0.8 for CD and 1.2 for UC. The mean age at the time of diagnosis was 42.3 years for CD and 46.4 years for UC. The incidences rates for CD and UC, definite and probable, are respectively 4.8 and 2.5 in the North and 6.6 and 2.3 in this county. *Conclusions:* 1) These preliminary findings revealed a high incidence of IBD in this county, and close to the highest incidences in the world for CD. 2) The incidence rate in France for UC is lower than CD, contrary to the other countries of Northern Europe. 3) This study doesn't show any North-South gradient for CD. *Clinical practice:* Epidemiology (non cancer) Intestinal disorders: IBD, basic } "Incidence of Inflammatory Bowel Disease (IBD) in the Puy-De-Dome Department of France in 1993-94"

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"P P 60 1456" P 60 1456 **Prevalence of Helicobacter Pylori (H.p.) Infection in Inflammatory Bowel Disease (I.B.D.) — A Controlled Study** L.S. Sousa,

\*A.M. Santos, T.C. Macedo, A.S. Pinto, A.C. Sousa, J. Reis, M.G. Quina

Clinica Universit'elria de Medicina Interna e Gastreterologia, Hospital de Pulido Valente, Lisboa, Portugal

*Objectives* To evaluate H.p. prevalence in patients with IBD submitted to several therapeutical regimens. *Material and Methods* 60 patients were studied prospectively. 30 with Crohn's disease (CD), median age – SD (38.46 – 14.63); 30 with Ulcerative Colitis (UC), median age – SD (43.13 – 13.19). Results were compared to those obtained in 60 healthy volunteers (control group – CG). These groups were matched by age. H.p. status was evaluated as follows: 1) Urea – <sup>13</sup>C Breath Test (n = 53 patients + 60 volunteers from CG); 2) Urease and Histology of antral biopsies from gastric mucosa in dispeptic patients (n = 11). Statistic analysis was carried out by { ? }<sup>2</sup> and Kruskal-Wallis tests. *Results* Prevalence of H.p. was as follows: IBD group = 56.6% (CD = 50% and UC = 63.3%) and CG = 62% (no difference between groups). Duration, extension, clinical activity or drug therapy (Metronidazol, Sulphasalazine, Mesalazine, Steroids and Azathioprine) were not correlated to H.p. status in the IBD group. When comparing H.p. status between operated (n = 22) and non-operated patients, a significant decrease in the prevalence of H.p. was verified in operated patients (31.8%) p = 0.003. *Conclusions* 1) Prevalence of H.p. infection was similar in IBD sub-groups and also between these and CG. 2) A significant decrease was shown in patients with previous surgery. These patients were submitted to intensive drug treatment (several antimicrobial agents) and had medical intractability. 3) In the IBD group no other factors were detected that may influence H.p. status. Oesophageal gastric duodenal disorders: Helicobacter Pylori Intestinal disorders: IBD, therapy }" "Prevalence of Helicobacter Pylori (H.p.) Infection in Inflammatory Bowel Disease (I.B.D.) / A Controlled Study"

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"P P 60 1457" P 60 1457 **General and Cancer Specific Mortality in the Follow-Up of a Cohort of IBD Patients in Florence**

\*D. Palli<sup>1</sup>, G. Trallori<sup>2</sup>, G. Masala<sup>3</sup>, C. Saieva, G. Bardazzi<sup>2</sup>, M. Milla<sup>2</sup>, A.G. Bonanomi<sup>2</sup>, F. Cimoli<sup>1</sup>, G. d'Albasio<sup>2</sup>, F. Pacini<sup>2</sup>, A. Amorosi<sup>4</sup>

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<sup>3</sup> Sez. Distaccata IST-CSPO, Firenze

<sup>4</sup> Ist. Anat. Patologica, Univ. di Firenze, Az. Osp. CAREGGI, Firenze A population-based study identified all the patients with a diagnosis of ulcerative colitis (UC) or Crohn's disease (CD) resident in the Florence area in the period 1978–1992. Overall, 920 patients were included in the follow-up since the date of diagnosis, January 1st 1978 (for cases diagnosed before the start of the study) or the date of migration into the area until death or end of study period (January 1st 1996). Approximately 9,000 person-years were available for observation, with a median follow-up of 9.7 years. A linkage with local town offices and the Regional Mortality Registry allowed the identification of 64 deaths and the retrieval of individual death certificates. Expected deaths were estimated on the basis of 5-year age group, gender and calendar year specific mortality rates of the general population in order to calculate Standardized Mortality Ratios (SMR) for overall mortality and selected groups of causes. Specific cancer sites were also considered; 95% confidence intervals (CI) were calculated assuming a Poisson distribution. General mortality was significantly lower than expected in UC (SMR 0.7; 95% CI: 0.5–0.9), due to a reduced number of cardio-vascular deaths. Smoke-related causes of death were also reduced in UC, in particular cancers of the respiratory tract (which tended to be increased among CD patients). Overall, there was only a limited evidence of an increased mortality for colorectal cancer (significant for rectal cancer in UC patients: SMR 5.0; 95% CI 1.0–14.6). A non significant excess of emolymphopoietic malignancies was observed Deaths due to non malignant gastrointestinal causes were increased among CD patients (SMR 3.9; 95% CI 1.1–10.0), but not in UC. These preliminary results suggest a specific mortality pattern for italian IBD patients. Clinical practice: Epidemiology (non cancer) Intestinal disorders: IBD, basic Oncology, specific: Colon, rectum } "General and Cancer Specific Mortality in the Follow-Up of a Cohort of IBD Patients in Florence"

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## "P P 60 1458" P 60 1458 The Polymorphism of Motilin Gene Differentiates Genetic Subgroups of Patients with IBD

\*V. Annese, G. Lombardi, A. Piepoli, F. Perri, L. Bisceglia, P. Gasparini, A. Andriulli

Gastroenterology and Human Molecular Genetic, e "CSS", I.R.C.C.S. Hospital, San Giovanni Rotondo, Italy

Several lines of evidence suggest the importance of genetic factors, such as the HLA class II genes, in the susceptibility of ulcerative colitis (UC) and Crohn's disease (CD). We have recently defined the subchromosomal localisation of the motilin gene very close to the HLA-DQ $\alpha$  locus (Hum Genet 1994; 94: 671). *Aim* of the study was to investigate DNA polymorphisms of the motilin gene in a population of inflammatory bowel disease patients. *Methods*: 88 patients with firm diagnosis of UC (49) and CD (39) were studied. Control values were obtained by 60 unrelated blood donors. Anti-neutrophil cytoplasmic antibodies (ANCA) were identified by indirect immunofluorescence (perinuclear pattern). PCR of the second exon of motilin gene was performed to study the different alleles (1 and 2) frequency of motilin gene. *Results*: are summarised in the table. Patients with CD had a significant increase of the allele 2 frequency ( $p < 0.03 - \chi^2$ ). After stratifying patients according to their ANCA reactivity, ANCA-negative CD patients did not differ from healthy subjects, while ANCA-positive subjects had a striking increase of allele 2 frequency ( $p < 0.02$ ). N. Allele 1 Allele 2 pControls 60 42% 58% UC 49 30% 70% n.s CD (total) 39 27% 73%  $< 0.03$  CD ANCA+ve 6 8.3% 91.7%  $< 0.02$

*Conclusions*: These results provide further evidence for genetic heterogeneity in patients with CD. It is also intriguing to hypothesize that the polymorphism of the motilin peptide produced by the nucleotide change might explain some of the intestinal motor abnormalities we found in CD patients (Gastroenterology 1993; 104: A470). Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Hormones and receptors: Molecular biology }

"The Polymorphism of Motilin Gene Differentiates Genetic Subgroups of Patients with IBD"

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"P P 60 1459" P 60 1459 **Prevalence of Antineutrophil Cytoplasmic Antibody in Unaffected Relatives of IBD Patients** G. Napolitano, A. Piepoli,

\*V. Annese, F. Perri, M. Astegiano, G. Iaquinto, P. Conoscitore, R. Clemente, S. Cucchiara, A. Andriulli

Departments of Gastroenterology and Pediatrics, San Giovanni Rotondo, Torino, Avellino, Napoli, Italy Presence of ANCA has been suggested as a genetic marker of disease susceptibility in ulcerative colitis (UC). However, a wide difference of their prevalence (3–30%) in unaffected first degree relatives has been reported. *Aim:* To determine the prevalence of ANCA in unaffected first degree relatives in families in which more than one member was affected with UC or Crohn's disease (CD). *Method:* 22 families which included 47 affected members (28 UC and 19 CD patients) and 94 unaffected first degree relatives were studied. ANCA reactivity was investigated by indirect immunofluorescence also in 169 consecutive blood donors and 275 patients without family history (195 UC and 80 CD). *Results:* are given in the table (values of p obtained with Fisher test). No significant difference of ANCA reactivity was found between patients with or without family history. Controls UC CD Relatives UC CD Familial Familial Sporadic Sporadic ANCA+ve 3.5% 31% 5% 1% 29% 7.5% p (vs Controls) < 0.001 n.s n.s < 0.001 n.s. There was no evidence of clustering of antibodies in particular families. In four out of seven families in which both UC and CD disease coexisted, all the affected members were ANCA negative. *Conclusions:* ANCAs are associated with ulcerative colitis. Their presence is neither increased in patients with family history nor in their unaffected first degree relatives. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics } "Prevalence of Antineutrophil Cytoplasmic Antibody in Unaffected Relatives of IBD Patients"

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## "P P 60 1460" P 60 1460 The Presence of ANCA Identifies Only a Weak Clinical Heterogeneity in Patients with IBD

\*V. Annese, G. Lombardi, G. Piepoli, F. Perri, N. Caruso, A. Andriulli

Gastroenterology, "CSS", IRCCS Hospital S. Giovanni R., Italy Antineutrophil cytoplasmic antibodies (ANCA) have been suggested as a potential marker of genetic heterogeneity in IBD. However, their relation to different clinical features of ulcerative colitis (UC) and Crohn's disease (CD) is unclear. *Aim:* To investigate a possible relation between ANCA reactivity and clinical characteristics of the patients. *Methods:* 237 UC (mean age 42 yrs, 147 male) and 94 CD patients (mean age 35 yrs, 53 male) were studied. The determination of ANCA reactivity was performed by indirect immuno-fluorescence also in 169 consecutive unrelated blood donors. Patients were characterized by clinical features: gender, age at onset, disease location and severity (Truelove-Witts and CDAI scores) need for surgery, pouchitis, extra-intestinal manifestations, clinical course (remission or frequent relapses [ $\geq 2$ /year]), therapy (need of steroids, need for immunosuppression). *Results:* ANCA positivity was infrequent in our patients being found only in 66 (28%) UC and 8 (8.5%) CD respectively. ANCA were found also in 2 (1.2%) blood donors. After stratifying patients according to their ANCA reactivity, the majority of clinical features were equally distributed between the two groups. ANCA reactivity was significantly more frequent only in UC patients using steroids (34% vs 19%;  $p = 0.019$ ) and in CD patients with colonic localisation (26% vs 1.5%;  $p = 0.009$ ). Moreover, a slight decrease of incidence was present in UC patients in remission (21% vs 46%;  $p = 0.047$ ). However, ANCA positivity had only a 32% accuracy in differentiating UC from CD colitis, and a 51% accuracy in predicting UC patients with steroids need. *Conclusions:* ANCA may well represent a marker of genetic heterogeneity. However, on clinical ground, the correlation with clinical features is rather weak with a poor accuracy and a low negative predictive value. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "The Presence of ANCA Identifies Only a Weak Clinical Heterogeneity in Patients with IBD"

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## "P P 60 1461" P 60 1461 **Antioxidant Enzymatic Systems in Inflammatory Bowel Disease**

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**Introduction:** The transmembrane redox enzymatic system has three main functions: growth control, reducing transferrin iron III and antioxidant actions through the recyclization of ascorbic acid, vitamine E and ubiquinone, and lipid hydroperoxide (HPR) inactivation. Oxygen free radicals have probably a role in either producing or amplifying the inflammatory response in Inflammatory Bowel Disease (IBD). **Aim of Study:** Activities of several enzymatic parameters of oxidative stress were measured in erythrocyte namely transmembrane reductase (RTM), methemoglobin reductase (RMetHb), and acid phosphatase (ACP1) and in plasma the epinephrine oxidasic activity (EO) in order to find out any difference between controls and IBD patients, ulcerative colites (UC) or Crohn's Disease (CD)), between male and female patients and state of disease. **Material and Methods:** 37 patients with IBD were studied, 16 male and 21 female, 18 with UC and 19 with CD. Age range between 17 and 72 years. A control group of 36 for RTM, 174 for RMetHb and 55 for ACP1 and 25 for EO, age and sex matched was used as comparison. Diagnosis of UC and CD was based on clinical, radiological, endoscopic and histological grounds. The activity of the RTM was assayed by the technique of Orringer and Roer modified by us; it is expressed in mmol/l cell/hour of ferricyanide reduced by intact erythrocyte. Other enzymatic systems were measured by standard spectrophotometric methods. The statistical analysis was done by parametric methods. **Results:** Patients with IBD showed RTM activity 4.625 – 2.079 while the controls showed 6.013 – 3.622 (difference statistical significant:  $p < 0.05$ ). No difference was found in men, while in female the mean values of 4.417 – 2.183 was statistically significant compared with female controls (7.145 – 4.510/ $< 0.05$ ). A non statistically significant difference was found neither between UC and CD patients, nor between the active or quiescent phases of the disease. Both RMetHb and ACP1 were statistically significant when compared with controls (17.62 – 4.87 in IBD patients vs 13.87 – 7.165 in controls  $p \{ \backslash \} 0.05$ ), (99.94 – 41.83 in IBD patients vs 307.2 – 154.7 in controls  $p \{ \backslash \} 0.001$ ), respectively. No statistically significant difference was found in EO. **Conclusions:** The results suggest an increased production of oxygen free radicals which can induce tissue injury. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, basic }" "Antioxidant Enzymatic Systems in Inflammatory Bowel Disease"

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## "P P 60 1462" P 60 1462 **Antiendotelial Cell Antibodies in IBD: A Marker of Vascular Injury?**

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<sup>1</sup> Clinica Medica I, Policlinico Umberto I, Roma, Italy Mesenteric vasculitis has been reported as a possible pathogenic mechanism in Crohn's disease (CD) [1]. Moreover it is well known that vascular endothelium plays an active role in inflammatory and immune processes through expression of endothelial adhesion molecules and of class I and II HLA molecules, cytokine production and expression of procoagulant activity. Antiendothelial cells antibodies (AECA) have been detected in various autoimmune vasculitides and there is some evidence that these antibodies can mediate endothelial injury and correlate with disease activity [2]. Recently AECA have been detected in inflammatory bowel disease (IBD) [3] but their clinical significance is still unknown. Aim of the present study was to assess the prevalence of AECA in IBD as compared to normal controls. Sera of 70 patients with IBD (47 UC; 23 CD) and 40 normal controls were tested for AECA by ELISA on unfixed human umbilical vein endothelial cells. Sera positive for AECA were found in 20/70 (28.5%) IBD patients and in 3/40 (7.5%) controls ( $p < 0.01$ ). No statistical difference has been observed in the prevalence of AECA in UC (13/47; 27.3%) as compared to CD (7/23; 30.4%).

The presence of AECA showed no correlation with age, sex, disease duration, disease extent and disease activity. However a higher prevalence of AECA was observed in UC patients treated with steroids as compared to patients treated with 5-ASA alone (54% vs 18%;  $p < 0.05$ ). The presence of AECA in about 30% of IBD patients suggests that endothelial damage can have a pathogenic role and provides further evidence of disturbed immunity in IBD. The higher prevalence of AECA in UC patients treated with steroids may reflect an association with a more severe disease requiring steroid treatment. This observation needs to be confirmed by prospective studies.

Reference: Wakefield AJ et al *Gastroenterology* 100 1279 1991

Leung DYM et al *J Clin Invest* 77 1428 1986

Sawyer AM et al *Dig Dis Sci* 39 1909 1994 Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD diagnosis, monitoring } "Antiendotelial Cell Antibodies in IBD: A Marker of Vascular Injury?"

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## "P P 60 1463" P 60 1463 **Leukery in Inflammatory Bowel Disease; A Test in the Assessment of Disease Activity**

\*F. Hamsioglu, A. Dobrucali, N. Bagatur, A. \c7elik, M. Tuncer, K. Bal, H. Uzunismail, I. Yurdakul, E. Oktay

Gastroenterology Section, Internal Medicine Cerrahpasa Medical Faculty, University of Istanbul, Istanbul-Turkey Assessment of disease activity is very important in the management and follow-up of the patients with inflammatory bowel disease (IBD). In spite of many efforts relying on clinical and laboratory parameters, there is still a lack of an inexpensive, rapid and convenient method in the evaluation of the IBD severity. In this study we evaluated leukery phenomenon manifested as an aggregation of leucocytes in citrated whole blood in the assessment of the IBD activity. We studied 8 Crohn and 17 Ulcerative Colitis (UC) patients in various disease activities, Crohn Disease Activity Index (CDAI) described by Pam van Hees, and Ulcerative Colitis Activity Index (UCAI) described by Mitsuru Seo were used. We performed endoscopy, ESR, CRP and albumin measurements, whole blood count and leukery to each patient. As a control group we used 30 age and sex matched healthy volunteers with no evidence of any inflammation. In all the IBD patients leukery values were significantly elevated. The mean leukery value in control group was  $3.33 \pm 2.6$ , in UC  $20.58 \pm 5.49$ , and in Crohn  $19.51 \pm 5.11$ . Moreover the leukery test could effectively discriminate between various grades of disease activity. Using correlation analysis we found out that leukery was the most accurate test in differentiation between various inflammatory states of IBD. Leukery v UCAI  $r = 0.89$   $p < 0.0001$ , CRP v UCAI  $r = 0.264$   $P = 0.305$ , ESH v UCAI  $r = 0.5691$   $p = 0.017$ , Endoscopy v UCAI  $r = 0.6804$   $p = 0.003$ , Histology v UCAI  $r = 0.6804$   $p = 0.003$ , Leukery v CDAI  $r = 0.7857$   $p = 0.021$ , CRP v CDAI  $r = 0.4286$   $p = 0.289$ . ESH v CDAI  $r = 0.0714$   $p = 0.867$ . This study has shown that the leukery this very rapid and economical test is the best indicator in the assessment of the IBD activity. It is obviously superior to other acute phase reactants, and It is even more accurate than endoscopy score defined by Baron and histology scores defined by Truelove. Intestinal disorders: IBD diagnosis, monitoring } "Leukery in Inflammatory Bowel Disease; A Test in the Assessment of Disease Activity"

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"P P 60 1464" P 60 1464 **Inflammatory Bowel Disease in People of Afro-Caribbean Descent**

\*N.I. McNeil, LONDON IBD Forum

Ealing Hospital, Southall, UK Inflammatory bowel disease had been considered uncommon in immigrant populations in the UK, until studies in Leicester found a high incidence of ulcerative colitis in people of Indian origin. Early studies in Afro-Caribbean immigrants described Crohn's disease only. A postal questionnaire to all doctors registered with the London IBD Forum asked for details of patients of Afro-Caribbean origin having inflammatory bowel disease. Twenty one patients were identified, 13 being female. Eleven patients were born between 1960 and 1969, and 14 out of 18 born in the United Kingdom. Thirteen patients were aged under 30 at the time of diagnosis. Twelve patients had ulcerative colitis (6 total) with only 6 having Crohn's disease. 2 cases were classified as indeterminate colitis. This survey has established that in people of Afro-Caribbean origin: ulcerative colitis is more common than Crohn's Disease. The majority of patients were born in the UK and the disease started at an early age. Immigrants from the Indian subcontinent also have ulcerative colitis more frequently than Crohn's Disease. However inflammatory bowel disease is mostly diagnosed in the immigrant generation with a mean interval of 11 years after arrival in the UK. This survey has demonstrated differences in the occurrence of inflammatory bowel disease that may encourage research into environmental factors in their aetiology. Intestinal disorders: IBD, etiology and genetics Clinical practice: Epidemiology (non cancer) } "Inflammatory Bowel Disease in People of Afro-Caribbean Descent"

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"P P 60 1465" P 60 1465 **Quality of Life and Physical Functioning are Different in Crohn's Disease and Ulcerative Colitis** L. Neumann, L.R. Odes,

\*H.S. Odes, D. Buskila

Departments of Epidemiology and Gastroenterology and Rheumatic Diseases Unit, Soroka Medical Center and Ben Gurion University, Beer Sheva, Israel Crohn's Disease (CD) and Ulcerative Colitis (UC) are chronic, debilitating diseases; controversy surrounds their impact on patients' functioning. The aim of this study was to assess and compare the Quality of Life (QOL) and the Physical Functioning of patients with CD and UC. *Methods:* Patients with CD and UC attending consecutively at the Gastroenterology Out-Patient Clinic were evaluated using the Flanagan-Burckhardt 16-item QOL questionnaire (a 7-point scale, where 1 = highly dissatisfied and 7 = highly satisfied) and the Burckhardt 10-item Fibromyalgia Impact Questionnaire (FIQ, a 4-point scale, where 0 = best and 3 = worst functioning). Data were calculated as mean – SD. *Results:* The response rate was 98%. There were 41 CD and 72 UC patients; their ages (43.8 – 14.5, 41.8 – 16.0 yr.), M/F ratio (0.64, 0.89), educational status, percentage working (46%, 47%), mean disease duration (6.8 – 5.3, 8.8 – 8.5 yr.), disease activity indices, and drug treatments were comparable. The QOL of CD patients (5.9 – 1.0) was significantly worse than UC patients (6.3 – 0.6,  $p < 0.01$ ). Specifically, CD patients were less satisfied with relationships with relatives ( $p < 0.025$ ), relationship with spouse ( $p < 0.001$ ), active recreation ( $p < 0.025$ ) and independence ( $p < 0.001$ ). The QOL of 20 CD patients who had undergone surgery (6.0 – 0.9) was not different from 21 CD patients who had not had surgery (5.7 – 1.1). Physical Functioning was worse in CD (0.8 – 0.8) than UC patients (0.4 – 0.6,  $p < 0.005$ ). In particular, the items on physical functioning ( $p < 0.005$ ), ability to do the job ( $p < 0.01$ ) and fatigue ( $p < 0.002$ ) were worse in CD. *Conclusions:* While QOL and Physical Functioning are impaired in both CD and UC, the deficit is appreciably greater in CD patients. This difference cannot be attributed to the demographic or clinical characteristics which were similar in CD and UC. Greater recognition of these impairments will alter the clinical approach to these patients. Intestinal disorders: IBD diagnosis, monitoring } "Quality of Life and Physical Functioning are Different in Crohn's Disease and Ulcerative Colitis"

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"P P 60 1466" P 60 1466 **Computerized Clinical Guidelines in Inflammatory Bowel Disease (IBD)** E. Ricci,

\*G. Rocca, V. Giura, M. Ribotto, R. Sostegni, M. Astegiano, S. Greco, M.T. Fiorentini, M. Rizzetto, A. Pera

Dipartimento di Gastroenterologia, Ospedale Molinette, Torino, Italia *Purpose* HOLMES is an hybrid artificial intelligence system that integrates three software tools: a) an Expert System b) an Hypertext c) Computer based training. The aims of this Windows 95 based environment are: 1) Interactive teaching and training of practical strategies in IBD related problems for students or practicing physicians 2) Patient specific clinical guidelines for medical decision support in the diagnosis and treatment of suspected IBD 3) Assisted compilation of accurate Computerized Clinical Patient Record 4) Computer guided collection of relevant data in a specific data base. *Software* The medical knowledge of the system is based on the practical experience of gastroenterologist collected by the Delphi's method in a national survey, epidemiological data and a systematic review of the medical literature (1980–1996). The knowledge base consists of production rules compiled in an expert system language developed in C and based on the Rete algorithm. The hypertext is highly integrated with the expert system and can explain the reason for each question and the line of reasoning followed in suggesting or confirming a diagnosis or treatment hypothesis. Patient data activate specific modular agents of the knowledge base and the conclusion of the rules fired suggest the best clinical decision or diagnostic hypothesis. In the first stage, data from medical interview, physical examination and simple laboratory tests are used to decide if the criteria for the hypothesis of IBD are satisfied and the differential diagnosis among ulcerative colitis, Crohn's disease and indeterminate colitis is calculated by the OMGE score. Parallel processing of the same data is used for ongoing differential diagnosis and for the calculation of all the important validated severity scores. Treatment guidelines for Crohn's disease are based on the clinical pattern, global evaluation of the patient and severity scores. Treatment of ulcerative colitis is based on severity scores and extension of the disease. In 50 patients affected by IBD the diagnostic accuracy of the program compared with the independent diagnosis made by expert clinicians and confirmed by 2 year follow up was 94% In 3 cases the correct diagnosis was suggested in the diagnostic list but not as the most probable. This promising preliminary results are being verified in a prospective multicentre study with different case-mix and differential diagnosis contexts. Intestinal disorders: IBD diagnosis, monitoring } "Computerized Clinical Guidelines in Inflammatory Bowel Disease (IBD)"

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## "P P 60 1467" P 60 1467 Which Factors Determine Bone Mineral Density in Inflammatory Bowel Disease?

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**Background:** Though low bone mineral density (BMD) is well recognised in inflammatory bowel disease (IBD), the relative roles of corticosteroids and systemic effect of inflammation are not well understood. **Patients and methods:** Three groups of IBD patients were studied. (1) Newly diagnosed patients – who had not received any treatment (15 Crohn's disease (CD), 12 ulcerative colitis (UC)); (2) Patients with intermediate duration of disease (median 3 years) – 14 CD patients (median 3.2 gm corticosteroids) and 10 UC patients (median 2.8 gm corticosteroids); (3) Patients with longstanding disease (median 8 years for CD and 7 years for UC) – 28 CD patients (median 9.5 gm corticosteroids) and 26 UC patients (median 8.6 gm corticosteroids). Lumbar 1–4 and forearm BMD was measured by dual energy X-ray absorptiometry. Records were kept of their smoking status, alcohol intake, bone fracture history, menstrual history, and experience of oral contraceptive pill and hormone replacement therapy. Body mass index was measured, Crohn's disease activity index and Powell-Tuck index (for UC) calculated, and their physical activities graded. **Results:** Both newly diagnosed and intermediate duration patients with CD had a significantly lower lumbar and forearm BMD Z-scores compared with patients with UC. However, in longstanding disease, both CD and UC patients were equally osteopenic. In UC, duration of disease ( $r = -0.78$ ) and cumulative steroid dose ( $r = -0.66$ ) were significantly correlated with BMD Z-scores. In CD however, low BMD Z-scores were not related to CDAI scores at the time of measurement. Biochemical parameters of bone metabolism were normal in all but one patient with CD. Multivariate analysis identified cumulative steroid dose as the variable associated with osteopenia in both CD and UC, with the duration of disease being an additional variable in CD. **Conclusion:** Osteopenia is a feature of newly diagnosed patients with CD, but not UC. With longstanding disease, the role of corticosteroids become more important, and it is the sole cause of osteopenia in UC. Intestinal disorders: IBD diagnosis, monitoring Nutrition: Nutrients and gut function } "Which Factors Determine Bone Mineral Density in Inflammatory Bowel Disease?"

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"P P 60 1468" P 60 1468 **Postprandial Splanchnic Hemodynamics as an Activity Index in Inflammatory Bowel Disease (IBD)**

\*D. Ludwig, S. Wiener, G. Jantschek<sup>1</sup>, E.F. Stange

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<sup>1</sup> Dept of Medicine II, University of L\u00fcbbeck, Germany Increased splanchnic flow has been shown in IBD by different methods, including Doppler flowmetry. The aim of the present study was the assessment of changes in the overall splanchnic circulation under baseline and stimulated conditions. Nineteen patients with ulcerative colitis (UC, mean age 37 (17–80) yrs.), 20 with Crohn's disease (CD, mean age 30 (20–40) yrs.) and 13 healthy controls (mean age 27 (23–28) yrs.) were evaluated by Doppler US. Mean flow (Vm) and the cross-sectional area of the superior mesenteric artery (SMA), inferior mesenteric artery (IMA) and portal vein (PV) were measured before and 30 minutes after a standardized meal (Fresubin liqu. 5 ml/kgbw). Flow measurements and the derived resistive index were analyzed with regard to clinical and endoscopic criteria of disease activity. Compared to controls baseline Vm of the SMA and IMA was significantly increased in active CD (SMA 67.8%, IMA 100.7%;  $p < 0.001$ ), UC (SMA 28.7%, IMA 353%;  $p < 0.01$ ) and inactive CD (SMA 35.7%, IMA 73.3%;  $p < 0.05$ ). The closest relation to disease activity was observed in CD with ileocolic involvement ( $p < 0.001$ ) but in pancolitis ulcerosa for IMA flow ( $p < 0.005$ ). In active UC postprandial flow increase was maximal in SMA ( $p < 0.001$ ), but in active CD in IMA ( $p < 0.01$ ). Mean portal flow was not different to controls at baseline conditions, but the postprandial flow increase was significantly higher in active UC ( $p < 0.05$ ) and active ( $p < 0.01$ ) and inactive CD ( $p < 0.05$ ). Postprandial hyperemia is superior to basal flow in the differentiation of active versus inactive CD as well as UC. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: Splanchnic circulation, ischemia Radiology and ultrasound: Diagnosis } "Postprandial Splanchnic Hemodynamics as an Activity Index in Inflammatory Bowel Disease (IBD)"

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"P P 60 1469" P 60 1469 **Doppler Ultrasonography Assessment in Inflammatory Bowel Disease (IBD)** E. Rolfo<sup>1</sup>, S. Grosso, M. Bruno,

\*C. Sategna-Guidetti

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<sup>1</sup> D.E.A. Medicina, Azienda Ospedaliera S. Giovanni Battista, Torino, Italy *Aim.* to evaluate haemodynamic changes in the Superior Mesenteric Artery (SMA) by means of Echo-doppler ultrasonography in IBD patients. *Patients and Methods.* 32 patients (19 M, 13 F; aged 18–78 years) affected by Crohn's disease (CD) entered the study, of these 19 had active disease with CDAI > 150. 14 patients (8 M, 6 F; aged 21–61 years) were affected by ulcerative colitis (UC). The control group consisted of 14 healthy volunteers (7 M, 7 F; aged 20–73 years) without vascular or inflammatory diseases which could influence splanchnic blood flow. Echo-doppler was performed with the patient in supine position after an overnight fast, using an ultrasound equipment with anular phased probe 2.75 Mhz. In each subject we considered the following variables of the SMA: Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Resistance Index (RI) calculated as PSV-EDV/PSV. Statistics: results were expressed as mean values and Standard Deviation (SD) and statistical analysis was performed by means of One Way analysis of Variance (ANOVA). Significance was defined as  $p < 0.05$ . *Results:* PSV (m/s) EDV (m/s) RIC D 1.18 (SD 0.6) 0.3 (SD 0.21) 0.77 (SD 0.1) U C 1.2 (SD 0.35) 0.2 (SD 0.12) 0.84 (SD 0.06) Controls 1.14 (SD 0.2) 0.15 (SD 0.003) 0.86 (SD 0.0002)  $p > 0.8$  0.0226 0.0033 *Conclusions:* in Crohn's disease and in ulcerative colitis there is a blood flow increase, probably due to dilatation and congestion of mucosal and submucosal vessels. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: Splanchnic circulation, ischemia Radiology and ultrasound: Diagnosis } " Doppler Ultrasonography Assessment in Inflammatory Bowel Disease (IBD)"

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## "P P 60 1470" P 60 1470 Energy Expenditure and Body Composition in Inflammatory Bowel Disease

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Weight loss is a dominant feature in patients with Crohn's disease (CD), while few data at this regard are reported in ulcerative colitis (UC) patients. Aim of the study was to compare body composition, using both direct (bioimpedance) and indirect (anthropometry) methods and resting energy expenditure (REE), measured by indirect calorimetry, in 32 patients with biopsy-proven inflammatory bowel disease (IBD) (18 CD and in 14 UC) in clinical remission (CDAI < 120). The patients did not undergo steroid therapy nor receive parenteral nutrition. Twenty healthy volunteers, matched for sex, age and height were used as a control group. The average weight of CD was significantly lower than that of both controls (mean – SD: 58.1 – 8.17 kg vs 67.2 – 6.51 kg;  $p < 0.001$ ) and UC (58.1 – 8.17 kg vs 70.2 – 12.1 kg;  $p < 0.001$ ). Fat free mass was not different between the three groups examined, while fat mass content was significantly lower in CD than both UC and controls (respectively 12.5 – 2.69 vs 16.9 – 7.53 kg;  $P < 0.05$  and vs 17.5 – 4.01 kg;  $p < 0.001$ ). No difference was found in energy expenditure, both predicted by Harris-Benedict equations and measured by indirect calorimetry among the three groups, while normalizing the REE by body weight, a significantly higher value was found in CD with respect to UC (26.6 – 2.73 vs 24.2 – 2.63 kcal/kg/day;  $p < 0.05$ ) and to controls (26.6 – 2.73 vs 23.7 – 1.29 kcal/kg/day;  $p < 0.001$ ). The non protein respiratory quotient was significantly lower in CD compared to UC and controls (0.79 – 0.03 vs 0.83 – 0.02;  $p < 0.05$  and vs 0.86 – 0.04;  $p < 0.001$ ). In conclusion, CD and UC are substantially different. In fact, CD subjects showed a poor conservation of fat mass coupled with an enhanced utilization of lipids and a high energy expenditure per kg of body weight. These data must be considered in the nutritional management of these patients and as a contribution to lipid tissue wasting in CD.

Intestinal disorders: IBD diagnosis, monitoring  
Intestinal disorders: IBD, therapy  
Nutrition: Metabolism }

"Energy Expenditure and Body Composition in Inflammatory Bowel Disease"

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"P P 60 1471" P 60 1471 **Cyclosporin in Patients with Inflammatory Bowel Disease**

\*T. Naftali, B. Novis, I. Pomerantz, G. Leichtman, Y. Maor, R. Shapira, M. Moskovitz, B. Avidan, Y. Avni, Y. Bujanover

Departments of Gastroenterology Meir, Schnieder, Ichilov, Sheba and Wolfson, Israel *Aim:* to review the experience with cyclosporin in cases of severe inflammatory bowel disease IBD in 5 hospitals in central Israel. *Methods:* Files of all patients treated with cyclosporin for IBD were reviewed. Status of disease was measured by disease activity index (DAI) that gave a maximal score of 21 (NEJM, 1994: 330: 1841–5). End points were operation, relapse or sustained remission for at least 6 months. *Results:* data on 28 patients was available. 15 were females and 13 males, average age was 24.8 (range: 11–48) Two had Crohn's disease and 26 Ulcerative Colitis. Average duration of disease was 37 months, (range: one to 180 months). All patients had an acute severe exacerbation of their disease that did not respond to IV. steroid therapy. Average duration of treatment with cyclosporin IV was 12.7 days (range 9 to 28 days). Average DAI was 14.6 before treatment (range 9 to 21), but dropped to 3.8 after first two weeks of treatment (only 2 patients had an index of more than 10). Complications included 6 cases of hirsutism, one case of allergy, one of pneumonia one of hypertension and one of hemolysis. In no case was treatment stopped because of complications. Despite the good initial response, 8 patients needed a total colectomy within 6 months from the start of cyclosporin, and 6 patients after 6 months, One patient with CD had a good initial response but relapsed after 18 months. In 1 patient treatment was stopped because of non compliance and one was lost to follow up. 11 patients maintained remission for an average of 14 months (range: 7 to 32 months) *Conclusion:* cyclosporin is an effective and safe treatment for induction of remission in acute IBD. In about 50% of patients, long term remission is maintained and they do not need an operation. }" "Cyclosporin in Patients with Inflammatory Bowel Disease"

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## "P P 60 1472" P 60 1472 Effect of *Sacharomyces Boulardii* on cAMP Dependent Cl<sup>-</sup> Secretion in T84 Cells

\*D. Czerucka, P. Rampal

Laboratoire de Gastroenterologie, Facult\ 'e9 de M\ 'e9decine, Nice, France The massive secretory diarrhea observed in cholera pathogenesis results from the modification of cAMP regulated Cl<sup>-</sup> secretion in cryptic cells by cholera toxin (CT) and by mediators (PGE<sub>2</sub>, VIP) which are released from subepithelial cells. *Saccharomyces boulardii* (S. boulardii) has been shown to inhibit the CT-induced secretion in rat jejunum. We have identified in the conditioned medium of S. boulardii (Sb-CM), a 120 kD protein which reduces CT and FSK-induced cAMP in intestinal cells. *Aim:* The current study was performed to evaluate the effect of Sb-CM on cAMP mediated Cl<sup>-</sup> secretion in T84 cells. *Methods:* Secretagogues activation of Cl<sup>-</sup> secretion was assessed by monitoring the rate of <sup>125</sup>I efflux (r.min<sup>-1</sup>) and the stimulation of cAMP (pmol/min/mg) synthesis by RIA. *Results:* The rate of <sup>125</sup>I efflux and cAMP content were determined 2 minutes after addition of PGE<sub>2</sub>, VIP or FSK to control monolayers (0 min) or to monolayers exposed for 30, 60 or 90 min to Sb-CM prior the secretagogues addition. The results reported in this table show that these parameters are significantly modified in cells exposed 60 and 90 min to Sb-CM. (Data show mean – SEM, n = 7, \* p < 0.05) 0 min 30 min 60 min 90 min PGE<sub>2</sub> cAMP 28.9 – 1.4 22.1 – 3.5 14.3 – 1.8\* 11 – 1.4\*(0.2 \b5M) r.min<sup>-1</sup> } 0.71 – 0.03 N.D. 0.49 – 0.04\* 0.47 – 0.04\* VIP cAMP 193 – 25.2 147.5 – 32.5 139 – 8\* 112 – 14.5\*(1 \b5M) r.min<sup>-1</sup> } 0.59 – 0.03 0.48 – 0.03 0.42 – 0.04\* 0.35 – 0.04\* FSK cAMP 48.1 – 2.72 40.2 – 4 34 – 2.3\* 26.2 – 2.9\*(1 \b5M) r.min<sup>-1</sup> } 0.49 – 0.04 0.39 – 0.02 0.36 – 0.03\* 0.31 – 0.01\* Experiments performed with CT, show that the stimulation of cAMP and <sup>125</sup>I efflux occurs 45 min after toxin addition to the incubation medium. In cells exposed 60 min to CT and Sb-CM, CT-stimulated cAMP is reduced by 50% (2.84 – 0.34 vs 5.41 – 0.59 in toxin treated cells) and the CT-induced <sup>125</sup>I efflux rates the basal level (0.11 – 0.01 vs 0.34 – 0.09 in toxin treated cells). We determined by LDH leakage assays, that T84 cells viability was not affected by Sb-CM. *Conclusions:* *In vitro*, Sb-CM counteracts the stimulation of cAMP synthesis and related chloride secretion induced by CT and others cAMP mediated secretagogues in T84 cells. These data contribute to the explanation of the beneficial effects of the yeast therapy in certain intestinal disorders. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport } "Effect of *Sacharomyces Boulardii* on cAMP Dependent Cl<sup>-</sup> Secretion in T84 Cells"

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"P P 60 1473" P 60 1473 **Olsalazine versus Sulphalazine Concerning Sperm Motility, Sperm Count and Sperm Morphology in Patients with Inflammatory Bowel Disease**

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Department of Gastroenterology and Hepatology and Department of Obstetrics and Gynecology, Karolinska Institute, Huddinge University Hospital, Stockholm, Sweden

**Background:** Sulphalazine is a well established drug in the treatment of inflammatory bowel disease (IBD), e.g. ulcerative colitis and Crohn's disease in the colon. However, in approximately 10–20% of the patients side-effects occur. The most common are allergy, headache and more seldom severe side-effects such as agranulocytosis and hepatitis. A well known side-effect is reversible oligospermia which can cause infertility. Almost all of the adverse reactions can be attributable to the sulphapyridine moiety of the drug. New 5-ASA compounds such as olsalazine does not contain sulphapyridine. Olsalazine consists of two salicylate radicals linked by a diazo bond. Previous case reports in patients allergic to sulphalazine have shown an improved sperm count and sperm quality when given olsalazine (J. Scherpenisse et al, Hetzel et al).

**Aim:** To characterize the changes in sperm quality in patients initially treated with sulphalazine, and then switched to treatment with olsalazine.

