3.22 (mean \pm SE) per mil). 3 patients had a negative test at one week (excess 2 $^{13}\text{CO}_2$ excretion = 1.5 ± 0.7 (mean \pm SE) per mil) which however turned to be positive at the second week evaluation (excess 2 $^{13}\text{CO}_2$ excretion = 11.5 ± 2.8 (mean \pm SE) per mil) Conclusions: $^{13}\text{C-UBT}$ can assess Helicobacter pylori eradication as soon as one week after treatment withdraw. When performed at two weeks it shows the same sentivity and specificity of the test performed at four weeks after withdrawing medications.

2066

Effect of Omeprazole and Clarithromycin Plus Tinidazole on the Eradication of Helicobacter pylori and the Recurrence of Duodenal Ulcer

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Although it is presently recognized that *Helicobacter pylori* (*H.p.*) infection is the main acquired factor in the pathogenesis of duodenal ulcer (DU) disease and that DU patients must be treated with antimicrobials in order to greatly reduce, or even abolish, the risk of recurrence, a consensus agreement for the optimal therapy (greatest efficacy with least untoward effects and lowest cost) has yet to be accomplished. We have recently reported (Gastroenterology, 1993; 104: A40) that in patients with *H.p.* gastritis, a short term and low dose therapy with clarithromycin (C.), omeprazole (O.) and tinidazole (T.) is highly effective for long term eradication and that absence of side effects and good compliance are likely to be major determinants of effectiveness.

Aim: In the present study we aimed to investigate the effect of combining one week administration of low dose C. plus T. with a conventional four week healing treatment with O. on the eradication of *H.p.* in DU patients and on the rate of recurrence of duodenal ulcer.

Methods: 171 patients (115 males; 56 females, mean age \pm SE 53.9 \pm 1.0 yrs) with active DU and H.p. infection received a 4 weeks administration of O. 20 mg u.i.d. and, during the first week, a combination antimicrobial treatment with C. 250 mg b.i.d. plus T. 500 mg b.i.d.. H.p. infection, as well as eradication or relapse, was established by urease test, histology and 13 C-urea breath test (56 pts) or brush cytology (115 pts). Upper GI endoscopy with antral biopsies and brush cytology or 13 C-urea breath test were performed prior to treatment and at month 1, 3, 6 and 12 after treatment withdrawal. Drug tolerability was evaluated by patient interview and compliance by pill counting.

Results: All, but one single patient who complained of nausea and vomiting, tolerated well and completed the treatment, and took more than 90% of the prescribed medication. At month 1 after the end of treatment, ulcers were healed in 167 patients and H.p. was eradicated in 158 (94.6%). Follow-up evaluations performed at month 3 (114 pts), 6 (74 pts) and 12 (48 pts) showed persistent eradication and no ulcer recurrence in all cases.

Conclusions: One week administration of clarithromycin 250 mg b.i.d. plus tinidazole 500 mg b.i.d. combined with four weeks administration of omeprazole 20 mg u.i.d., is highly effective for long term eradication of *H.p.* infection also in DU patients, and, in this group of patients, was able to fully abolish ulcer recurrence.

2068

Pancreatic Ultrasonographic Measurements in Non-insulin Dependent Diabetes Mellitus (NIDDM) Patients

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We evaluated the pancreatic size and structure in diabetic patients (NIDDM) and control subjects by ultrasonography. 20 healthy control subjects (7 male and 13 female), 19 NIDDM patients (5 male and 14 female) with no history of alcohol intake or pancreatitis were studied.

A real time system was used for ultrasonographic measurements of the maximum anteroposterior diameters of the head, body and tail of the pancreas of transverse/oblique images.

Table shows the differences between the diameters \pm SD of the head body and tail of the pancreas in NIDDM and control subjects.

	Pancreas		
	Head (mm)	Body (mm)	Tail (mm)
NIDDM patients	28.17 ± 0.83	13.13 ± 0.40	20.35 ± 0.59
Control subjects	26.66 ± 0.58	13.56 ± 0.38	19.38 ± 0.37
t value	1.511	0.718	1.431
p value	>0.05	>0.05	>0.05

These results were not related to age, sex or body size. Pancreatic image was hyperechogenic in both NIDDM and control subjects, 72%, 70% respectively.

Due to the results of our study, no difference between diameters and echogenity of pancreas in NIDDM and control subjects was determined.

207

Serum Apoprotein A_1 and B_{100} Levels in Liver Cirrhosis and in Chronic Active Hepatitis

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Important changes in cholesterol metabolism are common findings in chronic liver diseases. Apoprotein A₁ and B₁₀₀ (Apo A₁ and B₁₀₀) are the major proteins in HDL and LDL respectively. Unfortunately, few detailed studies are now available on serum Apo A_1 and B_{100} in liver cirrhosis (C) and in chronic active hepatitis (CAH). Aims of our study were to compare Apo A₁ and B₁₀₀ serum levels among C, CAH and control subjects (CS) and to evaluate their relation with Child classes of C patients. The distribution of cholesterol in the serum lipoprotein fractions was also evaluated. We studied 18 consecutive patients with histologically proven cirrhosis (15 M, 3 F; age 58.0 ± 11.2 yrs, m \pm SD; Child classes: 7 A, 8 B, and 3 C; billary cirrhosis was excluded), 16 patients with histologically proven CAH (9 M, 7 F; age 51.0 \pm 14.7 yrs) and 29 control subjects (24 M, 5 F; age 55.7 ± 17.4 yrs). Control subjects were selected among patients admitted to our Unit for diseases unrelated to liver impairment, with liver function tests within the normal range and without any major metabolic disease. No significant differences among groups were observed as far as sex and age were concerned. Apo A₁ and B₁₀₀ serum levels were measured by specific antibodies; triglycerides, total (TC) and HDL cholesterol were measured by enzymatic methods; LDL and VLDL were calculated. The Student t test was used to compare data among groups, while the ANOVA trend was used to test their relation with Child classes. Results. Mean \pm SD values (mg/dl) of Apo A₁ and B₁₀₀, as well as TC, LDL HDL and VLDL, are reported in the table.

	Apo A ₁	Apo B ₁₀₀	TC	LDL	HDL	VLDL
С	98 ± 50**	75 ± 24°	132 ± 47**	79 ± 33**	34 ± 14**	19 ± 6
CAH	155 ± 41	89 ± 29°	174 ± 33	110 ± 31	45 ± 10	19 ± 5
CS	138 ± 29	111 ± 29	186 ± 41	122 ± 37	42 ± 11	22 ± 8

**P < 0.05 vs. CAH and CS; *P < 0.05 vs. CS.

In C, serum Apo A₁, TC, LDL and HDL resulted significantly decreased in comparison with CAH and CS. In addition, they progressively decreased (P < 0.05) with the increase of the severity of the disease from Child A to C. Apo B₁₀₀ was significantly lower in C and CAH than in CS. In conclusion, serum Apo A₁ and B₁₀₀ could add potentially useful informations for the clinical evaluation and the management of chronic liver disease. In addition, these results may be of use in a better understanding of the relationship between cholesterol and protein metabolism during liver disease.

2078

Endoscopic Sphincterotomy for the Prevention of Further Attacks of Acute Pancreatitis in Patients with Galibladder In Situ

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Acute pancreatitis (AP) is a complication which affects 6%-8% of all patients with symptomatic gallstones; although, this percentage may be higher than 20% in those with microlithiasis. In the absence of cholecystectomy the risk of further attacks of AP is about 40%. The aim of this study was to evaluate the usefulness of endoscopic sphincterotomy (ES) to prevent recurrences of AP in patients with biliary stones and gallbladder in situ. Twenty-seven acute biliary pancreatitis patients (7 M, 20 F, mean age 70 years, range 40-86) were studied. The diagnosis was based on typical abdominal pain associated with a two-fold increase of serum lipase and was further confirmed by imaging techniques. On the basis of Atlanta criteria, 22 patients had mild acute pancreatitis and 5 a severe disease. Ultrasonography showed hillary lithiasis in 25 of the 27 patients studied. ERCP, performed within 72 hours from hospitalization, showed lithiasis or microlithiasis of the gallbladder in 23 patients and of the common bile duct in 23; papillary stenosis was found in 10 patients; all the subjects underwent urgent ES. Mean follow-up period of the 27 patients was 14 months (range 1-43 months). Three patients complained early complications related to endoscopic procedures: one had intestinal perforation resolved with nasobiliary drainage and medical treatment; two patients had moderate bleeding and one of these required two units blood transfusion. There were no fatal complications. The mean length of hospitalization was 11 days (range 6-48 days). During the follow-up period, 3 patients underwent to urgent cholecystectomy for gallbladder empyema (one patient on the 15th day, the 2nd, on the 40th day and the 3rd, 16 months after ES). During the follow-up period, relapse of acute pancreatitis was nil. In conclusion, results of our study suggest that ES is useful to prevent further attacks of acute pancreatitis in patients with gallbladder in situ in which cholecysteetomy is inadvisable.

2081

Intestinal Permeability in Chronic Liver Diseases

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Alterations in intestinal permeability reflect one component of intestinal ep-

A242 4th UEGW Berlin 1995

ithelial barrier function. Factors affecting the intestinal uptake and urinary excretion of ⁵¹&r-labelled ethylenediaminetetra-acetate (⁵¹Cr-EDTA), have been investigated in normal subjects and different patient groups in different disease except chronic liver disease (CLD). The objective of this study was to assess the degree of derangement of intestinal permeability in CLD.

Making use of 51 Cr-EDTA as a permeability marker, we measured intestinal permeability in a group of 144 patients with CLD (58 male aged 18–71 mean 44.2, 86 female aged 16–68 mean 44.7) and 38 control subjects (23 male aged 22–36 mean 28, 15 female aged 18–39 mean 34). After an oral dose of 100 μ Ci 51 Cr-EDTA was administered, urinary ex-

After an oral dose of 100 μ Ci³¹Cr-EDTA was administered, urinary excretion levels (in 6th, 12th and 24th hours) were progressively monitored in every patient. Urinary excretion levels at 6th, 12th and 24th hours were al found higher when compared to the control but only the excretion levels of 6th hour and 12th hour were found to have increased statistically significant (p < 0.05).

These results suggested that intestinal permeability is prone to increase in varying levels in patients with CLD especially during the passage of the ⁵¹ Cr-EDTA in small intestine. Besides, these findings shed light upon the explanation of the pathogenesis of bacterial translocation and endotoxemia which is predominantly seen in patients with CLD.

2082

Hepatitis C Virus Genotypes and Response to Interferon Treatment in Turkey

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The distribution of HCV genotypes throughout the world has been mostly reported. While type 1 and 2 dominate in Europe and North America, type 4 was recently reported to be frequent in the Middle East (Hepatology 1994; 20: A596). In this study, we aimed to explore the distribution of HCV genotypes, and its effect on treatment response to interferon in Turkey, the "bridge" between Europe and Asia.

Patients and Methods: 39 patients (pts) (25 men. 14 women, mean age: 52 (34-75) with biopsy proven chronic hepatitis C (positive serum anti HCV and nested PCR detected serum HCV RNA) were enrolled into the study. HCV genotyping was performed using type specific primers for the core region with amplification of core gene sequences by nested PCR according to Okamoto'z method. Of the 39 pts, 27 pts with high liver enzymes for 6 months (17 CAH and 10 cirrhosis) were treated with interferon 2 alfa (IFN), 3 MU (tiw) for 6 months. Post-treatment follow-up for 6-12 months is available for all pts. Pts', in whom ALT levels were normal at follow-up were considered to have a complete response (CR), pts, whose enzymes relapsed at followup had a partial response (PR) and the rest had no response (NR). Results: Genotype distribution 2 pts (5%) had type 1a (I); 34 pts (87%) had type 1b (II); 3 pts (8%) had type undetermined. Of the type 1b pts, 21 had CAH, 9 had cirrhosis, and 4 had cirrhosis + HCC. Of the 27 pts on IFN therapy, 24 had genotype 1b, and 3 had type 1a. 7 pts (26%) had a CR, 9 pts (33%) a PR, and 11 pts (41%) a NR. Conclusion: 1. The results indicate that HCV genotype 1b is the most common in Turkish pts with chronic hepatitis C. 2. The CR rate of 26% in a mostly genotype 1b patient population, though slightly higher, is comparable to results obtained in other areas of the world with a similar genotype pattern.