**Methods:** Nine patients, 20–40 years of age, with colonic IBD in remission having received long-term maintenance treatment with sulphalazine, 1 g b.i.d or t.i.d, were offered to participate in the study. The first sperm sample was obtained during sulphalazine treatment. The patients were then switched to olsalazine in an average dose of 500 mg b.i.d. After approximately 4 weeks of olsalazine treatment a second sample was obtained with a third sample after three months. Sperm variables were analysed by CASA, and morphology evaluated using strict criteria.

**Results:** A statistical improvement of the sperm quality could be seen between the two samples. Motility was significantly ( $p < 0.05$ ) improved from 32% to 57% ( $p < 0.05$ ). A tendency to improved sperm count and morphology was observed already in the second sample. One patient had azoospermia unrelated to sulphalazine.

**Conclusions:** The improvement in sperm motility during treatment with olsalazine suggests that the sulphapyridine or its metabolites are responsible for the seminal toxicity and infertility in patients treated with sulphalazine. The impairment of sperm production seems to be reversible in most cases.

Intestinal disorders: IBD, basic } "Olsalazine versus Sulphalazine Concerning Sperm Motility, Sperm Count and Sperm Morphology in Patients with Inflammatory Bowel Disease"

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"P P 60 1474" P 60 1474 **The Effect of Rectal Prednisolone on Markers of Bone Turnover in Inflammatory Bowel Disease**

\*R.J. Robinson, S.J. Iqbal, R.P. Whitaker, K. Abrams, J.F. Mayberry

Gastrointestinal Research Unit, Leicester General Hospital, Gwendolen Road, Leicester, U.K. Very little is known about the effect of rectal steroids on bone metabolism in inflammatory bowel disease. The aim of this study was to determine the effects of rectally administered prednisolone metasulphobenzate on bone turnover in patients with distal colitis. *Methods:* Study design: A longitudinal study comparing biochemical markers of bone turnover before, during and after two weeks of prednisolone metasulphobenzoate (Predfoam, Pharmax) 20 mg twice daily. Patients: Ten patients with active distal colitis were recruited to the study. Oral steroids within previous 8 weeks, rectal steroids within 4 weeks, and disease beyond the sigmoid colon were exclusion criteria. Biochemical analyses were performed on samples obtained before treatment, after 7 and 14 days of treatment and 1 week after cessation. Bone formation markers measured were serum osteocalcin (BGP), procollagen carboxy-terminal propeptide (PICP, ng/ml) and bone specific alkaline phosphatase (BALP). Urinary deoxypyridinoline (dPyr) corrected for creatinine was measured to assess bone resorption. *Results:* Bone turnover markers are presented as mean (SD) in the table. Pre-steroids 7 days 14 days Post-steroids BGP (ng/ml) 7.57 (1.8) 6.99 (2.7) 7.01 (1.8) 7.4 (2.3) BALP (U/L) 20.14 (6.5) 20.31 (6.6) 19.0 (6.6) 18.69 (6.9) \*PICP (ng/ml) 96.0 (27.2) 95.0 (35.7) 114.0 (40.5) 113.6 (28.0) dPyr (NMOL/L) 6.03 (2.3) 5.28 (1.58) 5.38 (2.26) 9.44 (10.4) \*BALP fell significantly after 14 days (Difference in means = 1.14 (1.33) 95% C.I. 0.12 to 2.17, p = 0.03) and was still low 1 week after cessation (Difference in means = 1.46 (1.17), 95% C.I. 0.56 to 2.36 p = 0.006). There was a non significant fall in osteocalcin and no significant change in the other bone turnover markers. *Conclusion:* Alkaline phosphatase and osteocalcin fell during treatment with rectal prednisolone. This suggests an impairment of bone formation which if sustained could lead to osteoporosis. Further study of the effects of rectal steroids on bone metabolism is warranted. Intestinal disorders: IBD, therapy }" "The Effect of Rectal Prednisolone on Markers of Bone Turnover in Inflammatory Bowel Disease"

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"P P 60 1475" P 60 1475 **Lupus-Like Syndrome Caused by the Use of 5-Aminosalicylic Acid in Patients with Inflammatory Bowel Disease**

\*F.M. Habal, A. Kirkpatrick

The Toronto Hospital, University of Toronto, Toronto, Ontario, Canada The newer 5-aminosalicylic acid (5-ASA) preparations used to treat inflammatory bowel diseases (IBD) are reported to have fewer side effects than the Sulfasalazine, a combination of 5-ASA and sulfapyridine. Four patients with IBD, 2 with Crohn's colitis and two with ulcerative colitis developed antinuclear factor antibody positive migratory arthralgia with acute inflammation following the institution of 5-ASA at a dosage of 2 gm–4 gm daily. The arthralgia was asymmetric involving small and large joints. None of these had extraintestinal manifestation prior to the introduction of the drug. All four patients went into remission while the arthropathy began. Despite the use of nonsteroidal anti-inflammatory medications and steroids, the patients continued to suffer from the arthritis. Within 2–6 weeks following the discontinuation of the 5-ASA all their symptoms cleared and the ANA serology became negative. Over a follow-up period of 1–3 years none of the patients developed further arthropathy and remained seronegative. The patients had only minimal gastrointestinal symptoms without further therapy.

Test	Patient profile	Pre	Post 1	2	3	4
ANA	1:320/0	1:320/0	1:640/0	1:640/0	1:640/0	1:640/0
Anti-DNA ( <i>Crithidia</i> )	+/{ - }	+/{ - }	+/{ - }	+/{ - }	+/{ - }	+/{ - }
Anti-DNA (Farr)	{ - }/{ - }	+/{ - }	{ - }/{ - }	+/{ - }	{ - }/{ - }	+/{ - }
ESR (mm/h)	35/16	25/22	48/22	42/40		

We recommend that patients treated with 5-ASA compounds experiencing acute inflammatory symptoms or clinical deterioration not related to their gastrointestinal disease be screened to rule out a lupus-like reaction. Clinical practice: Management strategy Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Lupus-Like Syndrome Caused by the Use of 5-Aminosalicylic Acid in Patients with Inflammatory Bowel Disease"

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"P P 60 1476" P 60 1476 **I.O.I.B.D. Questionnaire on the Clinical Use of Azathioprine, 6-Mercaptopurine, Cyclosporine-A and Methotrexate in the Treatment of I.B.D.**

\*S.G.M. Meuwissen, K. Ewe, M.A. Gassull, K. Geboes, D. Jewell, F. Pallone, D. Rachmilewitz, J. Rask-Madsen, R.H. Riddell

PO Box 7057, 1081 HV Amsterdam, the Netherlands *Purpose and Methods:* A questionnaire was mailed on behalf of the I.O.I.B.D. (International Organisation of Inflammatory Bowel Disease) to 300 gastroenterologists, living in the USA/Canada (US/C) (n = 76) and Europe (Eu) (n = 224) (12 countries), to obtain information on the clinical experience of azathioprine (AZA), 6-Mercaptopurine (6-MP), Cyclosporine-A (CSA) and Methotrexate (MTX) in the treatment of patients with I.B.D.. 168/298 (56.4%) of the respondents worked in Unvers. Hospitals (UniH) and 58/298 (19.5%) in Gen. Hospitals (GenH). 65% had > 10 y. experience in GI. *Results:* Personal experience existed with AZA (88.4%), 6-MP (33.3%), CSA-A (48.7%) and MTX (36.3%). AZA was prescribed more frequently in Eu (92.6%) than in US/C (74.2%) (p = 0.0002), 6-MP less frequently in the Eu than in the US/C respondents (23.8 and 53.3% resp., p < 0.0001). 69.7% of the respondents always prescribed AZA together with steroids to CD patients, in 62.4% for periods longer than 24 mo. 77.9% had experience with AZA in UC., Eu > US/C (p < 0.0001). AZA had been prescribed by 69 respondents in pregnant patients, without apparent toxicity and acute pancreatitis was seen after AZA by 56.7% respondents; 25 malignancies were mentioned (lymphoma 6{\b4}, leukemia 3{\b4}, colon 3{\b4} and renal carcinoma 4{\b4}, others 9{\b4}). CSA-A had been prescribed in acute UC by 140/291 respondents (63.9% treated < 5 patients per centre, 36.1% 6- > 20 cases) (US/C 45.1%, Eu 49.1%, n.s.). CSA-A results were considered good in 29.5%, acceptable but with recurrences in 58.6% and poor in 14.3%. MTX was prescribed in US/C by 47.8% of the respondents, and by 33.9% in Eu (p = 0.478). Several significant differences were observed between the prescription behaviour of respondents working at UniH and GenH, in relation to participation in clinical trials. *Conclusion:* considerable experience exists in the use of immunosuppressive therapy in IBD, both in US/C and Eu, however differences exist in the choice of immunosuppressives. UniH participate more frequently in clinical trials. The study results may contribute to a better insight in the use of immunosuppressive agents in I.B.D. by a large group of experienced gastroenterologists. Intestinal disorders: IBD, therapy Clinical practice: Management strategy }" "I.O.I.B.D. Questionnaire on the Clinical Use of Azathioprine, 6-Mercaptopurine, Cyclosporine-A and Methotrexate in the Treatment of I.B.D."

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"P P 60 1477" P 60 1477 **Ferric Maltol Corrects Chronic Iron Deficiency Anaemia in Ferrous Sulphate Intolerant Patients with Inflammatory Bowel Disease**

\*R.S.J. Harvey, L.A. Doig, R.P.H. Thompson, J.J. Powell

Gastrointestinal Laboratory, The Rayne Institute, St Thomas' Hospital, London, SE1 7EH, UK Iron deficiency anaemia may occur in inflammatory bowel disease (IBD) but use of oral iron therapy is limited by poor absorption and gastrointestinal side effects. Hence, ferrous sulphate intolerance is common in IBD leading to chronic mild anaemia or necessitating parenteral iron. Ferric maltol is a novel iron compound in which ferric ( $\text{Fe}^{3+}$ ) iron is chelated by the sugar derivative maltol. This complex has low side effects and high bioavailability compared to iron salts and we now report its efficacy in ferrous sulphate intolerant patients with IBD. Eleven patients with IBD (8 Crohn's) and iron deficiency anaemia (ferritin  $< 15$  + haemoglobin  $< 12$  F or  $13$  M) were recruited. All had documented intolerance to ferrous sulphate precluding its use. Ferric maltol was given b.d. ( $2 \times 30$  mg of elemental iron) for three months. At baseline, ten symptoms were assessed and each graded from 0 (none)–3 (serious). During treatment, patients similarly recorded their third week of each month symptoms in a diary, and these are presented as the mean daily symptom score per patient (MDSS). Haemoglobin and ferritin levels were measured monthly. All patients fully tolerated ferric maltol. Completed data was obtained for 9/11 patients and all corrected their anaemia. (n = 9) Pre- Treatment Treatment Treatment treatment Month 1 Month 2 Month 3 Haemoglobin (mean – SD) g/l 10.9 – 1.8 11.9 – 1.6 12.7 – 1.4 13.4 – 1.0 Ferritin (mean – SD)  $\mu\text{g/l}$  7.4 – 3.8 14.0 – 7.3 15.0 – 6.2 21.8 – 8.7 MDSS (mean – SD) 2.44 – 2.65 2.0 – 1.62 0.76 – 0.49 0.57 – 0.72 Despite documented ferrous sulphate intolerance causing chronic anaemia in all patients, there was complete tolerance to ferric maltol and correction of anaemia. A double blind multi-centre trial is in progress. Intestinal disorders: IBD, therapy Nutrition: Metabolism } "Ferric Maltol Corrects Chronic Iron Deficiency Anaemia in Ferrous Sulphate Intolerant Patients with Inflammatory Bowel Disease"

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"P P 60 1478" P 60 1478 **5-ASA Enemas Increase Mucosal Availability of Mesalamine up to Splenic Flexure**

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<sup>2</sup> Clinical Methodology Units, University of L'Aquila, L'Aquila, Italy *Introduction*

Pharmacological effects of 5-ASA in ulcerative colitis (UC) is mainly due to its mucosal concentration. 5-ASA is often given by enema to treat left-sided UC, but no data exist either on mesalamine mucosal concentration or the extent of treated mucosa during chronic topical treatment. *Aim* This study was carried out to measure mucosal concentration of 5-ASA in patients with UC treated with both topical and oral 5-ASA (double treatment) compared to patients treated with oral 5-ASA alone (control). *Materials and methods* Sixteen patients with mild to moderate UC limited to the left colon were randomized to receive 2.4 gr. of oral mesalazine (9 patients) or 2.4 oral plus 4 gr. topical mesalazine (7 patients). After two weeks, two endoscopic biopsies were taken in the rectum (inflamed mucosa) and two biopsies at the splenic flexure (normal mucosa). The specimens were weighted, immediately frozen in liquid nitrogen and stored at  $\{-\}80^{\circ}\text{C}$  for later assay. HPLC method was used to determine 5-ASA and Acetyl 5-ASA concentrations (ng/mg) in tissue homogenates. The Wilcoxon's rank test was used for statistical analysis. Data are expressed as median. *Results* Mucosal 5-ASA of both rectal and proximal tracts was significantly higher in double treatment group than in controls. Median values of rectal mucosa were 51.5 and 1.6 ng/mg in double treatment group and in controls respectively ( $p < 0.001$ ). Median values of proximal mucosa were 65.6 and 17.6 ng/mg in double treatment group and in controls respectively ( $p < 0.02$ ). No differences were observed in Acetyl 5-ASA concentration. *Conclusion* Topical treatment significantly increased mucosal 5-ASA concentration at least up to splenic flexure. This finding supports the rationale to treat left-sided UC with 5-ASA enemas and explain the good results obtained in clinical trials in which this treatment was tested. Intestinal disorders: IBD, therapy }" "5-ASA Enemas Increase Mucosal Availability of Mesalamine up to Splenic Flexure"

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**"P P 60 1479" P 60 1479 Colitis, Non-Steroidal Anti-Inflammatory Drugs (NSAID'S) & Salicylates — A Strong Association**

\*M.H. Gleeson, J.V. Hardman, C. Clinton

The General Hospital, Jersey, Channel Islands, UK A prospective study of 62 consecutive new cases of colitis from November 1993 to May 1996 revealed 45 patients who had been taking NSAID's or salicylates. Mean age of patients with NSAID-associated colitis was 40.5 years (range 20–77) and of the others (idiopathic colitis) was 49.9 (range 23–90). No patients had a previous history of colitis and diagnosis was always established by colonoscopy. Patients with NSAID-associated colitis had either distal disease identical in endoscopic appearances to ulcerative colitis (59%), or proximal disease with rectal sparing and discontinuous disease, similar to Crohn's colitis. Crypt abscesses, ulceration and a mixed inflammatory infiltrate were seen but no granulomas. All patients received standard treatment for inflammatory bowel disease, and 8 (47.1%) of the NSAID group required systemic steroids compared to 18 (40.0%) of the idiopathic group and 15 patients with NSAID-associated colitis have relapsed without further exposure to NSAID's or salicylates and appear to be developing a chronic colitis. A drug history was obtained from a control group of 513 attenders at a minor injuries clinic. The age range of this series was 18–90 (mean 38) years. 38 (7%) were taking NSAID's or salicylates. This compares to 45 (75%) of 62 patients taking NSAID's or salicylates in the colitis group. This gives an odds ratio of 33.1 significantly supporting a causal association between these agents and colitis. They appear to be an important aetiological trigger factor in inflammatory bowel disease. Intestinal disorders: IBD, etiology and genetics Endoscopy, specific: Colon, rectum Intestinal disorders, absorption: Pathophysiology of diarrhea } "Colitis, Non-Steroidal Anti-Inflammatory Drugs (NSAID'S) & Salicylates / A Strong Association"

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"P P 60 1480" P 60 1480 **Effectiveness of Heparin in the Treatment of Inflammatory Bowel Diseases: Anticoagulant or Immunomodulatory Effect?** F. Brazier<sup>1</sup>, V. Gouilleux-Gruart<sup>1</sup>, T. Yzet<sup>2</sup>, J.C. Duchmann<RID = 2), B. Roussel<sup>3</sup>,

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Activation of procoagulant factors and inhibition of fibrinolysis may be involved in the pathogenesis of inflammatory bowel diseases. It has been suggested that heparin, acting by its anticoagulant and/or immunomodulatory properties, may be useful in the treatment of inflammatory bowel diseases. *Aim:* To evaluate the effects of heparin on marker of coagulation (F1 + 2), fibrin degradation products (FbDP) and cytokines (IL6, TNF{ a}) serum levels during the treatment of patients with Crohn's disease (CD) or ulcerative colitis (UC). *Methods:* 12 patients (8 CD, 4 UC, age 19–43 yrs) with clinically active disease were included. 4 patients had chronically active CD treated by prednisolone 20–40 mg/d unchanged in the 3-weeks period before and during the study. All patients received heparin either IV (3000 UI/4 hrs), or SC (2500 UI/10 kg bid) for 1 week. F1 + 2, FbDP, IL6 and TNF{ a} blood levels were determined before and after 1-week heparin treatment. *Results:* significant clinical improvement was observed after 1-week heparin therapy in 7/8 patients with CD and 2/4 patients with UC. Normal day 0 day 7 PF1 + 2 nmol/l < 1.1 2 1.5 NSmean (95% CI) (1–3) (0.6–2.5)FbDP ng/ml < 450 617 405 NSmean (95% CI) (159–1075) (134–676)CRP mg/l < 5 79 36 P < 0.02mean (95% CI) (38–120) (15–56)IL6 pg/ml 3–8.5 74.3 42.0 P < 0.02mean (95% CI) (41.7–106.9) (26.6–57.3)TNF{ a} pg/ml 3–20 40.8 27.9 NSmean (95% CI) (22.8–58.9) (22.9–33.9)*Conclusions:* These results suggest that effects of heparin are more likely related to its immunomodulatory than its anticoagulant properties. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } "Effectiveness of Heparin in the Treatment of Inflammatory Bowel Diseases: Anticoagulant or Immunomodulatory Effect?"

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## "P P 61 1481" P 61 1481 Acute Phase Reactants in Pediatric Crohn's Disease (CD): Interest and Predictive Values

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<sup>1</sup> Pediatric Gastroenterology

<sup>2</sup> Biostatistics

<sup>3</sup> Biochemistry, Hospital Robert Debr'e9, Paris In order to assess the activity of CD in children, clinical and/or biological scores (Harvey-Bradshaw [HB], Pediatric Crohn Disease Activity Index [PCDAI]) have been defined. Biologic data included hematocrit (HT), erythrocyte sedimentation rate (ESR) and albumin (ALB). Recent laboratory parameters have been shown to be well correlated with CD inflammation in adults: C reactive protein (CRP), orosomucoid (ORO) and haptoglobin (HAP), but pediatric data are scarce. *Population*: 34 children (17 M, 17 F) treated for CD, mean age of 15 years. Follow-up: 21 months (Feb 92–Nov 93), mean interval between 2 measurements of 24 days. *Results*: On the 127 blood samples, the univariate study shows a highly significant difference of the three parameters between the acute (A) (PCDAI > 30, HB > 6) and the quiescent (Q) status of CD. We observed an excellent reproductibility of the 2 scores (correlation coefficient = 0.98). Variable A Q P (p < 0.01) Sen Spe PPV NPV (%) (%) (%) (%) HT 32.9 – 1.4 36 – 0.4 0.01 17 89 20 87 VS 43 – 6.5 25.8 – 1.7 0.004 94 23 16 96 ALB 29.9 – 1.5 35.6 – 0.6 0.004 29 95 50 89 CRP 18.45 – 8.3 7.55 – 0.6 0.0005 58 70 23 91 ORO 1.66 – 0.17 1.1 – 0.03 < 0.0001 94 16 14 94 HAP 3.85 – 0.53 2.64 – 0.1 0.002 94 15 14 94 Statistical diagnostic tests shows that sensibility (Sen) of ORO and of HAP is high (94%) as much as ESR, but their specificity (Spe) is low (15–23%). CRP seems to be the more specific biologic parameter (70%) but is not sensible (58%). However, NPV of these 3 acute phase proteins is very high (NPV {\'b3} 87%) but their PPV is still poor (VPP {\'a3} 50%). In multivariate study, CRP remains the best indicator of CD activity (OR 4.55; CI 1–20). These results suggest that no single laboratory test appears an adequate reflect of CD activity in childhood. Their increase is well correlated to CD activity index, mainly CRP. Their normality has a strong negative predictive value. Their poor PPV may reflect the weak correlation between clinical and endoscopic scores of CD activity. Intestinal disorders: IBD diagnosis, monitoring Immunology and microbiology: Inflammation }" "Acute Phase Reactants in Pediatric Crohn's Disease (CD): Interest and Predictive Values"

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## "P P 61 1482" P 61 1482 **Thrombotic Risk Markers in Inflammatory Bowel Disease (IBD) in Children**

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<sup>1</sup> Pediatric Gastroenterology

<sup>2</sup> Biological Hematology

<sup>3</sup> Biostatistics, Hospital Robert Debr\`e9, Paris Severe thromboembolic events (TEE) are not uncommon in IBD. Their incidence ranges from 1 to 39%, occurring mainly during severe episodes with extensive colic lesions and after surgery. In adults, these TEE have been found to be associated with coagulation/fibrinolysis anomalies, probably related to intestinal vasculitis and increased cytokine production. *Aim of the study:* assessment of the thrombotic risk in children IBD in order to recommend a preventive treatment *Patients and methods:* 34 children (139 samples) with IBD (Crohn disease (n = 29), undetermined colitis (n = 5)) were clinically assessed by the Pediatric Crohn disease Activity Index (PCDAI) (flare-up defined by a PCDAI > 30). The thrombotic risk has been assessed by platelet numeration, dosage of main coagulation factors (I, II, VII + X, V, VIII, von Willebrandt factor (vWF)) and inhibitors (antithrombin, proteins C and S), fibrinolytic activity (tissue-plasminogen activator (t-PA) and its main inhibitor, PAI-1), markers of coagulation activation (D-Dimers, thrombin-antithrombin complexes) and endothelial markers (thrombomodulin (TM) in addition to vWF and t-PA). *Results:* In univariate analysis comparing active and quiescent disease, it has been found a significant increase of platelets (p = 0.005), fibrinogen (p = 0.00001), D-dimers (p = 0.01) and factors V (p = 0.005), VIII (p = 0.003) and vWF (p = 0.0002). Coagulation inhibitors, fibrinolytic system components and TM remained unmodified. In multivariate study, vWF and fibrinogen were significantly increased in active disease, with OR values of 21.2 (CI = 3.2–141) and 21.9 (CI = 1.84–262) respectively. In summary, during active IBD in children a hypercoagulable state with coagulation activation, able to induce TEE, has been observed, associated with anomalies of one marker of endothelial lesions (vWF). A preventive anticoagulation should be proposed in high-risk relapses of IBD in children in order to reduce the thrombotic risk (which can be fatal), and perhaps have a therapeutic effect on the intestinal vasculitis. Intestinal disorders: IBD diagnosis, monitoring } "Thrombotic Risk Markers in Inflammatory Bowel Disease (IBD) in Children"

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## "P P 61 1483" P 61 1483 Crohn's Disease in Children 8 Years Old and Younger

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Diagnosis of Crohn's disease (CD) before 8 years is rare. Few studies interested about this population. The purpose of this report was to examine the presentation, course and outcome of CD in children < 8 years old and to compare them with a group of older children.

**Population:** We studied retrospectively 61 children in whom diagnosis of CD was made. Patients were categorized as the age at onset of disease in two groups. First one (G1) included 16 children < 8 years old at date of onset of disease (11 boys, 5 girls); group 2 (G2) (control group) included 45 children whose disease had been diagnosed after 8 years (26 boys, 19 girls).

**Methods:** To compare them, records as diagnosis delay, clinical features, topography of lesions, recurrences and long term prognosis were reviewed. Statistical analysis was made with the Student's t test and Chi 2 test.

**Results:** the difference of mean diagnosis delay between G1 and G2 was significative (respectively 22 months versus 12 months,  $p < 0.05$ ). Anorectals lesions, bloody stools and anal fissures were more frequent in the G1 ( $p < 0.05$ ). Ileocolic or colic localisations represented 94% of children of G1 et 62% of G2 ( $p < 0.05$ ). Parenteral nutrition (PN) was longer in G1 than in G2 (42 months versus 12 months,  $p < 0.001$ ). Surgical colic or ileocolic resections were more frequently necessary in G1 (84%) than in G2 (45%) ( $p < 0.01$ ). Ileostomy was done in 54% of patients in G1 versus 21% in G2 ( $p < 0.02$ ). Sequels as enterostomy were more frequent in the G1 (44%) than in the G2 (11%) ( $p < 0.01$ ). The definitive height was under  $\{-\}0.5$  SD (Standard Deviation) in 50% of the patients and under  $\{-\}1.5$  SD in 15% of the patients. There was no significative difference between the 2 groups.

**Conclusion:** in the childhood CD, the onset of the disease before 8 year's old is a index of severity. Colic localisation was more frequent. Aggressive medical (PN) and surgical therapeutics (large resections) were often necessary to control the illness. The sequels were more frequent than in children who began after 8 years (enterostomy). Thanks to that aggressive treatments, the height was similar in the 2 groups. }

"Crohn's Disease in Children 8 Years Old and Younger"

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"P P 61 1484" P 61 1484 **Congenital Secretory Diarrhea Associated with Choanal Atresia in Two Unrelated Children**

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Intractable diarrhea in infancy due to specific syndromes such as congenital microvillus atrophy, autoimmune enteropathy, chloridorrhea and defective jejunal brush-border Na/H exchange have been described. We report 2 cases of congenital diarrhea in association with choanal atresia in unrelated children and propose that this may constitute a new syndrome. *Case 1.* A newborn fullterm boy was referred to ICU for respiratory care due to bilateral choanal atresia. At 2 weeks age he developed severe watery diarrhea and became hyponatremic. The diarrhea persisted in spite of cessation of oral intake and has persisted until present age 20 months. Stool sodium was 125 mmol/l, stool osmotic gap < 50. Histological and electron microscopy (EM) examination of small bowel biopsy (A Phillips, London), autoantibodies against gut-epithelium (R. Marakian London), gastrointestinal peptides, tests for inborn errors of metabolism, chromosome analysis, EM of nasal cilia, xylose challenge were all normal. By performing an ileostomy at 15 months of age we demonstrated an ileal output of 100–120 ml/kg/d but no secretion from the large intestine. He is maintained on TPN, linear growth and psychomotor development is normal. *Case 2.* A fullterm girl was admitted to ICU at 2 weeks of age for dehydration and hyponatremia with seizures due to severe watery diarrhea. The diarrhea has since persisted, in spite of no oral intake. Stool sodium 110 mmol/l, fecal osmotic gap < 50, histological examination of small and large bowel and biopsies, EM of small bowel biopsy, gastrointestinal peptides, metabolic tests, chromosome analysis, autoantibodies against gut-epithelium were all normal. At 2 months of age unilateral choanal atresia was demonstrated by CT scan. She also has a congenital defect in factor V causing severe coagulopathy and requires i.v. warfarin for maintaining vascular access for TPN. Her linear growth and psychomotor development is normal, she is on full TPN with minimal enteral feeding. Further studies to elucidate this proposed syndrome are warranted.

Intestinal disorders, absorption: Pathophysiology of diarrhea  
Intestinal disorders, absorption: Malabsorption syndromes } "Congenital Secretory Diarrhea Associated with Choanal Atresia in Two Unrelated Children"

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"P P 61 1485" P 61 1485 **High Prevalence of Positive Antibody Response Against Gliadin in Children and Parents of Children with Coeliac Disease**

\*S. Belmer, Y. Lebedin

Russian Media University, Moscow, Dept. of Pediatrics Coeliac disease is a gluten intolerance with malabsorption syndrome, based on any genetic disorders. Serum IgA and IgG antibodies to alpha (AGA) or crude (CGA) gliadin by commercial EIAs (Labodia and Pharmacia, respectively) were measured in children with biopsy-proven coeliac disease and their first-degree relatives. Among 18 full family records (AGA test), at least one of the parents was positive in 6 cases; both of the parents – in 10 cases. AGA test reveals more positive relatives than CGA EIA. False-negative results for CGA were obtained in 43% against IgA AGA and 50% against IgG AGA. None of AGA positive adults showed clinical symptoms of coeliac disease. The gluten-free diet influenced to level of antibodies. All patients with untreated coeliac disease expressed serum IgA and IgG antibodies to bovine serum albumin (BSA) and only 1/5 of these expressed serum IgA and IgG antibodies to ovalbumin (OVA). In cases of treated coeliac disease the level of antibodies to BSA decreased and antibodies to OVA on the contrary increased. The first-degree relatives expressed low level of mentioned antibodies and unimportant differences with non-coeliac patients and their parents. *Conclusions.* The positivity for anti-gliadin (especially alpha-gliadin) antibodies in healthy parents could represent a risk factor of development of full scale coeliac disease in children and, probably, represent the genetic predisposition of immune system to abnormal response on gliadin but not to gut affection. The limitation of bovine products and eggs in coeliac patient's diet should be discussed. Intestinal disorders, absorption: Malabsorption syndromes Intestinal disorders, absorption: Gluten enteropathy Intestinal disorders, absorption: Malabsorption: children } "High Prevalence of Positive Antibody Response Against Gliadin in Children and Parents of Children with Coeliac Disease"

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"P P 61 1486" P 61 1486 **Mediators of Inflammation in Children with Inflammatory Bowel Disease**

\*S. Nousia-Arvanitakis, M. Hatzistilianou-Sidiropoulou, C. Agguridaki, V. Tsavdaridou, M. Xefteri, A. Galli

4th and 2nd Depts of Paediatrics and Serology Laboratory, Aristotle University of Thessaloniki, Thessaloniki, Greece Inflammatory bowel disease in children remains the most challenging problem in gastroenterology. Crohn's disease and ulcerative colitis are characterised by an activation of intestinal mononuclear cells and T-cells within the inflamed lesions. The aim of the present study is to determine whether circulating inflammatory mediators, such as interleukins and adhesion molecules, represent useful markers of immune activation in vivo and to characterise their respective roles in monitoring disease activity. Serum concentrations of IL-2, IL-6, IL-8, IL-10, sIL-2R, sICAM-1 and sVCAM-1 were measured in 18 patients with inflammatory bowel disease, 8 with Crohn's disease (CD), 10 with ulcerative colitis (UC) and in 25 healthy subjects (control group, CG). The mean values and standard errors are shown in the table. Inflammatory CD UC CG mediators n = 8 n = 10 n = 25 IL-2 (pg/ml) 108 – 12 80 – 24 15 – 3 IL-6 (pg/ml) 49 – 5 39 – 4 9 – 2 IL-8 (pg/ml) 245 – 39 198 – 24 23 – 9 IL-10 (pg/ml) 167 – 25 138 – 28 41 – 7 sIL-2R (IU/ml) 5518 – 415 3778 – 790 984 – 85 sICAM-1 (IU/ml) 1632 – 116 852 – 34 254 – 18 sVCAM-1 (IU/ml) 2086 – 153 1459 + 127 576 – 27 *Conclusions:* All the inflammatory mediators are significantly increased in patients with CD and UC as compared to the control group. Pro-inflammatory mediators (IL-6, IL-8, IL-10) are elevated in the serum of patients with active disease, suggesting that they act as naturally occurring initiators in the acute inflammatory process. Increased IL-2 and sIL-2R levels reflect T-cell activation. Increased circulating sICAM-1 and sVCAM-1 levels may reflect increased adhesiveness and signal transmission across cells, probably as a result of shedding of the parent molecule during local cellular immunoresponses in vivo. The measurements of all these mediators may be useful adjuncts to clinical assessment and to routine laboratory testing in pediatric patients with CD and UC. Intestinal disorders: IBD diagnosis, monitoring } "Mediators of Inflammation in Children with Inflammatory Bowel Disease"

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"P P 61 1487" P 61 1487 **Carbohydrate Intolerance after Gastroenteritis — A Disappearing Problem also in Polish Children?**

\*H. Szajewska, M. Kantecki, J. Antoniewicz, P. Albrecht

Dept of Pediatric Gastroenterology & Nutrition, Warsaw University Medical School, Poland *Background:* Frequency of carbohydrate intolerance after acute gastroenteritis, and its importance, varies widely from centre to centre. In Western Europe its frequency decreased from 50–70% in 1970's to 0–5% in 1990's. The change from high-solute to low-solute, less sensitising modern adapted formula is considered to be a key factor. *Aim:* to investigate the incidence of carbohydrate intolerance after acute gastroenteritis in Polish children. *Method:* 125 consecutive children less than 3 years of age who were admitted to our hospital with acute gastroenteritis (defined as acute onset of watery or extremely loose stools with or without vomiting for no more than one but less than five days) were entered into the study. Standard treatment – ORS for 4–12 hours followed by refeeding with the usual diet – was given. Carbohydrate intolerance (diagnostic criteria: > 0.5% reducing substances and stool pH < 5.5) was assessed. *Results:* carbohydrate intolerance was diagnosed in 16 of the 125 [12.8%] of the children: lactose intolerance was present in 12 [9.6%] patients; glucose polymer intolerance in 3 [2.4%] and monosaccharide intolerance in 1 [0.8%]. 75% of the children (12 out of 16) with carbohydrate intolerance were under 12 months. The most important predisposing factor was rotavirus. In all cases the carbohydrate intolerance was transient resolving by five days. *Conclusions:* The study confirms the observation from Western Europe that carbohydrate intolerance after acute gastroenteritis is infrequent event also in Polish children though its incidence is higher compared with other countries. Restriction of lactose containing foods (use of lactose free formula) for the vast majority of children with gastroenteritis does not appear to be justified. Immunology and microbiology: GI infection, children } "Carbohydrate Intolerance after Gastroenteritis / A Disappearing Problem also in Polish Children?"

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"P P 61 1488" P 61 1488 **Cyclosporin Induced Remission for Children Suffering from Ulcerative Colitis**

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Cyclosporin has been used successfully in adults suffering from fulminant refractory ulcerative colitis (UC), by avoiding immediate surgery in 75% and inducing long term remission in 55% of patients. Over the last five years we studied the effectiveness of cyclosporin in 12 children aged 10–17 years (mean 14.25 years). They were admitted to the hospital for fulminant refractory UC. Treatment was begun with intravenous cyclosporin 4–8 mg/kg/24 h, aiming at blood trough level of 150–250 ng/ml. Oral cyclosporin therapy was begun after remission was achieved, usually within 2 weeks. *Results:* Clinical improvement was noticed in all the patients but one (91.7%) within 3–10 days. Five patients are in remission, 14–34 months after cyclosporin treatment for 6–8 months. Another patient is in remission 2 months after initiation of therapy. Four patients had an exacerbation of the disease while on cyclosporin treatment. Remission lasted 8.7 weeks on the average, with a range of 2–24 weeks. Another patient had an exacerbation one year after cessation of a six month cyclosporin course. All of these 5 patients subsequently underwent surgery. *Conclusions:* Cyclosporin is effective in achieving clinical remission in 91.7% of children suffering from UC, Although surgery may only be delayed in about 50% of the cases, it can be done under non emergent conditions. Intestinal disorders: IBD, therapy } "Cyclosporin Induced Remission for Children Suffering from Ulcerative Colitis"

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"P P 61 1490" P 61 1490 **Comparison of Absorption of Macronutrients from a Defined Semi-Elemental Diet Containing Medium and Long Chain Triglycerides (MCT and LCT) in Children with Persistent Diarrhoea (PD)**

\*P.K. Bardhan, N.H. Alam, M.A. Wahed, S.M. Akramuzzaman, D. Mahalanabis, K. Gyr

International Centre for Diarrhoeal Disease Research, Bangladesh

Dept. of Gastroenterology, Basle University, Switzerland Persistent diarrhoea (an episode of diarrhoea continuing for > 2 weeks) in children is associated with malabsorption (particularly of fat), malnutrition, and a high mortality rate. This study compares macronutrient absorption in children with PD treated with a diet containing either coconut oil (relatively rich in MCTs) or soybean oil as the source of dietary fat. *Methods:* Seventy male patients aged 3–12 months with PD were randomly assigned to one of the two dietary groups. The study diets contained minced chicken meat, glucose, and either coconut oil or soybean oil. A 72 hours balance study was started after a 24-hr prebalance. Aliquots from 72-hr homogenized stool, vomitus, urine, study diets and breast milk samples were preserved at  $-70^{\circ}\text{C}$  until analysed. The coefficients of absorption of fat, protein and carbohydrate were calculated as percentages, and the results are expressed as mean – SEM. *Results:* Thirty three and 37 patients received diet 1 (coconut oil-based) and diet 2 (soybean oil-based) respectively. The patients belonging to the two groups were comparable in age, body wt., nutritional status, duration of diarrhea, and socioeconomic status. The coefficients of absorption of the macronutrients are: Diet 1 Diet 2 pFat 60.4 – 4.8 61.0 – 4.0 0.924 Protein 32.3 – 3.6 34.3 – 3.0 0.666 Carbohydrate 64.4 – 4.8 62.7 – 5.5 0.813 There were no significant difference between the two groups on stool output, nutrient intake or subsequent clinical course. *Conclusion:* There is significant malabsorption of macronutrients, particularly fat, in children suffering from PD, and dietary substitution of LCT containing dietary fat (soybean oil) by MCT-rich coconut oil has no effect upon macronutrient absorption. Intestinal disorders, absorption: Malabsorption: children Nutrition: Nutrition: children } "Comparison of Absorption of Macronutrients from a Defined Semi-Elemental Diet Containing Medium and Long Chain Triglycerides (MCT and LCT) in Children with Persistent Diarrhoea (PD)"

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"P P 61 1491" P 61 1491 **The Frequency of Surgery in Children with Crohn's Disease** Gabriella Palmer<sup>1</sup>, Andreas Henschen<sup>2</sup>, Rutger Bennet<sup>2</sup>,

\*Yigael Finkel<sup>2</sup>

<sup>1</sup> Dept of Pediatric Surgery, Karolinska/S.t G\`f6ran's Children's Hospital, Stockholm, Sweden

<sup>2</sup> Dept of Pediatrics, Karolinska/S.t G\`f6ran's Children's Hospital, Stockholm, Sweden  
The treatment of children with IBD in our hospital has changed during the last 15 years. New medical and nutritional therapies have been introduced, and a closer cooperation between the paediatric and paediatric surgery units has been established. This retrospective study has focused on the frequency of surgical procedures on patients with Crohn's disease from diagnosis in childhood to adulthood. *Subjects:* During 1980-1992 117 children with IBD were diagnosed and followed for 3–15 years. 52 had Crohn's disease, 44 ulcerative colitis, 21 indetermined colitis. 23 of the patients with Crohn's disease were referred to internal medicine/surgical departments at 18 years of age. *Results:* 52 patients with Crohn's disease were diagnosed at a mean age of 11.9 years. 35 underwent surgery at one or more occasions in our departments before the age of 18 years. After 2.5 years of disease duration 50% of the children had undergone therapeutic surgery, the main indications being growth failure and/or retarded puberty in spite of intensive medical and nutritional therapy. In the first surgical event the majority of operated children (17/35) underwent an ileocecal resection, anal fistula operations was performed in 8/35 and other resections of ileum and/or colon were performed in 7/35. 2 children underwent explorative laparotomy. Elective operations preceded by nutritional therapy were predominant and only two emergency operations were carried out. 5/23 referred to other departments were operated after the age of 18. *Conclusion:* Surgical treatment remains important in the therapy of Crohn's disease in children in spite of new therapeutic modalities. Close cooperation between paediatricians and paediatric surgeons improves the right timing of the procedures. } "The Frequency of Surgery in Children with Crohn's Disease"

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"P P 61 1492" P 61 1492 **Screening for Coeliac Disease in Autoimmune Thyroid Disease** M. Bruno, S. Predebon, A. Carlino, E. Mazza, C. Brossa, S. Grosso,

\*C. Sategna-Guidetti

Dipartimento di Medicina Interna. Università di Torino, Italy An increased frequency of thyroid abnormalities has been reported in patients with coeliac disease (CD), while the occurrence of CD among patients with autoimmune thyroid disease (ATD) is still poorly documented. *Aim:* To evaluate CD prevalence in an adult population with ATD. *Method:* The study was entered by 103 patients (18 males, 85 females) with either Hashimoto's thyroiditis or Graves' disease, none of whom taking steroids nor medications able to interfere with immunological response, nor with selective IgA deficiency. The serological screening was performed by means of IgA antiendomysium antibodies (EmA) appraised by indirect immunofluorescence on commercial slides of monkey oesophagus. Statistical analysis was performed by calculating the 95% confidence intervals of the standardised ratio (observed number/expected number of CD patients); the ratio was considered as significant ( $p < 0.05$ ) if the confidence interval did not contain 1.00. *Results:* EmA positivity was found in 3 out of 103 patients (2.91%). All 3 underwent intestinal biopsy that showed in all total or subtotal villous atrophy. None of these subjects had overt clinical signs of malabsorption nor impaired nutritional indexes. Considering that CD prevalence is close to 1:300, the expected number of CD patients would have been 0.34 (Standardised Ratio = 8.82 with confidence intervals from 1.8 to 25.78) [ $p < 0.05$ ]. *Conclusions:* Prevalence of CD among ATD patients is significantly higher than in the general population, probably because of a genetic link through same HLA apotypes. We consider worthwhile the screening of ATD patients for silent CD. Intestinal disorders, absorption: Gluten enteropathy } "Screening for Coeliac Disease in Autoimmune Thyroid Disease"

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"P P 61 1493" P 61 1493 **Postheparin Plasma DAO Activity and Xylose Absorption Test-Correlations with Jejunal Biopsy in Children with Protracted Diarrhoea** E. Toporowska-Kowalska, K. Wasowska-Kr\`f3likowska, W. Fogel, W. Kozlowski

Medical University, Polish Academy of Science, Military Academy of Medicine, Lodz, Poland The aim of the present paper was to attempt to answer the question, whether postheparin plasma DAO activity test may be an indirect non-invasive exponent of the morphological findings of small intestinal mucosa in children with protracted diarrhoea (pd) and its comparison with xylose absorption test. DAO is an enzyme whose main source is the alimentary tract where the highest DAO's activity is observed in mature enterocytes. The study was carried out in a group of 45 children with pd. In all the children with pd jejunal biopsies, xylose absorption test and DAO test were performed. The applicability of both tests was assessed by determining their correlation with the degree of jejunal villous atrophy. Only a weak negative correlation of xylose absorption test with the degree of jejunal villous atrophy was observed in children below 2 years of age ( $r = -0.36$ ;  $p < 0.1$ ). The percentage of consistent findings was only 36%. Analogous statistical analysis carried out for the DAO test demonstrated that as the atrophic changes in small intestinal villi progress, postheparin plasma DAO activity values, corresponding to the particular degrees of jejunal villous atrophy as well as those obtained for control group demonstrated statistically significant differences (0.60 vs 1.12 vs 1.62 vs 2.43 pmol/min/mg protein; ) *Conclusions:* 1/postheparin plasma diamine oxidase activity test (DAO test) allows for the differentiation of patients with normal and damaged jejunal mucosa barrier; 2/DAO test is correlated with the degree of jejunal villous atrophy and other morphological indices of mucous membrane damage; 3/DAO test- unlike the xylose absorption test- is correlated with the degree of jejunal villous atrophy; independently of the age of children with protracted diarrhoea and stage of the diagnostic process. Intestinal disorders, absorption: Malabsorption syndromes }" "Postheparin Plasma DAO Activity and Xylose Absorption Test-Correlations with Jejunal Biopsy in Children with Protracted Diarrhoea"

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"P P 62 1494" P 62 1494 **Beneficial Effects of DA-9601, Extract of *Artemisia Asiatica*, in TNB-Induced Experimental Colitis in the Rat**

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Dept. of Gastroenterol., Ajou Univ. School of Med. and Research Lab., Dong-A pharmaceutical, Suwon, Korea

The aim of the present study was to investigate the effect of DA-9601, extracts of *Artemisia asiatica*, which was known to possess mucoprotective effect either by free radical scavenging effect or increase of mucus secretion, against experimental colitis induced by trinitrobenzene sulfonic acid (TNB) in a rat model of inflammatory bowel disease. Colitis was induced in 7 week-old male SPF Sprague-Dawley rats by a rectal administration of TNB (20 mg in 1 ml of 30% ethanol). To investigate the effects of DA-9601 on experimental colitis, rats were provided with diet containing mesalazine 25 mg/kg/day (group 1), mesalazine 50 mg/kg/day (group 2), DA-9601 5 mg/kg/day (group 3), DA-9601 25 mg/kg/day (group 4), and DA-9601 125 mg/kg/day (group 5) or vehicle (saline 1 ml). 10 rats participated in each treated group and control group. Rats were sacrificed at the 7th and 15th day after each drug treatment. Macroscopic and microscopic damage score of the last 10 cm of colon was determined according to the criteria by Wallace (J Physiol Pharmacol 66: 422, 1987) and Murthy (Dig Dis Sci 38: 1722, 1993). Thiobarbituric acid-reactive substances (TBA-RS) and myeloperoxidase (MPO) activities in the colonic homogenates were determined. TNB induced severe colonic lesions and significant decreases in antioxidants in the colonic mucosa. In all TNB colitis group treated with DA-9601 (group 3, 4, 5), histologic damage scores were significantly improved when compared with their respective controls and mesalazine group. Macroscopic damage scores were significantly lower in DA-9601 treated group compared with those of control or mesalazine treated group (0.60 – 0.8 vs 3.7 – 2.8,  $P < 0.01$ ). In comparison with control and group 1, 2, group 3, 4, 5 showed decreased MPO and TBA-RS activities dose-dependent manner. In conclusion, DA-9601 was effective in reducing macroscopic and histologic scores in TNB induced colitis and could be a promising drug for the therapy of inflammatory bowel disease.