2085

Comparison of Dual (Omep. and Amox.) and Triple (Omep. and Amox and Metr.) Therapy in Eradication of Helicobacter pylori

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In this study, we have studied the effectiveness of Omep razole in combination with other drugs in the treatment of Hp. Materials and Methods: In this study 72 patients with positive Hp, 42 with peptic ulcer and 30 with gastroduodenitis, were investigated. The age range of patients was 42 \pm 11 years with 39 of patients being male and 33 female. All the patients have undergone endoscopic examination and three biopsy specimens were taken from each patient. One of the specimens was used for urease test, the second one for Gram staining and third one for culture. The patient was classified as Hp positive if the culture or both of the other two tests were found positive. 26 of cases were treated with Omep. 40 mg/day for one month and Amox. 2 g/day for two weeks. 46 of the cases were treated with Omep. 40 mg/day for one month and Amox. 2 g/day for 10 days and Metr. 750 mg/day for 10 days. The control endoscopy were done for all subjects after 1, 5-6 months (average: 4, 7 months) following the end of treatment. The specimens obtained at the control endoscopy were subject to the same tests and culture for Hp detection

Results: The eradication rate in triple therapy (Omeprazole and Amoxicilline and Metranidazole) was found to be 65.2%, whereas the eradication rate with dual therapy (Omep. and Amex.) was 46.2%.

Conclusions: The eradication ratios achieved with dual and triple therapy in türkiye were found to be lower ratios reported in developed countries. We believe that these low eradication rate in türkiye are due to the fact that the population becomes infected by Hp in early stages of life.

2086

Effect of Body Position on Esophageal Acid Clearance Time in Patients with Systemic Sclerosis

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In patients with systemic sclerosis, gastroesophageal acid refluxes are longer in the supine than in the upright position. Gravity does not significantly affect esophageal acid clearance time (ACT) in healthy subjects, whereas in patients with systemic sclerosis studies on esophageal transit suggest that gravity plays a determinant role in esophageal clearance. Aim: To evaluate the effect of body position on esophageal ACT in patients with systemic sclerosis and healthy controls. Methods: We studied 15 consecutive patients with systemic sclerosis (14 women, 1 man; mean age 48 yr, range 18-68), and six healthy subjects (3 women, 3 men; mean age 34 yr, range 27-49). All subjects underwent esophageal manometry, and after intraesophageal infusion of 15 ml HCl 0.1 N, ACT was measured in three body positions (supine, trunk elevated at 30° and 90°) in randomized order. The subjects swallowed at 30s intervals after each acid infusion, for a period of ten minutes. Esophageal peristalsis was considered impaired when the amplitude of distal contractions was less than 19 mmHa. ACT was defined as the interval between the end of the acid infusion and the first rise of pH above 4. Results: Based on esophageal manometry, the patients were allocated into two groups, one with impaired and one with normal esophageal peristalsis. In both groups of patients ACT was significantly longer than in controls in supine position. Moreover, in patients with impaired peristals is the ACT was shorter when the trunk was elevated at 90° than when they were supine. ACT (mean \pm SEM, s) according to body positions are shown in the Table:

	Body position	ì	
	Supine	30°	90°
Healthy subjects	235 ± 41	302 ± 75	280 ± 84
Systemic sclerosis:			
with peristalsis	497 ± 42*	405 ± 74	310 ± 84
with impaired peristalsis	569 ± 34°	452 ± 61	357 ± 68#

Tukey test: $^{\bullet}P < 0.01$ vs healthy subjects; $^{\#}P < 0.05$ vs supine.

Conclusions: In systemic sclerosis, gravity plays a major role in esophageal ACT, its effect increasing the more esophageal motility is impaired. Thus, ACT measurements in the supine position may detect initial esophageal involvement in the disease.

2087

Serum Levels of Interleukin-2 and Interleukin-2 Receptors in Chronic Active Hepatitis Type C

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T-lymphocytes produced Interleukin 2 (IL-2) as well as IL-6, and IL-2 responsiveness intimately associated with the expression of a receptor for IL-2 (IL-2R) on the surface of the cells. Cytokines released by infiltrating T cells may contribute to the hepatic injury in chronic active hepatitis. The aim of this study was to compare serum levels of interleukin 2 (IL-2) and interleukin 2 receptors (IL-2R) in patients with verified chronic active hepatitis associated to hepatitis C virus infection, with those in healthy subject Twenty-two patients (8 female, 14 male, mean age 42.6) were included in this study. Eighteen age and sex matched control subjects were used as control. Serum IL-2 and IL-2R levels were measured by ELISA. Serum IL-2 levels were 64.81 \pm 22.49 in chronic active hepatitis, and 59.05 ± 16.91 in control subject. Serum IL-2R levels were 3148.64 \pm 3393.12 and 1168.49 \pm 486.04 in patients with chronic active hepatitis and controls respectively. Significantly higher levels of IL-2R was found in patients with chronic active hepatitis compared with controls (p = 0.003). In contrast, no difference was found for serum IL-2 levels between two groups (p = 0.144). Resting T cells do not express the form of IL-2R required for the transmission of a proliferative signal. It was known that the presence of high affinity IL-2R on stimulated but not on resting T cells. Altered cytokine homeostasis has been implicated in the pathogenesis of chronic active hepatitis. In addition, the relationship between cytokines and the finding in chronic active hepatitis type C should be evaluated in detail. Conclusions: This study suggests that serum IL-2R levels may be important and may play a role in the pathogenesis of chronic type C hepatitis.

2088

High Urinary Neopterin Levels in Familial Mediterranean Fever (FMF) Patients with Acute Attack

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Familial Mediterranean Fever (FMF) is a genetic disease of unknown etiology characterized by recurrent episodes of fever, polyserositis, and arthritis. An inflammatory reaction occurs during acute attack. Various studies suggesting an autoimmune etiology in FMF have been reported. Since the production of neopterine closely reflects activation of T-lymphocyte-mediated-immunity, we measured urine neopterine level in asymptomatic and symptomatic FMF patients. Thirty four asymptomatic FMF patients (15 female, 19 male, ages 17–53), and thirty eight patients (20 female, 18 male, ages 17–42) with acute

attack were included in this study. Fourteen age and sex matched subjects were used as control. Urinary neopterine was measured by High Pressure Liquid Chromatography (HPLC). Urinary neopterine levels were found to be significantly higher in patients with acute attack (228.37 \pm 57.66) (p < 0.01), but not in asymptomatic patients (146.53 \pm 93.47) (p > 0.05) comparing with the control subjects (136.94 \pm 57.66). Urinary neopterine levels were also significantly higher in FMF patients with acute attack than asymptomatic patients (p < 0.01). Neopterine is released from macrophages and monocytes following interferon-gamma stimulation, the latter being a product of activated T-lymphocytes. Thus, neopterin is a non-specific marker of T-cell activation. Neopterin measurements have been used for monitoring disease activity where there is activation of cellular immunity. Increased neopterin level in FMF patients with acute attack comparing to the asymptomatic patients and control subjects suggests that T-lymphocytes are activated in acute attack. Conclusions: this study shows that urine neopterin concentrations may be a marker of FMF disease activity, and further support the importance of activated T lymphocytes in the pathogenesis of FMF.

2089

Serum Levels of Interleukin-2 and Interleukin-2 Receptors in Familial Mediterranean Fever (FMF)

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Familial Mediterranean Fever (FMF) is disease characterized by recurrent episodes of fever, abdominal pain, polyserositis, and arthritis. Several acute phase reactants have been shown to be elevated in FMF patients. Tlymphocytes produced Interleukin 2 (IL-2) as well as IL-6, and IL-2 responsiveness intimately associated with the expression of a receptor for IL-2 (IL-2R) on the surface of the cells. In order to investigate the role of Interleukins in FMF patients, serum levels of IL-2 and IL-2R were measured. Twenty patients (13 female, 7 male, mean age 28.2) during asymptomatic period (group A), and acute attack (group B) were included in this study. Eighteen age and sex matched control subjects were used as control (group C). None of the patients were on colchine therapy during the study. Serum IL-2 and IL-2R levels were measured by ELISA. Serum IL-2 levels were 51.25 \pm 19.20 in group A, 54.90 ± 59.06 in group B, and 59.06 ± 16.91 in group C. Serum IL-2R levels were (1776.00 \pm 901.72), (26.37 \pm 1651) and (1168.89 \pm 486.04) in groups A, B and C respectively. There were not any statistical differences among groups A, B and C regarding serum IL-2 concentrations. But IL-2R levels were significantly increased in group B as compared to group A and group C (P < 0.05). Resting T cells do not express the form of IL-2R required for the transmission of a proliferative signal. It was known that the presence of high affinity IL-2R on stimulated but not on resting T cells. Although it has been suggested that FMF is an error of metabolism, the inducing mechanism of the acute attack is still unknown. Increase in IL-2R level in FMF patients with acute attack implied that T cells probably were activated during this period. Conclusions: this study suggests that IL-2R may have a role in the pathogenesis of FMF especially during acute attack, and supports the presence of immune regulatory disorders in patients with FMF.

2090

Serum CA 19-9 Levels in Patients with Pancreatic Cancer and Liver Cirrhosis

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CA 19-9 is a tumor marker especially used in the diagnosing and monitoring of pancreatic adenocarcinoma. However, elevated CA 19-9 levels were reported in various malign and benign diseases. In present study, serum CA 19-9 levels investigated in patients with pancreatic adenocancer and liver cirrhosis. Forty-five patients with pancreatic cancer, 70 patients with liver cirrhosis and 40 adult subjects were included in the study. Serum CA 19-9 levels were measured by FLISA and cut-off value was accepted as 55 u/ml (1.5 fold of upper limit). Serum CA 19-9 levels found elevated in 35 (77.7%) patients with pancreatic cancer, 31 (44%) patients with liver cirrhosis and 2 (5%) controls. The mean(\pm SEM) values were 174.1 \pm 24.6 u/ml in cancer group, 102.7 + 18.1 u/ml in cirrhosis and 14 + 2.2 u/ml in controls. The mean levels and elevation incidence of ca 19-9 in cancer patients were statistically significant compared to patients with cirrhosis and controls (p < 0.05). The difference between cirrhosis and controls were also statistically significant (p < 0.05). This results showed that CA 19-9 is valuable and has a high sensitivity for pancreatic adenocancer but benign disease such as liver cirrhosis limits its specificity. Conclusion: it is very important to bear in mind other conditions that can possibly cause to elevated CA 19-9 levels to avoid misinterpretations. The presence of a pre-existing liver cirrhosis should be excluded before the rise of CA 19-9 can lead to any conclusions.

2091

Is Oesophageal Manometry a Useful Test in the Evaluation of Adult Patients with Idiopathic Megacolon?

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Idiopathic megacolon embraces a heterogeneous group of disorders. The presence of oesophageal motor abnormalities in these patients may suggest

that the disease is not limited to the colon. Aim: To assess oesophageal motility in a series of consecutive adult Italian patients with long-standing idiopathic megacolon. Methods: In a 2-year period, we studied 11 patients (9 M, 3 F, mean age 40 yr, range 16-69) with longstanding megacolon (mean time since diagnosis 9 yr, range 2-22), whose symptoms, when present, started after the age of 10 yr. The maximal colonic width at double contrast barium enema was greater than 9 cm in at least one colonic segment; in three patients the rectum was also dilated. A mechanical obstruction of the colon, associated megaduodenum, and chronic dilatation of the small bowel were ruled out by barium radiology. Neurological, endocrine, metabolic and collagen diseases were excluded. None of the patients had travelled in countries where Chagas disease is endemic or taken drugs affecting gastrointestinal motility. One patient was mentally retarded. Oesophageal symptoms and bowel function were assessed by a questionnaire. Patients underwent oesophageal and anorectal manometry with water perfused catheters connected to a low compliance perfusion pump and external transducers. Results: All patients were troubled by distension and none reported dysphagia. Constipation was reported by five of them. Oesophageal peristalsis after wet swallows was impaired in four (36%); in three normal peristalsis was substituted by low amplitude-multiple peaked simultaneous contractions, and contraction waves in the distal oesophagus were undetectable in one; the amplitude of contractions was significantly lower in patients with impaired than in those with normal peristalsis (mean \pm SD: 24 \pm 25 vs 88 \pm 44 mmHg; P < 0.05). In two of the patients with impaired peristalsis the resting pressure of the lower oesophageal spincter was reduced, the post-deglutitory relaxation was undetectable, and the rectoanal inhibitory reflex was absent. In the remaining nine patients the function of the two sphincters was normal. Conclusions: Impaired oesophageal peristalsis is not uncommon in adult Italian patients with idiopathic megacolon. This suggests that in some subjects with idiopathic megacolon the disorder is not limited to the colon, and that a visceral neuromuscular alteration is likely. Oesophageal manometry could be used as a simple test to detect such an alteration.