Intestinal disorders: IBD, therapy } "Beneficial Effects of DA-9601, Extract of *Artemisia Asiatica*, in TNB-Induced Experimental Colitis in the Rat"

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## "P P 62 1495" P 62 1495 **Beneficial Effects of SR140333, a Novel Substance P Antagonist, in a Rat Model of Experimental Colitis**

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Medical Unit, "G. D'Annunzio" University, Pierangeli Clinic, Pescara, Italy

<sup>3</sup> Department of Human Pathology, "G. D'Annunzio" University, Pierangeli Clinic, Pescara, Italy

<sup>4</sup> Institute of Visceral and Transplantation Surgery, University of Berne, Switzerland *Purpose and aims:* The etiology of inflammatory bowel disease is not clearly understood; there is evidence that several neuropeptides, including substance P, play a role. Therefore, we evaluated the ability of a novel SP-antagonist (SR140333) in modifying the course of experimental colitis induced in the rat by trinitrobenzensulfonic acid (TNB). *Methods:* Colitis was induced in 12 rats using TNB administered with an intrarectal enema. Six rats were treated with SR 140333 by intraperitoneal route (1.0 mg/kg) 30 minutes before the administration of TNB and every day until the sacrifice. Ten rats receiving only an intrarectal 0.9% saline served as controls. Rats were killed 14 days after the induction of colitis. 1 cm strips were collected for morphological and contraction studies. *Results:* The TNB group showed a higher score of inflammation, as assessed by histology and a greater weight of strips than controls; in addition, smooth muscle contractility was significantly reduced in inflamed colon than in controls. SR 140333 reduced inflammation and motor alterations caused by TNB. TNB Controls TNB + SP antag Weight (gr.) 0.303 – 0.03 \* 0.135 – 0.01 0.191 – 0.03<sup>#</sup> Infl. score 8.6 – 0.27 \* 1.6 – 0.19 4.0 – 0.7<sup>#</sup> CARB (mg/mm<sup>2</sup>) 91.3 – 24.4 \* 257.1 – 32.2 150.9 – 15.3<sup>#</sup> SP (mg/mm<sup>2</sup>) 22.1 – 4.4 \* 83.4 – 9.3 32.5 – 3.1<sup>#</sup> KCl (mg/mm<sup>2</sup>) 47.7 – 1.7 \* 89.9 – 15.1 125.9 – 12.1<sup>#</sup> \*p < 0.01 vs. controls; <sup>#</sup>p < 0.01 vs. TNB *Conclusions:* Treatment with SR140333 reduces the degree of inflammation and the concomitant alterations of contractility during TNB colitis. These findings suggest a role by substance P in the pathogenesis of colitis. The blockade of substance P may represent a reliable strategy in the treatment of intestinal inflammation. Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation Motility, general: Innervation } "Beneficial Effects of SR140333, a Novel Substance P Antagonist, in a Rat Model of Experimental Colitis"

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"P P 62 1496" P 62 1496 **Recombinant Factor XIII Replacement Therapy: Studies in a Rat Model of Experimentally Induced Intestinal Inflammation**. Grossmann, K.H. Sprugel, C. Hart, P. Strange,

\*P.D. Bishop

ZymoGenetics, Inc., Seattle Washington USA and D'Argenio G, Cosenz V. Cattedra di Gastroenterologia, Universita' Federico II, Napoli, Italy Coagulation factor XIII (FXIII) is the plasma borne transglutaminase which serves as the terminal enzyme in the clotting cascade. There is growing evidence that FXIII levels in the plasma of UC and CD patients are lower than normal and that there is a significant inverse correlation of FXIII with clinical severity. In order to better understand the potential use of FXIII replacement therapy in IBD, we have investigated the effects of recombinant FXIII treatment in a widely used animal model for IBD; TNBS induced chronic inflammation and ulceration of the rat colon. The effects of FXIII were assessed vis a' vis both positive (5-ASA), and negative (BSA) controls over a 28 day time course. The severity of lesions was determined by colon weight, macroscopic and histologic scores and transglutaminase activity was measured in both serum and colon tissue. Results indicate that in this model, lesion severity inversely correlated with transglutaminase levels. Consistent with these observations, rFXIII treatment restored serum and tissue transglutaminase levels and very significantly reduced lesion severity. Additionally, rFXIII treatment reduced the time to recovery for both developing and established lesions and was efficacious for at least 18 days after treatment was discontinued. These results indicate that FXIII replacement therapy is effective in an animal model of induced colitis and suggests its potential usefulness in the treatment of human inflammatory bowel disease. Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy Intestinal disorders: IBD diagnosis, monitoring } "Recombinant Factor XIII Replacement Therapy: Studies in a Rat Model of Experimentally Induced Intestinal Inflammation"

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## "P P 62 1497" P 62 1497 Changes of Fecal Short-Chain Fatty Acids in Experimental Murine Ulcerative Colitis

\*K. Ariake<sup>1</sup>, T. Ohkusa<sup>1</sup>, S. Hosi<sup>2</sup>, T. Yajima<sup>2</sup>, I. Takashimuzu<sup>1</sup>, K. Fujiki<sup>1</sup>, A. Araki<sup>1</sup>, K. Shimoi<sup>1</sup>, K. Honda<sup>1</sup>, Y. Enomoto<sup>1</sup>, T. Sakurazawa<sup>1</sup>, T. Horiuchi<sup>1</sup>, S. Suzuki<sup>1</sup>, K. Ishii<sup>1</sup>

<sup>1</sup> First Department of Internal Medicine, Tokyo Medical and Dental University School of Medicine, Tokyo

<sup>2</sup> Nutrition Science Institute, Meiji Milk Products Co., Ltd., Tokyo, Japan We reported that *Bacteroidaceae* significantly increased in the intestinal microflora of mice with experimental colitis induced by dextran sulfate sodium (DSS). It was reported that succinic acid was a major fatty acid by-product of *Bacteroidaceae* metabolism and impaired phagocytic killing function of neutrophils. Therefore, we investigated the relation between fecal short-chain fatty acids (SCFA), included succinic acid, and the occurrence of colorectal ulceration in this colitis model. **Methods:** Experimental colitis was induced by 14 days-administrations of 3% DSS (M.W. 52,000) to CBA/J female mice. Control mice were given distilled drinking water for 14 days. After sacrifice, stool specimens were obtained from cecum, proximal colon, and distal colon. Fecal SCFA were measured by HPLC. **Results:** Histological observation indicated predominant severity of ulceration on the distal colon with less ulceration on the cecum and proximal colon in DSS mice. In fecal SCFA analyses, succinic acid significantly increased in cecum, proximal and distal colon ( $p < 0.05$ ) of DSS mice. Mean fecal succinic acid concentrations were significantly higher ( $p < 0.05$ ) in the distal colon ( $3.42 \mu\text{mol/g}$ ) than in the proximal colon ( $1.71 \mu\text{mol/g}$ ) and in the cecum ( $1.90 \mu\text{mol/g}$ ). Butyric, acetic, and propionic acids significantly decreased in cecum, proximal and distal colon of DSS mice ( $p < 0.05$ ) when compared with the control. **Conclusion:** Fecal succinic acid mainly produced by *Bacteroidaceae* spp. may be the ulcerogenic agent of this experimental ulcerative colitis. Intestinal disorders: IBD, basic Intestinal disorders: IBD, etiology and genetics Immunology and microbiology: Inflammation } "Changes of Fecal Short-Chain Fatty Acids in Experimental Murine Ulcerative Colitis"

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"P P 62 1498" P 62 1498 **The Effect of Diltiazem on Acetic Acid-Induced Colitis in Rats**

\*A. \d6. \d6z\ftemiz, B. \dcnsal, M. Alkanat, K. Aks\ 'f6z, \c7. Din\ 'e7er, Y. Batur

Depts. of Gastroenterology and Pathology of Ege University Medical Faculty, Izmir, Turkey

Dept. of Gastroenterology of Atat\ 'fcrk State Hospital, Izmir, Turkey In inflammatory bowel disease, prostaglandins (PG) are mucosal protective whereas leukotrienes (LT) are proinflammatory. (Recent evidence suggests that the formation and action of LTs are calcium-dependent, whereas the formation and action of PGs are not. *In this study we examined* a calcium channel blocker, diltiazem (DLTZ), as a therapeutic agent on acetic acid (AA)-induced colitis in rats. *Methods:* Male Swiss Albino rats were divided into the 4 groups (n = 10). I-Rats were administered 1 ml 4% AA intrarectally, II-DLTZ was given i.m., in a dose of 2 mg/kg, for 7 consecutive days before instillation of AA, III-DLTZ was given i.m., in a dose of 2 mg/kg plus indometacin 5 mg/kg s.c., for 7 consecutive days before instillation of AA. In group IV rats were administered 1 ml of saline alone intrarectally. The rats were sacrificed two days later and the distal colons were scored (grade 1–4) macroscopically and tissue myeloperoxidase (MPO) activity was determined. Results (mean – SEM): Groups MPO U/g. wet weight Macroscopic score I-AA 19.8 – 2.7 (a) 3.74 – 0.32 (a) II-DLTZ + AA 3.4 – 1.0 (b, d) 1.42 – 0.23 (c) III-DLTZ + Indo. + AA 5.5 – 1.7 (b, d) 1.57 – 0.28 (c) IV-Saline 0.8 – 0.04 1.00 (a): different from group IV, p < 0.001 (b): different from group I, p < 0.001 (c): different from group I, p < 0.01, (d): different from group IV, p < 0.05 (Student's- t test) *In conclusion,* 1-Diltiazem plays a protective role on AA-induced colitis in rats, 2-Inhibition of endogenous PG biosynthesis has no effect on this protection. Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy }" "The Effect of Diltiazem on Acetic Acid-Induced Colitis in Rats"

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## "P P 62 1499" P 62 1499 Comparison of OR-1384 and Hydrocortisone in a Rabbit Colitis Model

\*A. Koponen, P. Aho, K. Haasio, I.-B. Lind

Orion Pharma Research, Espoo, Finland OR-1384 (3-[[4-(methylsulfonyl)phenyl]methylene]-2,4-pentanedione) is a novel thiol modulating agent intended for the treatment of inflammatory bowel disease (IBD). This compound has been effective in several animal models of ulcerative colitis. In this study the effect of OR-1384 was studied in rabbit immune complex colitis and compared to that of hydrocortisone (HC). *Methods:* The colitis was induced in New Zealand White rabbits by introducing dilute formalin into the lumen of the colon and by injecting preformed immune complexes into the marginal ear vein two hours later. Different concentrations of formalin (1% or 0.45%) were used in order to induce "severe" or "mild" colitis, respectively. The rabbits were killed two days ("mild" colitis) or three days ("severe" colitis) after formalin application. The colonic lesions were scored and the tissue was examined histologically. The colonic mucosal eicosanoid production was also measured. The rabbits were treated with OR-1384 or HC enemas (2 ml/kg): 10 mg/kg for the "severe" colitis and 3 mg/kg for the "mild" colitis. OR-1384 was dosed once daily and HC twice daily. The dose dependency of OR-1384 was tested in the "severe" colitis using doses 3, 10 and 30 mg/kg. *Results:* OR-1384 induced a dose related protective effect against the "severe" rabbit colitis. The dose 10 mg/kg inhibited the lesion score by 61% and reduced the formation of prostaglandin E2 (PGE2) by 50% and leukotriene B4 (LTB4) by 58%. HC was not effective in the "severe" colitis. In the "mild" colitis both compounds had a favourable effect. However, OR-1384 was more effective protecting against mucosal lesions by 79% and decreasing PGE2 by 61% and LTB4 by 82%. The corresponding figures for HC were 44%, 51% and 13%. The results from the histological evaluation were in line with the macroscopic scores. *Conclusion:* In the rabbit immune complex colitis locally administered OR-1384, dosed once daily, was shown to be more effective than HC, dosed twice daily. Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy Immunology and microbiology: Inflammation } " Comparison of OR-1384 and Hydrocortisone in a Rabbit Colitis Model"

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"P P 62 1500" P 62 1500 **Fish-Oil Enriched Diet Inhibited Leukotriene Release in Experimental Trinitrobenzene Sulfonic Acid (TNB) Colitis in Rats**

\*H. Y\fcceyar, \d6. \d6z\ftemiz, A. H\fcseyinov, M. Alkanat, S. Bor, I. \c7oker, Y. Batur

Depts. of Gastroenterology & Pathology, University of Ege, Izmir, Turkey  
The etiology of inflammatory bowel disease (IBD) is still unknown and the treatment of recurrences of IBD is also insufficient. In this study, we investigated that the protective role of fish oil (FO)-enriched diet in a rat model of TNB colitis. 20 male Wistar- Albino rats were randomized into 2 groups (n = 10). All of them were fed along 6 weeks with standard diet (group-1) and standard diet plus FO (%8) [group-2], At the end of this period, TNB (30 mg in 0.25 ml of %30 ethanol) were intrarectally administered. After two weeks, rats were sacrificed and the distal colon was removed. Specimens were histopathologically evaluated. Myeloperoxidase (MPO) enzyme activities (Ug/wet weight) were measured and leukotriene B4 (LTB4) (pg./mg tissue protein) and leukotriene C4 (LTC4) levels (pg./mg tissue protein) were determined by radioimmunoassay. The results were showed in table. Groups MPO LTB4 LTC4 Pathologic scores  
Group 1 30.41 – 1.9 372.1 – 65.2 450.0 – 6.45 2.125 – 0.3  
Group 2 2.43 – 0.4 34.5 – 8.1 64.0 – 10.46 1.555 – 0.2  
There were significant differences in MPO activities, LTB4 and LTC4 levels and histopathological scores between two groups (respectively p = 0.0108, p = 0.0034, p = 0.0024, p = 0.002). In conclusion, FO-enriched diet could reduce the colon damage in TNB colitis in rats.  
Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy }  
"Fish-Oil Enriched Diet Inhibited Leukotriene Release in Experimental Trinitrobenzene Sulfonic Acid (TNB) Colitis in Rats"

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"P P 62 1501" P 62 1501 **The Effect of Fish on Enema in Trinitrobenzene Sulphonic Acid (TNB) Induced Colitis in the Rat**

\*H. Y\fcceyar, \d6. \d6z\fcctemiz, A. H\fcseyinov, M. Alkanat, S. Bor, I. \c7oker, M. Tun\ey\fcrek, C. \c7oker, Y. Batur

Depts. of Gastroenterology & Pathology, University of Ege, Izmir, Turkey In recent studies, it has been shown that fish oil (FO)-enriched diet has a protective role in experimental colitis models. However, there was no sufficient knowledge about using of intrarectally FO administration during long periods. In this study, we investigated whether intrarectally FO administration has a protective role in TNB colitis. In the first step, 20 male rats were randomized into two groups (n = 10). TNB (30 mg in 0.25 ml of %30 ethanol) was intrarectally administered into each group. After one day, 1 ml of saline or FO enemas were administered in every day along two weeks. At the end of this period, the distal colons were removed. The specimens were histopathologically evaluated. Myeloperoxidase (MPO) enzyme activity (Ug/wet weight) and leukotriene B4 (LTB4) and LTC4 levels (pg/mg tissue protein) were measured by RAI (Mean – SEM). While there was no significant difference between group-1 and 2 in the comparison of MPO activities and pathologic scores. The LTB4 and LTC4 levels of FO group were less than the measurements of saline group (respectively p = 0.0081 and p = 0.0051). In the second step, 20 male rats were randomized into two groups. 1 ml of saline (group-3) or FO (group-4) enemas were administered in every day along three days. At the fourth day, TNB was given 0.25 ml intrarectally. After 24 hours, rats were sacrificed. We could not find any significant difference between group-3 and 4 in all parameters. In conclusion, although FO-enriched diet could reduce the colon damage in experimental TNB colitis, according to our results (in the first and second steps) the short periods of FO enemas do not play protective role in TNB colitis. Groups MPO LTB4 LTC4 Pathologic scores Group-1 6.5 – 2.3 257.1 – 60.6 514.2 – 23.9 2.25 – 0.31 Group-2 4.0 – 0.9 138.1 – 25.6 146.5 – 36.9 1.87 – 0.29 Group-3 25.01 – 3.5 285.0 – 59.6 502.1 – 124.5 2.85 – 0.14 Group-4 19.7 – 3.1 394.5 – 64.3 652.3 – 125.6 2.14 – 0.33 Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy } "The Effect of Fish on Enema in Trinitrobenzene Sulphonic Acid (TNB) Induced Colitis in the Rat"

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## "P P 62 1502" P 62 1502 **The Effect of Fish Oil Enema in Acetic Acid-Induced Colitis and Ethanol-Induced Colonic Damage in Rats**

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The importance of dietary fish oil (FO) is a well-known concept in the treatment of inflammatory bowel disease (IBD). In recent studies, it has been shown that FO-enriched diet reduces the level of some mediators -PAF, leukotrienes- which have noxious effects on the colonic mucosa. But there are a few reports indicating the effect of FO enema in the treatment of IBD. In this study, we investigated the protective role of FO in acetic acid (AA)-induced colitis and ethanol-induced colonic injury. 60 male Wistar rats was divided into AA and ethanol groups (n = 30). Each group was divided into FO, corn oil (CO) and saline subgroups (n = 10). Each subgroup was given 1 ml of FO, CO or saline via rectal route into to lumen of the colon using a rubber cannule. 1 hour later, 1 ml of 4% AA was given to the AA group and 0.25 ml of 30% ethanol was given to the ethanol group in the same manner. The rats were sacrificed two days later and the distal colons were scored histopathologically and myeloperoxidase (MPO) activity (U/g wet weight) was determined. Groups MPO Pathologic score  
FO + AA 8.72 – 4.87 1.142 – 0.142  
CO + AA 11.28 – 0.28 1.428 – 0.331  
Saline + AA 13.55 – 1.78 1.571 – 0.534  
FO + ethanol 12.60 – 3.26 1.285 – 0.289  
CO + ethanol 13.72 – 2.82 1.571 – 0.369  
Saline + ethanol 14.45 – 3.77 1.571 – 0.202  
No significant differences was found between subgroups. In conclusion, FO and CO does not play a protective role in acetic acid-induced colitis and ethanol-induced colonic damage in rats.  
Intestinal disorders: IBD, basic  
Intestinal disorders: IBD, therapy } "The Effect of Fish Oil Enema in Acetic Acid-Induced Colitis and Ethanol-Induced Colonic Damage in Rats"

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"P P 63 1503" P 63 1503 **Ten-Year Outcome of Restorative Proctocolectomy for Ulcerative Colitis**

\*C. Penna, P. Gasne, R. Parc

Service de Chirurgie Digestive, Hopital Saint-Antoine, Paris, France Restorative proctocolectomy (RP) is the treatment of choice for patients with ulcerative colitis. However, little is known about complications, risk of pouchitis and bowel function over the long term. *Aim:* To study the results of RP for UC in a cohort of patients with a minimum of 10 years follow-up. *Patients and Methods:* Among 500 RP patients, 40 consecutive subjects (18 males, median age 40 at operation) were identified who had the operation for UC prior to 1986. The occurrence of late complication, pouchitis and the bowel function were prospectively recorded. *Results:* One patient died of unrelated cause. Two patients (5%) were identified as having Crohn's disease 2 and 3 years after RP and pouch removal was mandatory in one case. There was no other pouch failure. Six complications occurred after the first year: 1 bowel obstruction and 3 anastomotic strictures were treated medically, 2 incisional hernias were operated. Pouchitis occurred in 5 patients (13%) and was chronic in only one case. Between the first and the 10th year bowel function remained unchanged. Median bowel frequency was 5.3 at 1 year and 4.9 at 10 years, daytime continence was perfect in 86% at 1 year and 91% at 10 year, nighttime continence was perfect in 69% at 1 year and 77% at 10 year. At 10 year only 11% of patients followed a strict diet (versus 33% at 1 year,  $p < 0.05$ ). Nine patients were more than 50 years old at RP and bowel function was also unchanged in this subgroup after 10 years. *Conclusions:* Long term follow-up of RP for UC showed that late morbidity was minimal, pouchitis easily amenable to treatment and that bowel function did not deteriorate with time, confirming RP as the treatment of choice for most patients with chronic UC. Intestinal disorders: IBD, therapy } "Ten-Year Outcome of Restorative Proctocolectomy for Ulcerative Colitis"

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"P P 63 1504" P 63 1504 **What Are the Functional Results of Colonic Pouch Anal Anastomosis (CPAA) in Aged Patients?**

\*N. Dehni, J.D. Singland, R.D. Schlegel, M. Guiguet, E. Tiret, R. Parc

Centre de chirurgie digestive, Hospital Saint Antoine, Paris, France Many low rectal cancers can be treated radically by proctectomy with mesorectal excision followed by CPAA. In aged patients, the fear of a poor function might reduce indications of CPAA in favour of abdomino-perineal excision with end stoma. The aim of this study was to evaluate the long term results of CPAA in patients over 75 years. *Methods* Among 198 patients with CPAA operated on between 1984 to 1992 for low rectal cancer, 20 patients over 75 years old were alive without recurrence at the time of telephone interview (July 95). Minimal follow up was 3 years for all patients. *Results* mean age at intervention was 74 years (66–87), mean age at interview was 82 years (75–93). Mean time follow up was 8 years. The functional results are listed herein. No bowel movements/day 1.1 (0.4–3.5) Urgency\* 3 (15%) Fragmented defecation\* 5 (25%) Constipation 8 (40%) Needs for micro-enemas\* 7 (35%) Laxatives\* 6 (32%) Incontinence for feces\* 3 (15%) Satisfaction 18 (90%) Incontinence for flatus\* 8 (40%)\*events occurring once or more per week. Incontinence for feces was only occasional in 3 cases. *Conclusion* These results show that functional outcome may be good to excellent in aged patients after CPAA and compare well with those obtained in younger patients in our series. However, constipation may be more frequent in the aged. Age is not a contraindication for CPAA if the sphincter tone is clinically normal. Oncology, specific: Colon, rectum } "What Are the Functional Results of Colonic Pouch Anal Anastomosis (CPAA) in Aged Patients?"

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## "P P 63 1505" P 63 1505 Lack of Postprandial Motor Response in Pouches with Temporary Ileostomy

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Ileal and rectal tone increases after a meal in healthy subjects; this response to feeding is preserved in isolated colonic loops. In a previous study in six patients with ileal pouch-anal anastomosis (IPAA) we observed an increase in pouch tone after a meal.

**Aims:** To confirm the increase in pouch tone after a meal in a larger group of patients and to verify whether this response is preserved in an isolated pouch.

**Methods:** We studied 13 patients with IPAA (5 men and 8 women, age range 18–55 yr), 9 with IPAA and ileostomy closure performed 18–66 months before and 4 with IPAA and temporary ileostomy performed 3 months previously. All pouches were S-shaped. All patients were studied after an overnight fast. In patients with gut continuity the pouch was cleaned with 500 ml water enema 4 hs before the study. Pouch tone was recorded for 1 h in fasting conditions and for 1 h after a 1000 kcal liquid meal (250 ml, 20% of lipids). A polyethylene bag was placed in the pouch and connected to an electronic barostat. The bag volume reflected pouch tone; changes in bag volume > 10% of the baseline volume were considered as phasic volume events. Statistical analysis was performed with Wilcoxon's test. Data are given as mean – SEM.

**Results:** The intrabag operating pressure was similar in patients with gut continuity and in those with ileostomy (6.4 – 0.5 and 7.0 – 1.6 mmHg respectively; P = NS). Pouch volumes were greater in the former than the latter group. In patients with gut continuity pouch volume decreased and the frequency of phasic volume events increased after the meal whereas both variables were unaffected by the meal in patients with ileostomy (Table).

	Volume (ml)	Phasic vol. events (n/h)	Fasting	Postpr.	Fasting	Postpr.
Pouch in continuity	149 – 5	72 – 16*	11 – 2	22 – 2*		
Pouch with ileostomy	69 – 3**	72 – 2	15 – 4	17 – 4*		

\*P < 0.05 vs fasting; \*\*P < 0.05 vs patients with pouch in continuity

**Conclusions:** Pouch tone is greater in patients with IPAA and temporary ileostomy than in those with gut continuity. The lack of motor response after a meal in patients with ileostomy suggests that the decrease in pouch volume observed in patients with IPAA after ileostomy closure may not be due to an increase in tone, but to the arrival of intestinal contents in the pouch.

Motility, specific: Small bowel }

"Lack of Postprandial Motor Response in Pouches with Temporary Ileostomy"

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## "P P 63 1506" P 63 1506 Prognosis and Blood Coagulation Disorders in Venous and Arterial Mesenteric Infarction with Short Bowel

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<sup>2</sup> INSERM U353, Paris, France Blood coagulation disorders either primary through decrease in anticoagulant activity or secondary through increase in procoagulant activity might be a major problem in mesenteric infarction (MI) patients. The aim of this study was to determine in MI patients with short bowel (SB) (remaining small bowel length < 150 cm): 1) frequency and characteristics of blood coagulation disorders, 2) comparative probability of survival. *Methods:* Exhaustive blood coagulation were tested in 16 out of 34 cases of arterial MI (AMI) and in all (14 cases) of venous MI (VMI). Prognosis was analyzed in 48 patients (34 AMI and 14 VMI) by survival probability expressed in actuarial curves according Kaplan-Meier and compared by log-rank test. *Results:* Age was significantly higher ( $p < 0.05$ ) in AMI (mean: 53 yr) than in VMI (43 yr). Small bowel (45 cm (0–130) and colon remnant lengths (66% of normal length { - }0 to 100%) were not different between the 2 groups. Among AMI 10 (63%) had blood coagulation disorders: 4 had decrease of anticoagulant activity, 3 with protein S or C deficiency, one with resistance to activated protein C; 7 had antiphospholipid-antibody syndrome (APAS). Among VMI 5 (36%) had blood coagulation disorders: 2 had decrease of anticoagulant activity, one with resistance to activated protein C and one with hypoplasminogenaemia; 3 had APAS. Among the 15 patients with blood coagulation disorders 12 had previous vascular events and 12 had confounding vascular risk factors. Five-year survival probability was 66 (95% CI: 49–83)% with a worse prognosis for AMI (53%, 95% CI: 33–73) than VMI (100%) ( $p < 0.05$ ). Six of the 11 deaths in AMI group were related to vascular extradigestive complications. *Conclusion:* Blood coagulation disorders were highly prevalent in MI (50%) regardless of site, A versus V, and confounding risk factors. APAS was the most frequent abnormality (33%). The worse prognosis observed for AMI was mainly linked to extradigestive vascular events. Intestinal disorders: Splanchnic circulation, ischemia Intestinal disorders, absorption: Malabsorption syndromes Clinical practice: Management strategy } "Prognosis and Blood Coagulation Disorders in Venous and Arterial Mesenteric Infarction with Short Bowel"

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"P P 63 1507" P 63 1507 **DNA-Aneuploidy in Mucosal Biopsies with No or Slight Atrophy from the Ileal Pelvic Pouch in Patients with Colonic IBD**

\*D. Stahlberg, K. Gullberg, L. Liljeqvist, B. Veress, B. Tribukait, R. L'f6fberg

Department of Medical and Surgical Gastroenterology, Huddinge University Hospital, Sweden *Background:* Total colectomy followed by formation of a pelvic pouch (PP) is an established treatment for patients with ulcerative colitis (UC). Some UC-patients with a PP develop atrophy in the PP-mucosa. We have previously shown that patients developing moderate and severe atrophy of the PP mucosa also are at risk for development of DNA-aneuploidy and dysplasia. *Aim:* To determine if no or slight atrophy in the PP-mucosa also is associated with subsequent development of dysplasia and/or DNA aneuploidy. *Patients and Methods:* Twenty-five patients with PP colectomized due to ulcerative or indeterminate colitis and with no or only slight atrophy in the PP mucosa were included in the study. The median PP-duration was 73 months (range 20–182 months). The patients were examined with a flexible video endoscope and biopsies were taken from 5 locations [the afferent small intestine, upper portion of the pouch, mid portion (2 locations), and lower portion of the pouch]. From each location 1–2 biopsies were taken for histological assessment of dysplasia and 1–2 biopsies were taken for flow cytometric DNA-analyses. *Results:* DNA-aneuploidy was found in three of the patients. In one of them aneuploidy was seen also in the afferent small intestine. In three further patients hyperploidy was seen. No dysplasia was found. One of the patients with aneuploidy was colectomized due to colonic cancer and one patient with hyperploidy underwent surgery due to dysplasia/DALM. *Conclusion:* Patients colectomized due to colonic IBD with a PP displaying no or only slight mucosal atrophy also have a risk for neoplastic transformation of the pouch mucosa as detected by an aneuploid DNA-content. The risk seems to be lower than in patients displaying moderate or severe mucosal atrophy. We suggest that all patients with PP due to IBD should be monitored with endoscopy and biopsy sampling. Intestinal disorders: IBD diagnosis, monitoring Oncology, general: Screening, prevention Oncology, specific: Colon, rectum }" "DNA-Aneuploidy in Mucosal Biopsies with No or Slight Atrophy from the Ileal Pelvic Pouch in Patients with Colonic IBD"

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"P P 63 1508" P 63 1508 **Pre- and Postoperative Diagnosis in Colonic IBD Patients Undergoing Colectomy — Is There a Shift in Diagnosis Towards Crohn's Disease? A Four Year Follow Up Study**

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Karolinska Hospital, Huddinge University Hospital, Söder Hospital, Danderyds Hospital, Karolinska Institute, Stockholm, Sweden

**Background:** In ulcerative colitis (UC), but not Crohn's disease (CD) or indeterminate colitis (IC), patients undergoing colectomy are usually offered a restorative proctectomy. Difficulties to separate these entities, both clinically and histologically, have caused problems in selecting cases for this type of operation. **Aim:** To compare the pre- and postoperative diagnosis in colonic IBD patients undergoing colectomy, and reviewing diagnosis at follow up four years after surgery. **Methods:** All patients with IBD undergoing colectomy during 1986 to 1990 at the four major hospitals in Stockholm were investigated. The clinical diagnosis at the time of operation was accepted as the preop diagnosis. Postop diagnosis was based on the macroscopical findings at operation as well as the histology. All case records were followed up four years after surgery. **Patients:** 83, 52, 45, and 26 patients from the 4 different hospitals, all-together 206 (96 women) were included. The median age at diagnosis was 28 (range 4–78) years, the duration of disease at operation was 7 (1–61) years and the median age at operation 39 (19–78) years. Subtotal colectomy with ileostomy was done in 147 (71%), IRA in 24 (12%), proctocolectomy in 16 (8%) and pelvic pouch procedure in 19 (9%). **Results:** The preop diagnosis were UC 145 (70%), probable UC (pUC) 5 (3%), IC 4 (2%), CD 41 (20%), and probable CD (pCD) 11 (5%). 34/145 (23%) UC cases were reclassified as CD postop. Another 7 patients (5 from pCD, 1 each from IC and pUC) were changed to CD, adding up to 41 "new" CD cases. During follow up, 5 more patients with CD were added. In total, CD increased from 41 preop to 80 postop and 85 at follow up compared to a decrease in UC from 145 to 107. The increase in CD was most evident at the two hospitals with the largest numbers of patients operated. The initial CD cases were only reduced by 2, that were reclassified as UC postoperatively. **Conclusions:** One fifth of all patients with UC before colectomy, had this diagnosis questioned with a subsequent suggestion of CD. This may be due to lack of sufficient histological information preoperatively, and the final numbers may more truly reflect the prevalence of UC and CD in the society. Different patterns from different hospitals suggest that pathologists and clinicians look differently on histological signs supportive of CD. The benign course in the reclassified CD cases may justify surgery with pouch procedure in such CD patients. Intestinal disorders: IBD diagnosis, monitoring }

"Pre- and Postoperative Diagnosis in Colonic IBD Patients Undergoing Colectomy / Is There a Shift in Diagnosis Towards Crohn's Disease? A Four Year Follow Up Study"

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"P P 63 1510" P 63 1510 **Mucosal Associated Ileal Flora after Ileocolic Resection for Crohn's Disease** E. Lederman, C. Neut, P. Desreumaux, O. Klein, P. Baron, L. Gambiez, P. Quandalle,

\*J.F. Colombel

C.R. Inserm-4U004B, Laboratoire de bactériologie, Faculté de Pharmacie, CH et U, F-59037 Lille **Background/Aim:** After an ileocolic resection for Crohn's disease (CD), an endoscopic recurrence occurs in the neoterminal ileum in 40–60% of cases 3 months after surgery and almost in 80% of cases at 1 year. Clinical and experimental evidence support the role of bacterial flora in this recurrence. The aim of this study was to identify mucosal associated bacterial flora in the neoterminal ileum of patients operated on for CD in relation to the presence or not of an endoscopic recurrence. **Methods:** Ileal biopsies were obtained per-operatively in the healthy ileum of 10 patients at time of an ileocolectomy for CD, 3 months after surgery in 17 patients and 12 months after surgery in 18 patients. An endoscopic recurrence defined as score  $\geq 2$  (according to Rutgeerts et al., 1990) was documented in 7/17 patients at 3 months and 11/18 at one year. Samples were inoculated and incubated under aerobic or anaerobic conditions. After counting predominant colonies were subcultured and identified. **Results:** log<sub>10</sub> Colony Forming Unit/g of tissue (mean – SD) Per-operative samples 3 months 12 months (n = 10) (n = 17) (n = 18) Aerobic incubation 4.2 – 0.5 6.1 – 1.1\* 7 – 1.5\* Anaerobic incubation 4.7 – 0.8 7 – 1.1\* 7.9 – 0.9\*<sup>§</sup> \*p < 0.001 vs per-operative samples; <sup>§</sup>p < 0.05 vs 3 months. Among the aero-anaerobic flora, the predominant species at 3 and 12 months were: *Escherichia coli*, *Bacteroides* and *Clostridium* species. There were no quantitative differences in the bacterial flora in patients having or not an endoscopic recurrence either at 3 or 12 months. **Conclusion:** Mucosal associated ileal flora is significantly increased after surgery in CD with predominant species characteristic of a fecal-type flora. Other factors appear necessary for the onset of an endoscopic recurrence. Intestinal disorders: IBD, etiology and genetics Intestinal disorders: IBD, basic }" "Mucosal Associated Ileal Flora after Ileocolic Resection for Crohn's Disease"

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"P P 63 1511" P 63 1511 **Influence of Azathioprine on Postoperative Recurrence after Ileocecal Resection for Crohn's Disease** F. Mauvais,

\*Y. Panis, J. Nemeth, P. Hautefeuille, P. Valleur

Digestive Surgical and Pathology Departments, University Hospital Lariboisière, 2 rue Ambroise Paré, 75010, Paris, France Recently, it has been demonstrated that mesalamine was effective in decreasing postoperative recurrence rate after surgery for Crohn's disease (CD). The possible effect of azathioprine on postoperative recurrence remains unknown. *The aim of this retrospective study* was to assess the possible effect of postoperative azathioprine administration (and 5-ASA) on long-term clinical recurrence rate after ileocecal resection for CD. *Patients and Methods:* From 1980 to 1995, 93 patients (pts) underwent ileocecal resection for CD. There were 49 women and 44 men (mean age – SD: 31 – 12 years). Indication for resection was: failure of medical therapy (n = 47); obstruction (n = 6); fistula (n = 23); abscess (n = 9); peritonitis (n = 6) and miscellaneous (n = 2). *Results:* Mean follow-up was 71 – 42 months (extr. 1–178); 6 pts were excluded: 4 for azathioprine disruption early after surgery; 2 patients received other treatment (methotrexate and solupred enemas). No treatment Azathioprine 5-ASA (n = 53) (n = 15) (n = 19) Mean follow-up 88 – 41 44 – 34 53 – 26 (months) Total recurrence rate (%) (a) 64% (34/53) 13% (2/15) 26% (5/19) 5-year recurrence rate (%) 52% 17% 50% Mean delay of recurrence 40 – 38 39 – 33 29 – 21 (months) (a): No treatment vs azathioprine or vs 5-ASA: p < 0.02; azathioprine vs 5-ASA: N.S. *Conclusions:* This preliminary study suggests that azathioprine could be effective for reducing postoperative recurrence rate after surgery for CD. A randomized study comparing azathioprine versus 5-ASA after surgery for CD should be undertaken. Intestinal disorders: IBD, therapy } "Influence of Azathioprine on Postoperative Recurrence after Ileocecal Resection for Crohn's Disease"