2093

Spontaneous Chromosomal Fragility in Patients with Familial Visceral Myopathy with Megaduodenum

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Familial visceral myopathy with megaduodenum is a rare cause of intestinal pseudo-obstruction. The disease is transmitted as an autosomal dominant trait. However, linkage or cytogenetic analysis to map the responsible gene was not performed in the 17 families described so far. Aim: To verify the karyotype of the patients and to evaluate their frequencies of chromosomal aberrations as compared with those of age and sex-matched controls. Methods: Four patients from 2 unrelated families with the disease were studied. The patients in family 1 included a 31 yr woman (the proband, whose mother died at 52 yr of esophageal carcinoma) and her 48 yr old maternal uncle. The patients in family 2 were a 30 yr woman (the proband) and her 55 yr old father. Chronic obstructive symptoms were reported by the 2 probands. In all the patients, megaduodenum was observed at X-ray, and esophageal aperistalsis, a motor abnormality also associated with the disease, at manometry. A full thickness duodenal biopsy of proband 2 showed vacuolar degeneration and fibrosis of smooth muscle characteristic of the disease. Two unaffected family members (the 58 yr old father of proband 1 and 55 yr old mother of proband 2) as well as 3 unrelated healthy subjects (2 women, 1 man, 23, 24 and 40 yr) were also studied as controls. Cytogenetic analysis was performed on chromosomal spreads from 72-hr cultured peripheral blood lymphocytes. Chromosomal aberrations (CA), classified according to the ISHCN, were scored blindly on 200 metaphases for each subject. Mean and 95% confidence intervals (CI) are reported. Results: CA were significantly more frequent in patients than controls (19%; Cl 10 to 29% vs 3%; Cl 1 to 4% respectively; P < 0.01). The various classes of CA, expressed in % of total aberrations, are given for each patient in the Table:

Fam-Pat	Sex	Age	Chromatid-type (%)		Chromosome-type (%)	
			Gaps	Breaks	Breaks	Rearrangements
1-1	F	31	35	23	33	9
1-2	M	48	46	21	25	8
2-1	F	30	28	41	9	22
2-2	М	55	33	18	40	9

CA in controls consisted only of chromatid gaps and breaks. *Conclusions:* This is the first evidence suggesting that familial visceral myopathy with megaduodenum may be included among the mendelian chromosomal instability syndromes predisposing to cancer. Cytogenetic analysis may be useful for preclinical and non invasive diagnosis of the disease.

2094

Does Interferon Produce a Cardiotoxic Effect in Chronic Active Hepatitis Patients?

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Interferons are naturally occurring proteins with antiviral, antitumor and immune-modulating activities. Recently, cardiovascular complications have

A244 4th UEGW Berlin 1995

been reported in clinical trials of interferon. Most of the patients in this study however, had an advanced malignant disease and previous cardiac status of these patients had not been known. In this study, the cardiovascular side effects of recombinant interferon alpha (R-IFN-α) were prospectively studied in 13 patients with chronic active viral hepatitis (CAH) B and C. The cardiac status of all patients were evaluated and monitored with a detailed history. physical examination, electrocardiography, telecardiography, echocardiography and with heart rate variability tests at the beginning of the study and at the first and sixth months of IFN therapy. No cardiovascular disorder with the exception of hypertension in a patients was revealed before treatment. R-IFN- α at a dose of 4.5 mü for CAH-B and 3 mü for CAH-C was administrated thrice weekly for six months. Nine patients (6 CAH-B, 3 CAH-C) were completed the study. No significant changes have been detected in physical examination and cardiovascular tests of patients during and at the end of treatment. Although a small number of patients have been evaluated in present study, we concluded that IFN therapy can be used safely in CAH patients with no pre-existing heart disease. Beside that, cardiological monitoring of patients in high-risk for a cardiac disease is advised.

2095 HCV Infection and Related Risk Factors in 1552 Inpatients Representative of a General Population

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Aim: To evaluate the prevalence of anti HCV positivity and possible related risk factors in a hospitalized setting considered representative of the whole population, Setting: Department of Traumatology of Salò Hospital serving an area of about 45,000 inhabitants. Patients and Methods: 1552 consecutive inpatients, 912 men and 640 women with mean age 40.6 (range 1-93) and 69.8 (range 2-98) years respectively (p < 0.01). Anti HCV positivity was tested by RIBA II. Student's t and chi-square tests were used for statistical analysis. Results

Classes of age (yr)	Men		Women		p < Overall		
	n	%	n	%		n	%
<30	11/336	(3.3)	0/87	(-)	0.001	11/423	(2.6)
31–60	17/415	(4.0)	10/188	(5.3)		27/603	(4.5)
>60	4/161	(2.5)	33/365	(9.0)	0.001	37/526	(7.0)
	32/912	(3.5)	43/640	(6.7)		75/1552	(4.8)

Anti HCV positivity was higher in women than in men (p < 0.005) and increased with age (X^2 10.3, p < 0.05). Overall prevalence (4.8%) was significantly higher (p < 0.001) than the 1.1% observed in 2830 blood donors (1815 men and 1015 women, age 18-56 yr) from the same area. As compared to anti HCV negative cases, heroin addiction, concomitant HBsAg positivity and number of patients with increased AST and ALT levels were significantly higher in anti HCV positive patients (5.3 vs 0.9%, 9.3 vs 2.3% and 30.7 vs 5.5% respectively, p < 0.001 in all cases).

In about one third of the cases the source of infection was unidentifiable and in a further 10% current heroin addiction was in cause. Conclusions: Considering the natural history of chronic HCV infection, our data indicate that it represents a major epidemiologic problem in this part of Northen Italy.

2097

Efficacy of Azathioprine in Steroid-Resistant and **Steroid-Dependent Ulcerative Colitis**

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The therapeutic use of azathioprine (AZA) in ulcerative colitis (UC) is controversial. The outcome of 56 patients (M 39, F 17, mean age 34, range 14-65) receiving AZA for either steroid-resistant UC (10 patients - group A) or steroid-dependent (46 patients - group B), otherwise requiring surgery, was evaluated retrospectively. Patients were followed up for a mean of 29 \pm 17 (median 27) months. Twenty-four had left-sided colitis, 5 subtotal colitis, and 27 total colitis. The mean duration of disease was 51 months (range 2-192). At the beginning of AZA (time 0), all patients had a clinically severe disease according to a Truelove and Witts classification, and were on prednisolone 40 mg/day. AZA was used in addition to steroid therapy at a dosage of 2 mg/kg/day. The need for steroids, expressed as median cumulative steroid dose (MCSD), and the number of clinical relapses (requiring steroid therapy) in the two years before AZA treatment, were compared to those of the 3 years follow up on AZA. A positive response to AZA was defined as: a) avoidance of colectomy, and b) a significant decrease of MCSD and of clinical relapses (expressed as number/patient-year)

One patient in group A withdrew due to painful dyspepsia and 2 patients in group B were lost to follow up. Two out of 9 patients in group A, and 2 out of 44 patients in group B underwent colectomy after a mean period of 15 months and 24 months, respectively.

Year	-2	-1	0	1	2	3
Relapse (no/pt/yr)	1.40	2.25		0.34	0.32	0.33
MCSD	2035	3692		664	509	509
Off steroids (no)	0	0		33/53 (62%)	23/35 (66%)	18/26 (69%)

In conclusion, azathioprine is effective and safe in avoiding colectomy in

patients with steroid-resistant and steroid-dependent ulcerative colitis; its use decreases both steroid requirements and clinical relapses.

Role of Ultrasonography (US) in the Evaluation of **Activity of Ulcerative Colitis (UC)**

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So far the monitoring of UC activity relies on clinical, endoscopic and biochemical parameters. Although recent studies have suggested the potential usefulness of abdominal US in the diagnosis of UC, its role in current practice

We aimed to investigate the role of US in the evaluation of the severity and the response to treatment of UC.

We studied 20 consecutive patients (pts) (12 male) with mild and moderate-severe active UC before and after a short term course (2-3 months) of systemic steroid therapy. Pts with proctitis only were exlcuded from the study. Each pt underwent both US and colonoscopy, before and after treatment. US scans were obtained with a 3.5 MHz and a 7.5 MHz convex and linear probes (Aloka SSD-680). The maximum wall thickness (WT) observed, expressed in millimiters, was used as the US marker of activity. Disease activity was assessed by colonoscopy, Truelove index, ESR and CRP.

UC activity was mild in 6 pts and moderate-severe in 14 cases. There was a significant correlation between WT and clinical (P:0.0001), biochemical (r:0.7 for ESR and r:0.73 for CRP) and endoscopic (P:0.001) activity. After treatment 10 pts had a complete clinical and endoscopic remission (A group); the clinical and endoscopic score was unchanged in 6 pts (B group), slightly improved 2 pts (C group) and worsened in 2 pts (D group) respectively. In A group WT significantly decreased after treatment (7.8 \pm 1.9 and 5.2 \pm 1.1), while it remained unchanged in B group (7.5 \pm 1.9 vs 7.8 \pm 1.1). In the C and D group WT improved and worsened respectively. These WT variations were well correlated with ERS and CRP.

We conclude that US evaluation of WT may be a non invasive, simple and reliable tool in assessment activity and follow-up of UC.

2100 Two Weeks Treatment with Omeprazole and Various Omeprazole/Amoxicillin Combinations for Eradication of Helicobacter pylori

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In order to investigate the efficacy of omeprazole (OM) and various OM/amoxicillin (AM) combinations in Helicobacter pylori (Hp) eradication, 138 dyspeptic patients with Hp infection were studied. All patients underwent upper gastrointestinal endoscopy and three gastric biopsy specimens were taken from both antrum and corpus regions for histological examination and urease test. Hp infection was diagnosed when urease test was positive and characteristic Hp microorganisms were seen on histological examination. Patients were treated with either OM 2 \times 20 mg for 14 days (group 1, n = 15), or one of the following OM/AM combinations: OM 2 \times 20 mg/14 days + AM 4 \times 500 mg/1–8.days (group 2, n = 30), OM 2 \times 20 mg/14 days + AM 4 \times 500 mg/7–14.days (group 3, n = 29), OM 2 \times 20 mg/14 days + AM 4 \times 500 mg/-14.days (group 4, n = 30) and OM 2 \times 20 mg/14 days + AM 4 \times 500 mg/14 days (group 5, n = 34). Patients were controlled one month after discontinuation of the therapy and Hp eradication rates in the groups were found to be 0%, 0%, 31%, 43.3% and 64.7%, respectively.

The results of this study suggest that, 1.) two weeks therapy with OM alone or in combination with AM for the first week are ineffective in Hp eradication; 2.) administration of AM for two weeks together with OM gives higher eradication rates than the other treatment regimens, in which AM is given for a shorter time; 3.) pretreatment with OM does not appear to reduce the success rate of OM/AM combination therapy.

2103

Bone Mineral Density (DEXA) in Celiac Children and Adolescents Before and During Gluten-Free Diet

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Previous studies demonstrated a remarkable decrease of bone mineral content of the forearm in children with untreated celiac disease (CD). No data are available yet about the vertebral and whole body bone mineral density (BMD) in such patients

We assessed the BMD of lumbar vertebrae (L2-LA) and of total body with a dual energy x-ray absorptiometer (DEXA, LUNAR DPX-L, Madison, WI, USA) in 25 celiac children and adolescents at CD diagnosis (5 of them were also affected by insulin dependent diabetes mellitus), in 15 after 6 months of glutenfree diet (GFD) and in 12 after 12 months of GFD. The mean age at diagnosis was 8.8 ± 5.7 years, 13 girls and 12 boys. Diagnosis has been made according to ESPGAN criteria. None of the patients needed calcium or vitamin D supplementation during the study. BMD was also measured in 103 healthy control children and adolescents (mean age 11.0 \pm 5.3 year, 44 girls and 59 boys). BMD is expressed as g/cm². Multiple regression analyses for the comparison between CD patients and controls were done: BMD was considered

A245 4th UEGW Berlin 1995

the dependent variable, sex and CD were the independent variables and age was the confounding one.

BMD difference between diabetic and non-diabetic CD patients was not significant ($\beta = 0.106$, P = 0.1). Lumbar spine BMD was significantly reduced in CD patients both at diagnosis ($\beta=0.096, P=0.003$), and after 6 months of GFD ($\beta=0.104, P=0.008$), as it was in total body BMD ($\beta=0.078, P=0.008$). = 0.002 at diagnosis and β = 0.083, P = 0.003 at 6 months of GFD). After 12 months of GFD no significant differences in BMD were observed both in spine ($\beta = 0.062$, P = 0.15) and in whole body ($\beta = 0.041$, P = 0.17).

Our data indicate that osteoporosis complicates celiac disease during childhood and adolescence both in spine and in total body and GFD alone is able to remarkably improve bone mineralization. Complete recovery of BMD does not occur as rapidly as other nutritional parameters, but it requires longer time of GFD.

2106

Effect of Morphine on Oesophageal Motility: A Clue to its Antipropulsive Action?

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Morphine has been shown to inhibit propulsion in the gastrointestinal tract of various species. The target neural pathways and the receptors through which morphine exerts its action have not been fully clarified. In the oesophagus the motor response to intraluminal distension is considered to be primarily controlled by the enteric nervous system, whereas the one to swallowing is initiated centrally. The aim of our study was therefore to investigate the effect of morphine on the oesophageal response to swallowing and oesophageal distension in 8 healthy volunteers (aged 19-25 yr; 5 men), and to evaluate whether these effects are mediated by opioid receptors.