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"P P 63 1512" P 63 1512 **Therapeutic Implications of Endoscopic and Histologic Informations Collected after Subtotal Colectomy for Fulminant Colitis**

\*C. Penna, O. Chapuis, R. Parc

Service de Chirurgie Digestive, St. Antoine Hospital, Paris, France Fulminant colitis unresponsive to medical therapy requires sub-total colectomy (STC). Examination of the specimen and of the rectal remnant may help to better classify the colitis between ulcerative colitis (UC) and Crohn's disease (CD) and consequently to guide the type of restoration of bowel continuity (ileorectal (IRA) or ileoanal (IAA) anastomosis). *Aim:* to evaluate the consequences of the changes in initial diagnosis made after a STC for fulminant colitis. *Patients and methods:* between 1984 and 1994, 89 patients (mean age 33 years, 57 men) had STC for a fulminant colitis of 3 to 12 days duration. Bowel continuity was restored 4 to 7 months later. Preoperative diagnosis was compared to the diagnosis before restoration of bowel continuity and to the definitive diagnosis taken on clinical, endoscopic and pathological basis after a mean follow-up of 42 months (14 to 111). *Results:* initial diagnosis was UC in 62 cases, CD in 8, indeterminate colitis (IC) in 19. Between the STC and the restoration of bowel continuity, the diagnosis was changed in 24 cases. The 8 CD were confirmed, patients had an IRA but definitive diagnosis appeared to be UC in 2 cases. UC was confirmed in 57 patients who had a IAA but 4 further appeared to have CD. UC was changed in CD in 5 patients (aphtoid ulcerations, granulomas) who had IRA but for whom follow-up confirmed UC. IC were classified in 6 CD and 13 UC with 1 error in each group at follow-up. *Conclusions:* endoscopic and histologic examinations after STC was useful for IC but did not preclude to perform IAA for CD and diversion colitis was responsible for erroneous changes from UC to CD. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy Endoscopy, specific: Colon, rectum } "Therapeutic Implications of Endoscopic and Histologic Informations Collected after Subtotal Colectomy for Fulminant Colitis"

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## "P P 63 1513" P 63 1513 **Adaptative Hyperphagia and Net Digestive Absorption after Massive Small Bowel Resection**

\*P. Crenn, L. Beloucif, M.C. Morin, F. Thuillier, J.C. Rambaud, B. Messing

Hospital Saint-Lazare and INSERM U290, 75010 Paris, France *Aim:* to quantitatively describe free oral intake and net digestive absorption (NDA) of protein and fat in Short Bowel (SB) patients. *Methods:* Nonactive digestive SB (n = 90) patients, mean age 51 yr (range: 19–81), were studied during 3-day periods for oral ingesta and fecal excreta, with a total of 247 exams. Digestive losses were measured for protein and fat using Kjeldahl and Van de Kamer techniques respectively. We analyzed: a) last NDA exam after (43 (1–240) month) resection (n = 90), b) NDA before and after (2.2 (0.5–14) month) re-establishment of colonic continuity (n = 12), c) early (< 6 month, mean: 2.3) and late (> 6 month, mean: 29.6) NDA after re-establishment of colonic continuity (n = 14). *Results:* a) Remnant length for jejunum and ileum (opisometry) was 71 cm (0–200) and 9 cm (0–120) respectively; the remnant colon in continuity was 66% (0–100) of normal length. The  $47 - 15 \text{ kcal}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$  (mean – SD) oral diet consisted of 46% carbohydrate, 34% fat and 20% protein. NDA (%: In – Out:In) was 53 – 24% for fat, and 60 – 22% for protein (p = 0.05 vs fat). Stool weight was related to percent colon in continuity (p < 0.0001), jejunum (p < 0.001) and ileum length (p < 0.05) and calorie ingesta (p < 0.05). NDA for protein was related to jejunum (p < 0.001) and ileum length (p < 0.01), and presence of rectum (p = 0.05); NDA for fat was related to jejunum (p < 0.01) and ileum length (p < 0.05), presence of ileocecal valve (p = 0.05) and fat ingesta (p = 0.05). b) After re-establishment of colonic continuity there was a decrease in stool weight (4000 vs 1215 g, p < 0.001), an increase in NDA for protein (32 vs 69%, p < 0.001) and fat (38 vs 66%, p < 0.01). c) Between early and late periods despite a significant increase in ingesta ( $39 - 14$  vs  $51 - 21 \text{ kcal}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ ) (p < 0.05) there was a non significant change of stool weight (2038 vs 1838 g), of NDA for fat (51 vs 49%) and of NDA for protein (48 vs 57%). *Conclusion:* These data confirms hyperphagia in SB patients and show the importance of colonic continuity for an increase in protein and fat NDA. Over time, since hyperphagia increase and % NDA do not change an increase of NDA *per se* was observed. Intestinal disorders, absorption: Malabsorption syndromes Nutrition: Nutrients and gut function } "Adaptative Hyperphagia and Net Digestive Absorption after Massive Small Bowel Resection"

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"P P 63 1514" P 63 1514 **Small Intestine Transplantation in the Rat- Comparison of Immunogenicity of Foetal and Adult Allografts** M. Francelina Lopes, A.S. Cabrita, J.A.B. Patr\`edcio

Laboratory of Animal Experimentation, University Hospital of Coimbra, and Faculty of Medicine, University of Coimbra, Portugal

**Introduction:** Rejection remains one of the principal causes of morbidity in clinical intestinal transplantation. Ontogenic studies have shown that foetal intestine has a relatively immature immune system, therefore the use of foetal intestinal grafts for small bowel transplantation might have some immunological advantages over the use of adult donor intestine. This experiment was designed to study this hypothesis as an immunological bi-directional rat model, with different histocompatibility barriers.

**Materials and methods:** Fifty-six small bowel transplantation were made, across a minor histocompatibility barrier (outbred Wistar-Wistar and a stronger one (Wistar-Sprague Dawley). Donor rats were Wistar and recipients were Wistar and Sprague Dawley. Animals dying on the first 48 h post-transplantation were excluded.

**Experimental Groups:** Adult rats (Wistar and Sprague-Dawley) underwent accessory jejunal (4 cm) transplantation, using the technique described by Zhong et al (Microsurgery 12: 268–274, 1991). They were grouped as follows: Group A: Wistar-Wistar, N = 9 and Group B: Wistar-Sprague-Dawley, N = 10. Jejunal grafts (4 cm) of Wistar foetuses (gestation age of 19 days), were transplanted into omentum of adult Wistar or Sprague-Dawley rats, using the technique of Kellnar et al (J Pediatr Surg 27: 799–801, 1992). They were grouped as follows: Group C: Wistar-Wistar, N = 18 and Group D: Wistar-Sprague-Dawley, N = 18. The recipients of the groups A, B, C and D were further divided into three subgroups, which received intramuscular cyclosporine A, for 21 days, beginning on the day of transplantation, 10 mg/Kg/day (subgroups A1-N = 3, B1-N = 3, C1-N = 6 and D1-N = 6) and 2 mg/Kg/day (subgroups A2-N = 3, B2-N = 3, C2-N = 6 and D2-N = 6) or no immunosuppressive therapy (subgroups A3-N = 3, B3-N = 4, C3-N = 6 and D3-N = 6). Sixteen adult rats (Wistar and Sprague-Dawley) were used as controls: they underwent a sham operation, without immunosuppressive therapy or with intramuscular cyclosporine, for 21 days (2 mg/kg/day and 10 mg/kg/day). All recipients of intestinal grafts were weighed and inspected daily for the typical signs of graft-versus-host disease (GVHD) and rejection, until dead or until 21 days after transplantation. All animals were submitted to autopsy. Relative spleen weight was calculated; is an indication of GVHD, if > 1. Specimens for histology were obtained from graft, native intestine, liver, spleen, mesenteric lymph-nodes and skin. Graft specimens were assessed using a histologic grading system considering the appearance of the villi, cripts, lamina propria, and muscularis mucosa. According to this criteria rejection was divided in severe (without villi, epithelium and cripts and significant cellular infiltration), moderate (partial loss of villi, focal epithelium denudation, significant cellular infiltration) or mild (few slightly shortened villi, mild oedema and initial cellular infiltration).

**Results:** Subgroups A1 and B1: jejunal grafts were well vascularized and had a normal appearance at autopsy. Histological study showed normal intestinal appearance or slightly short villous. Subgroups A2, A3, B2 and B3: Jejunal grafts with turner aspect, with intense fibrous reaction. Two of 13 recipients had a relative spleen weight > 1. Histological signs of moderate to severe rejection were observed in all cases. Subgroups C1 and D1: all foetal grafts were well developed with histological appearance of normal intestine of slightly short villi. Subgroups C2 and D2: all foetal grafts had visually detectable growth but in all cases there were signs of rejection (moderate or severe). Subgroups C3 and D3: 8 of 12 of the transplanted fetal intestine segments were detectable but fibrotic. All of them with signs of moderate or severe



rejection. *Conclusions:* Our study indicate that in our model, foetal intestine allografts, under no immunosuppressive or low dose therapy, failed to grow and at least were rejected even across a minor histocompatibility locus. None of foetal intestinal recipients suffered from graft-versus-host disease, but doubts remain about this immunological advantage. }" "Small Intestine Transplantation in the Rat- Comparison of Immunogenicity of Foetal and Adult Allografts"

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## "P P 63 1516" P 63 1516 **Superoxide Dismutase Increases Oxygen Consumption and Arterial Flow in Acellular Reperfusion of Small Bowel Grafts**

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*Introduction:* the protector effect of SOD in ischaemic-reperfusion syndromes is related to enzyme administration prior to ischaemic or reperfusion damage, and use to be related to act in the neutrophil's physiopathologic pathway. *Aim of the study:* to determine the role of S.O.D. in a model of acellular reperfusion. *Material and Methods:* 30 male WAG rats (250 g) were used for harvesting the small bowel graft with a modified technique of gut procurement. The isolated bowels were stored in Collins solution during a period of 6 hours, therefore divided in three experimental groups (n = 10) and perfused during 40 min.: A) guts perfused with Ringer's with glucose and bicarbonate (pH 7.4, 300 osmoles/kg). B) guts perfused after harvesting with a modified Ringer's (pH 7.4, 31 osmoles/kg) solution with verapamil and norepinephrine. C) Same solution as group B but adding SOD. Aliquots of arterial flow, portal outflow, gut luminal effluent, were recollected during the experiment, and O<sub>2</sub>, CO<sub>2</sub>, pH, Na<sup>+</sup>, K<sup>+</sup>, and Ca<sup>++</sup> measured. At the end of the perfusion ileal tissue was excised and microscopically evaluated (Chiu scale). The data was collected and studied with the repeated measures ANOVA, and the Mann-Wihtney test. *Results:* in group A the experiments failed after 15 min. of perfusion. Groups B and C maintained the perfusion during 40 minutes. Arterial flow, portal outflow, edema, oxygen consumption, mean arterial pressure and histologic damage was significantly different (p < 0.001) in SOD treated small bowel grafts. *Conclusions:* SOD ameliorates preservation-reperfusion injury in a cell free perfusate, improving the tissue perfusion of the graft, due to a protector effect produced during the reperfusion injury in endothelial layers. Intestinal disorders: Splanchnic circulation, ischemia }

"Superoxide Dismutase Increases Oxygen Consumption and Arterial Flow in Acellular Reperfusion of Small Bowel Grafts"

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## "P P 63 1517" P 63 1517 Immunogenicity of Foetal Intestine Allograft

\*M.F. Lopes, A.S. Cabrita, J.A.B. Patr\`edcio

Faculty of Medicine of University of Coimbra, Coimbra, Portugal This experiment was designed to study the hypothesis of immunological advantage of the use of foetal over adult intestine, in small bowel transplantation. We choosed an immunological bi-directional rat model, with different histocompatibility barriers. *Methods:* Fifty-six small bowel transplantations were made. Donor rats were Wistar and recipients were Wistar (outbred) and Sprague Dawley. *Experimental Groups:* Adult rats underwent accessory jejunal (4 cm) transplantation. They were grouped in Group A: Wistar-Wistar, N = 9 and Group B: Wistar-Sprague Dawley, N = 10. Jejunal grafts (4 cm) of foetuses (gestation age of 19 days), were transplanted into omentum of adult rats. They were grouped in Group C: Wistar-Wistar, N = 18 and Group D: Wistar-Sprague Dawley, N = 18. The recipients of the groups A, B, C and D were further divided into three subgroups, which received IM cyclosporine A, for 21 days, beginning on the day of transplantation, 10 mg/Kg/day (subgroups A1-N = 3, B1-N = 3, C1-N = 6 and D1-N = 6) and 2 mg/Kg/day (subgroups A2-N = 3, B2-N = 3, C2-N = 6 and D2-N = 6) or no immunosuppressive therapy (subgroups A3-N = 3, B3-N = 4, C3-N = 6 and D3-N = 6). Relative spleen weight was calculated (sign of graft-versus-host disease, if > 1). Gross and hystology of graft specimens were studied. *Results:* Subgroups A1 and B1: jejunal grafts were well vascularized and had a normal appearance at autopsy. Histological study showed normal intestinal appearance or slightly short villous. Subgroups A2, A3, B2 and B3: Jejunal grafts with tumour aspect, with intense fibrous reaction. Two of 13 recipients had a relative spleen weight > 1. Histological signs of moderate to severe rejection were observed in all cases. Subgroups C1 and D1: all foetal grafts were well developed with histological appearance of normal intestine or slightly short villi. Subgroups C2 and D2: all foetal grafts had visually detectable growth but, in all cases, there were signs of rejection (moderate or severe). Subgroups C3 and D3: 8 of 12 of the transplanted fetal intestine segments were detectable, but fibrotic. All of them with signs of moderate or severe rejection. *Conclusions:* Our study indicates that, in our model, foetal intestine allografts, under no immunosuppressive or low dose therapy, failed to grow and at least were rejected even across a minor histocompatibility locus. None of foetal intestinal recipients suffered from graft-versus-host disease, but doubts remain about this immunological advantage. Immunology and microbiology: Host defense mechanisms } " Immunogenicity of Foetal Intestine Allograft"

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"P P 63 1518" P 63 1518 **Malnutrition Induces Perturbation in Jejunal Mucosa Permeability *in vitro* in Rats Starved before Bowel Resection** Mikael Wiren

Surgery, University Hospital, 581 85 Linköping, Sweden Intestinal integrity is essential to avoid gut associated septic states after major abdominal surgery. Malnutrition as well as surgical trauma affects the intestinal mucosa. The purpose of this study was to analyze whether malnutrition, surgery, anesthesia or a combination of factors was responsible for increased permeability of  $^{51}\text{Cr-EDTA}$ . **Methods:** Male Wistar rats, weight 240–270 g, were used. One group was starved for 48 h until the time of analysis (S = starvation). One group had a 5 cm small intestinal resection of mid-jejunum performed (R = resection). One group was given anesthesia without surgery (A = anesthesia). The control group had free access of food and water (C = control). One group of animals was starved for 48 h and subjected to anesthesia and resection (S + R = starvation + resection). After 2 h. recovery the anesthesia was repeated and jejunal segments starting from 5 cm. distal to the ligament of Treitz were taken out and immediately immersed in cold, oxygenated Krebs' buffer. Stripped mucosal segments (R; n = 16, S; n = 15, S + R; n = 16, A; n = 8, C; n = 15) were mounted in Ussing chambers where transepithelial potential difference (PD) and electrical resistance (ER) was continuously recorded. Transmucosal flux of  $^{51}\text{Cr-EDTA}$  was studied for 60 min. and analyzed by  $\beta$ -counting. The apparent permeability coefficient  $P_{\text{app}}$  was calculated. **Results:** PD and ER were stable during experiments. Jejunal permeation of  $^{51}\text{Cr-EDTA}$  was significantly increased in the combined starvation and resection group compared to the controls ( $p < 0.001$ ). The  $P_{\text{app}}$  of the starved animals (S) was also significantly increased compared to controls ( $p < 0.01$ ). Surgery or anesthesia alone did not increase permeability compared to controls significantly. On the other hand the  $P_{\text{app}}$  of the starved animals was lower than in the combined starvation and resection group and the addition of permeability perturbation achieved by surgery was needed to reach the same degree of change in permeability. **Conclusions:** We consider malnutrition mainly responsible for the disturbance in intestinal integrity seen in this *in vitro* rat model. However, there can be additive effects of malnutrition and trauma causing an increase in intestinal permeability very early after surgery. Intestinal disorders, absorption: Enterocyte biology Intestinal disorders, absorption: Epithelial transport Nutrition: Nutrients and gut function } "Malnutrition Induces Perturbation in Jejunal Mucosa Permeability *in vitro* in Rats Starved before Bowel Resection"

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"P P 64 1519" P 64 1519 **Is Pancreatitis an Important Risk Factor for the Development of Pancreatic Cancer? A Brazilian Experience** R. Dani, C.E.D. Nogueira

Santa Casa de Misericórdia and Hospital Israel Pinheiro, Belo Horizonte, Brazil The aim of this study is to report on the possible relationship of pancreatic carcinoma (PC) and chronic calcifying pancreatitis (CCP) as observed in a southeast Brazilian city. *Methods:* From January 1963 to January 1996 the authors prospectively cared for 528 cases of CCP and 200 cases of PC, including here 15 cases with the association of the two diseases. Twelve of the 15 patients were males and the mean age was 50.3 – 9.8 years (range 33–64); 10 patients were white and 5, colored. Eight were male heavy chronic alcoholics and 7 were considered idiopathic CCP cases. Mean age of the alcoholics was 53.4 – 9.3 years (range 40–64) and 46.7 – 10 years (range 33–57) for the idiopathic group. PC was diagnosed 94 – 124 and 45 – 95 months after the clinical onset of CCP, respectively for alcoholics and abstemious patients. Four out of the 8 alcoholics showed pancreatic calcifications whereas all idiopathic cases had pancreatic calcifications. Tabagism was present in 7 alcoholics and in 2 idiopathic CCP patients. Clinical changes that signaled the possibility of cancer were noticed from 1 to 36 months before the diagnosis of cancer was set, mean of 12.5 – 15 months for the alcoholics and 4.6 – 3.6 for the idiopathic cases. The incidence of PC in the general population is 1.9/100,000 inhabitants. *Results:* The incidence of PC among CCP patients was 2.8%. Considering that 473 of our patients with CCP were alcoholics (89%), 42 idiopathic (8%), 10 "tropical" CCP (1.9%), and 3 (0.6%) were hereditary CCP cases, it seems that PC is much more common in patients with idiopathic CCP (16.7%) than in alcoholic CCP (1.7%), and the difference is significant ( $p < 0.05$ ). It seems, also, that the risk of PC is increased in CCP patients, especially in idiopathic cases. *Conclusion:* PC seems to be more frequent in CCP patients, particularly among idiopathic cases. Pancreas: Pancreatitis, chronic Oncology, general: Epidemiology Oncology, specific: Pancreas } "Is Pancreatitis an Important Risk Factor for the Development of Pancreatic Cancer? A Brazilian Experience"

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"P P 64 1520" P 64 1520 **Serum Neurotensin in Human Pancreatic Cancer**

\*G. Tessari, T. Meggiato, C. Ferrara, M. Plebani<sup>1</sup>, M. De Paoli<sup>1</sup>, G. Del Favero

Dept. of Gastroenterology

<sup>1</sup> Laboratory Medicine, University of Padua, Italy The role of neurotensin as a physiological regulator of exocrine pancreatic secretion is known, but only recently it has been recognised as important mitogen in vitro on human cancer cells. The aim of this study was to evaluate the variations of serum neurotensin levels in pancreatic cancer as compared to other pancreatic and extrapancreatic diseases. We studied 58 patients: 13 control subjects (CS), 20 pancreatic cancer (PC), 11 chronic pancreatitis (CP) and 14 extrapancreatic diseases (EPD). Serum neurotensin was found significantly different among groups (one way Anova  $F = 2.82$ ,  $p < 0.04$ ); significantly higher levels were detected in CP as compared to PC ( $p < 0.05$ ). No difference was found between PC and the other groups studied. In CP patients the serum neurotensin correlated to serum amylase ( $r = 0.95$ ,  $p < 0.01$ ). Lower values were found in stage IV PC as compared to stage I–II ( $t = 1.82$ ,  $p < 0.04$ ). and in grade II as compared to grade I ( $t = 2.21$ ,  $p < 0.05$ ). Significant correlations were found between neurotensin and two indices of nutrition: albumin ( $r = 0.60$ ,  $p < 0.05$ ) and the percentage reduction in body weight ( $Z = 2.20$ ,  $p < 0.02$ ). No correlations were found between serum levels of this hormone and size of tumour ( $t = 1.18$ ,  $p$ : ns), or the survival of the patients ( $< 12$  vs  $> 12$  months) ( $t = 0.65$ ,  $p$ : ns). We can conclude that serum variations of neurotensin do not seem to be related to the progression of human pancreatic cancer. The variation of serum levels of the hormone can be linked to a patient's poor nutritional status. Oncology, specific: Pancreas Oncology, general: Proliferation, carcinogenesis Oncology, general: Screening, prevention } "Serum Neurotensin in Human Pancreatic Cancer"

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## "P P 64 1521" P 64 1521 How to Deal with Serous Cystoadenoma of the Pancreas?

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<sup>1</sup> Pathological Department, University of Verona, Italy

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Out of 108 pts. suffering from cystic tumour of the pancreas who underwent surgery from 1985 to 1995, thirty one (28.7%) had a histologically proven Serous Cystoadenoma (CAS). The male/female ratio was 7/1. The mean age was 58.8 years (range 27.8–72.7). The more frequent symptom was abdominal pain in 19 (61.3%), anorexia in 4, vomit and weight loss in 2, diarrhea in one. The diagnosis was occasional in 10 pts. (32.2%). All underwent preoperative US and CT. The underlined lesions were in average of 4.5 cm. (range 1–15). The imaging has been able to set diagnosis of CAS in the 55.5% of the cases; in the remainder 45.5% a mucinous neoplasm was suspected, because of the macrocystic aspect of the lesion. No pseudocyst was diagnosed. Preoperative needle aspiration, performed in 10 pts, recognized the CAS in 6 cases (60%), in 3 was not diagnostic. In one case (still alive at the follow up after 80 months) an adenocarcinoma, then disavowed from the histology, was suggested. Twenty-one patients (67.7%) underwent radical resection, 7 a cystojejunostomy and 3 a laparotomy. Perioperative mortality was zero. Postoperative stay was 17.3 days in average. Seven pts. (22.6%) experienced complications; 4 low output pancreatic fistulas and 1 biliary fistulas, abdominal collection and bleeding (requiring operation) respectively. All patients are alive and symptoms free in a mean follow up of 45 months (range 3–118). No resected patients present recurrence. The problem in distinguishing the potential malignant pancreatic cystic tumours is still open. Moreover a careful follow up is necessary because 4 cases of serous cystadenocarcinomas of the pancreas are reported in the literature. These considerations justify the aggressive attitude we adopted in the last decade. Our policy is conservative only in the microcystic CAS, of small dimensions, symptom free and particularly when located in the head. Oncology, specific: Pancreas } "How to Deal with Serous Cystoadenoma of the Pancreas?"

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"P P 64 1522" P 64 1522 **Cystic Neoplasms of the Pancreas: Study of 72 Cases** M.A.C. Machado<sup>1</sup>,

\*G. Spiliopoulos<sup>1</sup>, P. Volpe<sup>2</sup>, A.L. Montagnini<sup>2</sup>, C. Stasik<sup>1</sup>, T. Bacchella<sup>2</sup>, J.E.M. Cunha<sup>2</sup>, J.P. Campion<sup>1</sup>, M.C.C. Machado<sup>2</sup>, B. Launois<sup>1</sup>

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Cystic neoplasms are an uncommon group among pancreatic tumors. These lesions are seen more frequently in recent surgical practice, probably because of advances in diagnostic and surgical techniques. The aim of this study is to describe the diagnostic features and therapeutical options in the management of cystic tumor of the pancreas. We report here our experience with 72 patients with pancreatic cystic tumors over a ten-year period. Sixty-two four patients were women and ten were men. The mean age of patients was 55.2 years (range, 21 to 81 years). Mild abdominal pain was the main symptom in 70% of patients. The lesion were incidental finding in 10% of patients. CT scan provided the diagnosis of cystic tumor in 94% of patients while ultrasonography provided the same diagnosis in 78% of patients. All patients underwent surgical treatment. The pathological diagnosis was: thirty patients with mucinous cystadenoma (41.7%), thirty-two patients with serous cystadenoma (44.4%), ten patients with mucinous cystadenocarcinoma (13.9%). There was no operative mortality. Seven of ten patients with cystadenocarcinoma ultimately died of the disease. One patient with extended resection is still alive 3 years after surgery without recurrence of the tumor. The survival rate was 20.5% at 3 years. All patients with cystadenomas (mucinous or serous type) that underwent complete resection are alive or died from other causes. Only complete resection of the cystic tumors of the pancreas provides certain pathological diagnosis, the best chance of cure and may remove the risk of malign transformation of the cystadenomas, particularly of the mucinous type, with minimum operative risk. Clinical practice: Management strategy Oncology, specific: Pancreas Oncology, general: Therapy } "Cystic Neoplasms of the Pancreas: Study of 72 Cases"

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## "P P 64 1523" P 64 1523 Phorbol Esters Induce Apoptosis in Pancreatic Cancer Cell Lines

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The growth and progression of cancer may involve both an increase in cell proliferation and a reduction in apoptosis (programmed cell death). Protein kinase C (PKC) is a serine/threonine kinase which has an important role in cell proliferation and survival including the control of apoptosis. This study aims to investigate the effect of phorbol esters on cell proliferation and whether down regulation of PKC isoforms is associated with the induction of apoptosis. Pancreatic cancer cell lines (SUIT 2 and BXPC3) grown in serum-free conditions were treated for 24 hours with tumour promoting phorbol esters 12-0-tetradecanoylphorbol-13-acetate (TPA) and 12-deoxyphorbol-13-0-phenylacetate-20 acetate (DOPPA) which activate PKC. Cell proliferation was assessed by the incorporation of <sup>3</sup>H thymidine. DNA laddering and acridine orange staining was used to assess apoptosis. Western antibody blotting was used to assess PKC isoform expression. Treatment of SUIT 2 and BXPC3 pancreatic cancer cell lines with TPA, a pan activator of PKC isoenzymes inhibited cell proliferation in a dose-dependent manner and induced apoptosis (p < 0.02). In SUIT 2 cells, down regulation of PKC { d } and { g } at 6 hours was associated with the earliest detection of apoptosis. DOPPA which is thought to be specific for the { b } isoform of PKC induced apoptosis at 24 hours and also induced down-regulation of PKC isoforms. Phorbol esters inhibit proliferation and induce apoptosis of pancreatic cancer cell lines. This effect appears to be mediated by the down-regulation of selective isoforms of PKC. A greater understanding of mechanisms of apoptosis may enable the development of new therapeutic strategies in the future. (Statistics: one sample t-test) Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis Oncology, specific: Pancreas }

"Phorbol Esters Induce Apoptosis in Pancreatic Cancer Cell Lines"

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## "P P 64 1524" P 64 1524 Pancreatic Adenocarcinoma Cells Block Liver Glucose Metabolic Pathway

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<sup>2</sup> Clinica Medica I, Universita' degli Studi di Padova, Italy MIA PaCa2 cell culture supernatants cause hyper-glycemia "in vivo". The aim of the present study was to verify the effects of MIA PaCa2 cell culture medium on liver glucose metabolic pathway. MIA PaCa2 cells were cultured in DMEM with 10% FCS. Conditioned medium (A) was collected after 6 days. Medium B was non conditioned DMEM. Five separate sets of experiments with hepatocytes, isolated from in situ perfused rat liver, were made. The hepatocytes were divided into 4 fractions: 2 were incubated with medium A with or without insulin (100 nM) and the other 2 with medium B with or without insulin. The hepatocytes were placed in an oxygenated atmosphere at 37 C for 3 hours. Every 5 min. glucose, lactate, pyruvate and insulin were measured in the supernatant, while pyruvate kinase (PK) and hexokinase (HK) (spectrophotometric assays) and cAMP (RIA) were measured in hepatocyte lysates. Protein kinase C activity (PKC) was measured in hepatocyte cytosolic and membrane fractions after PMA stimulation, measuring phosphate incorporation from ATP into saturating amounts of a PKC selective peptide. Glucose slowly decreased when hepatocytes were incubated with both medium A or B, treated or not with insulin. Lactate progressively increased in medium B (increase = 1.3 + 0.4 mmol/L, mean + SEM) and was not influenced by insulin; this increase was significantly higher than that found in medium A (0.4 + 0.1 mmol/L; Student's t test: t = 2.19, p < 0.05). Pyruvate behaved closely to lactate. HK slightly increased in each set independently from the medium and insulin presence and correlated with glucose (r = -0.82, p < 0.01). PK activity in hepatocytes incubated in medium B after insulin stimulation, peaked after 5 minutes (activation) and between 20 and 45 minutes (gene induction); these activations completely lacked in the presence of medium A. In the hepatocytes treated with medium A a significant increase of cAMP was observed in the first 10 minutes (20 + 6%, mean + SEM; % vs basal) as compared to the hepatocytes treated with medium B (4 + 3%) (t = 2.42, p < 0.05). A reduced activation of PKC after PMA stimulation was found in hepatocytes incubated in medium A, suggesting that this enzyme has been previously activated. In conclusion: MIA PaCa 2 cells release one or more factors which interfere with hepatic glucose metabolism. These factors block both glucose metabolism to lactate and insulin action, possibly through adenylate cyclase and PKC intra-cellular signal pathways which could counteract the cascade of insulin activated protein kinases. Oncology, specific: Pancreas Hormones and receptors: Growth factors } "Pancreatic Adenocarcinoma Cells Block Liver Glucose Metabolic Pathway"

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**"P P 64 1525" P 64 1525 Pancreatic Cancer Growth and Spread Are Differently Influenced by Epidermal Growth Factor (EGF), Interleukin-1 Alpha (IL-1a) and Beta (IL-1b) and Transforming Growth Factor Beta 1 (TGFb)**

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The integrity of extracellular matrix (ECM) surrounding neoplastic cells may counteract tumor spread from the primary site. A reduced production or an enhanced degradation of ECM components (e.g. collagen, fibronectin, laminin, etc.) could represent one of the first steps in metastasis. Aims of the present study were to evaluate the effects of EGF, IL-1a, IL-1b and TGFb on 1. the pancreatic cancer cell line MIA PaCa 2 growth, 2. the production by the above cell line of the aminoterminal propeptide of type III procollagen (PIIIP), plasminogen activator (uPA) and plasminogen activator inhibitor (PAI1), the latter two both involved in the regulation of ECM degradation. MIA PaCa 2 cells (100,000/25 cm<sup>2</sup> flasks) were cultured in DMEM supplemented with 10% FCS for the first three days, followed by 1% FCS for the subsequent three days. EGF (10 and 100 ng/mL), TGFb (0.1 and 1.0 ng/mL), IL-1a and IL-1b (10 and 100 pg/mL) were daily added to cell culture medium from day 3 to day 6. On days 4, 5 and 6 the cells were harvested and counted; PIIIP was measured in cell lysates (ELISA, CIS-France), while uPA and PAI1 were assayed in cell culture media (ELISA, Biopool-USA and Diagnostica Stago-France). Each experiment was run in triplicate; the results from day 5 will be further reported, being in agreement with those found on days 4 and 6. EGF stimulated cell growth in a dose dependent manner (128% and 160% for 10 and 100 ng/mL respectively), while inhibiting PIIIP (83% and 46%), uPA (76% and 52%) and PAI1 (74% and 51%) levels. An opposite pattern was found when TGFb was used at the dosage of 0.1 ng/mL: cell growth was inhibited (78%), while PIIIP (109%), uPA (142%) and PAI1 (165%) levels were increased. TGFb used at a higher dosage (1 ng/mL) exerted only minor effects on the analysed parameters. IL-1a and IL-1b had similar effects; when used at the dosage of 10 pg/mL they slightly stimulated cell growth (120% and 125%) while inhibiting PIIIP (64% and 56%), uPA (38% and 83%) and PAI1 (60% and 47%) levels. At a higher dosage (100 pg/mL) they did not significantly influence the parameters studied. *Conclusions:* Cytokines which exert a positive effect on cell growth (EGF, IL-1a and IL-1b) seem at the same time to favour tumor spread by reducing the production of ECM components like PIIIP and by altering the balance between ECM degrading enzymes and their inhibitors. On the contrary cytokines which inhibit pancreatic cancer cell growth (TGFb) seem to inhibit also tumor spread. These findings might have in the future therapeutical implications. Oncology, specific: Pancreas }

"Pancreatic Cancer Growth and Spread Are Differently Influenced by Epidermal Growth Factor (EGF), Interleukin-1 Alpha (IL-1a) and Beta (IL-1b) and Transforming Growth Factor Beta 1 (TGFb)"

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"P P 64 1526" P 64 1526 **Resection for Pancreatic and Periapillary Tumours in 956 Patients: Results from UK Specialist Units**

\*J.P. Neoptolemos, UK Pancreatic Cancer Group (UKPACA)

Dept. Of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH, UK *Background:* A survey of 13,560 patients of pancreatic cancer from general surgical units in the UK of whom 2.6% underwent resection revealed a post-operative mortality of 28%. No data are available from specialist units in the UK. Moreover, previous studies have suggested no relationship between caseload and surgical outcome. *Aims:* The purpose of this study was to review the outcome from specialist units for comparison with the previous study in the UK and also 5 surveys of general units and from nine large specialist units published since 1990. *Summary of Results:* There were 956 resections reported by 30 surgeons from 20 units in the UK with 56 (5.8%) re-operations for complications and with 57 (5.9%) post-operative deaths. Mortality was significantly lower in the specialist units compared to the general units from the UK ( $\chi^2_1 = 43.1, 2p < 0.0001$ ). Combining the UKPACA data from those from published specialist units ( $n = 29$  units;  $n = 1750$  cases) they were compared with the published surveys from general units ( $n = 338$  units;  $n = 1396$  cases). The median [95% CI] mortality was lower in the specialist units (4.9%, [3.1%, 8.0%]) compared to general units (9.8% [2.5%, 23.2%];  $2p = 0.008$ ). The caseload was significantly lower in specialist units (8.2 [7.0, 13.5] cases per unit per year) compared to general units (0.4 [-0.3, 2.0] cases per unit per year;  $2p = 0.007$ ). *Conclusion:* Specialist units from the UK have comparable results to other specialist units in other countries. Overall specialist units have a significantly lower post-operative mortality and a higher caseload than general surgical units. Oncology, specific: Pancreas Oncology, general: Epidemiology Oncology, general: Therapy } "Resection for Pancreatic and Periapillary Tumours in 956 Patients: Results from UK Specialist Units"

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"P P 64 1527" P 64 1527 **Proto-Oncogene Jun Expression is Induced in the Rat Pancreas by Cerulein Infusion**

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Dept. of Internal Medicine I, University of Ulm -Germany-

<sup>1</sup> Dept. of Gastroenterology, University of Padova -Italy-

<sup>2</sup> Dept. of Pathology, University of Padova -Italy- Colecystokinin (CCK) can stimulate pancreatic acinar cell growth. To study the effects of in vivo stimulation with cerulein (a CCK analog), we analyzed the expression of the proto-oncogenes jun, myc and fos in terms of both mRNA and protein expression. RNA and proteins were extracted from the pancreas of rats administered an infusion of cerulein 10 ug/kg/h (Group A) or 0.25 ug/kg/h (Group B), or saline (Group C) and sacrificed 2, 4, 6 hours after beginning of the infusion and 0, 12, 24 hours and 2, 4, 6 days after completing a 12-hours cerulein (submaximal or supramaximal dosages) or saline infusion period. Transcript levels were analyzed using Slot Blot and in-situ hybridization. Protein expression was studied using Western Blot and Immunohistochemistry. No changes were found for the expression of proto-oncogenes myc and fos either on the transcript or protein levels. Significantly higher jun mRNA levels were found in Group A than in Groups B or C ( $P < 0.05$ ), particularly after 2 h of infusion and 12, 24, and 48 hours after the end of 12 h cerulein infusion. No significant difference was observed in Groups B and C. The jun protein behavior seemed similar in Groups A and B, revealing an early peak during infusion and another later on, after the end of 12 h cerulein infusion. Jun mRNA and jun protein were found in the acinar cells. In conclusion: (1) acinar cells respond to cerulein stimulation by increasing the expression of jun, a proto-oncogene mainly involved in cell proliferation; (2) in vivo, high dosages of cerulein increase jun mRNA and jun protein levels, whereas low dosages only raise protein levels; (3) myc and fos are apparently uninfluenced by cerulein administration. Pancreas: Pancreatitis experimental Hormones and receptors: Molecular biology } "Proto-Oncogene Jun Expression is Induced in the Rat Pancreas by Cerulein Infusion"

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## "P P 64 1528" P 64 1528 TGF{ b}1 Modulate the Expression of Adhesion Molecules in Pancreatic Tumour Cell Lines

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<sup>1</sup> Dept of Ob/Gyn, University of D\fcsseldorf, Germany *Purpose* The reasons for the aggressive growth and metastatic behaviour of pancreatic cancer are poorly understood. Recently, we showed the expression of matrix proteins, integrins, and growth factors in pancreatic tumours (Br J Cancer 69: 144–151, 1994; Pancreas 12: 248–259, 1996). Other studies indicated the possible role of overexpressed growth factors and their receptors suggesting paracrine and/or autocrine effects in tumour development. Furthermore, CD44 variants, VLA { a}6, and ICAM-1 may be involved in tumourigenicity and metastasis of pancreatic cancer. In the present study we examined whether TGF{ b}1 can influence the expression of different cell adhesion molecules. *Methods* The an pancreatic tumour cell line PANC1 was transfected with an expression vector containing full length TGF{ b}1 using the DOTAP method (Boehringer). The TGF{ b}1-production was assayed with a TGF{ b}1 ELISA (R&D). The expression of CD44st, CD44v5-v7, ICAM-1, and VLA { a}2 and { a}6 was measured by flow cytometry. Untransfected PANC1 cells were incubated with TGF{ b}1 (Sigma) for 48 hrs and ICAM-1 expression was assayed, too. *Results* Transfected cells showed an increase in TGF{ b}1 production. Transfected cell expressed slightly increased CD44 v5–v7. Expression of { a}6 was unchanged and decreased of { a}2, CD44st, and ICAM-1 in comparison to the untransfected cells. The incubation of untransfected PANC1 with various concentrations of TGF{ b}1 reduced the ICAM-1 expression, too. *Conclusion* The overexpression of transfected TGF{ b}1 as well as exogenous TGF{ b}1 modulated the expression of different adhesion molecules associated with cell-matrix interaction and metastasis. Further investigations are necessary to determine the role of these effects on tumour progression and metastatic potential. Oncology, specific: Pancreas Hormones and receptors: Growth factors } "TGFβ1 Modulate the Expression of Adhesion Molecules in Pancreatic Tumour Cell Lines"

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"P P 64 1529" P 64 1529 **Growth Inhibitory Effect of an Essential Fatty Acid Containing Lipid Emulsion on Pancreatic Cancer Cell Lines in-vitro**

\*D. Ravichandran, A. Cooper, C.D. Johnson

University Surgical Unit, Southampton General Hospital, SO16 6YD, UK Treatment of inoperable pancreatic carcinoma is unsatisfactory at present and a new chemotherapeutic agent with minimal side effects would be welcome. Essential fatty acids (EFA) such as gamma linolenic acid (GLA) and eicosapentaenoic acid (EPA) have antitumour effects. We tested the effect of a lipid emulsion containing GLA and EPA on 2 human pancreatic ductal carcinoma cell lines Panc1 and MIA PaCa2. Cells were grown as monolayer on plastic under standard conditions in culture medium containing 10% FBS, harvested and seeded at 2500 cells in 100  $\mu$ l of medium per well in 96 well cell culture plates. GLA/EPA emulsion (containing 10 g of each EFA in 100 mls) (Scotia, Stirling, UK) in 100  $\mu$ l of medium was added 24 hours later to achieve final concentrations varying from 2.5 to 640  $\mu$ mol/l of each fatty acid. Control experiments were run with culture medium alone and a with a control lipid emulsion (Ivelip, Clinitec, UK) to exclude a nonspecific fat overload effect. Cell growth was assessed by a microculture tetrazolium (MTT) assay after 7 days. GLA/EPA emulsion showed a significant dose and time dependant growth inhibitory effect on both cancer cell lines. Cell growth was not affected by the control lipid emulsion. Preliminary nude mice studies have shown that this compound is well tolerated when administered IV, with no toxic effects. GLA/EPA emulsion is a non-toxic formulation of both EFA's and may provide a useful therapeutic adjunct in patients with pancreatic cancer. Oncology, specific: Pancreas Oncology, general: Therapy } "Growth Inhibitory Effect of an Essential Fatty Acid Containing Lipid Emulsion on Pancreatic Cancer Cell Lines in-vitro"

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"P P 64 1530" P 64 1530 **Effect of Liposomal Lithium Gamma Linolenic Acid in Pancreatic Cancer**

\*D. Ravichandran, A. Cooper, S.J. Karran, C.D. Johnson

University Surgical Unit, Southampton General Hospital, SO16 6YD, UK Lithium salt of Gamma Linolenic Acid (LiGLA) has been reported to prolong the survival of patients with inoperable pancreatic cancer. We studied the effect of LiGLA on 2 pancreatic ductal cancer cell lines (Panc1 and MIA PaCa2) in vitro and the effect of liposomal LiGLA on MIA PaCa2 derived pancreatic tumour in athymic mice. For in vitro study the cells were seeded in 96 well culture plates. LiGLA (Scotia, Stirling, UK) was added 24 hrs later (5–490  $\mu$ mol/l). A human fibroblast cell line was used as the control. Oleic acid (OA), Palmitic Acid (PA) and Lithium Chloride (LiCl) controls were used to exclude a nonspecific fat overload effect and a lithium effect. The cell growth after 7 days was assessed by the MTT say. For in vivo studies, Balb c nude mice were inoculated subcutaneously with 5 times;  $10^6$  MIA PaCa2 cells. Once progressive tumour growth was confirmed they were treated with liposomal LiGLA IV over 10 days (total dose 0.8 mg/g body weight). Control animals received blank liposomes. The tumour size was measured weekly for 4 weeks following therapy. LiGLA showed a selective and significant dose and time dependent growth inhibitory effect on both cancer cell lines in vitro. The IC<sub>50</sub> of cancer cell lines were 10 times lower than the IC<sub>50</sub> of fibroblasts. OA, PA and LiCl had no effect. A reduction of tumour growth was also achieved in nude mice with pancreatic tumours that received liposomal LiGLA, compared with controls. LiGLA has no side effects of conventional chemotherapy and may prove useful in patients with pancreatic cancer. Oncology, specific: Pancreas } "Effect of Liposomal Lithium Gamma Linolenic Acid in Pancreatic Cancer"

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## "P P 64 1532" P 64 1532 Preoperative Laparoscopy: Do We Need it in Patients with Pancreatic Malignancies?

\*H. Friess, H.U. Baer, W. Uhl, Ch. Seiler, J.-C. Silva, Ch. Sadowski, M.W. B\fcchler

Department of Visceral and Transplantation Surgery, University of Bern, Switzerland  
The role of laparoscopy prior to laparotomy in patients with pancreatic or periampullary malignancies is controversial. Recently, several studies have been published reporting that in up to 36% of the patients, metastasis can be detected by laparoscopy which were not found by contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). The aim of our present study was to investigate the potential role of laparoscopy prior to laparotomy in patients undergoing laparotomy for pancreatic or periampullary malignancies. *Patients:* Between 11/1993 and 12/1995, 127 pats (57 women, 70 men, median age: 67 years, range: 29–84 years) underwent laparotomy due to pancreatic (97 pats) or periampullary (30 pats) cancer. Preoperatively, all pats underwent CT scanning to assess resectability of the tumor. In addition, ultrasonography or MRI was performed facultatively before the operation. According to the findings of these imaging techniques, the pats were scheduled either for tumor resection or for a palliative operation. *Results:* 25 pats were preoperatively scheduled for non-resectional surgery due to distant metastasis or retroperitoneal tumor infiltration. In none of these pats was the operative strategy changed. In 102 of 127 pats (80%) a pancreatic resection was planned preoperatively. 71 pats (70%) underwent pancreatic resection. In the remaining 31 pats preoperatively planned for tumor resection, removal of the tumor was not possible: in 21 this was due to tumor infiltration into the retropancreatic vessels, and in 10 this was because liver or peritoneal metastasis could be detected for the first time intraoperatively. Those 10 pats (10%) could have benefited from laparoscopy. Similar results were found in 97 pats with pancreatic cancer. 71 pats were planned for tumor resection and 26 pats for palliative operation. Of 71 pats preoperatively planned for tumor resection, 46 pats (65%) underwent pancreatic resection. In the remaining 25 pats preoperatively planned for tumor resection, removal of the tumor was not possible: in 16 this was due to tumor infiltration into the retropancreatic vessels, and in 9 this was because liver or peritoneal metastasis could be detected for the first time intraoperatively. These 9 pats (13%) would also have benefited from laparoscopy. *Conclusion:* Preoperative computed tomography is a reliable technique to detect tumor metastasis in patients with pancreatic or periampullary cancer. In contrast to other studies, we found that only 10% of pats with periampullary/pancreatic cancer and 13% of pats with pancreatic cancer might profit from laparoscopy. Due to this low percentage, laparoscopy cannot generally be recommended in pats with pancreatic or periampullary cancer prior to laparotomy, particularly if we take into account the risk of tumor dissemination probably caused by laparoscopy. *Laparoscopic surgery: Diagnosis* Oncology, specific: Pancreas } "Preoperative Laparoscopy: Do We Need it in Patients with Pancreatic Malignancies?"

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"P P 64 1533" P 64 1533 **Indeterminate Pancreatic Masses: Failure of Modern Imaging Methods to Exclude Malignancy**

\*T. R. Rofsch, J.R. Roder, T. Decassian, P. Born, H.J. Dittler, W. Bautz, H.D. Allescher, P. Gerhardt, J.R. Siewert, M. Classen

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The precise differential diagnosis of indeterminate pancreatic masses is still a major problem in deciding on the appropriate diagnostic approach. In this retrospective study we blindly assessed the accuracy of computed tomography (CT), ERCP and endoscopic ultrasonography (EUS) in the differential diagnosis of these tumors. Follow-up information about patient survival was also obtained. 75 patients (47 male, age 36–76 years) with pancreatic head tumors undergoing a Whipple procedure over a period of 5 years were included. ERCP and CT images as well as EUS tapes were reviewed completely blindly by three different examiners. Sensitivity and specificity were calculated for diagnosis of malignancy. Follow-up information was obtained from hospital charts, interviews with patients' physicians or through a local tumor registry. Of the 75 patients, 51 had cancer, 5 benign tumors (3 endocrine, functionally inactive) and 19 focal chronic pancreatitis. During follow-up (mean: 38 months), 2 patients originally diagnosed as focal chronic pancreatitis returned with liver metastases and histological work-up of the previous resection specimen in one revealed a very small cancer focus. Sensitivity and specificity for the diagnosis of malignancy were as follows: 73%/73% for the tumor marker CA 19-9, 19%/86% for CEA, 81%/50% for CT, 86%/43% for ERCP and 81%/27% for EUS. 61% of patients underwent some form of preoperative biopsy (ERCP or percutaneous) which had a sensitivity of 50% only. In 50% of cases post-operative complications were encountered (half of them minor) which necessitated relaparotomy in 16% of all cases. Follow-up revealed a 3 year survival of 10% for tumors and 95% for focal chronic pancreatitis. Since imaging procedures and also biopsy attempts often fail to diagnose malignancy with a sufficient specificity, our data show that proceeding to a Whipple operation is currently the best way to establish the diagnosis, although the prognosis of cancer patients is very poor.

Endoscopy, specific: Biliary Radiology and ultrasound: Diagnosis } "Indeterminate Pancreatic Masses: Failure of Modern Imaging Methods to Exclude Malignancy"

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"P P 64 1534" P 64 1534 **Effects of CCK, Bombesin and EGF on Growth of Human Pancreatic Cell Lines PANC-1 and CAPAN-2**

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<sup>2</sup> 1st Dept. Surgery, Semmelweis Univ. Med., Budapest

<sup>3</sup> Dept. Med. I, Univ. Ulm Numerous studies have reported diverse effects of gut-derived regulatory peptides on growth of the normal pancreas, pancreatic neoplasms induced experimentally in animals, and pancreatic cancer cell lines. The results of these investigations are rather controversial. In the present study the growth of human adenocarcinoma cell line PANC-1 and CAPAN-2 were characterized in vitro, and the effects cholecystokinin (CCK), bombesin and epidermal growth factor (EGF) were determined. Cells were maintained at 37°C in a humidified atmosphere of 5 percent CO<sub>2</sub> and 95 percent air in DMEM medium supplemented with 10 percent fetal calf serum (FCS). In each experiment cells were initially plated in media containing FCS for 24 h. Then cells were incubated with medium devoid of FCS in the absence (control) or the presence of the peptides. Growth effects of peptides were determined by cell counting after 6 days, and by [<sup>3</sup>H]thymidine incorporation into DNA after 24 h incubation. Our data show that FCS is not required for maintaining growth in PANC-1 and CAPAN-2 cell lines. In serum free medium the number of PANC-1 cells more than doubled during the six days incubation period (day 0: 100.000 cells, day 6: 265.000 – 37.000 cells). Either bombesin or cholecystokinin (both in 10<sup>-11</sup>–10<sup>-8</sup> M) did not significantly affect the growth of the cells during this six-day treatment. DNA synthesis in PANC-1 and CAPAN-2 cell lines evaluated by [<sup>3</sup>H]thymidine incorporation increased 106% and 64%, respectively, over controls in response to EGF (10<sup>-8</sup> M) treatment (P < 0.01). Neither bombesin nor CCK altered significantly the incorporation of [<sup>3</sup>H]thymidine in concentration range 10<sup>-11</sup>–10<sup>-8</sup> M in these two cell lines. These data support a role for EGF as a growth factor for human pancreatic cancer cell lines PANC-1 and CAPAN-2. CCK and bombesin do not affect the cell proliferation in these pancreatic carcinoma cell lines. Hormones and receptors: Receptor characterization Hormones and receptors: Growth factors Oncology, specific: Pancreas } "Effects of CCK, Bombesin and EGF on Growth of Human Pancreatic Cell Lines PANC-1 and CAPAN-2"

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"P P 65 1535" P 65 1535 **Factors of Weight Loss in HIV-Infected Patients with Chronic Diarrhea: A Multidimensional Study**

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Departments of Gastroenterology and Infectious diseases, Hospital Rothschild, and INSERM U444, Paris, France

Body weight loss is a prominent clinical feature in HIV-infected patients with chronic diarrhea. The purpose of our prospective study was to look for the links between the degree of wasting, the level of food intake, and the severity of diarrhea. *Patients and Methods:* Between 1989 and 1996, 116 consecutive HIV-infected patients (109 males, 7 females, mean CD4 count  $50/\text{mm}^3$ ) with chronic diarrhea underwent a standardized gastrointestinal and nutritional evaluation, including: a) a questionnaire on the clinical severity of diarrhea; b) a prospective evaluation of 48-h food intake; c) a measurement of fecal weight, lipid and nitrogen output; d) a measurement of nutritional biological parameters from blood; e) a stool examination for bacteria and parasites; f) an upper gastrointestinal endoscopy and a rectosigmoidoscopy. *Results:* Diarrhea was associated with an infection by cryptosporidia, microsporidia, or other enteric pathogens in 27%, 24%, and 22% of the patients, respectively. Diarrhea appeared idiopathic in 27% of the patients. By multiple regression, the weight loss since the onset of diarrhea (15 – 8% of the initial weight, m – SD) was significantly related to four independent variables: the spontaneous caloric intake (25 – 8 kcal/kg/d), the maximal frequency of stools within the week before evaluation (8 – 7 movements/d), the stool weight (575 – 470 g/d), and the fecal nitrogen output (2.5 – 1.5 g/d). No significant correlation was found between the level of spontaneous caloric intake and the fecal parameters, neither by univariate study or multiple regression. *Conclusions:* Our results suggest that, in HIV-infected patients with chronic diarrhea, the degree of wasting is significantly related to the level dietary intake, and to the severity of diarrhea. However, no significant correlation can be demonstrated between the level of dietary intake and the severity of diarrhea. Immunology and microbiology: GI infections in adults }"

"Factors of Weight Loss in HIV-Infected Patients with Chronic Diarrhea: A Multidimensional Study"

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## "P P 65 1536" P 65 1536 Intestinal Absorption in HIV Infected Patients

\*S. Mouly, J.F. Bergmann, O. Chassany, C. Caulin

Unit of therapeutic research, Lariboisière Hospital, Paris, France *Objective:* To assess prospectively intestinal absorption and its relation to nutritional status, immunodeficiency, presence of diarrhea and/or parasites in stools, in 36 unselected HIV-infected patients. *Methods:* 29 men and 7 women HIV-positive with and without diarrhea (mean age, 40 years) were consecutively enrolled. A physical examination, with determination of Body Mass Index (BMI) was performed. The immunologic status was assessed by total blood CD4 cell count and detection of P24 antigenemia. Albumin and transferrin serum levels were performed, and 2 stool samples were analysed for the presence of parasites. Absorption tests were a standard D-Xylose test and a 72-hours fecal fat measurement. *Results:* 20 patients fulfilled criterias of AIDS-defining illness, 17 of whom presented with one or more secondary infections at the time of the study. Wasting Syndrome (WS) was present in 9 patients. CD4 cell count was below 200 in 24 cases, 7 of whom had positive P24 antigenemia. 13 patients had diarrhea (D), associated with WS (n = 6), and low CD4 cell count (n = 9). Weight, BMI, albumin and transferrin serum levels were all significantly lower in patients with diarrhea and/or WS ( $p < 0.01$ ). Eight patients had parasites in stools: cryptosporidia (n = 4), microsporidia (n = 4). Their mean CD4 cell count was 31. Six patients fulfilled criterias of "HIV-induced enteropathy", with malabsorption (n = 4), WS (n = 3), and a mean CD4 cell count of 146 ( $p < 0.05$ ). Association between diarrhea, WS and intestinal malabsorption are shown in the following table:

CD4 < 100	CD4 > 100	D	No D	WS	No WS	Parasites in stools
6	2	5	3	3	5	Xylosemia < 1.7 mM/l
4	3	5	2	4	3	Fecal fat > 6 g/day
2	1	2	1	1	2	Intestinal malabsorption

Intestinal malabsorption was not correlated with respectively, nutritional and immune status, diarrhea and parasites in stools among these unselected consecutive HIV-infected patients. *Conclusion:* In this prospective study, intestinal malabsorption was independent of nutritional and immune status, diarrhea and parasites in stools. Evaluation of intestinal absorption in HIV-infected patients might be helpful to improve therapeutic management at any stage of the disease. Intestinal disorders, absorption: Pathophysiology of diarrhea Intestinal disorders, absorption: Malabsorption syndromes Immunology and microbiology: GI infections in adults } "Intestinal Absorption in HIV Infected Patients"

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**"P P 65 1537" P 65 1537 Clinical Aspects of Pancreatic Disorders in 280 Patients with Aids, Submitted to *Post-Mortem* Studies**

\*I.C. Barros, C.A.B. Oliveira, C.E. Brandão-Melo, J.M.C.O. Coelho, M.C. Torres, P.A. Lima-F.

H.U. Gafrão Guinle, UNI-RIO, HUAP, Universidade Federal Fluminense, Rio de Janeiro, Brazil Aiming at evaluating the incidence, the main etiologies and the clinical profile of pancreatic disorders in AIDS, the authors analysed the *post-mortem* studies of 280 patients, from which they selected 82 with some form of pancreatic disease. These encompassed 31 cases with non-specific disorders (13 with acute pancreatitis, 14 with chronic fibrosis and/or duct dilation of the pancreatic canaliculus and 4 with vascular alterations); 11 cases with neoplastic involvement (9 with Kaposi's sarcoma and 2 with metastatic adenocarcinoma) and 40 cases with pancreatic opportunistic infections (14 with *Mycobacterium tuberculosis*, 11 with *Cytomegalovirus* (CMV), 8 with *Cryptococcus neoformans*, 5 with *Histoplasma capsulatum* and 2 with *Toxoplasma gondii*.) On a second phase, the authors made a correlation between these data with those obtained from a 40 patients group with no pancreatic alterations. In this control group we observed a higher incidence of abdominal symptoms that, in clinical practice, could simulate a pancreatopathy. The majority of these patients died due to infectious or neoplastic causes, which affected either the nervous system or the respiratory tract. None of the patients received the diagnosis of pancreatopathy as "*causa mortis*". After the statistical analysis, the authors concluded that: 1. The pancreatic disorder in AIDS was less frequent in our group when compared to previous reviews ( $p < 0.001$ ); 2. The behavior of the pancreatic disorders in AIDS is subclinical, benign and completely atypical if compared to the classical forms; 3. Tuberculosis stood out as the major cause of pancreatopathy ( $p < 0.001$ ) and CMV's pancreatitis was less frequent in our study than in other communications ( $p < 0.001$ ); 4. Pancreatic involvement by *Histoplasma capsulatum*, not previously reported, was identified in 5 cases. Laparoscopic surgery: Diagnosis Immunology and microbiology: GI infections in adults Clinical practice: Management strategy } "Clinical Aspects of Pancreatic Disorders in 280 Patients with Aids, Submitted to Post-Mortem Studies"

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"P P 65 1540" P 65 1540 **Immunohistological Study of the Mesenteric Nodes in Deceased Children with AIDS**

\*R. Ilie<sup>1</sup>, N. Tudose, C. Ilie, M. Lesovici<sup>1</sup>

<sup>1</sup> University of Medicine and Pharmacy Timisoara-Romania

Clinical Children Hospital "Louis Turcanu" Timisoara-Romania  
Acquired immunodeficiency syndrom (AIDS) in children is a multisystemic disease with the modification of the proportions of T-helper and T-suppressor cells in sense of increase the latter in the mesenteric nodes is in accordance with blood lymphocitic values achieving an "mirror" appearance. *Materials and method.* There was taken mesenteric nodes, necroptic pices. There were 9 deceased children with AIDS in the "Children Hospital Louis Turcanu" and "Infectious Diseases Clinic" Timisoara from which the samples were obtained. The confirmation of the diagnose was intra-vitam made by sequential serological determination of the virus through ELISA and Westttern-Blott techniques. The prelevated pieces were fixed in neutral formalin and then was performed ordinary procedure for processing until we obtained the paraffine blocks and studied that by comparing the Hematoxylin-eosin and immunohistochemical coloration. *Results:* 1. Numerical increase sometimes excessive of the CD8, T lymphocytes into the germinative centers and lymph node sinuse and spleen. 2. A depletion of different degrees of CD4, T lymphocytes into the germinative centers and profound cortex of the lymph nodes, in the periarteriolar lymphoid muffs and speen's Malpighi corpuscles. 3. The variable fragmentation of dendritic cells from germinative ganglionic centers and epitheloid cells from thymic paramedular zone. The described modifications were constantly present to all studied cases confirming the different degrees of immunodepession in AIDS. The germinative ganglionic centers are the most important virus tank in the patients with AIDS, they being precociously infected in the course of the disease. The progressive and slowly destruction of germ centers takes place over all the length of disease. Immunology and microbiology: GI infections in adults  
Immunology and microbiology: GI infection, children } "Immunohistological Study of the Mesenteric Nodes in Deceased Children with AIDS"

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"P P 65 1541" P 65 1541 **Cytotoxicity Influences Hydrophobic Surface Properties of Helicobacter Pylori** D. Risberg, H. Enroth, L. Engstrand, A. Uribe

Department of Medicine, Karolinska Institute, Danderyd Hospital, Stockholm, Sweden

Department of Microbiology, University Hospital, Uppsala, Sweden Bacterial adherence to epithelial cells is dependent on their surface hydrophobicity, which is of importance for an unspecific attachment of the microorganism to the mucosal surface. Thereafter a specific, receptor-mediated, binding may occur. Our aim was to examine the surface hydrophobicity of different strains of *Helicobacter pylori* (*H. pylori*) by means of contact angle measurements. *Methods:* 18 different strains of *H. pylori* including knock-out mutants lacking vac A cytotoxic protein (A5 vac A and 17874 vac A), and *H. mustelae*, were processed for contact angle measurements. After cultivation, the viable bacteria were centrifugated and the pellets were evenly spread on glass slides. After 30 minutes of air drying, a droplet of saline was applied and the contact angle was measured using a goniometer. A mean value of four different measurements on each slide was calculated. *Results:* The contact angles of the strains A5 vac A and 17874 vac A were lower than those of A5 and 17874 respectively ( $p < 0.001$ ). Similarly, the contact angle of SVA40 was lower than that of GZSVA40 ( $p < 0.001$ ). Urease-negative *H. pylori*, *H. mustelae* and strains of *H. pylori* obtained from patients with duodenal ulcer disease, antral gastritis or gastric cancer showed significant differences in contact angles ( $p < 0.01$ ). *Conclusions:* The presence of vacuolising A protein increases surface hydrophobicity which may contribute to bacterial adherence and facilitate their cytotoxic action. The differences in contact angles observed in the various examined strains may be of importance for the pathogenic actions of certain *Helicobacter pylori* strains on the human gastric mucosa. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: GI infections in adults Immunology and microbiology: Host defense mechanisms } "Cytotoxicity Influences Hydrophobic Surface Properties of Helicobacter Pylori"

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## "P P 65 1542" P 65 1542 Oral Cavity as Permanent Reservoir of *Helicobacter Pylori* (Hp) and Potential Source of Gastric Reinfection

\*J. Pytko, E. Karczewska, J. Majka, S.J. Konturek

Inst Physiol & Dept Conserv Dent, Univ Sch Med, Krakow, Poland *Purpose:* Studies in developed countries showed that neither dental plaques (DP) nor dentures are important reservoir for Hp, whereas studies in developing countries revealed a high prevalence of Hp in DP, though elsewhere successful bacterial culture in the material from mouth cavity was rare. This study was designed to compare the incidence of Hp in mouth cavity and in the stomach of 10 healthy and 100 peptic ulcer (PU) patients 18–69 yr old. *Methods:* <sup>14</sup>C-oral urea breath test (UBT) (with <sup>14</sup>C-urea dissolved in water and confined for 5 min only to the mouth cavity — without swallowing), CLO-test, Hp culture on special "Hp Agar" and PCR for Hp DNA in saliva, gingival pockets and DP were used to assess the presence of Hp in mouth cavity. In the stomach, <sup>14</sup>C-gastric UTB (<sup>14</sup>C-urea 1 \b5Ci in capsule dissolved in the stomach), endoscopy with biopsy for CLO-test, histology and culture were used to identify the Hp infection. *Methods:* Ten healthy subjects without symptoms and in 100 symptomatic patients with gastric or duodenal PU were tested just before the start and 4 weeks after the termination of 2 wk triple therapy (omeprazole 20 mg bd, clarithromycin 500 mg td and metronidazole 500 mg bd) when endoscopically PU were healed. All 10 healthy subjects were found to be Hp-positive in the mouth cavity but only 7 in the stomach. All PU patients before the therapy were found to be Hp positive both in the mouth and in the stomach. Following triple therapy in PU 86 patients became Hp negative in their stomach but only in 5 of them the Hp was not detected in the mouth by culture and PCR. *Conclusions:* the mouth is permanent reservoir of Hp both in healthy subjects and in PU patients before and after successful eradication of Hp from the stomach, being a potential source of reinfection. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Oesophageal gastric duodenal disorders: GD disorders, acid peptic } " Oral Cavity as Permanent Reservoir of *Helicobacter Pylori* (Hp) and Potential Source of Gastric Reinfection "

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## "P P 65 1543" P 65 1543 **Helicobacter Infection in AIDS Patients: Correlation between Morphologic Findings and Serum Levels of Pepsinogen I–II and Gastrin**

\*C. Giannelli, R. Paloscia, A. Cianetti<sup>1</sup>, S. Ciarletti, M.G. Graziani, M. Luminari

Department of Gastroenterology

<sup>1</sup> Clinical Laboratories, S. Camillo Hospital, Rome, Italy The prevalence of H. Pylori infection in HIV positive pts is much lower than for HIV negative population (10–15% vs 70%). The cause of this lower prevalence is not yet known. Several authors believe that this can be consequence of reduced chloridropeptic secretion which can create an hostile environment. Shaffer in 1992 clearly demonstrated a normal chloridric secretion in these patients. Aim of our study was to verify the peptic secretion as well, by pepsinogen I and II serum levels, (RIA Sorin) correlating it with serum gastrin (RIA-Sorin) and endoscopic and histologic findings, (Giemsa) in 26 AIDS pts. 21 of them were males and 5 females, mean age 37.6 y (28–51). All were symptomatic for dyspepsia or epigastric pain. The HP infection (only in antral biopsies) was present in 8 pts (31%). This prevalence was higher than 10% reported in our previous study in 423 unselected patients. The results of serum data, endoscopic and histologic findings are showed in Tab 1

Parameter	HP pos.	HP neg.
Total	99 (DS37)	74 (DS55)
Gastrin	14/26 (50%)	6/23 (23%)
Pepsin. I	108 (DS35)	70 (DS39)
Pepsin. II	24 (DS23)	4/8 (50%)
End. posit. Activ. c. gastr.	4/8 (50%)	2/18 (11%)

Our experience indicates normal peptic secretion and normal gastrin serum levels in AIDS pts, without difference between HP pos. and HP neg groups. Only Pepsinogen II serum levels were higher in HP pos. pts. This higher level could be related to the active c. gastritis usually present in these patients (50% vs 11%).

Reference: Shaffer R.T. et Al Am. J. Gastroent. 1992 87(12) 1777–80

Giannelli C. et Al: W. Congresses G. Enter. Los Angeles 1994 Oesophageal gastric duodenal disorders: Helicobacter Pylori Oesophageal gastric duodenal disorders: Secretion: mechanism, regulation Immunology and microbiology: GI infections in adults } "Helicobacter Infection in AIDS Patients: Correlation between Morphologic Findings and Serum Levels of Pepsinogen I-II and Gastrin"

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"P P 65 1544" P 65 1544 **Relevance of Splenic Histopathology in Early Diagnosis of Disseminated Infections in 150 Patients with Aids, Submitted to *Post-Mortem* Studies (1984–1995)**

\*I.C. Barros, A.R. Cordovil Pires, P.E. Helayel, D.P. Fernandes, P.A. Lima-F.

Universidade Federal Fluminense, Rio de Janeiro, Brazil With the purpose to evaluate the relevance of spleen biopsy in clinical practice, the authors analyzed the *post-mortem* studies of 150 patients with AIDS. Some form of splenic disorder was found in 123 of these patients (82%). This group encompassed 85 cases with non-specific disorders (40 with splenitis, 18 with white hyperplasia, 12 with splenic congestion, 7 with lymphocitary depletion, 5 with splenic infarcts, and 3 with abscesses); 33 cases with splenic opportunistic infections (13 with miliary tuberculosis (39%), 5 with cryptococcosis (15%), 4 with histoplasmosis (12%) and 3 with splenic toxoplasmosis (9%)) and 5 patients with neoplastic disorders (4 with Kaposi's sarcoma and 1 case with metastatic adenocarcinoma). On a second phase, our purpose was to outline the profile of such patients, the authors made a correlation between the data gathered from the clinical and *post-mortem* reports and the data obtained from the 27 patient control group (with no splenic disorders). After the analysis of the data, the authors concluded that: a) the splenic disorders in AIDS were asymptomatic and more frequent in our environment when compared with the current medical literature 82% vs 30% ( $p < 0.0001$ ); b) non-specific disorders, stood out as the major cause of splenic involvement in our study; c) there was high statistical significance between the evidence of splenic involvement by opportunistic agents in patients with disseminated infections, frequently not detected in life ( $p < 0.0001$ ). Clinically, we observed opportunistic infections in 45 cases (30%), acute neurologic symptoms in 20 cases (13%), neoplasias in 14 (9%). Severe gastrointestinal complaints were detected in 9 cases (6%). Prospective studies should be done to confirm the clinical benefits of the laparoscopic biopsy of the spleen in the management of patients with AIDS complications. Clinical practice: Epidemiology (non cancer) Immunology and microbiology: GI infections in adults Pancreas: Pancreatitis, chronic } "Relevance of Splenic Histopathology in Early Diagnosis of Disseminated Infections in 150 Patients with Aids, Submitted to Post-Mortem Studies (1984-1995)"

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"P P 66 1545" P 66 1545 **Butyrate Inhibits Cyclin-Dependent Kinase 2 (cdk2) and Stimulates Cyclin D Expression in HT-29 Epithelial Cells** S. Siavoshian,

\*H.M. Blotti re<sup>1</sup>, C. Cherbut<sup>1</sup>, B. Kaeffer<sup>1</sup>, J.P. Galmiche

Human Nutrition Research Center INSERM, CHU 44035 Nantes Cedex, France

<sup>1</sup> INRA-LTAN, CHU 44035 Nantes Cedex, France Butyrate, a four-carbon fatty acid produced by colonic fermentation of resistant starch and dietary fibre, can modulate colonic epithelial cell proliferation *in vitro*. In a variety of cell systems, butyrate has been found to block cells in G<sub>1</sub> phase. The G<sub>1</sub> phase is controlled by kinases which consist of a regulatory subunit (primarily one of the D cyclins) and a catalytic subunit (named cyclin-dependent kinase). In human cells, cdk2 can combine with cyclin E in the G<sub>1</sub> phase, and regulate the progression toward S phase, moreover, it can be associated with cyclin A during S phase. The aim of our study was to investigate the mechanisms by which butyrate may inhibit cell cycle progression toward S phase. *Methods*: HT-29 cells were synchronized by exposing the culture to fetal calf serum-deprived DMEM medium. Cells were then exposed to complete medium (10% fetal calf serum) in the presence or absence of increasing concentration of sodium butyrate (from 2 to 8 mM) for 4 days. Proteins were extracted, and cyclin D and cdk2 expression were studied by Western blotting. *Results*: After exposition to 2 mM sodium butyrate, a strong stimulation of cyclin D expression was observed which was optimal at 8 mM. This stimulation was associated with a decrease in cdk2 level in the presence of butyrate. Expression of cdk4 and cdk6 was not affected by butyrate at all the concentrations tested. *Conclusions*: These results confirm that butyrate blocks cell proliferation in G<sub>1</sub> phase. The increased level of cyclin D may not be involved directly in the inhibitory mechanism, but be a marker of the blockade in G<sub>1</sub> phase. However, the decreased expression of ckd2 which leads to the inhibition of events that are essential for DNA replication, may participate directly in the mechanism of action of butyrate on cell proliferation. Nutrition: Nutrients and gut function Oncology, general: Proliferation, carcinogenesis }" "Butyrate Inhibits Cyclin-Dependent Kinase 2 (cdk2) and Stimulates Cyclin D Expression in HT-29 Epithelial Cells"

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"P P 66 1546" P 66 1546 **G-Protein Activator Mastoparan Decreases Transepithelial Permeability of T<sub>84</sub> Cells by Activating Potassium Channels and Actin Disassembling** R. Gerhard, J. Ries, W.F. Caspary, J. Stein

II. Dep. of Internal Medicine, J.W. Goethe-University Frankfurt/M., Germany *Background:* Mastoparan (MP), a tetradecapeptide isolated from the vasp venom, is known to stimulate heterotrimeric and small molecular GTP-binding proteins. The aim of this study was to investigate the role of mastoparan stimulated GTP-binding proteins in the regulation of transepithelial resistance and ion secretion of the intestinal cell line T<sub>84</sub>. *Methods:* Cells were grown on filters in DMEM/F12 supplemented with 5% newborn calf serum, 100 mg/ml streptomycin and 100 U/ml penicillin until confluency and mounted in modified Ussing chambers to measure electrical parameters. Cyclic AMP was measured by ELISA, Ca<sup>2+</sup> was determined by using fura-2. Cells were labelled with myo[2-<sup>3</sup>H]inositol to study the generation of inositol-phosphates by HPLC after stimulation with MP. F-actin was estimated by bound rhodamin-phalloidin, G-actin was measured by its ability to inhibit Dnase. *Results:* Mastoparan decreased the transepithelial resistance up to 80% in a range of 5 μM to 10 μM only when added apically. Stimulation with mastoparan did not elevate the cAMP level in the cells, but led to an increase of intracellular calcium without affecting inositol phosphate metabolism. Chloride-free medium as well as blocking the Na<sup>+</sup>/K<sup>+</sup>/Cl<sup>-</sup>-cotransport by 100 μM bumetanide reduced the chloride secretion of T<sub>84</sub> cells from 8.3 – 3.5 μA/cm<sup>2</sup> to 3.9 – 3.1 (p < 0.01) and 5.1 – 1.9 (p < 0.1) respectively, but did not abolish the effect of mastoparan on the transepithelial resistance. Addition of the potassium channel blocker barium (2 mM) prevented both, the decrease in the resistance and ion secretion, indicating that mastoparan does not directly activate chloride channels, but that chloride secretion is only due to K<sup>+</sup> efflux. F-actin content showed a biphasic modulation with initial increase and subsequent decrease, G-actin content showed 2.5 fold increase after 45 min. *Discussion:* From these data we hypothesize; that changes in the transepithelial resistance of T<sub>84</sub> cells after stimulation with mastoparan are based on selective activation of G-proteins that directly activate potassium channels. Efflux of K<sup>+</sup> results in membrane hyperpolarisation and activation of voltage dependent calcium channels and leads to an increase of intracellular calcium and remodeling of the cytoskeleton. } "G-Protein Activator Mastoparan Decreases Transepithelial Permeability of T84 Cells by Activating Potassium Channels and Actin Disassembling"

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"P P 66 1547" P 66 1547 **Edible Mushroom (*Agaricus Bisporus*) Lectin, a Reversible Inhibitor of Cell Growth, Concentrates around the Nuclear Envelope after Internalization and Blocks Nuclear Protein Import**

\*L.G. Yu, J.A. Smith<sup>1</sup>, O.V. Gerasimenko<sup>2</sup>, O.H. Petersen, J.M. Rhodes

<sup>1</sup> Department of Medicine Biochemistry, University of Liverpool, Liverpool L69 3BX, UK

<sup>2</sup> Department of Physiology, University of Liverpool, Liverpool L69 3BX, UK *Purpose:* The Thomsen-Friedenreich (TF) antigen (Gal{ b }1-3GalNAc{ a }-) is a common onco-fetal carbohydrate antigen in intestinal epithelia. Our previous work has shown that the non-cytotoxic TF-binding lectin from the edible mushroom *Agaricus bisporus* (ABL) inhibits proliferation in a range of malignant and normal epithelial cells (Cancer Res. 1993; 53; 4627) and has to be internalized to produce its inhibitory effect (Gastro. 1995; 108 (4); A558). The present study was designed to investigate the mechanism of its effect on cell proliferation. *Methods:* 1) HT29 colon cancer cells were incubated with FITC-ABL for 6 hours in 1% FCS Dulbecco's Modified Eagle's Medium and the distribution of FITC-ABL was observed by confocal microscopy. 2) The SV40 T antigen wild type nuclear localization sequence (NLS) containing peptide (cgggPKKKRKVED) was synthesized and conjugated to bovine serum albumin (BSA) and FLUOS (carboxyfluorescein-N-hydroxysuccinimide ester). HT29 cells cultured in chamber slides were permeabilized in 40 μg/ml digitonin for 6 mins at 4°C before application of cellular cytosol extract, ATP-generated system and NLS-BSA-FLUOS with or without the presence of 100 μg/ml ABL for 30 mins at 30°C. Distribution of NLS-peptide was observed by fluorescence microscopy. *Results:* FITC-ABL was observed to accumulate around the nuclear membranes after internalization. This led us to speculate that the lectin might interfere with transport through nuclear pores. Almost total inhibition of nuclear import of NLS-peptide was demonstrated in the cells treated with ABL (n = 3). *Conclusion:* These results suggest that inhibition of nuclear protein import is a likely explanation for the anti-proliferative effect of ABL. This has further implications for the importance of O-glycosylation in the regulation of proliferation. *Motility, specific:* Colon, anorectum *Oncology, general:* Proliferation, carcinogenesis *Hormones and receptors:* Growth factors } "Edible Mushroom (*Agaricus Bisporus*) Lectin, a Reversible Inhibitor of Cell Growth, Concentrates around the Nuclear Envelope after Internalization and Blocks Nuclear Protein Import"

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"P P 66 1548" P 66 1548 **Inhibition by Heparin of Neutrophil Adhesion to Human Intestinal Microvascular Endothelial Cells *in Vitro***

\*J. Wilson, S.L. Bloom, J.M. Rhodes

Department of Medicine, University of Liverpool, Liverpool, L69 3BX, UK *Purpose.* There have been several reports of clinical improvement and histological evidence of remission associated with use of heparin in patients with Ulcerative colitis (UC). Patients with UC have extensive infiltration of neutrophils into the lamina propria and as adhesion of leucocytes to the gut endothelium is a central event in the inflammatory process, we have used isolated human intestinal microvascular endothelial cells (HIMECs) to examine the effects of heparin on the adhesion of neutrophils *in vitro*. *Methods.* HIMECs were isolated from specimens of bowel (colon and small intestine) obtained from patients undergoing resection for colonic cancer or inflammatory bowel disease as previously described (Gut 38: A635, 1996), and cultured in endothelial growth medium (Clonetics) containing 20% pooled human AB serum. Neutrophils were derived from fresh peripheral venous blood using Mono-Poly resolving medium (ICN) and labelled with <sup>51</sup>Chromium for 1 hour. Endothelial monolayers grown to confluence in 24 well plates were treated with various concentrations of either high molecular weight heparin (Monoparin) or low molecular weight heparin (Fragmin) for up to six hours, and then overlaid with  $5 \times 10^5$  neutrophils/well. After 30 minutes, neutrophil adhesion was assessed by scintillation counting and expressed as counts/well. *Results.* Untreated endothelial monolayers bound 5% of the neutrophils added, however, pre-treatment of endothelial monolayers with both high and low molecular weight heparin significantly blocked the adherence of neutrophils by up to 50% (n = 3; \* p < 0.05 ANOVA) Untreated Heparin concentration (Units/ml) 0.1 1.0 10 High M.W. 190 – 3.7 92 – 10\* 119 – 2.7\* 124 – 5.7\* Low M.W. 184 – 12.4 105 – 15.9\* 102 – 16.4\* 120 – 5.1\* *Conclusions.* The pre-treatment of HIMECs with both heparins inhibits the binding of neutrophils indicating that they disrupt the adhesion mechanisms involved in leucocyte-endothelial interactions. This suggests that low molecular weight heparin may have therapeutic potential in the treatment of Inflammatory Bowel Disease. Immunology and microbiology: Inflammation Intestinal disorders: IBD, basic } "Inhibition by Heparin of Neutrophil Adhesion to Human Intestinal Microvascular Endothelial Cells in Vitro"

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## "P P 66 1549" P 66 1549 Aspirin and NSAIDs Induced Apoptosis in SW480 Cells

\*P. Planchon<sup>1</sup>, R. Benamouzig<sup>1</sup>, E. Jullian<sup>2</sup>, S. Chaussade<sup>2</sup>, D. Couturier<sup>2</sup>, J. Rautureau<sup>1</sup>

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<sup>2</sup> Facult\`e de M\`e9decine de Cochin, 75014 Paris Colorectal cancer is a frequent malignancy in western countries and despite recent progress, current treatment strategies have little effect on survival. Experimentally, NSAIDs have chemopreventive effects in rodent models of colorectal carcinogenesis, reducing the incidence and multiplicity of premalignant and malignant lesions. NSAIDs such as aspirin and sulindac have recently shown considerable promise as agents effective in the chemoprevention of colorectal cancer and large trials are conducted. Although the NSAIDs mechanisms of action remain unknown. In vivo as well as in vitro preliminary studies in HT-29 cells have suggested a salicylate-induced apoptosis mechanism. The aims of our study were to evaluate the effects of indomethacin, aspirin and lysin acetylsalicylate (Aspegic) in the RER+ phenotype human colon cancer cell-line SW480 which also present Ki-ras and p53 mutations. Indomethacin 25 to 400 \b5M induce a 17 to 90% decrease in SW480 cellular proliferation. A 10- and 20-fold higher doses are needed to observe a similar effect with aspirin and aspegic respectively. In this way a similar dose-effect pattern was observed in cell cycle analysis showing a G0/G1 cell accumulation. Indomethacin induced a strong apoptosis phenomenon (45% at 72 h) which was not observed with neither aspirin nor aspegic at the concentrations used. In conclusion, our results shown differences in apoptosis induction by indomethacin and salicyled derivatives in SW480. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum Oncology, general: Therapy } "Aspirin and NSAIDs Induced Apoptosis in SW480 Cells"

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## "P P 66 1550" P 66 1550 Interaction of ICAM-1 and E-Selectin in Gastrointestinal Tumor Cells

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<sup>2</sup> Surgical Department, University of Frankfurt, Theodor Stern-Kai 7, 60590 Frankfurt, Germany Regulation of cell adhesion is decisive for morphogenesis and integrity of solid tissue as well as immune defense. In many respects hematogenous metastasis of solid tumor cells is equivalent to the extravasation of leukocytes to inflammatory sites. Inflammatory cytokines, such as interleukin 1 and tumor necrosis factor { a }, stimulate the expression of several adhesion molecules on vascular endothelium and on tumor cells. However, the regulation of the individual adhesion molecules seems almost independent. Therefore, the interaction of E-selectin and the intercellular adhesion molecule ICAM-1 was studied in gastrointestinal tumor cells. Soluble immunoglobulin chimera consisting of the extracellular domain of E-selectin or ICAM-1, joined to the hinge region of IgG1 were immobilized in an adhesion assay (Walz 1990, Science). Two gastrointestinal tumor cells (liver, gallbladder) and the promyelocytic cell line HL60 were tested and it was shown, that cell adhesion to E-selectin plus ICAM-1 was up to 10 times stronger than to each single adhesion receptor. To further investigate costimulation of adhesion molecules tumor cells were incubated with the soluble fusion proteins of E-selectin and ICAM-1 for 1 h and 24 h and the expression of the adhesion receptors E-Selectin, ICAM-1 and VCAM and their ligands was determined in a flow cytometric analysis. The CD4-IgG chimera served as a negative control. We could demonstrate, that soluble E-selectin-IgG caused an specific increase of ICAM-1-positive tumor cells from 1% to 13% (1 h) and 70% (24 h) in the tumor cell lines. The ICAM-1-IgG1 fusion protein did not influence the expression of adhesion molecules. Stimulation was specifically blocked using monoclonal antibodies to E-selectin and ICAM-1. Our data indicate an interaction between the two adhesion receptors E-selectin and ICAM-1. We therefore suggest, that soluble E-selectin might result in a cell signal that directly stimulates ICAM-1. Oncology, general: Proliferation, carcinogenesis Oncology, general: Molecular biology, genetics Oncology, specific: Liver, biliary } "Interaction of ICAM-1 and E-Selectin in Gastrointestinal Tumor Cells"

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"P P 66 1551" P 66 1551 **Expression of the Placenta-Specific, 100 kDa Ras GTPase Activating Protein (*Ras* GAP 100) in Several Human Cancer Cell Lines and Normal Human Tissues**

\*Y. Araki, K. Nakamura, Y. Chijiwa, T. Kabemura, H. Nawata

Third Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan Point mutation of *c-ras* are frequently observed in human tumors, especially in colon cancers, and alteration of the Ras-mediated signal transduction may contribute to carcinogenesis. The *ras* GTPase activating protein (*ras* GAP), a regulator of Ras activity, has two isoforms; *ras* GAP 120 and *ras* GAP 100. The latter, whose molecular size is about 100 kDa, is generated by alternative splicing from the *ras* GAP 120 gene and has been considered to be placenta-specific, though the former is expressed ubiquitously. We evaluated the expression of *ras* GAP 100 in several human cancer cell lines, using immunoprecipitation and immunoblot analysis with an anti-GAP monoclonal antibody as well as reverse transcription-polymerase chain reaction. A protein of about 100 kDa was detected in some of colonic, gastric and lung cancer cell lines. The incidence of *ras* GAP 100 protein expression seemed to be higher in colonic cell lines than in those derived from other tissues. *ras* GAP 100 mRNAs were present in all cell lines and their amount tended to be higher in 100 kDa-expressing cell lines. In human normal tissues, we detected *ras* GAP 100 message in colon, stomach and liver. These findings demonstrate that *ras* GAP 100, previously thought to be placenta-specific, is expressed in other normal human tissues at mRNA level and its expression is augmented in some cancer cell lines, especially in colon cancer cell lines. So far, the function of *ras* GAP 100 is unknown, but further investigation for its role in cell proliferation is now on progress. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Colon, rectum } "Expression of the Placenta-Specific, 100 kDa Ras GTPase Activating Protein (*Ras* GAP 100) in Several Human Cancer Cell Lines and Normal Human Tissues"

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## "P P 66 1552" P 66 1552 Is Ornithine Decarboxylase Really a Marker of Premalignancy in the Gastrointestinal Tract?