Methods: motility in the pharynx, oesophageal body at 2, 8 and 14 cm above the lower oesophageal sphincter (LOS), LOS with a sleeve and stomach was recorded during three sequential 30 min periods, basal, after i.v. morphine (100 μ g/kg) and after i.v. naloxone (80 μ g/kg). An assembly incorporating a balloon placed 11 cm above the LOS was used. Eight water swallows and two series of 30-s distensions at 4, 6, 8 and 10 ml were performed in each period. Non parametric ANOVA was employed in the analysis

Results (median; IQ range): after swallows morphine almost doubled velocity of peristalsis and decreased duration and magnitude of LOS relaxation. During distensions it markedly increased contractile activity in the body below the balloon and decreased LOS relaxation, especially at 8 and 10 ml. All effects were blocked by naloxone.

		Basal	Morphine	Naloxone
Swallows	Perist. vel (cm/s) LOS relax (%)	2.9; 2.1–3.8 87; 82–95	5.0; 3.3–5.6° 63; 44–67.	3.2; 2.2–3.4 95; 81–98
Balloon distensions (10 ml)	Above balloon [#] Below balloon [#] LOS relax (%)	201; 12–264 1; 1– 18 88; 80– 95	158; 144–221 58; 37– 95* 65; 40– 84*	143; 118–171 26; 6– 49 100; 64–100

[#]mmHg/30 s; *p < 0.05 vs basal and naloxone

In conclusion, (1) the motor effects of morphine in the human oesophagus are mediated by opioid receptors. (2) the action of morphine on motility induced by oesophageal distension suggests the enteric nervous system as a site of action, and its interference with the inhibitory response below the distending balloon may represent at least one of the mechanisms responsible for its antipropulsive effect.

2110

Endoscopy Nd-YAG Laser Therapy in Inoperable Colorectal Carcinoma

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Aim of our study is to estimate the effectivemness of Nd-YAG laser therapy in retrospective analysis of 22 consecutive patients (9 females, 13 males, mean age 77.5 years), treated for palliation of colorectal carcinoma between January 1991 and January 1995. The indications for palliative chose were: extensive local progression or distant metastases, general inoperability, age and local relapse on surgical anastomosis. 14 patients (63%) had persistent bleeding and 8 (36.4%) had obstruction. The carcinoma was located in the rectum in 17 (77%) patients, in the colorectal junction in 3 (14%) and in 2 (9%) patients was on colorectal surgical anastomosis. Seven (32%) patients were affected by constricting tumor, 12 (54%) by polypoid-ulcerative tumor and 3 (14%) by ulcerative infultrative tumor. We used a Nd-YAG laser of 1064 nn wave length and 1 to 100 W power output with non contact fibers. We usually began the treatment at the proximal edge; 2 patients needed a dilation before therapy.

The mean number of sessions was 3.6; the mean energy for session was 3569 J (range 450-10200). Seven on 8 patients were relieved of obstruction symptoms; one needed colostomy. Laser was successfull in arresting macroscopic bleeding in all other 14 patients. There were no laser related complications. The mean survival was 10 months. Conclusions: 1) Nd-YAG laser therapy was effective in palliating both obstruction and bleeding of inoperable colorectal carcinoma. 2) Laser therapy may improve the quality of life avoiding colostomy. 3) Laser therapy is safe and may avoid the hospital admission of the patient

2112

Evaluation of a New Rapid Immunodiagnostic Assay for H. pylori Antibody Detection: Serological and **Histopathological Correlations**

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Helicobacter (H) pylori infection is known to elicit a specific systemic antibody response and detection of serum IoG represents a non-invasive method for the diagnosis of H pylori infection. The aim of our study was to evaluate sensitivity and specificity of a new rapid enzyme immunoassay for the detection of IgG to H pylori in human serum and plasma.

Seventy-eight consecutive outpatients (mean age ± SD: 54 ± 11, 33 M, 44 F) with gastrointestinal complaints were evaluated. All patients had upper endoscopic examination. Two biopsy specimens were taken from the antrum and the body of the stomach and 2 from cardiasic region. Biopsies were stained with H&E for routine histology and with modified Giemsa for H pylori identification. Before endoscopy, blood samples were taken and sera were tested using ImmunoCard H pylori (Meridian Diagnostics Europe, Mi, Italy).

Results. When compared with histology, the sensitivity and specificity of the assay were 91.6 and 98.2% respectively. False negative results were confirmed also by a quantitative in-house ELISA. The only false-positive was a patient with type A gastritis.

Conclusion. Our results show a very high sensitivity and specificity for the detection of IgG to H pylori in human sera for this new rapid serologic assay. Such an accurate, unexpensive, rapid and easy-to-use method may represent a first choice test for qualitative H pylori determination in epidemiological and screening studies.

2113

Gastroesophageal Reflux (GER) in Asthmatics

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To study the association between GER and asthma, and the aspiration of gastric acid in the respiratory tract in triggering bronchospasm, we performed 24-hour esophageal pH-monitoring in 25 asthmatics. A dual pH probe was placed 5 and 20 cm above LES. Results were compared with those of 14 patients with typical reflux symptoms (heartburn, regurgitation) and 16 control subjects. GER was definied by esophageal pH < 4, and the results were expressed by the number of GER episodes, number of GER episodes longer than 5 min, and the percentage of time with pH < 4.

	n° GER eps.		eps. >	eps. > 5 min		< 4	
	prox	dist	prox	dist	prox	dist	
Controls	6.5	31.2	0.06	0.5	0.43	1.8	
Asthma	14.1	56.2	0.54	2.9	1.35	6.7	
Heartburn	17.4	70.8	0.62	4.1	1.21	7.8	

Asthmatics and heartburn patients showed significantly longer % time GER in both distal (p < 0.05 and p , respectively) and proximal (p< 0.05, p < 0.05) esophagus, in comparison to control subjects. No significant difference between patients with respiratory and esophageal symptoms was recorded. Pathologic GER was present in 13 patients with asthma (52%) and in 9 with reflux symptoms (64%) in the distal esophagus, and in 8 patients with asthma (32%) and in 6 with reflux symptoms (43%) in the proximal esophagus.

In conclusion, our data show that abnormal GER is present in many asthmatics, but do not support the theory that proximal acid exposure, leading to aspiration due to close proximity to the respiratory tract, is more common in patients with pulmonary symptoms since no difference was observed in comparison to patients with typical esophageal symptoms.

2115

Reflux Esophagitis: Relationship Between Endoscopy and 24 Hours Gastroesophageal pH Monitoring

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Gastroesophageal reflux disease (GERD) encompasses a wide spectrum of disorders in which gastric refluxate causes symptoms and/or damage of esophageal mucosa. The pathogenesis of GERD is multifactorial and several mechanism are involved including: a) an incompetent anti-reflux barrier, b) an abnormal acid clearance, c) noxious effect of refluxate, d) and the resistance of esophageal mucosa. The esophageal exposure to acid seems to be the major determinant in the pathogenesis of reflux esophagitis (RE). Aim of this study was to evaluate the correlation between the parameters of 24 hr gastroesophageal monitoring and the degree of esophageal injury. Three-hundred and eighteen patients (191 males, mean age 48.3 yrs, range 14-72) suffering from typical symptoms of gastroesophageal reflux and endoscopic evidence of esophagitis (grade I° 97 pts, grade II° 181 pts, grade III° 40 pts according to Savary-Miller classification) underwent to simultaneous 24-hr esophageal and gastric pH monitoring using standard techniques. The following parameters were analyzed: total percentage of time pH < 4, percentage of time with pH < 4 in the upright (U) and supine (S) position, number of reflexes >5 min. An esophageal manometry was also performed in 190 patients. The Wilcoxon matched-pairs signed rank test was used for statistical A246 4th UEGW Berlin 1995

analysis. The correlation between RE and the pH parameters is showed in the table:

 $pH < 4 (mean \pm SD)$

	Grade I°	Grade II°	Grade III°	р
Upright	7.7 ± 1.4	10.4 ± 2.1	12.6 ± 4.7	ns
Supine	5.3 ± 1.8	18.6 ± 3.4	33.7 ± 2.7	< 0.05
Total	8.7 ± 2.1	16.3 ± 2.5	32.5 ± 3.7	<0.005

Refluxes >5 min were recorded in a larger proportion of grade II° and III° of pts (60 to 85%) as compared to grade I° pts (45%). Also a hypotensive LES and peristaltic contractions of lower amplitude were more frequently associated with severe esophagitis.

Conclusions: There was a good correlation between endoscopic classification of RE and pH parameters of acid reflux, especially in the supine position. Severe esophagitis was also associated with an impaired motility pattern.

2117

Colorectal Cancer in Slovenia: An Epidemiology Study

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Estimates of the crude and age-standardized incidence rate by sex of colorectal cancer in north-eastern part of the Republic Slovenia. We were interesting in diagnostic procedure, which brought us to diagnose, in symptoms and signs of disease, which were bringing along the patients to a doctor and the more popular method of therapy in our hospital. We have tried to find out also the most common type of colorectal cancer by Dukes classification.

2118 Long-term Effect of Anti-Helicobacter pylori Therapy on Gastric Malt Lymphoma. Histological and **Molecular Evaluation of 15 Cases**

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Histological regression of gastric low grade MALT lymphoma (ML) after eradication of Helicobacter pylori (H. pylori) infection has been reported. To assess the long-term efficacy of the antibiotic therapy, fifteen patients (7 females, age 34-76) with a diagnosis of gastric ML stage IE associated to H. pylori infection underwent anti-H. pylori therapy and bioptic follow up for 11-44 months (mean follow up 23 months). At each sampling, histological evaluation and PCR for immunoglobulin heavy chain gene rearrangement were performed.

H .pylori was eradicated in 14 cases and histological remission was found in 13 cases 2 to 4 months after the eradicating therapy. All the 13 cases with histological regression of lymphoma are free of disease and reinfection 8-30 months after eradication of H. pylori (mean 18 months). Monoclonality was demonstrated in 10 of the 13 cases with histological remission. Disappearance of PCR detected amplification bands following eradication of H. pylori was demonstrated in 6 cases and was synchronous to histologic remission in 4 of them whereas monoclonality persisted for 9 and 24 months in absence of histological evidence of lymphoma in the remaining 2. Monoclonality persists 13-27 months after eradication and histological remission in 4 cases.

The eradication of H. pylori induced a quick and persistent histological remission in 93% of cases. The molecular regression of ML seems to be much slower than the histological one.

2119

The Behaviour of Serum Procollagen III (sPIIIP) in Wilson's Disease

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The authors report an increased serum concentration of the procollagen III end-peptide in 12 patients with Wilson's Disease.

The increase seems to be associated with the hyperfibro-genetic activity of the liver in these patients and it is therefore hypothesized that the excessive copper accumulation which characterises the disease may play a precise role in indicing hepatic fibrosis. Copper is in fact an important co-factor of lysyl-oxidase, a cuprodependent enzyme, fundamental for the production of collagen fibres and consequently, for the formation of connective tissue.

To support this hypothesis, besides the intense hepatic fibrosis revealed by the histomorphological examination of the liver, a high rate of feebly alburnin linked plasmatic copper was observed, both in the subjects receiving penicillamine treatment and in the untreated subjects. It follows that the metal which is constantly present in high quantities, not only deposits it self passively in the various organic areas but is capable of inducing an increase in lysyl-oxidase activity, thus promoting collagen synthesis, especially at hepatic

In conclusion, the authors propose to use the sPIIIP as a marker to monitor the fibrogenetic activity of the liver in patients with Wilson's Disease.

Antiendomysium Antibody Determination for Coeliac Disease in Children

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Many attempts have been made to find precise screening tests for coeliac disease in order to reduce the need for biopsy or to achieve better selection criteria before intestinal biopsy. The aim of the 18-month study was to examine the usefulness of screening for antiendomysial antibody (EMA) in the diagnosis of coeliac disease in children. The research was carried out by an indirect immunofluorescent test on 355 serum samples of children with various gastrointestinal disorders in the age range 7 months to 18 years. 63 (17.7%) out of the total 335 were found to be positive for serum IgA class endomysial antibody. They included 40 (11.2%) strong positives, 10 (2.8%) positives, and 13 (3.7%) weak positives. All children with positive EMA had small bowel biopsy performed. In all children with strong positive EMA, severe villous atrophy was established (18 children were untreated, 20 were undergoing gluten challenge and 2 had Dermatitis herpetiformis). All 10 children with positive EMA had a diagnosis of coeliac disease (8 had a moderate villous atrophy, 2 partial villous atrophy).

5 children with weak positive results did not have coeliac disease, small bowel mucosa was normal or had partial villous atrophy consistent with nutritive allergy; others had coeliac disease. This study confirms a strong association between antiendomysial antibodies and coeliac disease.