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There is no biochemical marker of premalignancy that is known to antedate the appearance of histological changes in the gut epithelium. Although increased ornithine decarboxylase (ODC) activity has been described as a useful marker of neoplastic potential, longitudinal studies to assess the serial use of this measurement have not been reported. The aim of this study was to determine the value of mucosal ODC activity in patients with premalignant conditions of the GI tract and to try to identify high risk patients. Mucosal biopsy samples were obtained during endoscopy from 214 patients. ODC activity was measured using [<sup>14</sup>C]-ornithine bioassay and results were expressed in pmol/mg protein/h. Conventional histology was used to detect the presence of dysplasia which was graded according to established criteria. ODC activities obtained in the studied groups are shown in Table.

Diagnosis	n	Median	Range
Normal stomach	15	164	2–558
Gastritis	25	652	201–4247
Gastric adenomas	15	896	28–4287
Operated stomach	20	1204	199–8023
Gastric cancer	15	1821	762–11369
Normal duodenum	11	121	10–961
Duodenal polyps	15	1176	57–2900
Ca. of the papilla of Vater	10	2686	401–5818
Normal colon	10	185	1–695
Ulcerative colitis	20	526	2–7422
Familiar polyposis	11	929	5–3142
Colon adenomas	30	1423	185–3981
Colon cancer	17	3852	640–16561

ODC activity was significantly higher in all premalignant and malignant conditions than in normal tissue. However, our results have shown that high activities do not always indicate malignancy and low activities do not exclude the increased neoplastic potential. No significant difference according to the degree of dysplasia in the epithelium was observed (results not shown). This work was supported by the Polish Committee for Scientific Research (4 4335 92 03).

Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Stomach  
Oncology, specific: Colon, rectum }

"Is Ornithine Decarboxylase Really a Marker of Premalignancy in the Gastrointestinal Tract?"

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"P P 66 1553" P 66 1553 **Characterization of Polyamine-Transport Systems in the Cell Line Caco-2**  
Vladan Milovic, Wolfgang F. Caspary, J\fergen Stein

Division of Gastroenterology, Johann Wolfgang Goethe University, Frankfurt/Main Polyamines are polycationic molecules, essential for growth and differentiation in all eukaryotic cells. Recent work has focused on cell polyamine-transport systems as a way to regulate intracellular polyamine levels. We investigated the effects of epidermal growth factor (EGF) on polyamine uptake in Caco-2 cell monolayers. Caco-2 cells were exposed to 100 ng/ml EGF and the effects of treatment on putrescine uptake (putrescine, spermine) was measured over time. *Methods:* Caco-2 cells were grown in DMEM on porous filters. Serum was removed 24 h prior to uptake studies. Uptake was investigated after confluence (7 day old cells) or after differentiation (14 day old cells) *Results:* EGF stimulated polyamine uptake into Caco-2 cells in a dose- and time dependent manner. 100 ng/ml EGF had a maximally stimulatory effect on polyamine uptake at 12 h. Both basal and EGF-stimulated uptake rates were higher in 7 than in 14 day old Caco-2 cells. EGF increased both the affinity and capacity of the polyamine transporter ( $K_m = 33.7$  vs.  $19.4$   $\mu\text{mol/L}$  for putrescine [ $p < 0.05$ ] and  $23.6$  vs.  $12.6$   $\mu\text{mol/L}$  for spermine [ $p < 0.05$ ], in controls vs. EGF-stimulated cells, respectively;  $V_{max}$   $44.7$  vs  $82.5$   $\mu\text{mol}/10^6$  cells/2 h for putrescine [ $p < 0.05$ ] and  $32.3$  vs.  $55.1$   $\mu\text{mol}/10^6$  cells/2 h for spermine [ $p < 0.05$ ], in controls vs. EGF-stimulated cells, respectively). The enhanced polyamine uptake induced by EGF was not inhibited when protein synthesis was blocked by cycloheximide, implying that additional protein was not required for the effect of EGF on polyamine uptake. Similarly, brefeldine A had no effect indicating that EGF does not stimulate vesicular transport from the Golgi apparatus. However, the tyrosine kinase inhibitor, genistein, completely inhibited EGF-stimulated polyamine uptake, pointing to a possible role for tyrosine phosphorylation(s) in EGF-stimulated polyamine uptake in Caco-2 cells. *Conclusion:* In the present study we demonstrate that EGF stimulates polyamine uptake in Caco-2 cells. The mechanism of EGF-induced polyamine uptake likely includes an increase in the number of functional transporters in the plasma membrane, and/or modification of the transporter itself. }" "Characterization of Polyamine-Transport Systems in the Cell Line Caco-2"

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"P P 66 1554" P 66 1554 **Inflamed Synovial Tissue from Patients with Spondyloarthritis is Enriched with Activated Cells Carrying  $\beta$ 7 Integrins**

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<sup>4</sup> Dpt. of Pathology, University Hospital, Ghent, Belgium

<sup>2</sup> Dpt. of Nephrology, University of Western, Ontario, Canada *Introduction:* An intriguing relationship between gut and synovium exists in patients with spondyloarthritis (SpA). Previously, we demonstrated microscopically inflammatory gut lesions in 62% of these patients. A fraction of them (6.5%) ultimately evolved to clinically overt inflammatory bowel disease. The origin of the gut-synovium axis is as yet unknown. In this study, we tested the hypothesis that antigen-primed gut-derived lymphocytes would migrate into synovial tissue of patients with SpA, thereby mediating synovial inflammation (gut-iteropathy concept). *Methods:* Synovial biopsies were obtained by needle-arthroscopy from 5 patients with SpA and 6 with rheumatoid arthritis (RA) with peripheral synovitis (knee). All but one patients had less than 6 months of disease duration. To minimize sampling error 8 to 10 biopsies were taken from different sites within the inflamed joint. Activated T-cells were generated by expansion with IL-2 for 3 to 5 weeks from each single biopsy. In total 25 cell-lines were obtained (RA:14; SpA:11). Cell-lines were characterized by flowcytometry, with special reference for  $\alpha$ 4 $\beta$ 7 and  $\alpha$ E $\beta$ 7,  $\beta$ 7 integrins playing a critical role in the homing of lymphocytes to the gut. Results are expressed as mean % positive T-cells – SEM. The Wilcoxon rank sum test was applied for statistical analysis. *Results:* Activated T-cells from RA-synovium consist almost exclusively of CD4+ T-cells (RA:93.4 – 3.4; SpA:61.4 – 10.7,  $p < 0.01$ ), contrasting to SpA in which CD8+ T-cells are more abundant (SpA:36.5 – 10.0; RA:5 – 3.1,  $p < 0.01$ ) In contrast to RA, cell-lines from SpA patients highly expressed one of the gut homing integrins, either  $\alpha$ 4 $\beta$ 7 or  $\alpha$ E $\beta$ 7 (SpA:66.6 – 9.3; RA:35.3 – 7.4,  $p < 0.02$ ). The observed differences between SpA and RA are not merely due to the discriminating CD4/CD8 ratio, as the increase in  $\beta$ 7 integrins in SpA was similar on CD4 and CD8+ T-cell. *Conclusion:* Inflamed synovial tissue from SpA-patients with recent onset disease is enriched with activated T-cells expressing  $\beta$ 7 integrins  $\alpha$ 4 $\beta$ 7 or  $\alpha$ E $\beta$ 7. Intestinal disorders: IBD, basic }" "Inflamed Synovial Tissue from Patients with Spondyloarthritis is Enriched with Activated Cells Carrying  $\beta$ 7 Integrins"

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**"P P 66 1555" P 66 1555 Type IV Collagenase Expression is Integral to MMP Induced In-Vitro Invasion and is Inhibited by BB2516 and BB94**

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University Department of Surgery, Queen Elizabeth Hospital, Birmingham, B15 2TH, UK  
The matrix metalloproteinases (MMPs) are proteolytic enzymes that are capable of degrading the extracellular matrix. Their functional activity is controlled by the tissue inhibitors of the metalloproteinases (TIMPs). MMP activity is increased in most tumours but type IV collagenase activity appears to be the most important. Interest in this field has led to the development of low molecular weight MMP inhibitors (MMPIs), two of these (BB94 & BB2516, British Biotech, Oxford, UK) have been the subject of clinical trials. We studied the in-vitro invasion of a radiolabelled endothelial cell basement membrane by two pancreatic cancer (SUIT2 & BxPC3) and one breast cancer (MDA-MB231) cell lines. Each experiment was performed in triplicate and repeated three times. The ability of BB94 and BB2516 to inhibit invasion was then compared to the cell line expression of 72 & 92 kDa type IV collagenase and TIMP 1 & 2. The MMP and TIMP expression were measured using a quantitative RT-PCR technique. The MDA cell line were significantly more invasive than either the SUIT2 ( $p < 0.001$ ) or BxPC3 ( $p < 0.01$ ) cell lines. The addition of MMPIs to the MDA cell line resulted in a significant and dose dependent reduction of invasion ( $p < 0.03$ ) but this was not seen with either of the other two cell lines. All three cell lines produced TIMP mRNA but the MDA cell line produced significantly more type IV collagenase mRNA than either the SUIT2 or BxPC3 cell lines ( $p < 0.05$ ). This study supports the hypothesis that type IV collagenase action is necessary for basement membrane degradation and malignant cellular invasion and can be inhibited by both BB94 and BB2516 MMPIs. Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis Oncology, general: Therapy } "Type IV Collagenase Expression is Integral to MMP Induced In-Vitro Invasion and is Inhibited by BB2516 and BB94"

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"P P 66 1556" P 66 1556 **HIP/PAP Is an Adhesive Molecule Expressed in Hepatocellular Carcinoma, Normal Paneth and Pancreatic Cells** L. Christa<sup>1</sup>, F. Carnot<sup>2</sup>, M.T. Simon<sup>1</sup>, F. Levavasseur<sup>3</sup>, M.G. Stinnakre<sup>4</sup>, C. Lasserre<sup>1</sup>, D. Thepot<sup>4</sup>, B. Clement<sup>3</sup>, E. Devinoy<sup>4</sup>, C. Brechot<sup>1</sup>

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<sup>4</sup> INRA, Jouy-en-Josas, France We have previously identified a gene "HIP" overexpressed in around 25% of HCCs and not in normal nor cirrhotic livers. HIP is expressed in normal pancreas and intestine and is identical to pancreatitis associated protein (PAP). We have subsequently shown that HIP/PAP encodes for a C-type lectin, raising the hypothesis that it might be implicated in liver cells adhesion and spread. In the present study, we have established transgenic mice to drive the production of soluble recombinant HIP/PAP protein in the milk of lactating animals; in this model we showed that HIP/PAP protein was secreted after proper cleavage of the potential signal peptide. We have also produced HIP/PAP protein by *E. Coli* cultures to generate specific antibodies. These antibodies allowed us to detect the HIP/PAP protein in the cytoplasm of tumorous, but not non-tumorous hepatocytes. HIP was not detected in normal liver but present in normal intestine and pancreas: neuroendocrine and Paneth cells, pancreatic Langerhans islets and acinar cells. Finally, we tested HIP/PAP protein activity, showing that HIP/PAP induced adhesion of rat hepatocytes, and bound to the extracellular matrix proteins: laminin-1, fibronectin; HIP also bound, yet to a lesser extent, to types I and IV collagens and not to heparan sulfate proteoglycan. *In conclusion*, our results show that: 1. the recombinant HIP/PAP protein we have produced can be matured upon secretion. 2. HIP/PAP protein is specifically expressed in hepatocarcinoma, and not cirrhotic tissue 3. HIP/PAP acts as an adhesion molecule on hepatocytes and binds to key extracellular matrix proteins. Altogether, these results suggest that HIP/PAP protein might be implicated in HCC progression. } "HIP/PAP Is an Adhesive Molecule Expressed in Hepatocellular Carcinoma, Normal Paneth and Pancreatic Cells"

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## "P P 67 1557" P 67 1557 Hereditary Fructose Intolerance — Case Report with Molecular Study

\*A.I. Lopes, A.G. Almeida, A.E. Costa, A. Costa, M. Leite

Pediatric Gastroenterology Unit, Pediatric Department, Hospital Santa Maria, Lisboa, Portugal *Hereditary Fructose Intolerance (HFI)* is a rare metabolic disorder, resulting from a deficiency of aldolase B (fructose-biphosphate-aldolase) in the liver, kidney and intestine. Though classically considered an autosomal recessive condition, genetic heterogeneity is increasingly being recognized. Recent molecular studies [1] have identified the mutation A149P in most European affected patients. We describe the first case of HFI with molecular analysis in a Portuguese patient (a Caucasian boy, second child of nonconsanguineous healthy parents), presenting the same mutation of the aldolase B gene (A149P). The child presented at 3.5 months of age with vomiting, coincident with the introduction of a sucrose-containing formula. Diagnosis was confirmed at 7 months of age by conventional methods (enzymatic assay in liver tissue). Liver biopsy showed slight periportal fibrosis and hepatocyte fatty changes. Family study extensive to the mother and sibling, confirmed the presence of same single mutant aldolase B allele (A149P). This finding, associated with a typical nutritional history in the older brother, may be considered highly suggestive of the disorder and sufficient confirmatory evidence, avoiding more invasive tests. We emphasize the diagnostic contributory role of molecular studies in risky patients for HFI and their families. The authors thank Prof. T.M. Cox, University of Cambridge School of Clinical Medicine, Addenbrooke's Hospital, Cambridge, UK, who kindly performed molecular studies in patient and family.

Reference: Cross NCP, Cox TM et al. Molecular analysis of aldolase B genes in hereditary fructose intolerance. *Lancet* 1990; 335: 306–9 Liver and bile ducts, 1: Liver diseases, children Oncology, general: Molecular biology, genetics } "Hereditary Fructose Intolerance / Case Report with Molecular Study"

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"P P 67 1558" P 67 1558 **Structural and Functional Analysis of Apolipoprotein A-I**

\*C. B\fttner, M. Dogar, R. Haas, J. Genschel, S. Wagner, M.P. Manns, H.H.-J. Schmidt

Dept. of Gastroenterology and Hepatology, Medizinische Hochschule Hannover, D-30623 Hannover, Germany Apolipoprotein A-I (apoA-I) serves as an excellent predictor for liver protein synthesis. It is an important determinant of the concentration of HDL in plasma. We used normolipemic rabbits (NZW) as an in vivo model to gain more insights about apoA-I metabolism and its structural functions (Schmidt et al., *J. Biol. Chem.* 1995, 270: 5469–5475). ApoA-I has been shown to contain repeated sequences that presumably arose by intragenic duplication of 11- or 22-amino acid amphipathic segments. To study differences of metabolic behaviour and association with lipoprotein particles of various apoA-I variants we isolated apoA-I from different animal species (rabbit, human, macaca, mouse, rat, pig, calf and chicken) using ultracentrifugation, SDS gel electrophoresis, and electroelution, subsequently. The various apoA-I forms were analyzed by the in vivo catabolism. In addition mouse and rat apoA-I had a higher percentage of non-lipoprotein associated apoA-I. Comparing the protein sequence of the rabbit with rat and mouse apoA-I the major difference occurs within the amino acids 180–186, which represents a turn between helices using the predicted secondary structure of human apoA-I. In contrast the region of amino acid 125–135 seems to have no major impact on the catabolic rate of apoA-I. Therefore, we assume that the difference in metabolism among the studied proteins can be explained by their structural differences. Interestingly, the overall predicted hydrophobicity between mouse, rat and human apoA-I is almost identical. In conclusion, the structural properties of apoA-I may explain the association with human and rabbit HDL, which in turn determines its rate of catabolism. Therefore, the kinetic analysis of proteins isolated from different species have major implication to define their functional regions. Nutrition: Metabolism }" "Structural and Functional Analysis of Apolipoprotein A-I"

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"P P 67 1559" P 67 1559 **Energy Metabolism and Body Composition in Alcoholics**

\*G. Addolorato, E. Capristo, G. Mingrone, A.V. Greco, G.F. Stefanini, G. Gasbarrini

Cattedra di Medicina Interna II. Università Cattolica del S. Cuore, Rome and Università di Bologna, Italy Several controversies are still present in the literature on body weight (BW) and on alcohol energy contribution on the body mass in alcoholics. Aim of the study was to evaluate the effect of alcohol addiction on energy expenditure (REE) (measured with indirect calorimetry) and body composition (assessed by both anthropometry and bioimpedance) in 12 alcoholics (A) (6 men and 6 women) enrolled in the study on the basis of DSM III R criteria, with mean alcohol intake of 187 – 57.4 g/die for at least 5 years compared to a group of healthy social drinkers (C) with mean alcohol intake of 38.4 – 12.0 g/die (mean – SD) matched for sex, age and height. The caloric intake was computed on the basis of a food diary, compiled during the last 7 days and the calories provided by alcohol were also computed. 24 h urine and fecal collections were performed. The BW average of A was lower than that of C (60.7 – 9.99 vs 66.7 – 5.86 kg;  $p = ns$ ) with a significant decrease in fat mass (FM) in A (14.8 – 5.39 kg vs 19.0 – 3.50;  $p < 0.05$ ), while no difference was found in fat free mass (FFM). REE was not statistically different in the two groups, however, normalizing REE by BW, A showed higher values than C (27.1 – 3.21 vs 23.4 – 3.81 kcal/kg<sub>bw</sub>;  $p < 0.001$ ). REE resulted higher than that predicted in A ( $P < 0.05$ ), while not statistically different in C. The non-protein respiratory quotient was significantly lower in A than in C (0.76 – 0.03 vs 0.86 – 0.03;  $p < 0.001$ ) and A showed a significantly higher lipid oxidation and a lower carbohydrate oxidation than C ( $p < 0.05$ ). No statistical differences were found in dietary intake, urinary nitrogen excretion and fecal losses over 24 hrs. In conclusion alcoholics showed an increased REE over predicted values suggesting a possible cause of their lower BW. They showed a preferential lipid oxidation and this finding might be responsible for their reduced FM. Nutrition: Metabolism Nutrition: Nutrients and gut function } "Energy Metabolism and Body Composition in Alcoholics"

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"P P 67 1560" P 67 1560 **Alcohol Consumption in an Italian General Population: The CO.A.L.A. Project**

\*E. Scafato, A.F. Attili, A. Giorgi Rossi, L. Capocaccia, CO.A.L.A. Group

Dept of Clinical Medicine, Rome University "La Sapienza", Italy *Background:* Lack of data from studies on general population rates of subjects at higher risk for alcohol-related problems. *Objective:* To study dietary habits and alcohol intake in a general population with special focus on drinking patterns and differences related to age, sex, education, occupation, census, history of alcohol consumption, lifetime changing in alcohol consumption, diseases, geographical distribution. *Design:* Prospective population study. *Setting:* COALA Project, Latium, Italy. *Field activities:* January 1994–January 1995. *Participants:* 1660 family clusters, 1709 males (M) and 1878 females (F) (total 3587), over 15 years old, randomly sampled from the municipal censuses of 20 local authorities and stratified according to the size of the local authority. *Measurements:* Participants filled in a semi-quantitative food frequencies questionnaire. Total alcohol intake was calculated by summing the alcohol content of each beverage according to a standard glass of wine, can of beer and shoot of liquor (eleven precoded response categories for each alcoholic beverage). *Main outcome measure:* Age standardized prevalence, mean alcohol consumption, drinking patterns, drinking categories according to the targeted variable. *Results:* 1325 of the 3567 subjects (43.9%; 30.6 M, 56.1 F) declared to be teetotaler and/or abstinent and 2242 to be drinkers (56.1%; 69.4 M, 43.9 F). Of the latter 51.4% (63.4 M, 39.7 F) drank wine, 25.6% beer (36.2 M, 16.4 F) and 20% spirits (30.7 M, 10.3 F). The 15–20 year old age group had the lowest prevalence of drinkers (35.7% M, 25.2% F) of whom 19.3% drank wine, 24.8% beer, 6.9% spirits. The highest number of drinkers were males in the 31–50 age group and for females in the 21–30 and 61–70 age groups. 83.3% of these (87.1 M, 78.9 F) drank wine, 39.8% (47.4 M, 29.9 F) beer, 31.9% (41.5 M, 19.5 F) spirits. Alcohol was prevalently consumed at mealtimes (80% of M and 91.4% of F). Wine was consumed daily by 78% of M, 57.9% of F for wine, beer by 16.7% of M, 7.4% of F and spirits by 11% of M and 2% of F. Per capita alcohol consumption among drinkers was 25.8 gr/day (32.9 gr M, 15.5 gr F). 32.7% of M exceeded 40 gr/day, 29.7% of F 20 gr/day. *Conclusions:* A lower prevalence and a more moderate alcohol consumption was found among women and younger subjects. Alcohol consumption was within acceptable limits (low risk) for 67.3% of M and 70.3% of F drinkers but 1/3 of subjects could be considered at higher risk for alcohol related problems. The prevalent drinking pattern is wine consumption at mealtime although young people seem to promote new, less traditional patterns. (COALA PROJECT was supported by a grant from the Ministry of Agricultural, Food and Forestry Resources. Min Bill 55250/92) Clinical practice: Epidemiology (non cancer) } "Alcohol Consumption in an Italian General Population: The CO.A.L.A. Project"

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## "P P 67 1561" P 67 1561 Frequency of the Beta 3-Adrenergic Receptor Trp64Arg Mutation in Obese and Non-Obese Subjects in Germany

\*R. B\ 'fcttner, A. Sch\ 'e4ffler, H. Arndt, Diabetomobile Study Group, J. Sch\ 'f6lmerich, K.-D. Palitzsch

Dept. of Internal Medicine I, University of Regensburg, Regensburg, Germany *Objective:* To analyse the frequency of the Trp64Arg mutation of the beta 3-adrenergic receptor gene in relation to the body mass index (BMI) in a randomly collected sample of the German population. *Methods:* Out of 5800 participants in the Diabetomobile Study, an epidemiological survey to investigate the prevalence of diabetes mellitus and other metabolic disorders being carried out in Germany from 1993 up to now, 645 participants were randomly chosen and divided into four groups according to their BMI: [1] BMI  $\leq$  20, [2] BMI  $\leq$  25, [3] BMI  $\leq$  30 and [4] BMI  $>$  30. PCR and restriction digestion were performed on genomic DNA from these subjects. The Trp64Arg mutation of the beta 3-adrenergic receptor gene could then be recognised by restriction-fragment-length polymorphism. Subjects carrying the mutation were further analysed with respect to age, sex, and prevalence of diabetes mellitus, high blood pressure and hypercholesteremia. *Results:* The frequencies of the heterozygous mutation and the homozygous mutation were as follows: group [1] 10.32% and 0.00%; group [2] 8.85% and 1.04%; group [3] 8.62% and 1.15%; group [4] 8.50% and 0.65%. The overall frequency of the heterozygous mutation was 8.99% and of the homozygous mutation 0.78%, respectively. There were no significant differences between the prevalence of the homozygous or the heterozygous mutation in the group with high BMI [4] compared with the groups with lower BMI [1–3]. There were also no significant differences between age and sex distribution and prevalence of diabetes mellitus, hypertension or hypercholesteremia when comparing normal subjects with subjects carrying the mutation in the same subgroups. *Conclusions:* The heterozygous Trp64Arg mutation of the beta 3-adrenergic receptor gene is found commonly in Germany (8.99%), the homozygous mutation relatively rarely (0.78%). Neither the homozygous nor the heterozygous mutation are correlated with higher BMI, higher prevalence of diabetes mellitus, hypertension or hypercholesteremia. Nutrition: Metabolism Hormones and receptors: Molecular biology Clinical practice: Epidemiology (non cancer) } "Frequency of the Beta 3-Adrenergic Receptor Trp64Arg Mutation in Obese and Non-Obese Subjects in Germany"

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## "P P 67 1562" P 67 1562 **Glucose Control and Incretine Hormone Release Following Ingestion of Different Liquid Diets in Non-Insulin Dependent Diabetics**

\*H. Printz, B. Recke, A. Wagner, H.C. Fehmann, R. Arnold, B. G\|f6ke

Department of Internal Medicine, Philipps-University of Marburg, Marburg/Lahn, Germany Recently, for enteral nutrition of non-insulin dependent diabetics balanced liquid diets have been formulated. However, their beneficial influence on glucose control and metabolism still needs to be proven. In the present study, 10 non-insulin dependent diabetics (7 men, 3 women, age: 56 – 11 years) with a mean body mass index of  $26.2 \pm 3.6 \text{ kg/m}^2$  orally ingested 500 ml of either a standard liquid diet (Biosorb' Sonde) or a fibre containing diet (Biosorb' Plus Sonde) or a carbohydrate modified, fructose containing special "diabetes diet" (Fresubin' Diabetes). Oral antidiabetic therapy consisted in 6 patients of an average dose of  $9.3 \pm 1.8 \text{ mg/die}$  glibenclamide plus an average oral dose of  $175 \pm 113 \text{ mg/die}$  of the glucosidase inhibitor acarbose. Four patients were treated with diabetes diet plus an average oral dose of  $4.8 \pm 1.7 \text{ mg/die}$  glibenclamide without acarbose. Prior to testing, mean blood glucose values (07:00 am preprandial, 10:00 am, 04:00 pm) were  $133 \pm 37$ ,  $166 \pm 51$  and  $135 \pm 50 \text{ mg/dl}$ , respectively.  $\text{HbA}_{1c}$  ( $8.4 \pm 2.2\%$ ) and fructosamine concentrations ( $308 \pm 86 \text{ } \mu\text{mol/l}$ ) prior to liquid diet testing showed a satisfactory antidiabetic control. Intravenous glucagon stimulation indicated a sufficient residual  $\beta$ -cell insulin secretion capacity ( $10 \pm 4$  versus  $36 \pm 30 \text{ } \mu\text{U/ml}$  insulin 0 or 6 min after 1 mg glucagon iv). Each type II diabetic ingested in randomized order with 10 days intervals each liquid formula (with comparable carbohydrate amounts of  $\approx 60 \text{ g}$ ) after intake of the usual oral morning medication. Blood samples were collected at intervals for up to 180 min following diet consumption for determination of blood glucose, as well as IR-insulin, C-peptide, IR-GIP and IR-GLP-1 in plasma. Considering minor variations in the nutritional values of the diets, all liquid diet formulations showed comparable responses during the observed time period. Based on this data, we conclude that all diets challenged the entero-insular axis in non-insulin dependent diabetics to a comparable extent. Nutrition: Metabolism Nutrition: Nutrients and gut function Pancreas: Secretion, regulation } "Glucose Control and Incretine Hormone Release Following Ingestion of Different Liquid Diets in Non-Insulin Dependent Diabetics"

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## "P P 67 1563" P 67 1563 Paper- or Computer Based Quality-of-Life Questionnaires — Does It Matter?

\*L. Aabakken<sup>1</sup>, P. Tarnasky<sup>1</sup>, Y. Palesch<sup>2</sup>, H. Evangelou<sup>1</sup>, P. Cotton<sup>1</sup>

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<sup>2</sup> Dept. Of Biometry, Medical University of South Carolina, Charleston, US *Purpose:* The replacement of manual paper questionnaires with a computer based data acquisition system offers several potential practical advantages, but the validity of such a transition must be documented. The purpose of the present study was to compare data acquired by computer and data acquired by traditional paper questionnaires. *Material and methods:* Eighty-three consecutive patients attending our outpatient GI clinic were included in the study. After informed consent was obtained, they completed a 28 items standardized quality-of-life questionnaire, both a standard, self-administered paper form, and a computer based form, in a randomized order. The computer was a self-explanatory touchscreen-based system with a sound feature that reads out the questions, as well as the reply alternatives and additional explanations on demand. The paper-based questionnaire used a standardized 5 point Likert scale scoring frequency (of a symptom/complaint) or agreement (with a statement). The computer entry was done with an identical scale (n = 44) or with a visual analogue scale (n = 40) that was subsequently normalized symmetrically to a 5 point scale. Zero or one item difference between paper and computer was regarded concordant data. *Results:* The mean concordance between the paper and computer version was 91% with the normalized VAS and 92% with the Likert scale, and over-all statistically significantly greater than 80% for both scoring models. The mean time to complete the questionnaire was 345 seconds for the paper and 240 seconds for the computer version. However, in the paper form, 8 questions were not filled in by 7 patients, and another two patients entered erroneous data, circling more than one reply on individual questions. In contrast, all the computer data were complete. Moreover, 83% of the patients preferred the computer version on direct questioning while only 3% preferred the paper questionnaires. *Conclusion:* We found an acceptable concordance between paper- and computer-acquired quality of life data. The inherent error-control and additional practical advantages of using a computer makes this a promising technique for the routine acquisition of patient-based questionnaire data. *Clinical practice:* Management strategy Clinical practice: Quality assurance } "Paper- or Computer Based Quality-of-Life Questionnaires / Does It Matter?"

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## "P P 67 1564" P 67 1564 Utility of a Touch Screen Computer-Based Quality of Life Questionnaire

\*L. Aabakken<sup>1</sup>, P. Tarnasky<sup>1</sup>, Y. Palesch<sup>2</sup>, S. Javed<sup>1</sup>, H. Evangelou<sup>1</sup>, P. Cotton<sup>1</sup>

<sup>1</sup> Digestive Disease Center, Medical University of South Carolina, Charleston, US

<sup>2</sup> Dept. Of Biometry, Medical University of South Carolina, Charleston, US *Purpose:* Quality of life data are becoming increasingly important for assessment of efficacy and overall outcomes of treatment, but data acquisition may be cumbersome. The aim of this study was to assess the feasibility of computer based acquisition of quality-of-life data in a routine outpatient clinic setting. *Material and methods:* 127 consecutive outpatients (mean age 42, range 15–78) were studied. After informed consent and explanation by a nurse, they completed in randomized order both a paper version and a computer version of our standardized quality of life questionnaire of 28 questions. The computer consists of a touch screen with large screen buttons, and it has sound capabilities, that reads aloud questions, replies and explanations on demand. Patients were randomized to a visual analogue scale (VAS) or a 5 point Likert scale, and after completing the 28 questions, the first five questions were repeated, using the other scale, for intraindividual comparison. *Results:* Seventy-seven males and 47 females participated. 3 subjects refused both the paper and computer questionnaire. Seventy-seven percent of the participants liked the computer questionnaire, and an additional 20% found it acceptable, leaving only 3% that did not like it. Moreover, 82% felt the computer to be *better* than the paper form, and only 3% preferred the paper version. The sound feature was felt to be *very helpful* by 51%, and *somewhat helpful* by another 20%. No difference was found as to preference to VAS versus 5 point Likert scale. The mean time to complete the 28 questions was 240 seconds. The concordance between VAS and Likert scale scores was acceptable, but with a tendency toward end-point accumulation in the VAS scores. *Conclusion:* The touch screen computer with sound capabilities was very well accepted by the patients in this feasibility study. Only 3% preference to the paper version and a mean entry time of 4 minutes, together with the inherent simplification of data handling makes this a promising method for administering QOL instruments in a routine clinical setting. *Clinical practice:* Management strategy Clinical practice: Quality assurance } "Utility of a Touch Screen Computer-Based Quality of Life Questionnaire"

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"P P 67 1565" P 67 1565 **Direct Measurement of the Intraabdominal Pressure in Normal Subjects and Pathologic Conditions**

\*A. Shafik, A. El-Sharkawy, W.M. Sharaf

Department of Surgery, Cairo University, Cairo, Egypt *Purpose:* to standardize a method of direct measurement of the intraabdominal pressure (IAP), to correlate the results with the intrarectal pressure and to apply the method for surgical diseases. *Method:* Thirty-four subjects were studied in 4 groups: control (no = 11), hernia (no = 8) mass (no = 7) and obese (no = 8). A Veress needle was introduced into the peritoneal cavity through a 5 mm subumbilical incision and was connected to a Statham pressure transducer. Measurements of the IAP were recorded at rest and during straining, in supine and erect positions, and before and after anesthesia administration. Recording of the intrarectal pressure was done simultaneously with the IAP. *Results:* The hernia group showed significant IAP pressure reduction at rest ( $p < 0.01$ ) and on straining ( $p < 0.01$ ) compared to the controls. In both the mass and obese groups, the IAP showed no significant difference from controls at rest ( $p > 0.05$ ) and was higher on straining ( $p < 0.05$ ). All the groups exhibited significant IAP drop ( $p < 0.05$ ) after anesthesia. There was no significant difference ( $p > 0.05$ ) between the intrarectal pressure and IAP in the 4 groups. *Conclusion:* a method for direct IAP measurement is described in the control group and in subjects with some surgical conditions. The intrarectal pressure represented the IAP and can thus replace it. Motility, general: Functional GI disorders Intestinal disorders: Constipation Intestinal disorders: Anorectal disorders } "Direct Measurement of the Intraabdominal Pressure in Normal Subjects and Pathologic Conditions"

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## **OT77 1566A Novel Target Therapy for Squamous Cell Carcinomas Overexpressing EGF-Receptors with Apparent Safety: The Fusion between Human Pancreatic Ribonuclease1 and Human EGF**

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<sup>2</sup> Dept of Mol. Biology, Nat. Instit. of Agrobiol. Resources, Tsukuba, Japan Many of the immunotoxins constructed up to the present, have been evaluated over clinical trials for future use as anticancer agents, but toxicity or immunogenicity seem to be the dose limiting factors. In order to improve the whole immunotoxin concept we used two endogenous human proteins to construct a recombinant totally human "immunotoxin-like" agent. Ribonucleases have been shown to have antitumor activity. The gene coding for human pancreatic ribonuclease1 (hpRNase1), lately cloned from human pancreas by Seno et al., was fused with a gene coding for human epidermal growth factor (hEGF). The DNA was expressed in E. coli, the recombinant hpRNase1-hEGF was purified to homogeneity and assayed in vitro by the MTT colorimetric assay, for cytotoxic potential on several squamous cell carcinomas expressing different amounts of EGF-Receptors (EGFR). The protein was cytotoxic, EGFR number dependently with an IC50 ranging between  $10^{-7}$  M and  $10^{-6}$  M whereas the IC50 of free hpRNase1 was  $10^{-4}$  M. A mixture of free hEGF and free hpRNase1 had no greater effect than free hpRNase1 alone and a molar excess of hEGF blocked the cytotoxicity dose dependently. No cytotoxicity was detectable for EGFR deficient control cells suggesting that the fusion protein enters via EGFR and kills the cells presumably by RNA brake down. It has been demonstrated that many squamous cell carcinomas, especially those of esophagus, lung, head and neck and bladder appear with EGFR overexpression, are closely correlated to high aggressivity and poor prognosis and cannot be cured by surgery alone. Our data suggest that hpRNase1-hEGF may be a candidate for a safer approach in the multidisciplinary treatment of such carcinomas than conventional immunotoxins. Oncology, general: Molecular biology, genetics Oncology, general: Therapy Oncology, specific: Oesophagus } "A Novel Target Therapy for Squamous Cell Carcinomas Overexpressing EGF-Receptors with Apparent Safety: The Fusion between Human Pancreatic Ribonuclease1 and Human EGF"