However, not all patients with positive antibodies had coeliac disease. Small bowel biopsy remains the golden rule for the diagnosis of coeliac disease.

2121

Octreotide vs. Terlipressina in Association with **Endoscopic Sclerotherapy in the Treatment of Variceal Bleeding in Cirrhotics**

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Bleeding from esophageal varices is the most common and dramatic cause of death in cirrhotics. Endoscopic sclerotherapy is a treatment able to stop bleeding in about 90% of patients and, perhaps, to improve survival. Early rebleeding, occurring in the first week after sclerotherapy in 60% of cases is now the main problem. Aim of our work is to compare the action of two drugs, Octreotide or Terlipressina, in association with sclerotherapy in the first seven days, after bleeding and to evaluate their effect on early rebleeding and on one-month mortality rate. From 01.12.93 to 01.12.94, 40 cirrhotics with active variceal bleeding have been in our Department. Once vital signs had been stabilized and always in the first 12 hours, patients were submitted to sclerotherapy and then divided in two groups of twenty, omogeneous for age, sex, etiology and Child-Pugh's score. Group A was treated with Octreotide bolus and then in continuous infusion was given for 24 hours, then 0.1 mg s.c. t.i.d. for seven days. Group B was treated with Terlipressina 2 mg. i.v. every 4 hours on day 1, 2 mg i.v. every 6 hours on day 2 and then 1 mg i.v. every 6 hours from day 3 to 7 was given. All the patients received transdermic TNT 20 cm for 7 days. 4 patients from group A and 5 from group B dead, and seven from group A and eight from group B rebled.

There are not statistically significant differences, but our results show a positive trend on mortality and rebleeding in respect to sclerotherapy alone.

2126

H. pylori Eradication Rates in Patients with Autoimmune Diseases and with Dyspepsia

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Infection by H. pylori has been associated to the development of gastric Mucosa Associated Lymphoid Tissue (MALT) lymphoma. It is known that patients with autoimmune diseases such as Sjögren's syndrome often report unspecific dyspeptic symptoms sometimes attributed to a coexistent "chronic gastritis". Furthermore, it has been shown (NEJM 329: 172) that they appear prone to develop various MALT lymphomas. It is whether H. pylori is involved in the pathogenesis of these findings. A potential clue could come from the response to the eradication treatment in infected patients. In this study we compared the response to standard H. pylori eradication treatment (omeprazole 40 mg/day plus amoxacillin 2 g/day for two weeks) in patients with Sjögren's syndrome or with dyspepsia. Diagnosis of infection was done by histology and the urease test. Results: Of 9 patients with Sjögren's syndrome only one was eradicated by the treatment (11%) as opposed to an eradication rate of 72% in dyspeptic controls (n = 25). Of the patients belonging to the first group only two (including the one eradicated) were using corticosteroids. Conclusions: Patients with Sjögren's syndrome infected with H. pylori appear much more resistant to the eradication treatment than dyspeptic controls. It is possible that this phenomenon may reflect a gastric microenvironment more favorable to H. pylori survival in these patients. Alternatively, it may reflect a defect in the immune mechanism involved in the relationship host-pathogen. If confirmed in a larger series, this phenomenon could have

potential implications for the higher incidence of MALT lymphomas observed in patients with Sjögren's syndrome.

2127

IgA and IgG Class Antineutrophil Cytoplasmic Antibodies in Inflammatory Bowel Disease. A Study on **Estonian Patients**

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Antineutrophil cytoplasmic antibodies with perinuclear immunofluorescence staining (pANCA) are frequently found in ulcerative colitis (UC) but more rarely in Crohn's disease (CD), their pathophysiological significance being still unclear.

The aim of the study was to examine the prevalence and pattern of ANCA and the distribution of IgA and IgG class in patients with IBD.

We studied 56 sera of the patients with UC (25 M, 31 F; mean age 43.3 years) and 9 with CD (7 M, 2 F; mean age 28.2 years). Sera were analyzed for the presence of ANCA by the indirect immunofluorescence on ethanol-fixed neutrophils using either fluorescence labelled anti-lgG or anti-lgA

IgG ANCA was detected in 29/56 (52%) patients with UC and 3/9 (33%) patients with CD whereas IgA ANCA was detected in 17/56 (30%) patients with UC and 1/9 (11%) with CD. 13 patients with UC had the combination of IgA and IgG ANCA and 1 patient with CD had both types of antibodies. ANCA in UC patients was predominantly pANCA, but at the same time, ANCA with cytoplasmic pattern (cANCA) was also detected. We found IgG cANCA in 8 UC and 1 CD cases and IgA cANCA in 6 UC cases. There was no relationship between ANCA and the duration or extent of the disease.

We confirmed the high prevalence of IgG ANCA among UC patients in Estonia. However, also a significant number of UC patients with IgA ANCA was revealed. The ANCA pattern in UC is predominantly cytoplasmic perinuclear. The autoantigenic target for ANCA in UC needs to be determined in further

2129

Gastroesophageal Reflux and Cow's Milk Allergy: Evidence of a Close Relationship in Infants

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Recent reports have suggested that gastroesophageal reflux (GER) in pediatric patients may be secondary to food allergy. The aim of our study was to determine the frequency of the association between GER and cow milk protein allergy in patients in the first year after birth. We studied 204 consecutive patients (median age 6.3 months), who had been diagnosed for GER on the basis of 24-hour continuous pH-monitoring and the histological picture of the esophageal mucosa. Clinical history suggested a suspected diagnosis of cow milk allergy in 19 infants, while a further 93 had positive tests (serum lgG antilactoglobulin, Prick tests, circulating or fecal or nasal mucus eosinophils) but did not present symptomatology indicating cow milk allergy. Histology of the intestinal mucosa was evaluated before and 24 hours after cow's milk challenge to confirm or exclude the diagnosis of cow's milk allergy. The cow's milk-free diet and 2 successive "blind" challenges confirmed the diagnosis of cow milk allergy in 85 out of 204 patients with GER. The clinical presentations of the infants with GER + cow milk allergy and of those with GER only were different, in view of the greater frequency of diarrhea (p < 0.0001) and atopic dermatitis (p < 0.0002). In total, GER was associated with, and probably secondary to, cow milk allergy in 85/204 case (41.8%). Considering the frequency of this association patients less than 12 months old presenting symptoms of GER should be carefully examined to determine whether this disorder is primary, or rather, secondary to cow milk allergy

2130 Ulcerative Colitis and Genetic Markers

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There are three basic approaches to define the genetic susceptibility to inflammatory bowel disease: family epidemiolody, subclinical markers, and ge-

We have studied the peculiarities of the HLA-system antigen distribution among patients with ulcerative colitis (UC) in the Ukrainian popular

The identification of the main complex-antigens of histocompatibility was being carried out in microlymphocytotoxic test according to Terasaky by means of the panel of histotyping sera from the Sanct-Peterburg Scientific Research Institute of Hematology and Blood Transfusion discovery 39 specificities of A, B and C loci. The lymphocytes discharged from the periphepic heparinized venous blood served as the material of investigation.

An increased frequency of HLA B5 was noted in 43 of 107 UC patients (40%) compared with 66 of 282 healthy donors (11%) (p less then 0.0001, relative risk — 5.4). An increased frequency of HLA B51 was noted in 25 of 107 UC patients (23%) compared with 8 of 282 controls (3%) (p less 0.0001, relative risk - 9.98). The positive association was discovered between

indicated antigens and pseudopolyposis in patients with UC and high levels of humoral immunity.

Identifying the genes for UC should provide an answer to the question as to how genes designed for immunoprotection can go awry to lead to clinical disease, such understanding should provide new approaches to therapy and disease prevention.

2131

Circulating Intercellular Adhesion Molecule-1 in Patients with Hepatocellular Carcinoma

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Elevated serum levels of circulating soluble intercellular adhesion molecule-1 (sICAM-1), a ligand for lymphocyte function associated antigen-1, has been reported in hepatocellular carcinoma (HCC), and it has been suggested that they can play a role in tumor cell proliferation. In this study we measured serum levels of sICAM-1 (Bender-Med Systems, Vienna, Austria) in a group of patients with HCC-associated liver cirrhosis, and compared them with a group of cirrhotic patients and a control group. We also correlated sICAM-1 values with some biochemical parameters of liver function. Moreover, an immunohistochemical localization of ICAM-1 was carried out on liver tissue sections of patients with HCC. Levels of siCAM-1 were significantly higher in patients with HCC than controls (p < 0.0001), but not than the cirrhotic group (p = 0.06). A positive correlation was found between siCAM-1 values and ALT, Bilirubin, AP and GT serum values (p < 0.05), whereas a negative correlation was found with albuminemia values (p < 0.05). No correlation was found with alpha-feto protein values, but higher values ICAM-1 were found in HCC patients with large tumor size (>5 cm) than with small tumor size (<3 cm) (p < 0.01). Immunohistochemical localization showed no reaction for ICAM-1 of the hepatocytes in normal liver, while a positive membrane staining was observed on hepatocytes of HCC tissues. In conclusion these results suggest that high serum levels of s-ICAM-1 are associated with severe liver disease (such as LC and HCC), and that they tended to increase with deteriorated hepatic function, like in advanced HCC. Release from both activated lymphocytes and malignant hepatocytes can contribute to the high serum levels of the HCC group.

Effect of Omeprazole, Clarithromicin and Amoxicillin for a Short Time on Helicobacter pylori Eradication

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Aim of the study: To evaluate the efficacy, tolerability and compliance of a triple therapy with Omeprazole and amoxicilin plus clarithromicin for a short term in patients with antral gastritis and Helicobacter pylori (HP) infection.

Methods: 51 patients (30 males, 21 females, age range 18-79) with idiopathic dispapdia and antral gastritis with HP infection were recruited to a multicenter trial study. They were endoscoped before and two months after the end of treatment. HP was sought by biopsy urease test and histology of antral and corpus biopsies. Eradication was definited as all tests negative at the final endoscopy. The patients were treated for a week with Omeprazole 20 mg BID, Amoxicillin 1 gr BID, Clarithromicin 250 mg BID.

Results: At the endoscopy after two months HP was found in 8 patients (16%). The eradication was therefore reached in 43 patients (84%)

Conclusion: It is concluded that a one week administration of triple therapy with O meprazole, Clarithromicin and Amoxicillin is effective and well tolerated for the eradication of HP infection.

2134

Effect of Roxatidine and Amoxicillin Plus Tinidazole on the Eradication of Helicobacter pylori in Duodenal **Ulcer Patients**

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Persistent infection with Helicobacter pylori (HP) is associated with the recurrence of duodenal ulcer. The aim of this study is to investigate the eradicative effect of a triple therapy with roxatidine and amoxicillin plus tinidazole in patients with duodenal ulcer and HP infection

Methods: We treated 36 patients (22 males, 14 females, age range 23-59) with amoxicillin 1 gr BID plus tinidazole 250 mg BID gived orally for 15 days. All patients received roxatidine 150 mg BID for 15 days and 150 mg UID for 4 week. They were endoscoped before and 4 week after the end of treatment. HP was sought by biopsy urease test and histology of antral and corpus biopsies. Eradication was definited as all tests negative at the final A248 4th UEGW Berlin 1995

Results: 2 patients discontinued treatment because of side effects; HP was eradicated in 30/34 patients (85%).

Conclusion: In this study, the triple therapy with roxatidine and amoxicillin plus tinidazole is effective to improve the eradication of HP from gastric mucosa in duodenal ulcer patients.

2136 Patients with Diffuse Esophageal Spasm Show an **Abnormal Esophago-Cardiac Inhibitory Reflex**

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The esophagus may be involved in the genesis of some cardiac arrhythmias, spontaneous (i.e. "swallow syncope") or induced by strumental manipulations, including esophageal balloon dilatation used to reproduce angina-like chest pain. To investigate the mechanisms of these esophago-cardiac reflexes, we recorded in 8 normal subjects (N) and 10 patients with diffuse esophageal spasm (DES), the ECG during an esophageal manometric examination and measured the variations of RR intervals induced by dry swallows. swallows of solid boluses (bread) and intraesophageal balloon inflation at 100 mmHg for 10 sec. The percent variation of the RR interval of ECG from its mean basal value to its highest or lowest value observed after stimulation was calculated in both groups.

Results (%: mean ± SD):

Group	Dry swallows	Solid swallows(§)	Intraesophagea		
balloon			inflation	deflation	
N	-15 ± 5 [†]	$-8 \pm 4^{\dagger}$	+8 ± 3 [†]	+16 ± 7 [†]	-9 ± 5 [†]
DES	-14 ± 10	$-5 \pm 2^{\dagger}$	+ 16 ± 4 [†] *	$+29 \pm 8^{\dagger *}$	-5 ± 4

 $^{\circ}p<0.05$ versus the corresponding value of group N; $^{\dagger}p<0.05$ versus basal period; § biphasic response.

Comment. 1) Dry swallows induced a brief increase in heart rate. 2) solid swallows induced an increase in heart rate followed by a decrease, significantly more marked in DES group, 3) balloon inflation induced a decrease in heart rate significantly more intense in DES group, while balloon deflation was followed by a significant increase in heart rate in group N. In conclusion. the esophageal wall distension, either due to solid bolus or balloon inflation. elicits an inhibitory esophago-cardiac reflex that is more intense in patients with DES and might induce cardiac arrhythmias in predisposed subjects.

2138 Effect of Omeprazole on Interdigestive Gastroduodenal Motor Activity in Man

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Background. As acid secretory activity fluctuates with the same rhythm as gastroduodenal motor activity during the interdigestive period, we investigated the relationship between these two cyclic activities. Methods. In 9 normal subjects the interdigestive gastroduodenal motor activity and the intragastric pH were recorded after an overnight fasting by means of a manometric and pH-metric apparatus. Thirty minutes after the second phase 3 of the Migrating Motor Complex (MMC) recorded during saline administration, omeprazole (OME) was administered intravenously at a dose of 20 mg. Results. A typical gastroduodenal phase 3 with a duration of 4.5 sec \pm 1.2 (m \pm SD) in the stomach and 6.6 \pm 1.9 in the duodenum, appeared 19.5 min \pm 7.9 after OME administration, significantly before its expected occurrence. In fact the length of MMC cycle OME-related was 53.7 min \pm 7.4 (m \pm SD) and that of the spontaneous MMC cycle was 88 min \pm 16 (p < 0.01). The amplitude and frequency of antral pressure waves of the period from the end of OME administration to the beginning of phase 3 (67.8 mmHg \pm 12 and 9.1 waves/min ± 2.1, respectively) were not significantly different from those of a period of same length preceding the spontaneous phase 3 (63 mmHg \pm 8.6 and 8.4 w/min \pm 2.6, respectively), but were significantly (p < 0.001) different from those of a corresponding period starting 30 min after a spontaneous phase 3 (40 mmHg \pm 10.9 and 5.18 w/min \pm 1.5, respectively). The intragastric pH before OME administration (2.1 \pm 0.35) showed a significant increase just before the beginning of the gastric phase 3 following OME administration (2.6 \pm 0.3) and continued to increase up to the end of recording (5.1 \pm 1.01), while during the spontaneous MMC cycle it did non vary significantly. Conclusion. The fact that the block of gastric acid secretion is followed by the appearance of a typical gastroduodenal phase 3 suggests that the acid secretory activity may have some influence on the cyclic motor activity of the gastroduodenal tract.

2139

Levamisole Plus 5-FU vs Levamisole in Elderly Patients with Resected Colon Carcinoma: A Meta-analytic Study

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Levamisole is an efficacious anthelminthic drug that is used to improve monocyte and T-cell functions after chemotherapy-induced immunosuppression. Thus, levamisole is used as an adjuvant agent after surgical resection of several cancers. In our meta-analytic study we analyzed a total of 880 patients affected by colorectal carcinoma (Dukes B2, C). 440 of them were treated with combination therapy (5-Fluorouracil plus levamisole), while the remaining 440 were treated with levamisole alone. We applied Mantel-Haenszel-Peto method to the data based on 12, 24, 36, 48 months survival rates. Our results

- Meta-analysis at 12 months: Overall Odds Ratio (O.R.) = 0.734 (Confidence Interval = 0.448-1.205) Mantel-Haenszel-Peto Chi Square = 2.246
- Meta-analysis at 24 months: Overall Odds Ratio (O.R.) = 0.858 (Confidence Interval = 0.614-1.198) Mantel-Haenszel-Peto Chi Square = 1.26
- Meta-analysis at 36 months: Overall Odds Ratio (O.R.) = 0.604 (Confidence Interval = 0.453-0.807) Mantel-Haenszel-Peto Chi Square = 2.08
- Meta-analysis at 48 months: Overall Odds Ratio (O.R.) = 0.674 (Confidence Interval = 0.511-0.888) Mantel-Haenszel-Peto Chi Square = 7.34

Our study showed that in surgically resected colon cancer, adjuvant combination therapy with 5-FU plus levamisole improved survival rates during long-term treatment. The results may justify the use of levamisole as an adjuvant agent in chemotherapy for resected colorectal carcinoma.

2141

Folinic Acid + 5-FU vs 5-FU Aloe in Elderly Subjects with Advanced Colorectal Carcinoma: A Meta-analysis

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Many doubts surround the numerous forms of medical treatment of advanced colorectal carcinoma in elderly subjects. Our study aim was to reach more reliable conclusions on the real efficacy of two of these treatments: folinic acid (FA) + 5-fluorouracil vs 5-fluorouracil (FU) alone. We examined 9 randomized studies with a total of 1215 patients, 660 of whom were treated with combination therapy, while the remaining 555 were treated with 5-FU alone. We applied the Mantel-Haenszel-Peto method to the data we extrapolated based on the 6 months, 12 months, 18 months and 24 months survival rates reported by the authors.

The following results were obtained.

- Meta-analysis at 6 months: Overall Odds Ratio (O.R.) = 0.796 (Confidence Interval = 0.615-1.031). Mantel-Haenszel-Peto Chi-square = 11.4719.
- Meta-analysis at 12 months: Overall Odds ratio (O.R.) = 0.69 (C.I. = 0.544-0.874). Mantel-Haenszel-Peto Chi-square = 15.107.
- Meta-analysis at 18 months: Overall Odds ratio (O.R.) = 0.831 (C.I. = 0.635-1.089). Mantel-Haenszel-Peto Chi-square = 19.882.
- Meta-analysis at 24 months: Overall Odds ratio = 0.849 (C.I. = 0.617-1.169) Mantel-Haenszel-Peto Chi-square = 10.4909.

The results showed that in advanced colorectal carcinoma survival was not significantly improved by combination therapy. However, since overall survival was not improved by combination therapy, evaluation of quality of life could play an important role in the final analysis of our study.

2146

Factors Associated with Malignant Transformation of Colorectal Adenomas

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The aim of this study was to evaluate whether the size, histology, localization and finding of multiple colorectal adenomas influence on the frequency of appearing high degree dysplasia and invasive carcinomas.

Material: We analyzed 194 polypuses in 99 patients (mean age 49 \pm 10). Methods: We used Morson's classification for histological and Kozuka's for citological analyses. For statistical analyses we used descriptives (frequencies, grades, cross-tabulations), and analytical methods (Cruschal-Wallis).

Results: Percentage of malignisation was 7.2% in all polypuses. Degree of malignisation in adenomas with size to 10 mm, from 11-20 and over 20 mm, was, as follow: 1.62%, 13.04% and 27.22%. According to localization, they were eliminated: 62.3% from rectum and sigma, 16.3% from left and 21.43% from the right colon. All malignant adenomas found were tubular. The results show that there is correlation between size and degree of cell's dysplasia (p < 0.01), histology and degree of cell's dysplasia (p < 0.0001) and that there isn't correlation between: finding of multiple adenomas and degree of cell's dysplasia (p > 0.05) and localization and degree of cell's dysplasia (p > 0.05).

Conclusion: We must eliminate, endoscopically or operatively, all adenomas from colorectum regardless of size, localization and multiple finding.

2156

Comparative Study of Gastroduodenopathy Induced by Various Non-Steroid Antiinflamatories in Patients with Rheumatic Diseases

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The present study assesses the gastroduodenal disorders induced by various non-steroid antiinflamatories (NSAIs) after short-time administration in average doses: aspirin 1500 mg/day, Ibuprofen 600 mg/day, Indometacin 150 mg/day, Diclofenac 150 mg/day and Piroxicam 20 mg/day.

The study was conducted on 185 patients, 74 women and 111 men, with various rheumatic diseases: arthroses 129 patients, arthrites and spondylarthrites 40 patients, rheumatoid arthritis 16 patients. At the beginning of the study the patients, who had interrupted any medical treatment (including with NSAIs) for at least 30 days, presented normal endoscopic aspect of their stomach and duodenum (degree 0–1 according to the Lanza scale).

After 7 days of treatment with one type of NSAI, 41.6 % of the patients had mucosal damage at the level of the gastric body, pyloric antrum and/or duodenal bulb. 5.4 % of these patients presented an aspect of ulcer (damage in stage 4), and 30 patients (16.2%) had characteristic symptoms. The frequency and severity of the damage were correlated with the type of the antiinflammtory, the most aggressive being Aspirin (28 of 48 cases developed gastroduodenopathy) and piroxicam (7/13) versus Diclofenac which had the lesser effects (7/29). Some correlations regarding the intensity of the damage connected to age, sex, alcohol consumption, smoking, the inflammatory or degenerative character of the rheumatic disease, and the age of the disease were noticed.

2160 Gallstones in Adults with Peptic Ulcers Disease

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Purpose: We prospectively studied if the presence of ulcer (gastric-GU or duodenal-DU), as well as the submitting to gastric surgery (GS) for ulcer are influencing the prevalence of gallstone disease (GD) = gallstones or previous cholecystectomies, in adults.

Methods & material: We studied a batch of 347 subjects (125 F, 222 M), mean age of 50.1 ± 12.9 years (19–81) with endoscopically proven ulcer (GU, DU) or with previous GS (techniques: BI – Billrothl, BII – Billrothll, PV – pyloroplasty + vagotomy, PGEA – posterior gastroenteroanastomosis). GD was detected by US. We excluded the subjects suffering from other organic diseases

Results: After correction for age and sex, we compared the GD prevalence with that of the general adult population in our geographic area — 13.45%, obtained by our team & all on a batch of 1318 volunteers:

Batc	h	GU	DU	GU + DU BI	BII	PV	PGEA	GS	
NR	347	77	180	257	33	23	24	10	90
GD	92	18	33	51	18	5	13	5	41
%	26.5	23.4	18.4	19.8	54.5	21.7	54.2	50.0	<i>45.5</i>
p <	0.01	0.02	NS	0.05	0.001	NS	0.001	0.001	0.001

Comparing the patients with GD/without GD, we calculated the mean duration of ulcer for the entire batch: $10.3\pm9.4/15.4\pm9.7$ years (p < 0.0001) and for the GU + DU batch: $6.6\pm7.1/14.2\pm9.9$ years (p < 0.0001—unpaired t test).

Conclusions: Compared to the general population, the GD prevalence was significantly increased in our whole batch, as well as in the GU + DU and GS group, but not in the DU and BII patients. GD prevalence in GU was higher as in DU (p < 0.0001). The highest GD prevalence in GS was found in BI, followed by PV and PGFA. The duration of ulcer was significantly higher in the GD subjects, suggesting a possible role of ulcer in increasing the GD prevalence.

2161 Abdominal Tuberculosis

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Tuberculosis unfortunately continues as an important cause of morbidity and mortality. The case rate has been failing, but this trend has reversed with the rate having increased in last several years. Extrapulmonary tuberculosis is also fare more common than in last decade.

From 1992–1994, in our institute we recorded 10 patients with abdominal tuberculosis. All were HIV negative, and in only three cases poverty was identified as a risk factor. Vast majority of patients were from urban areas and had a solid economic status. The oldest patient was 52 year old.

In two patients tuberculous ileitis developed concomitantly with an extensive cavitary pulmonary disease. On a contrary, only one of six patients with TBC peritonitis had concomitant pulmonary disease. In two patients tuberculosis of the liver was a manifestation of subacute miliary tuberculosis.

In all patients diagnosis was confirmed after careful and sometimes invasive investigations: in all patients with TBC peritonitis laparoscopic biopsy was necessary for diagnosis since recovery of the organism from ascitic fluid was not possible. Colonoscopy with retrograde ileoscopy was a method of choice for TBC ileitis, since blind liver biopsy was performed in cases of liver tuberculosis.

Typical granulomas with caseation was observed in 6 pts, while in rest granulomas without necrosis, but with positive Zeihl-Neelsen staining were identified. Only one patient died due to massive pulmonary hemorrhage and ileus, since others were succesfully treated with antimaicrobs.

2169 Characteristics and Significance of Renal Involvement in Chronic Liver Diseases with Cryoglobulinemia

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The frequency, prognosis and therapeutic characteristics of renal involvement were investigated in 20 patients with chronic liver disease (CLD) and presence of cryoglobulins (CG), in comparison with a control group of 20 patients with CLD but without CG. Renal damage was detected in 60% of the cases with CG, its most common clinical manifestation being hematuria (12/12); renal failure was present in 3 cases. The prognosis and life quality were worse in the group with CLD and CG that in controls. The patients with CLD of viral etiology and CG did not respond to corticotherapy but could benefit, to a certain extent, of interferon administration.