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OT77 1567 **Unfrequent Microsatellite Instability in Esophageal Cancer**  
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*Background and Aims:* Genetic defects in the mismatch repair system can be monitored by examining Replication Errors (RER) at microsatellite loci in cancer cells. Microsatellite instability (MI) was first described in hereditary nonpolyposis and sporadic colorectal cancers. It has been reported that MI may play a role in the development of various cancers, but its role in esophageal cancer is debated. The aim of this study was to determine the frequency of MI in the two main types of esophageal cancer, squamous cell carcinoma (SCC) and Barrett's adenocarcinoma (BA).  
*Methods:* Surgically resected specimens were collected from 20 patients with SCC and 26 patients with BA, treated in the same hospital. Genomic DNA was extracted from primary tumours and adjacent normal gastric mucosa, and amplified by PCR at 39 poly CA microsatellite loci scattered throughout the genome. The PCR products were electrophoresed on denaturing gels and visualized by autoradiography.  
*Results:* Four of 20 SCC showed MI at one locus. Among 26 BA, 5 and 3 tumors showed MI at one and two loci, respectively. No MI was demonstrated in any of the remaining cases. The instability affected different loci on chromosome 3, 4, 6, 9, 17 and 18. There were no differences between tumors with and tumors without MI regarding the clinicopathological characteristics.  
*Conclusion:* We show that the frequency of MI in cancer of the esophagus is very low. The presence of few loci showing MI could be explained by the existence of a background of instability (< 10%) independent of genetic defects in the mismatch repair system. In this study, none of the esophageal tumors had a typical RER+ phenotype. These data suggest that genetic defects in the DNA mismatch repair system do not play a role in esophageal cancer.  
Oncology, general: Molecular biology, genetics  
Oncology, general: Proliferation, carcinogenesis  
Oncology, specific: Oesophagus } "Unfrequent Microsatellite Instability in esophageal Cancer"

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OT77 1568 **The Incidence of Esophageal Adenocarcinoma in Barrett's Esophagus in an Italian Population: First Report from Southern Europe** R. Ferraris<sup>1</sup>, L. Bonelli<sup>2</sup>, M. Conio<sup>3</sup>, H. Aste<sup>3</sup>

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<sup>3</sup> e I.S.T. Genova

<sup>2</sup> Epidemiologia Clinica, I.S.T. Genova The incidence of adenocarcinoma (ADC) of the esophagus is increasing in the U.S.A., Northern and Central Europe. Data from Southern Europe are still lacking. Since the alimentary attitudes and the lifestyle in these areas are different, it could be interesting to compare these data. *Aim:* to report the results of the prospective endoscopic histological surveillance of a large cohort of Barrett's esophagus (BE) patients enrolled in the Italian multicentric study G.O.S.P.E. (Gruppo Operativo Studio Precancerosi Esofagee). *Methods:* 345 BE patients with 3 or more cm. metaplasia were eligible to the yearly endoscopic follow up. 59 patients with esophagitis but not histologically proven BE were also eligible for a parallel follow up. *Results:* the mean duration of the follow-up period was 3 years (Range 12–81 months). 202 out of the 345 eligible BE patients (253 males and 92 females; aging 19–75 years) complied to the follow-up study (at least one follow-up examination). The compliance for the two main histological types of BE i.e.: gastric and intestinal metaplasia (IM) was similar, 58% and 60% respectively. Overall, BE was confirmed in 90% of the cases during the follow up, being the rate of confirmation higher in the IM. 29 of the 59 patients (50%) without histologically proven BE at the entry, showed BE at the final examination. At the entry, dysplasia was found in 5 patients who complied to follow-up, all with low grade dysplasia. During the surveillance period, dysplasia increased in frequency as well as in severity and was found exclusively in the IM type of BE. Dysplastic changes were found in 10 patients (8 low-grade; 2 high-grade) and ADC developed in 3 patients, all in the IM group. This prospective study shows an incidence of ADC in BE of 1 in 185 patient-year. When only IM patients were considered, the risk of ADC was about two folds higher than the whole BE group, suggesting a close surveillance for this high-risk subgroup. *Conclusion:* the present "ad interim" report of a prospective endoscopic study shows that the incidence of ADC in Italian BE patients is in the range of that reported from other Western countries. Our data may be representative of the epidemiology of the disease in Southern Europe. Oncology, general: Epidemiology Oncology, specific: Oesophagus Endoscopy, specific: Oesophagus } "The Incidence of Esophageal Adenocarcinoma in Barrett's Esophagus in an Italian Population: First Report from Southern Europe"

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## OT77 1569 Oesophageal Cancer: Aggressive Growth Behaviour Correlates with the Expression of Adhesion Molecules

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The intercellular adhesion molecule 1 (ICAM-1), the vascular cell adhesion molecule 1 (VCAM-1) and the endothelial leukocyte adhesion molecule 1 (ELAM-1) are cell-surface bound glycoproteins, which contribute to cell-cell interactions. Alteration of adhesion molecules have been suggested to play an important role in tumor progression and the development of blood-born metastasis. In the present study, we examined the expression of ICAM-1, VCAM-1 and ELAM-1 in oesophageal tissues obtained from patients with oesophagus cancer. *Patients:* Oesophageal cancer samples were obtained from 13 male patients with a median age of 58 years (range: 42–73) undergoing surgery for oesophageal cancer. Normal human oesophageal tissues, obtained from either 6 previously healthy organ donors or from resection material (6 patients) adjacent to cancer (1 female, 11 males, median age: 43.5 years), served as control. *Methods:* The tissues were frozen using O.C.T. compound medium in liquid nitrogen for histological analysis. For RNA analysis freshly resected tissue samples were frozen in liquid nitrogen and stored at  $-80^{\circ}\text{C}$  until analysis. Using Northern blot analysis and immunohistochemistry the expression and cellular localisation of ICAM-1, VCAM-1 and ELAM-1 were assessed. *Results:* ICAM-1, VCAM-1 and ELAM-1 mRNA expression was markedly increased in the oesophageal cancers in comparison with the normal controls. By densitometric analysis there was a 7-, 4.5-, and 4-fold increase in ICAM-1, VCAM-1 and ELAM-1 mRNA expression, respectively ( $p < 0.05$ ) in the oesophageal cancer samples compared with the normal controls. By immunohistochemistry intense ICAM-1, VCAM-1 and ELAM-1 immunoreactivity was found in the oesophageal cancer tissues, whereas weak to moderate immunoreactivity was present in the normal controls. *Conclusion:* The strong overexpression of the adhesion molecules, ICAM-1, VCAM-1 and ELAM-1, in oesophageal cancer, may have a crucial role in the dissemination of tumor cells and might contribute to the development of a metastatic disease. Oncology, specific: Oesophagus Oncology, general: Proliferation, carcinogenesis Oncology, general: Molecular biology, genetics } "Oesophageal Cancer: Aggressive Growth Behaviour Correlates with the Expression of Adhesion Molecules"

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## OT79 1570 Ileal Pouch-Anal Anastomosis for Distal Ulcerative Colitis

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Service de Chirurgie Digestive, Hopital Saint-Antoine, Paris, France Distal ulcerative colitis (UC) seldom require surgery for chronic debilitating symptoms and failed medical management. *Aim:* This study was designed to assess the outcome of ileal pouch-anal anastomosis (IPAA) in such patients. *Patients and methods:* From 1984 to 1994, among 263 IPAA for UC, 27 patients (16 men) were operated for distal UC. Bowel function and quality of life before and 1 year after IPAA were compared. *Results:* The mean duration of UC was 11 – 6 years. In the year before IPAA, those patients had a mean of 2 – 1 attack of colitis, 1 – 1 coloscopy, 2 – 2 rectoscopies, 11 received oral steroids and 10 had a microrectum. IPAA was performed at a mean age of 46 – 10 years, all the pouches were "J" shaped and protected with an ileostomy. The mean hospital stay was 25 – 10 days, 3 patients were reoperated (1 small bowel obstruction, 2 intra-abdominal abscesses). Previously unknown severe dysplasia was discovered on the colectomy specimen in 2 patients. After IPAA there was a significant decrease in day-time stool frequency (8.2 – 4 vs 4.7 – 2,  $p < 0.05$ ), night-time stool frequency (2 – 2 vs 1 – 1,  $p = 0.05$ ), and in the number of patients having urgencies (25/27 vs 1/27,  $p < 0.001$ ). Sexual life was improved in 8 patients, social life in 26 and professional life in 8. Twenty-six patients were satisfied with the results and 20 wished to have been submitted to surgery earlier in the course of their disease. *Conclusion:* IPAA can improve bowel function and quality of life in patients presenting disabling chronic symptoms of distal UC. Intestinal disorders: IBD, therapy }

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## OT79 1571 Longterm Outcome of Proctocolectomy with Ileal Reservoir for Ulcerative Colitis

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<sup>1</sup> Dept. of Gastroenterology, dept. of Surgery, Herlev Hospital, University of Copenhagen, Denmark *Aim:* To assess the outcome of ileal pouch-anal anastomosis (IPAA) in patients colectomised for severe or refractory ulcerative colitis. *Patients and Methods:* In all 151 patients were colectomised during 1980–1994. 52 patients had a permanent ileostomy performed primarily and 99 (66%) had an IPAA carried out. All patients who in April 1996 had a functioning pouch for > 12 month underwent interview by the same gastroenterologist. *Results:* 71/99 (72%) of the patients were included for interview, while 17/99 (17%) had had the pouch removed. 5/99 (5%) had a loop ileostomy and 6 (6%) were lost to follow up. 71 patients were interviewed, 35 men and 36 women, median age 36, range 18–71. 13/71 (18%) had J-pouch, and 58/71 (82%) had S-pouch. Median time since IPAA was 75 months, range 6–191. Subjective global assesment was: *satisfied* in 59 (83%) and *not satisfied* in 12 (17%). 61/71 (86%) stated that they would go through the same again to obtain their present condition. 66 (93%) had spontaneous defecation while 5 (7%) had to tubulate and 4 did both. Perfect continence was achieved in 23 (32%) while 22 (31%) had minor incontinence, and 26 (37%) had periodical incontinence (> 1 per month). Median number of bowel movements was 6, range 3–13. Nocturnal defecation was present > once per week in 45/71 (63%), in median 7, range 2–49 per week. Pouchitis occurred in 28/71 (39%) first time at a median of 8 months (range 1–138) after closure of the loop-ileostomy. Social life function was generally intact: 58/71 (82%) were working full-time, 53/71 (75%) were active in sport, 70/71 (99%) participated in social events, and 63 (89%) were able to travel abroad. 34 (97%) men and 25 (69%) women had unchanged active sexual activity, 2/35 (6%) men and 10/36 (28%) women had some fear of incontinence during sexual intercourse. *Conclusion:* Despite technical and individual difficulties, IPAA is an attractive alternative to ileostomy. The majority of patients are satisfied and have an intact social life. Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, basic Intestinal disorders: IBD, therapy } " Longterm Outcome of Proctocolectomy with Ileal Reservoir for Ulcerative Colitis "

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**OT79 1572 Post-Operative Recurrence of Crohn's Disease: A Study for the Development of Lesions in Treated and Untreated Patients R. Caprilli, A. Viscido,**

\*G. Taddei, G. Corrao, P. Torchio, D. Assisi

Univ. of L'Aquila, Italy and Gruppo Italiano per lo Studio del Colon/Retto\*It has been hypothesised that aphtae are the earliest lesions in Crohn's disease (CD). Ulcers seem to result of coalescence of aphtae and then spread superficially or transmurally leading to abscesses and fissurings. Stenosis seems to be a reparative late event. Nevertheless such a sequence of evolving lesions has never been demonstrated due to the lack of techniques which enable a continuous observation. By using the GISC trial data on 5-ASA (Aliment Pharmacol & Therap 1994; 8: 35-43) in the prevention of post-operative recurrence of CD, we have elaborated a mathematical model based on the hypothesis that CD's lesions develop following the aphtae-ulcer-fisuring-stenosis sequence. It was assumed that each endoscopic lesion observed during follow-up controls at 6, 12, 24, 36 months after surgery occurred between (half period) the previous negative observation and the present positive control. The cumulative probability of every lesion occurrences has been estimated using the life-table method and applied in both arms of patients, those treated with ASACOL 4 gr/day (55 pts) and those who remained untreated (55 pts). The *results* of the study is referred only to the development of aphtae and ulcers (fistula and stenosis were scarcely represented). The cumulative proportion of lesions reappearance after radical resection are shown in the diagram. Mean time of lesions recurrence were 423 days for aphtae and 584 days for ulcers in untreated pts and 580 and 704 days respectively in pts treated with ASACOL. The development of aphtae and ulcers resulted to be significantly delayed in pts treated with ASACOL vs those untreated ( $p = 0.006$  and  $p = 0.03$  respectively). The earliest lesions observed at 6 month after surgery were aphtae (20% of the cases), ulcers (8% of the cases) and aphtae associated with ulcers (10% of the cases). The multivariate analysis ""Marginal Proportional Hazard"" showed a relative risk (RR) of aphtae development of 0.4 ( $p < 0.01$ ) and a RR of ulcers development of 0.5 ( $p < 0.05$ ) in treated vs untreated pts. Limiting the results of the study to the observations made in untreated pts, the mean time of aphtae appearance was estimated to be about 14 months and that of ulcers 19 months. However about 30% of pts show aphtae already at 6 months after surgery. These data may be helpful for the study of natural history of recurrence and possibly of the disease.

Reference: G. Latella, G. Frieri, P. Vernia, (L'Aquila); A Tragnone (Bologna); G. D'Albasio G. Salvadori, I. Paladini, F. Ficari, G. Vannozzi (Firenze); D. Valpiani (Forl'ec); G.P. Rigo, M. Mastronardi, P.L. Codeluppi (Modena); G.C. Sturniolo, R. D'Inc'e0 (Padova); F. Pallone, L. Capurso, A. Andreoli, A. Gioieni, R. Lorenzetti, A. Ciaco, C. Papi, M. Luminari (Roma); F.P. Rossini, V. Ponti, A. Bertone (Torino). Intestinal disorders: IBD diagnosis, monitoring Intestinal disorders: IBD, therapy } "Post-Operative Recurrence of Crohn's Disease: A Study for the Development of Lesions in Treated and Untreated Patients"

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## OT79 1573 Outcome of Restorative Proctocolectomy after Recurrence of Crohn's Disease in the Reservoir

\*Y. Panis, A. Dusoleil, X. Penna, P. Francois, P. Lehur, A. Vignal, F. Carbonnel, L. Spiroudhis, L. Gosselin, L. Descos, R. Parc, P. Valleur, D. Couturier, S. Chaussade

Service de chirurgie et de gastroentérologie, Hospital Lariboisière, Saint Antoine, Rothschild, Paris, Rennes, Lyon, Nantes, France Restorative proctocolectomy with construction of an ileal pouch anastomosis is a procedure which is mainly proposed in the treatment of ulcerative colitis. Patients with Crohn's disease are generally regarded as unsuitable candidates for reservoir procedure because of the risk of recurrent ileal and anal disease. The consequence of the recurrence of a CD after ileo anal anastomosis is unknown. *The aim of this study* is to describe the clinical features and the evolution of the anal function of patients presenting a CD after an ileoanal procedure. *Method-Material:* 21 patients (6 males, 15 females) from 7 centers were included in this study. Proctocolectomy with ileo anal anastomosis and reservoir (J = 19, W = 2) was performed for severe colitis (19%), cortico-dependance (33%) or cortico-resistance (48%). The inclusion criteria to assume the recurrence of a CD was as follow: 1-Occurrence of ano-perineal disease suggestive of CD (abcess, fistula, anal ulcerations), 2-Occurrence of pouchitis with an inflammation in the small intestine at a distance of more than 10 cm beyond the reservoir or pouchitis with granuloma in any part of the gastrointestinal tract, 3-Occurrence of a fistula between the reservoir and the skin, the vagin on an other part of the small bowel at least 1 year after the surgical procedure. *Results:* CD have been suspected in 5 cases before the recurrence in the reservoir (presence of granuloma on the colonic specimen in 3 cases and chronic ileitis in 2 cases). The diagnosis of CD was made 36 – 20 months (12–94) after the construction of the reservoir. The diagnosis of CD was performed in 3 situations: pouchitis and ileitis proximal to reservoir (n = 3) or pouchitis with granuloma (n = 3), perianal disease (n = 10), or fistula between the reservoir and the skin, the small bowel or the vagin (n = 5). One or several surgical procedures were indicated in 16/21 cases (76%). Pouch excision or end ileostomy was performed in 30%. *Conclusion:* After ileo anal anastomosis, recurrence of a suspected or of an unknown CD is associated with pouch excision or ileostomy in 30% of the patients mainly for perianal disease. Intestinal disorders: Anorectal disorders } "Outcome of Restorative Proctocolectomy after Recurrence of Crohn's Disease in the Reservoir"

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## OT80 1574 *CagA* Status and Clinical Outcome in *H. Pylori* Infected Patients Treated with Omeprazole and Amoxicillin: A Prospective Study

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**Background:** It is unknown whether the presence of *cagA* selects patients (pts) who will have more benefit of *H. pylori* eradication therapy. We conducted a large prospective study to assess the relation of *cagA* status and clinical outcome of pts randomized for omeprazole-amoxicillin dual therapy. **Methods:** The relation between *cagA* and gastro-intestinal disease characteristics, the eradication success and the degree of gastritis (according to modified Sydney classification) before and after eradication therapy (4–6 weeks and a mean of 1 year) was assessed. **Results:** 155 consecutive *H. pylori*-positive (culture and histology) pts, were enrolled in the study. *cagA*<sup>+</sup> *H. pylori* were recovered from 122/155 pts (79%). *H. pylori* eradication was successful in 74% of *cagA*<sup>+</sup> and 52% of *cagA*<sup>-</sup> strain (p = 0.017). Pretreatment degrees of gastritis activity, superficial epithelial damage (SED), intestinal metaplasia (IM) and atrophy were significantly more pronounced in pts infected with *cagA*<sup>+</sup> *H. pylori* as compared to those infected with *cagA*<sup>-</sup> strains (p < 0.001). Following eradication therapy a significant improvement of the gastritis activity occurred (p < 0.001), however, the final gastritis scores were similar in both in *cagA*<sup>+</sup> and *cagA*<sup>-</sup> infected pts. *H. pylori* eradication did not affect the degree of IM and atrophy. Dysplasia was noticed in only one patient infected with *cagA*<sup>+</sup> *H. pylori*. **Conclusions:** Eradication efficacy and the degree of activity of gastritis, atrophy and IM correlated with the presence of *cagA*<sup>+</sup> *H. pylori*. Improval of the degree of active gastritis, following *H. pylori* eradication, was also correlated to the presence of *cagA*<sup>+</sup> *H. pylori*, although the final degree of gastritis was independent of the *cagA* status. The degree of IM and atrophy was unchanged despite cure of *H. pylori* infection. Oesophageal gastric duodenal disorders: Helicobacter Pylori }" "CagA Status and Clinical Outcome in H. Pylori Infected Patients Treated with Omeprazole and Amoxicillin: A Prospective Study"

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## OT80 1575 *In vivo* and *in vitro* Analysis of Inducible Nitric Oxide Synthase (iNOS) in Gastric Epithelial Cells in CagA Positive & CagA Negative *Helicobacter Pylori* Infections

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<sup>1</sup> University of Bologna, Italy **Purpose:** Increases in iNOS are associated with intestinal inflammatory conditions. Products of NO, such peroxynitrite, may be important mediators of mucosal damage. This study investigates i) whether infection with CagA<sup>+</sup> and CagA negative *H. pylori* results in quantitative differences in iNOS enzyme in the gastric epithelium using immunochemiluminescence imaging and ii) the ability of CagA<sup>+</sup> and CagA negative *H. pylori* to induce iNOS mRNA in a gastric epithelial cell line *in vitro*. **Methods:** Cryosections of antral biopsies (n = 23) were incubated with rabbit anti-iNOS antibody or normal rabbit serum. Bound antibodies were detected using a low light imaging luminograph following incubation with enzyme labelled second antibodies and chemiluminescent substrate. Kato-3 cells were cultured *in vitro* with CagA<sup>+</sup> and CagA neg *H. pylori*. At 3–30 hrs post-stimulation cells were harvested and mRNA for iNOS and an internal control gene G3PDH was examined by RT-PCR. **Results:** 14/18 (78%) HP<sup>+</sup> patients with chronic gastritis and 1/5 (20%) Hp negative with normal histology had a chemiluminescent signal for iNOS in the epithelium. No signal was detected with control rabbit sera. Median (IQR) iNOS levels were respectively 42.6 (10.8–66.4) photons/sec/unit area (HP<sup>+</sup>) and 0 (0–22.1) (HP neg; p < 0.05 versus HP<sup>+</sup>). 7/8 (88%) CagA seronegatives and 7/10 (70%) CagA seropositives were iNOS positive. Median iNOS values were 48.1 (21.7–72.9) (CagA neg) and 41.3 (0–63) (CagA<sup>+</sup>). iNOS mRNA was not present in unstimulated Kato-3 cells. Culture with CagA<sup>+</sup> and CagA negative *H. pylori* resulted in iNOS mRNA expression with maximum expression at 3 hrs. **Conclusions:** Sensitive chemiluminescence techniques can quantitatively detect iNOS in gastric epithelial cells. Infection with both CagA<sup>+</sup> and CagA negative strains is associated with increased epithelial iNOS message and protein. *H. pylori* induction of epithelial iNOS is mediated by factors common to both CagA<sup>+</sup> and CagA negative strains. Oesophageal gastric duodenal disorders: *Helicobacter Pylori* Immunology and microbiology: Host defense mechanisms Immunology and microbiology: Inflammation }" "In vivo and in vitro Analysis of Inducible Nitric Oxide Synthase (iNOS) in Gastric Epithelial Cells in CagA Positive & CagA Negative *Helicobacter Pylori* Infections"

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OT80 1576 **Rate of Apoptosis in Chronic Gastritis and Correlation with Antigastric Autoantibodies** H. Steininger, E. Dewald,

\*G. Faller, Th. Kirchner

Institute of Pathology, University of Erlangen-Nürnberg, Germany *Introduction:* Gastric atrophy is an obvious feature in autoimmune gastritis and in some cases of *H. pylori* gastritis. In the latter it has recently been shown that the occurrence of autoantibodies to canaliculi structures within parietal cells is associated with atrophic changes in the gastric mucosa. Since apoptosis is an important mechanism leading to cell death we aimed to investigate its role in different types of gastritis. *Methods:* Human gastric biopsy specimens from normal mucosa (n = 16), from *H. pylori* gastritis with (n = 19) and without (n = 16) anticanalicular autoantibodies and from autoimmune gastritis (n = 7) were included in our study. The rate of apoptosis was assessed in each case with the TUNEL-method using a commercially available Apoptosis Detection Kit (Oncor, USA). Autoantibodies to human gastric epitopes were detected by immunohistochemistry. *Results:* Normal gastric mucosa showed only very few apoptotic cells. In *H. pylori* gastritis the number of apoptotic cells in the foveolar epithelium and in the glands was significantly higher both in the antrum and in the body (p < 0.01). Furthermore in the *H. pylori* positive group *with* anticanalicular autoantibodies the rate of apoptosis was significantly higher in the gastric glands when compared with *H. pylori* gastritis *without* this type of autoantibodies (p = 0.01). In type A gastritis the rate of apoptosis in the body glands was highest in all groups tested (p = 0.0005). *Conclusion:* According to our data apoptosis seems to be an important mechanism leading to gastric atrophy not only in autoimmune (type A) gastritis but also in *H. pylori* gastritis. Furthermore in *H. pylori* gastritis, the host's antigastric autoimmune response in combination with apoptosis possibly induced by antigastric autoimmune reactions could determine the transition to chronic atrophic gastritis. } "Rate of Apoptosis in Chronic Gastritis and Correlation with Antigastric Autoantibodies"

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## OT80 1577 Relationship between H. Pylori Infection, Histological Gastritis and Non-Ulcer Dyspepsia

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<sup>1</sup> Dep. of Pathology, University of Ulm, Germany It is still controversial whether or not HP infection, histological gastritis and non-ulcer dyspepsia (NUD) are intercorrelated. We designed a prospective study to clarify this. *Methods.* 88 prospective NUD patients (age range 18–84 y) who did not show other disease than gastritis were investigated. In a questionnaire they were asked to report the presence or absence of 8 upper GI symptoms and to score from 0 (absence) to 3 (severe), whereupon a sum score was calculated. 40 age-matched patients with a NUD sum score < 3 served as controls (C). Biopsy specimens for histology and rapid urease test were taken. *Results.* HP infection was present in 43% of NUD and in 35% of C subjects (n.s.). None of the symptoms was correlated with HP infection. The median NUD score was 8.5 in HP-positive and 9.5 in HP-negative NUD pts.. Histological gastritis was not correlated with any of the symptoms. Medians of NUD scores were 10 in pts. without gastritis (G0), 7.5 in pts. with gastritis characterized by lymphoplasmacellular infiltration of the lamina propria (G1) and 9.0 in pts. featuring granulocytic epithelial lesions (G2). G2-gastritis was present in 34% of NUD pts. and in 30% of C subjects. Prevalence of G0/G1/G2 gastritis was 5%/32%/63% in HP-positive and 64%/24%/12% in HP-negative pts.. *Conclusions.* HP infection is not correlated with clinical symptoms of NUD. The same applies for histological gastritis. In contrast but well-documented, HP infection is associated with histological signs of gastritis. Our data imply that HP gastritis is not an important condition in the pathogenesis of dyspeptic symptoms. Oesophageal gastric duodenal disorders: GD disorders, acid peptic Oesophageal gastric duodenal disorders: Helicobacter Pylori Immunology and microbiology: Inflammation } "Relationship between H. Pylori Infection, Histological Gastritis and Non-Ulcer Dyspepsia"

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**OT80 1578A Serologic Survey of Helicobacter Pylori (HP) Infection in 3281 Patients Referred to Endoscopy through Italy**  
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*Purpose:* To assess: 1. the seroprevalence of HP in a large series of patients with upper gastrointestinal symptoms referred for their first upper gastro-intestinal endoscopy through Italy, 2. to evaluate the reliability of a commercially available ELISA (HELORI-TEST, EUROSPITAL, Trieste, Italy).

*Methods:* A total of 3,281 patients referred to endoscopy in 93 Medical Centers through Italy were enrolled. For each participant a blood sample for assessment of anti HP IgG antibodies by ELISA, and two biopsies of the antral gastric mucosa for histology (Hematoxylin & Eosin and Giemsa stain) were obtained. Presence of HP by Giemsa was considered the "gold standard".

*Results:* Endoscopic diagnosis ranged between normal mucosa (25.3%), gastro-duodenitis (51.6%), gastric and duodenal ulcers (3.7 and 14.9%, respectively) and other conditions including gastric cancer (0.8%). Overall, the seroprevalence of HP resulted 71.3% with a strong positive association with increasing age and male sex and a negative one with education level. According to endoscopic diagnoses, the association with HP seropositivity was highest for duodenal and gastric ulcer (OR: 6.1 and 2.2 respectively) and lowest for carcinoma (OR: 1). The comparison between serology and the Giemsa stained specimen showed a good reliability of IgG by ELISA particularly in a subgroup (n = 2,056) for which the histological interpretation was performed by a single dedicated pathologist: sensitivity and specificity reached 92 and 78%, respectively.

*Conclusions:* 1. We confirm an high prevalence of HP in dyspeptic patients through Italy with a positive association with age, male sex and low educational level; 2. a key factor for obtaining a real histological "gold standard" seems to rely in having a dedicated histopathologist.

Oesophageal gastric duodenal disorders: Helicobacter Pylori

Clinical practice: Epidemiology (non cancer) } "A Serologic Survey of Helicobacter Pylori (HP) Infection in 3281 Patients Referred to Endoscopy through Italy"

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## OT81 1579 **Central Effect of Pituitary Adenylate Cyclase Activating Polypeptide (PACAP) on Gastric Emptying and Small Intestinal Transit in Conscious Rats**

\*M. Ozawa, K. Mizuta, M. Aono, M. Moriga

The First Department of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto, Japan PACAP is new member of the secretin-glucagon-VIP peptide family. PACAP is widely distributed not only in the brain, but also in gastrointestinal tract. The present study was to investigate a possible effect of central administration of PACAP on gastric emptying (GE) and small intestinal transit (SIT) of a liquid meal in conscious rats. Male Wistar rats weighing 250–280 g were used. Rats were deprived of food for 24 hr but given free access to water in wide-mesh wire cages to prevent coprophagia. Under light ether anesthesia, saline, PACAP38 (2, 4, 8 nmol/rat) was administered intracisternally 1 min before ingestion of phenol red solution as liquid meal through an oral tube. The animals were sacrificed by deep ether anesthesia 1 hr after phenol red ingestion. The small intestine was divided into two segments of equal length. To examine the mechanism of the effect of PACAP, carbachol (50 ug/kg), atropine (1 mg/kg), hexamethonium bromide (10 mg/kg), phentolamine (2 mg/kg) or propranolol (2 mg/kg) was injected intraperitoneally 5 min before PACAP administration. Intracisternal administration of PACAP38 inhibited GE and SIT in a dose dependent manner. By contrast, intraperitoneal administration of PACAP (4 nmol) did not affect GE and SIT. Intracisternal administered PACAP partially suppressed GE and SIT accelerated by carbachol. The inhibitory effect of PACAP was additive to the inhibitory effect of atropine or hexamethonium bromide pretreatment. Pretreatment with propranolol or phentolamine did not affect the effect of PACAP. These results suggested that central administration of PACAP inhibited gastrointestinal transit in part by inhibition of vagal tone at peripheral level but not central level. Hormones and receptors: Brain gut axis Motility, specific: Stomach Motility, specific: Small bowel } "Central Effect of Pituitary Adenylate Cyclase Activating Polypeptide (PACAP) on Gastric Emptying and Small Intestinal Transit in Conscious Rats"

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OT81 1580 **Stress-Induced Visceral Hypersensitivity in Rats Involved Central CRF Pathway** M. Gu<sup>1</sup>, C. Del Rio, J. Fioramonti, L. Bu<sup>1</sup>

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<sup>1</sup> Institut de recherche Jouveinal, Fresnes, France Enhanced abdominal pain and colonic motor disturbances are commonly observed in IBS patients. Psychologic factors have long been implicated in the aetiology of IBS. In rats, stress alters colonic motility through central CRF pathway. Consequently, the aims of this study were to evaluate the influence of partial restraint stress (PRS) on abdominal cramps, in response to rectal distension (RD) and to determine the involvement of CRF; in addition, we have evaluated the effect of PRS on a somatic pain, such as tail flick and on rectal compliance. *Methods:* Male Wistar rats weighing 250 to 300 g were surgically prepared for electromyography with Ni/Cr electrodes implanted in the striated muscle of the abdomen and with a small polyethylene catheter for intracerebroventricular (ICV) injection. In a 1st series, 8 rats were leaved in cage (sham PRS) for 2 hours, whereas the 2nd group was submitted to PRS, consisting to restrain forelimbs with paper tape, for 2 hrs. Thirty min later, RD was performed by rectal insertion of a balloon (diam: 2 mm, length, 2 cm) at 1 cm from the anus, increasingly inflated with water step by step from 0.4 up to 1.2 ml. each step lasting 5 min. In a 2nd series, 8 rats were ICV injected with  $\alpha$ -helical CRF (5  $\mu$ g) 5 min before PRS, then rats were submitted to RD as in the 1st series; in a last series, 8 rats were ICV injected with CRF (0.5  $\mu$ g/kg) 30 min before RD. Finally, in a group of 8 rats the tail-flick test was used. The distal 4 cm of the tail was dipped into 48°C water and the latency of the withdrawal reflex was recorded at 15, 30 and 45 min after sham PRS or PRS. *Results:* In sham PRS rats, RD induced a volume-related increase in the number of abdominal cramps (0.4 ml: 5.0 – 1.3; 0.8 ml: 17.3 – 1.9; 1.2 ml 28.7 – 1.4). PRS significantly ( $p < 0.05$ ) enhanced the number of abdominal cramps at all volumes of distension (0.4 ml: 8.7 – 1.2; 0.8 ml: 27.6 – 1.4; 1.2 ml 38.8 – 1.8). This hypersensitivity to PRS was mimicked by ICV CRF (0.4 ml: 8.1 – 0.6; 0.8 ml: 26.1 – 1.3; 1.2 ml 36.9 – 1.8) and was antagonized by ICV pretreatment with  $\alpha$ -hel CRF. PRS-induced a significant delay on tail flick latency, at 30 and 45 min after PRS session. Furthermore, PRS had no effect on rectal compliance since none of the rats exhibited an increased pressure response to balloon inflation. *Conclusion:* These results show that, in contrast to its effects on somatic pain, stress enhances abdominal contractions in response to RD in rats and that these effects are mediated through central CRF pathway. } "Stress-Induced Visceral Hypersensitivity in Rats Involved Central CRF Pathway"

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## OT81 1581 Assessment of Rectal Sensitivity by a Reflexologic Technique in Healthy Humans

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Rectal distension studies with pharmacological tests and verbal questionnaires, have suggested the existence of two types of mechanoreceptors stimulated by different methods of distension. *Our aim* was to confirm this functional duality by using a reflexologic technique based on the recording of a nociceptive somatic reflex, the RIII reflex, which allows an objective evaluation of visceral sensitivity [1]. *Methods:* The effects of rectal distension on the RIII reflex were measured in 10 healthy volunteers. Rapid (900 mL/min) phasic distensions in a random order at 10, 20, 30, 40 mmHg, lasting 3 min each, and slow (40 ml/min) ramp distension up to a maximal volume of 600 ml or to discomfort threshold were performed with an electronic barostat. The RIII reflex was continuously stimulated and recorded on the lower limb for both types of distensions, and on the upper limb for phasic distensions. Reflex responses were recorded before (control period), during, and after each distension for 3 min, and expressed as percentages of control values. Volumes distending pressure and sensations (7 steps on verbal scale) were also measured. Results (m – SD) were evaluated by ANOVA. *Results:* On the lower limb, the RIII response was significantly increased (facilitation) by phasic distensions (129 – 15%, 160 – 20%, at 20 and 30 mmHg respectively  $P < 0.05$ ). At 40 mmHg, a biphasic response with a facilitation (128 – 20%,  $P < 0.05$ ) followed by an inhibition (66 – 18%,  $P < 0.05$ ) was noted. By contrast, the RIII response on the lower limb was significantly inhibited by slow ramp distension (53 – 17%,  $P < 0.05$ ) for a maximal distending volume of 397 – 101 mL, and the magnitude of inhibition was correlated with the intensity of the sensation elicited by the distension ( $r = 0.76$ ,  $P < 0.05$ ). On the upper limb, the RIII reflex response was significantly inhibited by phasic distensions (46 – 16% at 40 mmHg,  $P < 0.05$ ). *Conclusions:* Convergence onto the same spinal cord segment of afferent pathways coming from the rectum and from the somatic territory involved in the RIII reflex could explain the facilitation we noted. The inhibition of the RIII reflex corresponds to the classical phenomenon of counter irritation triggered by heterotopic stimulations. Our results give an objective confirmation for the presence in the rectum of healthy humans of two types of mechanoreceptors with different afferent pathways. Funded in part by the Institut de Recherche Jouveinal, Fresne, France.

Reference: Bouhassira et al. Gastroenterology 1994; 107: 985–992. } " Assessment of Rectal Sensitivity by a Reflexologic Technique in Healthy Humans "

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**OT81 1582 Differences in Response of Proximal and Distal Colonic Smooth Muscle Cells to Relaxant Agents**  
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Patterns of motor activity differ between the various segments of the colon and regional differences have also been observed in receptors and neurotransmitters distribution. We aimed a study to both characterize the patterns of relaxation and determine the relative signalling pathways involved in order to investigate in colonic smooth muscle cells (SMC) if cellular differences could reflect the different pattern of motor activity. The two main relaxant putative neurotransmitters are Nitric Oxide and VIP which induce respectively a cGMP-dependent and a cAMP-dependent response. SMC, isolated by collagenase digestion separately from proximal and distal circular muscle layer of guinea pig colon, were exposed to a maximal dose of carbachol (Cch) (30 nM) for 30 sec in order to determine peak contraction or preincubated, before Cch exposure, for 60 sec with a relaxant agent to examine relaxation. Contraction was expressed as % decrease in cell length while relaxation as % inhibition of contraction. cGMP-dependent response was induced by activation of guanylate cyclase with sodium nitroprusside (SNP: 1  $\mu$ M) or by cGMP (1 mM) while cAMP-dependent relaxation by activation of membrane receptors with VIP (1  $\mu$ M, 1 nM) or isoproterenol (ISO: 0.1  $\mu$ M, 0.1  $\mu$ M), of adenylate cyclase with forskolin (FK: 0.1  $\mu$ M, 0.1  $\mu$ M) or by cAMP (1 mM). Contractile responses were similar between proximal and distal SMC (Cch: 21.9 – 3.2 and 25.8 – 2.0% respectively). Differences were instead observed in relaxation depending on which intracellular pathway was activated. Proximal SMC relaxation was in fact cGMP-dependent while distal response was cAMP-dependent. cGMP-dependent agents relaxed proximal SMC without having any effect on distal SMC (SNP: 70 – 10 vs 6.8 – 3.6%, cGMP: 58.6 – 10% vs 6.9 – 3.6%). Maximal doses of each cAMP-dependent agent instead induced an higher degree of relaxation of distal than proximal SMC (VIP: 62 – 10 vs 37.6 – 10%, ISO: 53.2 – 2.4 vs 36.2 – 8.8%, FK: 54.4 – 10 vs 24.7 – 10%, cAMP: 58.2 – 10 vs 18.4 – 9.8%). Submaximal doses of these agents were still effective (20%) on distal SMC while were ineffective on proximal SMC, confirming that the high intracellular levels of cAMP stimulated by maximal doses are also able to activate cGMP-kinase. These results suggested that the distinct intracellular patterns of relaxation between proximal and distal colon might in part contribute to explain the different regional functional motor activities of this organ.

Motility, general:  
Receptors and signals  
Motility, specific: Colon, anorectum } "Differences in Response of Proximal and Distal Colonic Smooth Muscle Cells to Relaxant Agents"

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## OT81 1583 Anal Sensitivity: What Does It Measure and Do We Need It?

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*The aim of the study* was to determine the anal sensitivity (AS) in controls and in different patient groups and to determine factors that determine AS. *Methods.* Anorectal function tests were performed in 387 patients with different anorectal diseases. AS was measured in 36 controls. AS is measured by means of mucosal electrosensitivity using a catheter with 2 electrodes placed in the anal canal. A constant current (square wave stimuli 100  $\mu$ s, pulses per second) was stepwise increased from 1–20 mA until the threshold sensation was reached. Other tests were anal manometry (maximal basal pressure (MBP), maximum squeeze pressure, (MSP), rectal compliance (maximal rectal volume and pressure (MRP)), endosonography (defects and thickness internal (IST) and external sphincter EST), submucosal thickness (SMT), EMG (maximal contraction pattern (MCP grade 1 (solitary contractions) to 4 (interference pattern)) and pudendal nerve terminal motor latency (PNTML). Multiple regression analysis was performed. Postulated was that age, local conditions (anal scars, anal fissures, hemorrhoids, mucosal prolapse, proctitis, SMT, IST and EST) and neurologic factors could influence anal sensitivity. *Results.* Controls had an AS of 3.4 – 1.7. AS was significantly diminished compared to controls in patients with fecal incontinence, soiling, hemorrhoids, mucosal prolapse, constipation, anal scars, anal surgery and sphincter defects; patients with fecal incontinence had the lowest AS (6.7 – 4.3,  $p < 0.0001$ ). Patients with anal fissures and proctitis showed no differences compared to controls. AS correlated significantly with age ( $R = 0.29$ ), MBP ( $R = -0.29$ ), MSP ( $R = -0.32$ ), SMT ( $R = 0.19$ ), MCP ( $R = -0.39$ ), SF-EMG ( $R = 0.39$ ) and MRP (0.14). Multiple regression analysis showed that age, IST and SMT significantly influenced AS, but explaining only 10% of the variance. *Conclusion:* AS is diminished in all patients with anorectal diseases except for anal fissures and proctitis. There are correlations with other anorectal function tests. AS is determined for 10% by age and thickness of submucosa and anal sphincter. It therefore has limited clinical value and should be used in conjunction with other tests in a research setting.

Motility, specific: Colon, anorectum  
Intestinal disorders: Anorectal disorders  
Motility, general: Innervation } "Anal Sensitivity: What Does It Measure and Do We Need It?"