In conclusion, the CG presence in patients with CLD is not rare and they enhance the risk of renal involvement and renal failure. The response to corticosteroid therapy is unsatisfactory and the immunosuppressive drugs are indicated in the severe forms of autoimmune CLD with present CG, while interferon is recommended in the CLD of viral etiology and CG, associated with renal involvement. The efficacy of interferon in such cases is in course of evaluation.

2170

The EDTA Dysodic Treatment of the Reflux Esophagitis Associated with Pulmonary Symptoms

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This study is a second step toward eatablishing calcium upon acid gastric secretion. In vitro administration of EDTA dysodic, which is a calcium chelating substance was followed by a significant decrease of acid gastric secretion in normal condition as well as in stimulated ones, in a very short period of time. This effect was used successfully in intraoperative reflux esophagitis, caused by aspiration bronchopneumopathy. The objectives of this study concern the clinical, secretory and endoscopic modifications of reflux esophagitis associated with chronic obstructive bronchopneumonia after EDTA dysodic treatment. The study was performed on a lot of 28 patients with the mean age between 52 and 69 years, with reflux esophagitis correlated with chronic obstructive bronchopneumonia. Chronic obstructive bronchopneumonia manifestations, were unsignificant another therapy being unnecesarv. EDTA dysodic was administered in 10% solution, 0.3 mg/kg body/day doses; during 3 weeks. There were made gastrosecretory exploration concerning the secretory volume. H+ concentration and hydrochloric acid output of the basal secretion before and after the treatment. Endoscopical examinations were performed by Olympus Evis 100 Videoendoscop, biopsy pieces being taken before and after the treatment. Calcium concentration was determined with atomique absorption spectrofotometer AAS 30, using calcium electrosis Corning, during the period of prevalence basal gastric secretion and after EDTA dysodic treatment. The objectives were as follows:

- Acid gastric secretion evolution porameters.
- 2. Histopathologic and endoscopic aspects of reflux esophagitis.
- 3. Influences upon chronic obstructive bronchopneumonia reflux esophagitis induces manifestations and clinical manifestations of reflux esophagitis.

The results releave a significant decrease of all acid gastric secretion parameters.

Hour basal secretory volume decrease from a value of 115 \pm $-19\,\mathrm{ml}$ to a value of 30 \pm $-2.8\,\mathrm{ml}.$

H+ concentration decreases from the value of 51 + -2.7 mEg/l to 0 mEg/l. All the patients had a subjective acuses improvement, caused by reflux esophagitis as well as by chronic obstructive bronchopneumonia. Endoscopical and bioptical analysis reveale a good evolution of the esophagian lesions, macroscopic as well as microscopic. Calcium concentration decrease through inferior limit, respectively total calcium concentration decrease from 9.32 + -0.35 mg% to 9.04 + -0.26 mg% (P < 0.1). Ionic calcium concentration decreases from 4.53 + -0.28 mg% to 4.15 + -0.27 mg% (P < 0.02). There were no significant secondary effects. Our in vivo studies prove the favourable effects of calcium chelators in the treatment of reflux esophagitis associated with pulmonary manifestations. A significant decrease appear in the calcium concentration as well as in acid gastric secretion values. Calcium concentration decreases is correlated with acid gastric secretion decreases and clinical improvement, endoscopical and microscopical of reflux esophagitis. There was difficult to establish a correlation between acid gastric secretion values, digestive manifestations intensity, and ventilatory disfunction concerning the simptomatology of reflux esophagitis associated with chronic obstructive bronchopneumonia.

Calcium chelators strongly inhibit basal acid gastric secretion, showing calcium relation with acid hypersecretory states pathogeny. The improvement of associated pulmonary manifestations suggests a mutual secretory anomaly, which causes an acid and bronchial hipersecretion. This kind of treatment can be used successfully in the emergency therapy of reflux esophagitis.

A250 4th UEGW Berlin 1995

2189

Ulcer Disease in Association with Herpes Simplex Infection

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Purpose. To assess the influence of infection with Herpes Simplex virus (HSV) on duodenal picer.

Patients and Methods. Ulcer disease patients (n = 124), 36 with stomach ulcer (SU) and 88 with duodenal ulcer (DU), aged 18–78. The disease's duration varied from 1 to 25 years. Herpes nasalis and/or labialis had 88 patients with DU and 24 with SU. The anti-HSV-IgG was ELISA-detected in blood serum. The presence of HSV in the mucosa biopsy specimens was verified by fluorescein-iso-thio-cyanate-linked HSV-antibodies.

Results. The anti-HSV-IgG was found in blood in 73 patients. Biopsy specimen microscopy revealed HSV-specific luminescence (HSV-SL) in epitheliocytes (in DU n = 37 and in SU n = 12) that often occurred together with the mucosa lamina propria HSV-SL (in DU n = 33 and in SU n = 9). In case anti-HSV-IgG was present in blood and HSV-SL was absent in the mucosa, ulcer healing rate didn't differ from the present-day mean rate. The mucosa HSV-SL coincided with long-term SU and DU healing. The most resistant to therapy non-malignant ulcers were characterized by laboratory evidence of HP and HSV simultaneous presence in the mucosa.

Conclusion. HSV must cause immunosuppression with subsequent mucosa restitution depression and HP-infection aggravation.

2191

Disease-Rlated Endocrine Changes in Patients with Acute and Chronic Viral Hepatitis

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Purpose. To reveal the hormone changes pathways, if they are related to stress or to impaired hormone cleavage.

Patients and Methods. Non-endocrine patients: 140 with acute viral hepatitis (AVH), including 11 severe, 85 moderate and 44 mild cases, and 20 with chronic active hepatitis (CAH) were RIA-tested for ACTH, cortisol, TSH, T4, T3, TBG, insulin, C-peptide, and glucagon in blood plasma. The severe AVH patients were tested before glucocorticoid treatment. The CAH patients received reaferon.

Results. High ACTH, cortisol, T4, TBG, insulin, and glucagon and low TSH, T3 and C-peptide accompanied the AVH acute phase and the CAH exacerbation. As an exception, patients with severe AVH had normocortisolemia. The hormone levels approximated the healthy controls' ones (62 individuals) during convalescence or remission. Glycemia was normal, glucosuria didn't occur. Hypercortisolemia was higher in patients with mild AVH versus moderate. Maximal cortisolemia in each individual AVH and CAH patient used to occur simultaneously with maximal values of bilirubinemia and of AST and ALT activities in serum. Exacerbation either of AVH or of CAH evoked hypercortisolemia. AVH patients' strong correlations: positive — ALT-ACTH, ALT-TBG, ALT-T4, ACTH-TBG, T4-TBG, negative — cortisol-T3, ALT-TSH, ALT-T3, T3-T4, T3-TBG.

Conclusion. The highest cortisolemia in mild and the lowest cortisol in severe cases of AVH indicate towards stress but not to impaired cortisol cleavage, otherwise maximal cortisol would have occurred in the severe cases. Thus high ACTH and low TSH, T3 and C-peptide during either the acute phase of AVH or exacerbation of CAH are due to stress. Hyperinsulinemia despite low C-peptide and normoglycemia reveal resistance of patients' tissues to insulin.

2194

Bone Mass Changes in Chronic Pancreatitis

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Chronic pancreatitis in advanced stages is clinically manifested as a malabsorptive syndrome. Mineral deficiency may also be present. The aim of the study was to investigate bone density (DXA, Norland, USA) in patients with chronic pancreatitis. The group of patients suffering from the chronic pancreatitis was formed by 34 patients (18 premenopausal women and 15 men). In 20 patients the diseases was of biliary origin and in 14 patients of alcoholic origin. All patients had ERCP findings of grade II–III by Anacker and Loffler. We have found statistically significant diminished density of L2-4 spine (p < 0.001) and diminished density of hip (p < 0.05) in patients with chronic pancreatitis. We suppose that in such cases densitometry should be routinelly done and this findings considered in therapy of chronic pancreatitis.

220

The Follow-Up Results of Clinical Course of Primary Sclerosing Cholangitis in Ulcerative Colitis and Crohn's Disease

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In the series of long-term investigations (1975–1994), carried out at Moscow Medical Academy, in a group of patients with ulcerative colitis (UC-164) and Crohn's disease (CD-97), primary sclerosing cholangitis (PSC) was found in 25 (15.2%) and 13 (13.4%) of patients accordingly, that makes up 14.6% from the total number of patients with inflammatory bowel diseases (IBD). In 10

cases (UC-4, CD-6) PSC was diagnosed at the early stage without clinical manifestations of the disease according to biochemical indices proving the initial symptoms of cholestasis. During this observation progressive PSC has been found in 4 of these patients followed by 2 lethal cases (one patient has got cirrhosis of the liver, the other has developed cholangiocarcinoma). After diagnosing PSC in 28 patients (UC-21, CD-7) they have demonstrated both biochemical indices disorders and pronounced symptoms of the above mentioned disease. By the end of observation 6 patients had died of hepatic failure resulting from PSC followed by cirrhosis of the liver and 1 patient — of cholangiocarcinoma. 9 patients developed slow progressing PSC and transplantation of the liver was performed for two of them; 4 patients have been enlisted and waiting for transplantation. By the end of investigation clinical symptoms of PSC and biochemical indices remained stable in 8 patients. It was impossible to detect distant results in 4 cases. Thus, in 20 of 38 (53%) cases PSC has been in progress, won the first place in the clinical picture of associated diseases and defined their future prognosis. The results of our investigations are confirming the priority development of PSC in medio-severe and severe forms of UC with total affection of large intestine and chronic continuous inflammatory process there, as well as in permanently active large intestinal forms of CD.

2205

Surgical Management of Acute Necrotizing Pancreatitis

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The purposes of our study were: 1) to compare results of surgical treatment of necrotizing pancreatitis (NP) after operation of neurectomy and drainage (ND) and necrectomy and scheduled relaparotomies (NR), 2) to find out factors that could have influence to the outcome.

Retrospective analysis of 53 patients operated on because of NP in 1983–1993 was carried out. In 1983–1991 40 ND operations were performed, and in 1992–1993 13 NR operations were performed. Technique of NR. During the first operation the bursa omentalis is opened dividing omentum mayus from colon transversum. Abdominalization of pancreas, necrectomies, mobilisation of duodenum, mobilisation of flexura coli dextra and flexura coli sinistra is performed. Large drains are placed over pancreas. Later, every 2–3 days relaparotomies with necrectomies and lavage are carried out until mayority of necroses are removed.

There were 28 male (died 17–61%) and 25 female (died 19–76%) patients. Age range 20–89 years, mortality of patients up to 40 years of age was 7 out of 18 (39%), in the group above 41–29 out of 35 (83%), difference significant, p < 0.01. Alcoholic pancreatitis was in 17 cases, died 10 (59%), biliary — 19, died 14 (73%), postperative — 6, died 5 (83%), unidentified ethiology — 11, died 7 (63%). There were 59 complications, mayor septic (27), bleeding (11) and fistulae of GI tract (11). Overall mortality 68% (36 out of 53). Mortality of ND — 78% (31 out of 40), NR — 38% (5 out of 13), difference significant, p < 0.05.

 ${\it Conclusions.}$ (1) Prognosis is better in the age group below 40. (2) NR carries lower mortality comparing with ND.

2211

Membrane Regulation of Electrical and Contractile Aktivity of Smooth Muscle with 2-nd Messenger

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Electrical and contractile activity of smooth muscle (SM) taenia coli strip was studied by double sucrose gap. It was shown, forskolin (Fs)-adenylatcyclase activator- decrease electrical and contractile activity of SM. Tetraethylammonium (TEA) before Fs addition led to the strengthly decreasing inhibitory effect, but after Fs addition increasing it. It possibly, Fs partly stimulating of SM Ca²⁺ membrane conductance.

The protein kinase C (PK-C) activator phorbol ester (TPA) also leded taenia coli electrical and contractile activity decreasing. TEA after or before TPA addition, strength led to decreasing inhibitory effect. Taenia coli SM K+ membrane conductance increasing is main factor of inhibitory effect of cAMP and PK-C

In experiments with Na⁺/H⁺ membrane exchange inhibitor EIPA was shown, K⁺ membrane conductance increasing is result of citoplasma pH increase. The PK-C dependent pathway was directly connected with the Na⁺/H⁺ exchange and adenylate cyclase activity. It was shown, PK-C activation may be important way of decreasing enhancement effect realization of some mediators on SM.

PK-C of taenia coli SM plays main negative role of spontaneous electrical activity regulation. Na⁺/H⁺ exchange and K⁺ membrane conductance are the modulation effect of PK-activation.