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## OT81 1584A Study of the Functional Activity of the Sigmoid Colon and Rectum during Fecal Storage in the SigmoidA. Shafik

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*Purpose:* The incomplete information in the literature on the mechanism of sigmoid storage and evacuation and its relation to the rectum has initiated our study. *Methods:* In 18 mongrel dogs, a condom-ended catheter was introduced into the sigmoid and infused with carbon dioxide (CO<sub>2</sub>) at 2 rates: slow and rapid. The pressure responses of sigmoid colon, rectosigmoid junction (RSJ), rectum and rectal neck to sigmoid distension were determined; the EMG activity of the external anal sphincter and levator ani was also evaluated. *Results:* Upon slow sigmoid distension up to a mean of 93.6 – 3.2 ml, no pressure response occurred in the sigmoid, RSJ, rectum or rectal neck. Distension above this level induced an increase of sigmoid pressure ( $p < 0.001$ ), a decrease of RSJ pressure ( $p < 0.05$ ), but no change in rectal or rectal neck pressure ( $p > 0.05$ ); balloon was expelled to rectum. EMG of external anal sphincter and levator showed no activity. Balloon expulsion to the rectum effected a pressure increase in the rectum ( $p < 0.001$ ), a decrease in the rectal neck ( $p < 0.01$ ), and an increase in the RSJ ( $p < 0.01$ ), while the sigmoid showed no response ( $p > 0.05$ ), and the balloon was expelled to the exterior. Rapid sigmoid distension induced an increase of sigmoid pressure ( $p < 0.001$ ) and a decrease of RSJ pressure ( $p < 0.05$ ) at approximately half the volume needed with slow distension. *Conclusion:* Sigmoid colon adapts to the new contents until a certain volume is attained, when it contracts expelling its contents to rectum. Rapid distension induces sigmoid contraction at a smaller volume than slow distension. Rectum and rectal neck did not respond to sigmoid distension or contraction, and vice versa. Sigmoid contraction initiates RSJ relaxation, while rectal contraction evokes RSJ contraction. Motility, general: Functional GI disorders Motility, specific: Colon, anorectum } "A Study of the Functional Activity of the Sigmoid Colon and Rectum during Fecal Storage in the Sigmoid"

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## OT82 1585 Segmental Reversal of the Small Bowel: An Alternative to Intestinal Transplantation in Patients with Short Bowel Syndrome?

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Digestive Surgical and Gastroenterology Departments, Lariboisière and St Lazare Hospitals, Paris, France Although long-term survival is possible in patients with short bowel syndrome requiring home parenteral nutrition (HPN), its cost and morbidity rate have maintained interest in developing surgical alternatives to HPN. Intestinal transplantation has gained interest in clinical practice. However, actuarial patient and primary graft survival rate at 2 years are still about 60 and 50% respectively, making transplantation still a difficult and unreliable procedure. *The aim of this work* was to report the results of segmental reversal of the small bowel in patients with very short bowel syndrome definitely dependent on HPN. *Methods:* Eight patients with short bowel syndrome underwent segmental reversal of the distal (n = 7) or proximal (n = 1) small bowel. The mean length of the remnant small bowel was 46 – 18 cm (extr. 25–70), including a mean length of reversed segment of 12.7 – 2.8 cm (extr. 8–15). Five patients presented with jejunotransverse anastomosis, and one each with jejunorectal, jejunocolonic, or jejunocaecal anastomosis with left colostomy. *Results:* There were no postoperative deaths. Three patients were reoperated early, respectively for sepsis of unknown origin, wound dehiscence and acute cholecystitis. Three patients experienced transient intestinal obstruction which was treated conservatively. Mean follow-up was 38 – 36 months (extr. 2–108). One patient died 7 months postoperatively, of pulmonary embolism. By the end of follow-up, 3 patients were on 100% oral nutrition, and one patient had hydroelectrolytic perfusions only. For the three other patients, parenteral nutrition regimen was reduced. Parenteral nutrition cessation was obtained in 3/5 cases at 1 year, and 3/3 cases at 4 years. *Conclusion:* Segmental reversal of the small bowel could be proposed, as an alternative to intestinal transplantation, in the early stage of short bowel syndrome, before the possible occurrence of parenteral nutrition-related complications. Intestinal disorders, absorption: Malabsorption syndromes Nutrition: Techniques of nutrition } "Segmental Reversal of the Small Bowel: An Alternative to Intestinal Transplantation in Patients with Short Bowel Syndrome?"

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## OT82 1586 Correction of Malnutrition Following Gastrectomy with Cyclic Enteral Nutrition

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Service de Gastroent'e9rologie et Nutrition, Hospital de l'Archet, 06202 Nice cedex 03, France This prospective study was designed to evaluate the efficacy and tolerance of cyclic enteral nutrition (CyEN) in gastrectomized patients. *Methods.* 28 consecutive gastrectomized patients were treated with CyEN for at least two weeks. CyEN was performed during the night with a pump and the flow rate was maintained constant at less than 3 mL/min. We used a commercially available polymeric diet at the concentration of 1.33 kcal/mL to provide 20% protein, 45% carbohydrates and 35% fat. During the day, patients were allowed and encouraged to eat normally and to have physical activities. A Global Nutritional Deficit (GND), was calculated before the beginning of the treatment (D0), after two weeks (D15), and at the end of CyEN (Dn), using 10 anthropometric and biological parameters. After renutrition, patients were followed-up for one year. *Results.* Total (enteral + oral) energy intake (292% and 284% of resting energy expenditure in gastrectomized and non-gastrectomized patients, respectively) and the duration of CyEN (mean: 27 days) were similar in both groups. Tolerance was good and not different in the two groups. The GND significantly improved ( $P < 0.0001$ ) in the two groups with six of the ten nutritional parameters studied being significantly improved by renutrition (body weight, triceps skinfold, medium arm circumference, serum prealbumin, serum transferrin, 24 h. urinary creatinine). At Dn, the GND improved by 42.7 – 17.3% in the gastrectomized patients and 40.0 – 17.4% in the non-gastrectomized patients ( $P = 0.55$ ). After one year, the probability to be alive without relapse was 77.8% in the gastrectomized and 72.2% in the non-gastrectomized patients ( $P = 0.70$ ). Among the patients who did not relapse, oral energy supplements were still being given after one year to ten (48%) gastrectomized and eight (30%) non-gastrectomized patients. The efficacy of renutrition was similar regardless of the type of gastrectomy, and the GND improved by 39.4 – 16.5% in the patients with partial gastrectomy (20 patients) versus 50.3 – 17.8% in the patients with total gastrectomy (8 patients) ( $P = 0.14$ ). *Conclusion.* CyEN is a safe, effective and durable treatment for undernutrition in gastrectomized patients suitable for more widespread utilization. Clinical practice: Management strategy Clinical practice: Psychosomatics Nutrition: Techniques of nutrition } "Correction of Malnutrition Following Gastrectomy with Cyclic Enteral Nutrition"

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## OT82 1587 **Demonstration of Transforming Growth Factor Alpha (TGF-Alpha) in Neuroendocrine L-Cells of the Human Colon Mucosa by Immunoelectron Microscopy**

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Proteins of the epidermal growth factor (EGF) family are important for the maintenance of cell renewal and epithelial regeneration in the gastrointestinal tract. There are still open questions about the cellular depots, the source and the pathophysiological role of these growth factors in the gastrointestinal tract. Biopsies and surgical mucosa probes of the colon (n = 15) and of the gastroduodenum (n = 10) were parallelly processed through plastic embedding (Araldite and Lowicryl K4M) and paraffin histology. Single and double labelling immunohistologic techniques, serial sectioning and immunoelectron microscopy were applied to localize growth factors, hormones and other neuroendocrine markers on mucosal cells. Immunohistochemically TGF-alpha is localized in parietal cells of the gastric corpus and in a special subgroup of neuroendocrine cells of the colon mucosa. As evidenced by serial sectioning every colonic crypt harbours about 5 TGF-alpha positive cells in the lower half of the crypt and in the crypt neck. Double labelling experiments with neuroendocrine markers and other hormones show TGF-alpha to be present in 30% of all neuroendocrine colon cells and in 80% of colonic enteroglucagon-containing cells (so called L-cells). Ultrastructurally TGF-alpha is found to be copackaged along with other neurosecretory peptides within neurosecretory dense core granules of colonic L-cells. In acute inflammatory reactions of the colon mucosa the number of TGF-alpha cells is significantly reduced. This is the first study, which gives morphologic evidence of growth factor reservoirs in human neuroendocrine colon cells. Our results strongly support the idea of a growth factor secretion by neuroendocrine cells in the colon. These TGF-alpha cells are an interesting new element in the understanding of the colonic microenvironment, where the release of TGF seems to be under neuroendocrine control. Hormones and receptors: Growth factors Hormones and receptors: Brain gut axis Oncology, general: Proliferation, carcinogenesis } "Demonstration of Transforming Growth Factor Alpha (TGF-Alpha) in Neuroendocrine L-Cells of the Human Colon Mucosa by Immunoelectron Microscopy"

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## OT84 1592 Epinephrine Alone Vs Epinephrine Plus Ethanol for Injection Therapy of Bleeding Peptic Ulcers: An Interim Report of a Prospective Randomized Trial

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**Aim:** A prospective randomized trial was performed to assess whether the additional injection of absolute ethanol improves the results achieved by injection of 1:10,000 epinephrine alone in the therapy of bleeding peptic ulcers.

**Methods:** Among 157 patients who had peptic ulcer bleeding over a 8-month period, only patients with active bleeding (n = 20) or a nonbleeding visible vessel (n = 20) were randomized to receive injection therapy with epinephrine alone (group I, n = 20) or epinephrine plus ethanol (group II, n = 20).

**Results:** The two groups were comparable in age, size and site of ulcer, and severity of bleeding. The volume of injected epinephrine in group I and group II was 17.7 – 7.3 ml and 14.1 – 6.1 ml, respectively (p > 0.05). The volume of injected ethanol in group II was 1.9 – 0.7 ml. Initial hemostasis was achieved in 20 (100%) of group I and 19 (95%) of group II. Rebleeding occurred in 8 (40%) of group I and in 2 (11%) of group II (p < 0.05). Of 10 rebleeders, seven received a second injection with the same agents and five of them achieved ultimate hemostasis; one received surgical intervention directly; two received no intervention due to comorbid illness and died soon. Ultimate hemostatic rates of injection therapy were 80% (16/20) in group I and 90% (18/20) in group II (p > 0.05). No differences were found between the two groups in terms of surgery (10 vs. 10%) or mortality (15 vs. 0%).

**Conclusion:** There was a trend towards lower rebleeding with the epinephrine plus ethanol injection, as compared with the epinephrine injection alone. The final results of this ongoing study may clarify the value of additional injection of absolute ethanol after preinjection of epinephrine in the endoscopic hemostasis of bleeding peptic ulcers.

**Clinical practice:** Management strategy Oesophageal gastric duodenal disorders: GD disorders, acid peptic Endoscopy, general: GI bleeding }

"Epinephrine Alone Vs Epinephrine Plus Ethanol for Injection Therapy of Bleeding Peptic Ulcers: An Interim Report of a Prospective Randomized Trial"

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## OT85 1593 Intraepithelial Clonal T Cell Proliferation in the Gut of Patients with Refractory Sprue

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<sup>4</sup> INSERM Unit 429, Necker Hospital, University Paris V, France *Background.* The etiology of refractory sprue remains a matter of debate. To get further insight into its mechanism, phenotype and T-cell clonality of intestinal lymphocytes were studied in five adult patients. *Methods.* Small bowel and/or rectal biopsies were obtained from 5 adult patients with refractory sprue, 10 patients with uncomplicated active celiac sprue, 19 patients with normal intestinal histology and 2 patients with invasive intestinal T-cell lymphoma. Phenotype of intestinal lymphocytes was studied by immunohistochemistry on cryostat sections and, in two patients, by flow cytometric analysis of lymphocytes isolated from biopsies. Clonal T{ g } gene rearrangement was studied by multiplex PCR. *Results.* In patients with refractory sprue but not in controls, both the epithelia of the small intestine (5/5) and of the rectum (3/5) were infiltrated by CD103<sup>+</sup> CD7<sup>+</sup> lymphocytes of normal cytological appearance. Yet, these lymphocytes had an abnormal phenotype. They contained intracytoplasmic CD{ e } chain but lacked surface expression of CD3-TcR complexes and were CD4<sup>+</sup> CD8<sup>-</sup>. Clonal T { g } gene rearrangements in the V{ g }1 or V{ g }III families were detected in small intestinal (5/5) and rectal (3/5) biopsies of patients with refractory sprue, in the two specimens of invasive intestinal T cell lymphoma and not in controls. In one patient with refractory sprue, the study of lymphocytes isolated from biopsies indicated the clonal T { g } gene rearrangement was only detected in the phenotypically abnormal subset of CD103<sup>+</sup> lymphocytes lacking surface expression of CD3-TcR<sup>-</sup>. *Conclusions.* These results suggest that refractory sprue may be indicative of the onset of low-grade intraepithelial T cell lymphoma. Intestinal disorders, absorption: Malabsorption syndromes Intestinal disorders, absorption: Gluten enteropathy }" "Intraepithelial Clonal T Cell Proliferation in the Gut of Patients with Refractory Sprue"

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## OT85 1594 Extensive Small Intestinal Low-Grade T-Cell Lymphoproliferative Disease without Evidence of Celiac Sprue

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<sup>3</sup> Dept of Hematology, Saint Louis, Paris, France Most reported cases of small intestinal T-cell lymphoma are associated with celiac disease and termed Enteropathy Associated T-cell Lymphoma (EATCL). *Methods.* Among 22 cases of small intestinal T-cell lymphoma (including 11 EATCL), we observed 4 patients (between 1975 and 1995) whose clinicopathological picture was that of an extensive small intestinal low-grade T-cell lymphoproliferative disease (ESILT). *Results.* These 4 patients (3 male and one female) were aged 28–59 years, had long-standing chronic diarrhea with malabsorption and weight loss. Delay to diagnosis was 5 months to 7 years. Peripheral-blood count and smears were normal in 4/4 patients. Search for HIV, HTLV1 and antiendomysium/antigliadin antibody was negative in 3/3 patients. In the 4 patients, the small intestinal lamina propria was extensively and diffusely infiltrated by small T-lymphocytes with irregular pleomorphic nuclei which were CD2+ and CD3+ in 4/4 cases and CD4+, CD5+ and TCRF1+ in 3/3 cases. Noncaseating granulomas and eosinophils were found within the infiltrate in 3/4 cases. In no case there was evidence of associated enteropathy. Lymphoid cells were negative for HML-1 in 3/3 cases. Nucleic acid studies of the lymphoid infiltrate (2 cases) showed monoclonal rearrangement of the T-cell-receptor-chain gene in one case and monoclonal rearrangement of T-cell-receptor -chain gene in the other. Although none of the 4 patients responded to single or multiple drug chemotherapy, median survival was of 5 years being only 7.5 months in 11 EATCL patients. *Conclusion.* We suggest that ESILT is a new entity distinct from EATCL, characterized by heavy lamina propria infiltrate by small lymphoid cells expressing mature T-cell antigens and associated with a longer survival than EATCL. Oncology, specific: Small bowel Intestinal disorders, absorption: Malabsorption syndromes Oncology, specific: Lymphoma } "Extensive Small Intestinal Low-Grade T-Cell Lymphoproliferative Disease without Evidence of Celiac Sprue"

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OT85 1595 **Interaction between Food Proteins and Intestine: Antigen Absorption and Processing** K. Terpend, P. Lanier, F. Boisg'9rault<sup>2</sup>, J.F. Desjeux,

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<sup>1</sup> INSERM U290, Paris France

<sup>2</sup> INSERM U396, Paris France *Purpose:* The main function of Major Histocompatibility Complex class II (MHC II) molecules is to present antigenic peptides produced in antigen presenting cells to T lymphocytes. During intestinal inflammation, an overexpression of MHC II molecules in enterocytes is associated with an increased macromolecular transport. This study examines the relationship between MHC II expression and transepithelial transport and processing of the exogenous protein horseradish peroxidase (HRP). *Methods:* Transwell-grown HT29-19A intestinal cells were treated on their basal or apical side with IFN{ g } (100 U/ml). Surface expression of MHC II molecules was assessed. Transepithelial transport and processing of <sup>3</sup>H-HRP were also measured in HT29-19A cell monolayers mounted in Ussing chambers and ionic conductance (G) and <sup>22</sup>Na and <sup>14</sup>C-mannitol fluxes were used as markers of the paracellular pathway. *Results:* HT29-19A cells did not express MHC II molecules in basal conditions. IFN{ g } induced an increase in MHC II molecules. When IFN{ g } was placed on the basal compartment of intestinal monolayers, G, <sup>22</sup>Na, <sup>14</sup>C-mannitol and intact-HRP fluxes rose significantly (G: 7.2 – 0.2 vs 22.7 – 4.3 mS/cm<sup>2</sup>, <sup>22</sup>Na: 63 – 2 vs 184 – 24 \b5g/h.cm<sup>2</sup>, C-Mannitol: 5.6 – 0.3 vs 25 – 5 \b5g/h.cm<sup>2</sup>, intact HRP: 31 – 4 vs 193 – 56 ng/h.cm<sup>2</sup> in control vs IFN{ g }-treated cells) suggesting a paracellular leakage. Degraded-<sup>3</sup>H-HRP fluxes, reflecting a transcellular pathway, were also significantly increased in IFN{ g }-treated cells compared to controls. No such changes in permeability were observed when IFN{ g } was applied in the apical compartment. In IFN{ g }-treated cells, at least one additional peptide is found in the chromatographic profile compared to control cells, suggesting a different processing. *Conclusion:* These results suggest a possible relationship between MHC II expression and transepithelial transport of exogenous antigens in the HT29-19A intestinal cell line. Intestinal disorders, absorption: Epithelial transport Immunology and microbiology: Inflammation }" "Interaction between Food Proteins and Intestine: Antigen Absorption and Processing"

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## OT85 1596 { d } T Cell Receptor Repertoire in Monozygotic Twins Concordant for Celiac Disease

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Laboratory of Mucosal Immunology, Dept. of Medicine, University of California, San Diego, CA, USA Genetic factors determine host susceptibility to celiac disease. Thus, approximately 75% of monozygotic twins are concordant for celiac disease and disease susceptibility is associated with specific HLA class II alleles in the DQ subregion. One of the hallmarks of celiac disease, both active and treated, is an increased number and proportion of { g } / { d } intraepithelial T lymphocytes in the small intestinal mucosa, and an increased number of { g } / { d } T cells in the small intestinal mucosa has been associated with the inheritance of specific HLA class II genes. Nonetheless, the contribution of genetic factors to the development of the T cell receptor { d } repertoire in celiac disease and the specific role { g } / { d } T cells play in the pathogenesis of this disease are not known. To assess the contribution of genetic factors to development of the T cell receptor (TCR) { d } repertoire in celiac disease, we characterized the junctional diversity of TCR { d } transcripts expressed in the intestine and peripheral blood of a pair of monozygotic twins concordant for celiac disease. *Methods:* TCR V { d } 1, V { d } 2 and V { d } 3 transcripts from small intestinal and colon biopsies, and from peripheral blood mononuclear cells, were amplified by PCR and the complementarity determining region 3 domains of TCR { d } transcripts were analyzed by denaturing PAGE and direct nucleotide sequencing. *Results:* The repertoire of TCR { d } transcripts and complementarity determining region 3 amino acid motifs in the intestine and peripheral blood of monozygotic twins concordant for celiac disease exhibited no overlap. The TCR { d } repertoire in each twin was oligoclonal and complexity of the junctional regions of their TCR { d } transcripts was typical of the adult repertoire. *Conclusions:* Genetically identical individuals with celiac disease have distinct, non-overlapping TCR { d } repertoires. Genetic factors that determine disease susceptibility do not select for specific TCR { d } sequences or complementarity determining region 3 amino acid motifs. Intestinal disorders, absorption: Gluten enteropathy Immunology and microbiology: Inflammation Hormones and receptors: Molecular biology } " ð T Cell Receptor Repertoire in Monozygotic Twins Concordant for Celiac Disease "

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## OT85 1597 Activation and Cytotoxic Function of Intestinal Lymphocytes in Children with Ulcerative Colitis

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The phenotype characterization and the immune function of intestinal lamina propria T lymphocytes (LPL) in children with ulcerative colitis (UC) is not completely clarified. The present study defines cytotoxic and activation surface markers expression on LPL CD4 or CD8 and the cytolytic activity (CTL) exhibited by CD4+enriched and CD4- depleted colonic LPL in 5 acute phase UC children (mean age 4 years) and in 4 controls (mean age 2 years). LPL were isolated by DTT-EDTA-Collagenase digestion and characterized by double fluorescence flow cytometric analysis. The CTL were measured by PHA or anti-CD3-induced lysis of K562 and P815 target after 6 hrs incubation. In UC CD4 subset there was higher expression of CD69 (72 – 5%), HLA-DR (20 – 7%), ICAM1 (15 – 3.5%), in CD8 subset was increased expression of ICAM1 (27 – 6.8%), CD11b (8 – 4%) compared to normal subset (p = 0.05). All cell population showed low levels of cytotoxicity against K562 in accordance with experiments using LPL effector cells from normal and IBD adults. In contrast, the UC patients CTL, both stimulated by PHA (1  5g/ml) or anti-CD3 (1  5g/ml, TR66) against P815 is absent in CD4+subset, while in CD4- subset is significantly increased (10.5 – 0.1% and 9.6 – 2% respectively) compared to CD4- controls (1.5 + 0.5%, 2 + 0.7%) (p = 0.03, 0.05). Cytokine analysis of UC patients CD4- cells point out the  -IFN increased level (2.4 – 1 ng/ml) compared to CD4+ cells (0.3 – 0.02 ng/ml) (p = 0.03); IL4 and IL5 concentrations of all supernatants were undetectable. Together with phenotypic characterization, these functional studies provided further evidence that CD4+ activated subset in UC and Crohn's disease are unlikely to play a role in tissutal injury. Intestinal disorders: IBD, basic Immunology and microbiology: Inflammation } " Activation and Cytotoxic Function of Intestinal Lymphocytes in Children with Ulcerative Colitis"

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## OT86 1598N-Terminal Peptide of Type III Procollagen: an Early Indicator of Colorectal Cancer Recurrence

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<sup>1</sup> Divisione Chirurgica II, University of Padova, Italy Colorectal cancer follow-up is needed to identify as earlier as possible any recurrent disease. The first step in colorectal cancer spread is characterized by the ability of tumor cells to degrade and invade the extracellular matrix (ECM). Aims of the present study were 1. to evaluate the serum pattern of laminin, C-terminal peptide of type I (PIP) and N-terminal peptide of type III (PIIP) procollagens, indices of ECM synthesis, in the follow-up of patients surgically treated for colorectal cancer; 2. to assess their role in predicting recurrence in comparison with those of CEA, CA 19-9 and TPA. 32 patients, all subjected to radical surgery for colorectal cancer, were followed up from 6 to 36 months (median = 24 months) after surgery. During follow-up a serum sample from each patient was obtained every three months to measure laminin, PIP and PIIP (immunoradiometric assays, Cis, France) and the tumor markers CEA, CA 19-9 and TPA. Every six months the patients were subjected to abdominal ultrasound examination and chest X-ray. 21 patients did not have any sign of recurrence during follow-up (group 1), while the remaining 11 developed hepatic (n = 7) or pulmonary (n = 4) metastases (group 2). Serum bilirubin, alkaline phosphatase and alanine amino transferase were in the normal range during all follow-up in all the patients. Laminin did not significantly vary in both groups 1 (Anova one-way:  $F = 1.79$ ,  $p$ : ns) and 2 ( $F = 0.67$ ,  $p$ : ns). PIP and PIIP significantly increased three months after surgery in group 1 ( $F = 19.93$ ,  $p < 0.001$  and  $F = 69.76$ ,  $p < 0.001$ ) and, although at a lesser extent, in group 2 ( $F = 10.54$ ,  $p < 0.001$  and  $F = 6.70$ ,  $p < 0.01$  respectively). CEA, CA 19-9 or TPA did not vary in any group. The differences between basal and three months follow-up values of PIP and PIIP discriminated group 1 from group 2 patients with a sensitivity of 36% and 91%, a specificity of 71% and 71% and an overall diagnostic accuracy of 59% and 78% respectively. In conclusion: we may suggest the use of serum PIIP determination as an early prognostic indicator of colorectal cancer recurrence; the pathophysiological mechanism underlying this pattern is probably due to the persistence of aggressive tumor cells after surgery, which can inhibit ECM synthesis thus allowing their escape from the primary site to the metastatic foci. Oncology, specific: Colon, rectum } "N-Terminal Peptide of Type III Procollagen: an Early Indicator of Colorectal Cancer Recurrence"

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## OT86 1599 Disruption of the Cadherin-Catenin Complex in Gastric Carcinoma Cell Lines

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<sup>2</sup> Department of Histopathology, Hammersmith Hospital, London Dysfunction of the cadherin-catenin complex, a key component of adherens junctions, is thought to confer invasive potential to cells. In a recent study we demonstrated abnormal expression of the cadherin-catenin complex in the majority of gastric cancers. *Aims:* 1. To examine the expression of E-cadherin, { a }, { b }, and { g }-catenin in gastric carcinoma cell lines, and look for evidence of mutations and disruption of the cadherin-catenin complex. 2. To correlate these findings with a functional assay of cell-cell aggregation. *Methods:* Expression and function of E-cadherin, { a }, { b }, and { g }-catenin and p120<sup>cas</sup>, was examined in gastric (Kato3, HSC39, MKN7, MKN45, AGS) and colonic (HT29) carcinoma cell lines, using immunocytochemistry, Western blotting and cell aggregation assay. Complex composition was examined by immunoprecipitation with antibodies to { b }-catenin followed by Western blotting. *Results:* Bands of abnormal molecular weight suggesting mutations of E-cadherin (in Kato3 and MKN45), and { b }-catenin (in HSC39) were detected, while both E-cadherin and { a }-catenin were absent in AGS. MKN7 and HT29 showed bands of expected size for all components of the complex. There was loss of membranous localisation of complex components from the cell membrane, and loss of calcium dependent aggregation in all but HT29. Immunoprecipitation of { b }-catenin-associated proteins revealed loss of { b }-catenin binding to { a }-catenin in HSC39, and to p120<sup>cas</sup> in MKN7, HSC39 and Kato3, suggesting functional disruption of the complex. *Conclusions:* Mutations of E-cadherin, { a }- and { b }-catenin, were associated with abnormalities of E-cadherin-catenin complex composition, loss of membranous localisation to the adherens junction and loss of calcium-dependent aggregation in 4 gastric carcinoma cell lines. These findings support *in vivo* data and suggest that these cell lines may be an appropriate model for further study of these changes. Oncology, general: Proliferation, carcinogenesis Oncology, specific: Stomach } "Disruption of the Cadherin-Catenin Complex in Gastric Carcinoma Cell Lines"

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OT86 1600 **Cyclin D1 Protein Plays an Important Role in Maintaining the Transformed Phenotype in Human Colon Cancer Cells** N. Arber, Y. Doki<sup>1</sup>, E.K.-H. Han<sup>1</sup>, A. Sgambato<sup>1</sup>, P. Zhou<sup>1</sup>, N.W. Kim<sup>1</sup>, T. Delohery<sup>2</sup>, P.R. Holt, I.B. Weinstein<sup>1</sup>

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<sup>3</sup> Division of Gastroenterology, St. Luke's-Roosevelt Hospital Center, Columbia University, New York, NY *Purpose:* Cyclin D1 is a cell cycle regulator essential for progression through the G1 phase of the cell cycle. Cyclin D1 amplification or increased expression has been implicated in the pathogenesis of several types of human cancer. The cyclin D1 gene is frequently overexpressed in human colon cancer. The functional significance of this overexpression has not been established. We have previously shown that an antisense cyclin D1 cDNA inhibits growth and reverses the transformed phenotype of human esophageal cancer cells. *Methods:* To address the role of cyclin D1 in growth control and tumorigenesis in colon cancer we have overexpressed the same antisense cyclin D1 cDNA construct in the SW480E8 cells, human colon cancer cell line which expresses high levels of cyclin D1. *Results:* The integration and expression of the antisense construct was verified by Southern and Northern blot analysis, respectively, and resulted in decreased expression of cyclin D1 and Rb proteins. In addition the hypophosphorylated form of Rb was increased in the antisense cyclin D1 cells. p27<sup>Kip1</sup> levels were also reduced and the levels of Cyclin E were slightly decreased. Cyclin D1 kinase activity was reduced in the antisense cells without a change in cdk4 protein level. Derivative cells expressing antisense cyclin D1 mRNA displayed an increased doubling time and were more contact inhibited. They also demonstrated decrease in saturation density, plating efficiency and anchorage-independent growth in vitro, and tumorigenicity in nude mice in vivo. *Conclusions:* These findings provide direct evidence that the increased expression of cyclin D1 in certain colon tumor cells contributes to their abnormal growth. The ability to revert the transformed phenotype of these cells with antisense cyclin D1 suggests that cyclin D1 may be a useful target in the therapy of colon cancer. Oncology, general: Molecular biology, genetics Oncology, general: Proliferation, carcinogenesis } "Cyclin D1 Protein Plays an Important Role in Maintaining the Transformed Phenotype in Human Colon Cancer Cells"

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## OT86 1601 Overexpression of the Type I Receptor for Transforming Growth Factor $\beta$ (TGF- $\beta$ ) in Colorectal Carcinomas

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*Purpose:* Transforming Growth Factor  $\beta$  (TGF- $\beta$ ) is a potent regulator of cell growth and differentiation and is thought to play an important role in colorectal tumorigenesis. The in vitro progression from adenomas to carcinomas is accompanied by a reduced responsiveness to the growth inhibitory effects of TGF- $\beta$ . Recent reports suggest that the lack of growth inhibition by TGF- $\beta$  in several colon cancer cell lines may be due to a lack of expression of functional TGF- $\beta$  receptors.

*Methods:* The expression of the two TGF- $\beta$  receptors (T $\beta$ R-I and T $\beta$ R-II) and of their mRNAs was studied in surgical samples from 16 normal colons and 21 colorectal adenocarcinomas by immunohistochemistry using specific polyclonal antibodies and by semi-quantitative Reverse Transcriptase-Polymerase Chain Reaction.

*Results:* 94% and 6% of the normal colon samples showed a weak and strong expression of T $\beta$ R-I mRNA respectively whereas 31% and 69% of the normal samples showed a weak and strong expression of T $\beta$ R-II mRNA respectively. In the tumoral samples, 57% and 43% showed a weak and strong expression of T $\beta$ R-I mRNA respectively whereas 29% and 71% showed a weak and strong expression of T $\beta$ R-II respectively. By immunohistochemistry, the T $\beta$ R-I and T $\beta$ R-II proteins were weakly or not at all expressed in normal colonic mucosa. In contrast, both receptors were abundant in glandular tumoral cells from all specimens. The surrounding inflammatory stromal cells were also positively stained in both normal and tumoral samples.

*In conclusion,* the two TGF- $\beta$  receptors that are both required for TGF- $\beta$  activity, were differently expressed in normal and neoplastic colons: T $\beta$ R-I is weakly expressed in normal cells but abundant in tumors; T $\beta$ R-II is expressed similarly in normal and neoplastic tissues.

Oncology, specific: Colon, rectum  
Hormones and receptors: Growth factors

"Overexpression of the Type I Receptor for Transforming Growth Factor  $\beta$  (TGF- $\beta$ ) in Colorectal Carcinomas"

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## "S ST3 9001"ST3 9001 **The need for quality assurance programmes**

\*Dr B Holthof

Throughout the developed world, the traditional roles of players in the health-care system are changing. Governments are moving responsibility to control health-care quality and costs more and more to payers, physicians, hospitals, suppliers and patients. These changes are stimulating a move away from a fee-for-service reimbursement approach, such as a tariff for a specific operation, towards a capitation system based on a budget for each patient. Gastrointestinal (GI) conditions will be at the forefront of developments in managed care, because they are second only to hypertension in being the most expensive disease grouping to care for. This means that primary care physicians and gastroenterologists alike will have to become better in managing the quality and cost of integrated patient care processes. In support of this new task, three tools are becoming more widely available: management guidelines, practice profiling and outcomes analysis. However, most applications are still in the experimental stage. It would involve applying a management guideline such as the IGPCG plan to a group of physicians and then collecting and analysing outcomes and cost data in order to improve the guideline. This requires a comprehensive database of patient characteristics, in- and out-patient visit records, prescriptions and investigations linked to specific patients and physicians across the care continuum. In order to make the experiments successful, primary care physicians and gastroenterologists will have to create a new environment that allows them to start using these new tools. The nature of this environment will have to take into account the attitudes of the professionals involved. In particular, gastroenterologists, like most specialists, tend to be guarded about management guidelines until these can be discussed with colleagues. In addition, they are used to learning through fact-based scientific data of well-controlled trials. This implies that the best learning environment will probably be small, information-based, collaborative discussion groups of gastroenterologists and primary care physicians. These groups should adapt available guidelines such as the IGPCP plan, collect and analyse patient data to evaluate the impact of applying these guidelines and improve the guidelines over time. Unfortunately, most countries do not have the right financial incentives to encourage the formation of these professional development groups. The move from a fee-for-service approach towards a capitation system will facilitate the application of managed care principles to GI disorders to the benefit of patients, providers and payers. } "The need for quality assurance programmes"

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## "S ST3 9002"ST3 9002 **The right physician managing the right patient in the right way**

\*Dr M Whitaker, UK  
In order to optimize the management of patients with upper gastrointestinal (UGI) disorders a number of improvements have been identified. Among primary care physicians, there is a clear need for a better understanding of the pathophysiology of UGI disorders and their role in managing these conditions. The issues of symptom management and the care of *Helicobacter pylori* patients in particular are causing confusion among primary care physicians. There is also a need to generate closer and more focused communication links between all physicians involved in gastroenterology in order to increase specialists' confidence in the gastroenterological abilities of primary care physicians. In an attempt to address these issues, an international group of primary care physicians founded a working team, the International Gastro Primary Care Group (IGPCG) in 1994. With the advice of leading gastroenterologists, the group reached a consensus on how queries should be addressed and developed guidelines to assist the primary care physician in different countries to correctly diagnose and manage patients with UGI symptoms in the primary care setting. These guidelines were first presented at the World Congress of Family Doctors in the form of an algorithm, and introduced the concept of the predominant symptom. In a recent international survey of over 900 primary care physicians in 25 countries, the IGPCG found that over half of them were able to clearly establish a predominant symptom rather than a cluster of symptoms when presented with patients with UGI disorders. However, the ability to do this varied from 100% in Sweden and Italy to less than 40% in Slovenia and the Netherlands. Not surprisingly perhaps, the most common predominant symptom established was heartburn, followed by abdominal pain, bloating, fullness, acid regurgitation and other symptoms. In the IGPCG management plan, patients with non-gastrointestinal symptoms must first be excluded while those with alarm symptoms, such as GI bleeding, dysphagia and weight loss, are referred to a specialist for consideration of endoscopy. Specific management is required for those patients on non-steroidal anti-inflammatory drugs. For the remaining patients, the IGPCG is convinced that patients can be grouped and treated on the basis of the predominant symptom and reason for consultation. These three different groups include: Abdominal discomfort, bloating, fullness and nausea Localized epigastric pain Heartburn and regurgitation The management guidance then proceeds according to which of the three categories the patient's predominant symptom falls within. This approach, which is supported by a recent publication from Stanghellini *et al.*, offers the majority of patients a more appropriate therapy and can avoid unnecessary investigations. The IGPCG management plan has now been developed into a health economic model that can be used to calculate health-care costs associated with treating dyspeptic patients in a specific manner. In addition, the IGPCG is now undertaking other projects to provide broader services to the gastroenterological community. The first is an interactive problem-based educational package developed by family physicians with the help of gastroenterologists for primary care physicians and can be adapted for different countries and different health care systems. The second is an Internet site which will include a regular newsletter and information sheets on key topics in gastroenterology. It is hoped that these activities will provide a significant contribution to addressing the needs of all physicians involved in the care of patients with UGI disorders.

Reference: Stangellini V, Tosetti C, Paternic OA et al (1996) *Gastroenterology* 110: 1036-1042.  
}" "The right physician managing the right patient in the right way"

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## "S ST3 9003"ST3 9003 **The use of economic modelling to support clinical decision making in gastroenterology**

\*Dr A Haycox

Health economic models attempt to identify the therapeutic options that maximize health benefits utilizing the limited health-care resources available. Such models are being used increasingly to support clinical decision making in a wide range of therapeutic areas. The development of an economic model to support clinical decision making at the primary care level in upper gastrointestinal (UGI) disorders is of particular importance. Gastrointestinal disorders account for 10% of primary care consultations in the UK, of which UGI disorders represent approximately half of such presentations. As a consequence, gains to both the patient and the health service arising from an improvement in resource utilization in this area are potentially enormous. Clinical guidelines aimed at improving the management of UGI disorders at the primary care level have been developed by the International Gastro Primary Care Group (IGPCG). This presentation discusses the derivation, methodology and results of an economic model that analyses the resource implications arising from these clinical guidelines. In order to construct the economic model, it was necessary to identify:- Every potential therapeutic pathway that could be followed by patients- The nature and level of resources that would be consumed by patients along each pathway – The probabilities of following alternative options, at each stage of each pathway. Every branch of the algorithm represents a treatment pathway that has a defined level of resource use and a defined probability of use by patients. Where therapeutic options were not explicitly stated in the IGPCG algorithm, expert opinion and literature reviews were employed to complete the model. One crucial factor underlying the interpretation of results obtained from any economic model is the time period covered by the model. For example, expensive 'one-off' diagnostic procedures, such as endoscopy, which are undertaken in the early stages of a treatment pathway will inevitably have a greater significance in a short-term model. The model presented analysed the initial 12-month treatment period of 'new' patients presenting with UGI disorders. In order to test the implications of a longer term perspective, the model is currently being developed to analyse resource use over a 24-month period. The model has proven to be extremely accurate and demonstrates that utilizing the predominant symptom approach to the diagnosis and treatment of patients with UGI disorders appears to provide significant gains in terms of patient management and effective resource use. This factor, together with a more intensive use of eradication therapy, provides the potential to reduce the cost of drugs for the treatment of UGI disorders by approximately 15% in the UK. A major strength of the model is its adaptability to a wide range of clinical and cost scenarios. Such adaptability enables the model to effectively reflect the potential resource implications in countries exhibiting significantly different levels of cost and patient management. In this manner, the model provides one valuable method by which clinicians at primary and secondary care levels internationally can be supported in optimizing the management of UGI disorders within current resource constraints. }

"The use of economic modelling to support clinical decision making in gastroenterology"

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## "S ST3 9004"ST3 9004 **A vision of the primary care-gastroenterologist interface in the future**

\*Professor J-R Malagelada

As we move into the 21st century, it seems likely that the management of gastrointestinal (GI) disorders will place more emphasis on broadly applicable disease-specific prevention programmes and non-invasive diagnostic methods. Drug efficacy will be expected to aim towards complete disease control, while surgery will become minimally invasive and reparative with the widespread practice of transplantations. The growth of therapeutic and diagnostic options, and the ever increasing pressure to control health care costs across Europe, has already resulted in an increased involvement of primary care physicians in the management of upper GI disorders. This is reflected by the formation of the International Gastro Primary Care Group (IGPCG). As this involvement develops, we must address how to best complement the management tasks of the primary care physician and the gastroenterologist, both generally and for specific diseases. This division of labour must also take into account how different physicians practise, patients' circumstances and different health care systems. A disease-based division of tasks would be based on the type of condition, its severity and chronicity, and the ultimate prognosis. Taking these factors into account, it would be cost-effective for conditions such as GI bleeding and inflammatory bowel disease to be managed primarily by the gastroenterologist. This might also be the case for severe cases of dyspepsia, and peptic disorders, whereas it might be more appropriate for the primary care physician to take on this role for mild cases, although with ad hoc advice from a specialist colleague. Equally, the primary care physician might be the best practitioner to manage chronic cases with a poor prognosis and requiring minimal therapeutic intervention. In proposing such a division of tasks, however, it is important not to forget the areas in which the specialist and the primary care physician can work closely together, for example during informal consultations, formal clinical teaching sessions and communication about specialist procedures. Improved interaction is clearly one of the areas where the communications revolution could have a notable impact. For example, primary care physicians could receive one-to-one on-line consultations from gastroenterologists or from a specialist group on the Internet. It seems appropriate that the gastroenterologist would be responsible for providing accurate and up to date information to primary care physicians, overseeing the implementation of quality assurance programmes and monitoring patient outcomes. In parallel, the primary care physician would review all new management guidance, request more specific advice from a gastroenterologist and provide outcomes feedback. Although such interaction already occurs, it is clear that there is a need for new methods of communication, such as primary care physicians and gastroenterologists working in teams. With this vision, primary care and specialist physicians can work together with the common aim of efficient delivery of health care to patients with GI disorders. } "A vision of the primary care-gastroenterologist interface in the future"

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