2215

Experience of Complex Treatment of Severe Necrotic Pancreatitis

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Haemodynamical and septic complications are the leading causes of mortality in severe necrotic pancreatitis. 76 patients (52 men and 24 women) have

been hospitalized due to necrotic pancreatitis since to January 1984, median age 47.84 (19-71). Acute pancreatogeneous toxaemia was in 70 cases, but 6 patients on admission were in shock. All the patients were treated by i/v infusion, in average 3-4 1/24 h. On admission all patients had upper abdominal US and CT scans. In cases of pancreatic shock catetherisation of truncus coeliacus after Seldinger was done and 4-6 1/24 h of various solutions were given in regional artery i/arterial for 2 to 7 days. Different operations have been performed in 72 patients after ineffective medical treatment. The method of operative treatment was wide-ranging necrosectomy and long-standing washing and suction drainage of the retroperitoneal space (60 operations). Continuous washing and suction drainage was applied for an average of 34.6 days. In 9 cases abdominalisation of pancreas was done, 9 splenectomies to avoid arrosive bleeding, 6 parapancreatic abscess drainage were performed In cases of billiary pancreatitis cholecystectomy and CBD drainage (4) and cholecystostomy (1) was made. 3 feeding enterostomas due to duodenal compression and 1 caecostoma due to compression of colon transversum were made. 39 programmed relaparatomies in 14 patients were done. The overall postoperative mortality was 22.2% (16 npatients). The cause of death was late septic complications.

Conclusion: (1) I/aortal long-standing infusions system is very important method treating severe toxic pancreatitis. (2) Programmed relaparatomies with necrectomy, long-standing washing and suction drainage together with supportive medical therapy significally reduce postoperative mortality.

2218 Complications and Outcome of Chronic Pancreatitis — A 10-years Follow-up

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Aim: to improve outcome for patients with chronic pancreatitis by early recognition and treatment of complications

Method: Longitudinal study with clinical, ultrasound, functional and biochemical controls every 4 months.

Results: 68 patients with proven chronic pancreatitis (abdominal pain, US, ERCP, elevated urine amylase activity, low chymotripsin in stool activity). Mean age 46.

During 10-years follow-up 9 patients died. Causes of deaths: septic infections 4, pseudocysts rupture 1, pancreatic cancer 1, bronchial cancer 1, following abdominal surgery 1 (performed for duodenal stenosis), alcohol intoxication 1 patient. Mean age of those who died: 41 years. Diabetes among those who died was present in 7 out of 9 patients, pseudocysts in 6.

Ultrasound guided drainage of infected pseudocysts was performed in 17 patients, in 10 of them more than once.

Conclusion: The high incidence of septic complications and deaths was detected among patients with chronic pancreatitis, especially among those with diabetes. There is strong need for earlier recognition and intensive and prolonged treatment of infections in these patients. Pain as indication for surgical treatment should be taken only exceptionally.

2220

High Doses of Epirubicin and 5-Fluorouracil with or without Cisplatin in Advanced Gastric Cancer

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From September 1991 to January 1995 80 patients with advanced gastric cancer entered phase III clinical trial. The aim of the study was to determine activity of high doses of 5-fluorouracil and epirubicin (FE) vs. the same combination + cisplatin (FEP) in that group of patients.

Out of 80 patients 73 (52 males and 21 females) were evaluable (≥ 2 cycles of chemotherapy). The range of patient's age was 27-70 years (M = 56), and ECOG performance status was \leq 3. The treatment involved in FE arm 120 mg/m² of epirubicin i.v. on day 1, and 1000 mg/m² in 6-hour infusion of 5fluorouracil on days 1, 2, 3, 4, 5; in FEP arm the same combination + cisplatin 30 mg/m² on days 2, 4 was administered. The cycles were repeated after 4

In FE arm, 37 patients were evaluable with 10 partial and 1 complete remission (29.7%), and in FEP arm out of 36 evaluable patients 14 partial and 1 complete remission (41.7%) were observed. Median survival in FE group was 6.3 mos, and in FEP group 8.1 mos. Test results so far did not reveal the statistically significant difference between the two treatments applied. Toxicity was tolerable and reversible.

Our trial being still under way, the final results will provide a more accurate answer with regard to the value of the two administered protocols.

2222 Early Differentiation of Acute Pancreatitis Etiology

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Early differentiation of two most common etiologic groups of acute pancreatitis (alcoholic and biliary caused by gallstones) is very helpful because biliary pancreatitis can be treated early by endoscopic papillotomy whereas such a treatment is unnecessary in alcoholic.

Several studies attempted to define various biochemical models for this differentiation but were, mostly, not accepted into clinical routine because there were no significant differences between alcoholic and non alcoholic patients.

Hundred and twenty-one patients with diagnosis of acute pancreatitis were entered into the our study. The diagnosis was based on combination of clinical features, typical case history, elevation of serum enzymes and imaging studies (ultrasonography or contrast enhanced computed tomography).

Patients were divided into groups A (alcoholic etiology) and NA (non alcoholic etiology).

Our results showed that values of serum amylase (p < 0.001), alanine aminotransferase (ALT) (p < 0.001), alkaline phosphatase (ALP) (p < 0.001), aspartate aminotransferase (AST) (p < 0.01) and urine amylase (p < 0.05) were lower in patients with alcoholic pancreatitis, while mean corpuscular volume (MCV) (p < 0.001) and lipase/amylase ratio (p < 0.001) were higher in this group of patients. There were not statistically significant differences between groups in the values of lipase, bilirubin and gamma glutamyl transferase (GGT).

We conclude that multifactor analysis of biochemical parameters could be useful in early differentiation of acute pancreatitis etiology.

Plasma Concentrations of Xenin After Meals with **Different Composition and After Sham Feeding**

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Xenin is a 25 amino acid peptide, recently described in the gastric mucosa of the human (J. Biol. Chem. 267 (1992) 22305). The function of this peptide is unknown. In the present experiments we studied the response of immunoreactive xenin in untreated and in chromatographed plasma to meals of various composition and to sham feeding. Eight volunteers received isocaloric meals of 5 MJ, enriched (> 50%) with either fat, protein, or carbohydrate or a mixed meal in randomized order. Plasma xenin was determined with a ra-dioimmunoassay using ¹²⁵I-labelled xenin analog and an antibody (2815/3) against a 9 amino acid C-terminal fragment of xenin: Immunoreactive xenin was determined in plasma samples in 15 min intervals before and after the meal. In addition, 30 ml plasma obtained 30 min before and 30 min after the meal was chromatographed on Sep Pak C 18 followed by a μ Bondapack C 18 column (300 x 3.9 mm). Immunfiltration of unacified postprandial plasma on a hydrazido column with bound antibody 2815/4, eluted by acidification, and followed by C 18 HPLC was used in a separate group of volunteers. The eluates were screened with the radioimmunoassay for xenin. Immunoreactive levels of xenin in unextracted plasma rose after the meal. This rise was significant after the mixed meal (78 \pm 7 rising to 93 \pm 9 fmol/ml M \pm SEM) and after the carbohydrate rich meal (90 \pm 1 to 119 \pm 23 fmol/ml). No response was observed after sham feeding. Sep-Pak chromatography followed by HPLC revealed a significant rise of xenin immunoreactivity eluting at the time of synthetic xenin 25 after all forms of meal. Immune filtration followed by HPLC detected a rise of postprandial plasma xenin from 3.3 ± 0.5 to 6.1± 1.2 fmol/ml (M ± SEM). Xenin immunoreactivity appearing exactly at the position of synthetic xenin 25 after 2 different steps of chromatography indicates that the eluting moiety represents the molecular form of xenin 25. Xenin 25, therefore, seems to be part of total postprandial plasma xenin immunoreactivity. These observations are consistent with a physiological role of xenin during meals.

2224

Transabdominal Ileal Pouch-anal Reanastomosis

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From February 1980 to October 1994 a total of 89 patients underwent construction of an ileal reservoir. Two-limb J-shaped reservoirs were created in 4 patients, and three-limb S-shaped reservoirs were created in 85 patients. Between May 1983 and October 1994, 11 patients were subjected to reoperations for pouch-related complications concerning the Ileal Pouch-Anal Anastomosis. The transabdominal route was used for resection and reanastomosis and a covering loop ileostomy was applied. The pouch-anal anastomoses had been handsewn at the primary operation in all patients and furthermore a mucosectomy had been carried out above the dentate line in all but one of the patients.

From October 1989 the stapled ileo-anal anastomosis was introduced and none of the following 36 S-pouches required ileo-anal reanastomosis, p = 0.003 (Fisher's exact test).

Pouch excision ultimately was required in three of the eleven patients, and additional reoperation to restore spontaneous defecation was required in three patients. No deaths were encountered in the material.

In conclusion, using stapling technique for the ileal pouch-anal anastomosis significantly has reduced the need of salvage procedures.

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2226

Constructing a Health Related Quality of Life Questionnaire for Italian Dyspeptic Patient

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Despite ulcer like dyspepsia (ULD) is a common complaint, in Italy there is not any suitable questionnaire for assessing the Health Related Quality of Life (HRQoL) of ULD pts. We planned a study whose aim was the building of a specific questionnaire.

Three focus groups were assembled in three different towns and, during each meeting 15 pts were invited to discuss about their disease on the basis of a very preliminary questionnaire made during a meeting with some gastroenterologists. Finally, 48 items attributable to six domains (anxiety, daily living, food, pain, social relations, symptoms) have been obtained. The process of validation was carried out through the first part of a multicentre Italian study involving 170 digestive endoscopists who administered the "Questionario Paziente Dispeptico" (QPD) to 1772 pts suffering from ULD (Herqules — Health Related Quality of Life in dyspepsia Evaluation Status).

The results reveal the powerful emphases and functions of disease-specific questionnaires. Frequency distributions were calculated for all 48 items in QPD48. Reliability analyses were performed on all 48 items and on a number of sub-scales. The reliability of the trial 48 items scale was 0.89. Several items showed low item total correlation so they were removed and a total of 30 items was retained for standardisation. The 30 remaining items revealed an increase in reliability to 0.91, a satisfactory outcome. Factor analysis on the QPD showed five correlated factors accounting for the covariance among the items: *Primary QoL determinant* (pain-induced anxiety); *Primary QoL Determinant* (constrained daily living), Gastric Specific Sensitisation to triggering agents; Gastric Specific symptoms and OoL burden (family).

We consider our aim of developing a valid instrument for the assessment of QoL in gastric patients to be largely realised.



Local Excision and Mucosal Advancement for Anorectal Ulceration in HIV-infected Patients

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In HIV-infected patients no effective surgical procedure has been described for anorectal ulceration resistant to antibiotic/antiviral therapy. These patients used to be treated by excision. Due to disappointing therapeutic results, we combined excision with mucosal advancement in an attempt to resurface the defect. The aim of this retrospective study was to determine the effectiveness of surgical excision of anorectal ulcers, with or without mucosal advancement, on patients' complaints.

Methods: Medical records of HIV-infected patients presenting with anorectal ulcers between 1984 and 1994 were reviewed. Patients were divided into two groups with respect to treatment offered. All patients presenting between 1984 and 1990 (group A) were treated consecutively by excision only; those presenting between 1991 and 1994 (group B) underwent consecutively excision combined with mucosal advancement. Patient characteristics, duration of preoperative ulcer disease, immune status, cultures and histology of anorectal ulcers, and results of the two different types of surgical treatment were identified. Surgical treatment was considered successful, if relief of symptoms was achieved within 4 weeks after the operation.

Results: In this study 26 patients suffered from anorectal ulceration; all homosexual men (mean age: 39 years). Group A consisted of 16 patients who underwent ulcer excisions only. Group B consisted of 13 patients who underwent ulcer excisions with mucosal advancement; 3 patients previously had one or more unsuccessful ulcer excisions without mucosal advancement. Duration of preoperative ulcer disease was on average 5 months in both groups. CD4+-lymphocyte counts (group A: 110×10^6 /l; group B: 150×10^6 /l) were comparable for both groups. Anorectal ulceration was related to HSV infection in 30% and to CMV infection in 29% of the patients. All biopsies were negative for malignancy. Excision of an anorectal ulcer was successful in 7 of the 16 patients in group A. Symptom relief was achieved in 12 of the 13 patients in group B. In group B surgical treatment appeared to be significantly better in comparison with the results in group A (p = 0.02).

Conclusion: Operative treatment by excision in combination with mucosal advancement is significantly more effective than excision only for persistent symptomatic anorectal ulcers, unresponsive to medical therapy.



High Risk of Severe Complications in HIV-infected Patients with Perianal Sepsis

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Concerning perianal sepsis (fistulas, abscesses), the clinical presentation, due to the immunodeficiency, can be different from that in non-

immunocompromised patients. The infaust prognosis of the underlying disease and the already impaired sphincter function in many HIV-infected patients tend to discourage surgeons from performing surgery. The aim of this study was to determine the clinical presentation of perianal sepsis and its surgical treatment in HIV-infected patients.

Methods: Medical records of all HIV-infected patients were reviewed with special attention to perianal sepsis requiring surgical treatment between January 1st 1984 and September 1st 1994. All records were studied in detail to identify age, sex, risk factors for HIV infection, immune status (CD4+1/mphocyte counts), type and results of treatment and postoperative survival.

Results: During the study period 1342 HIV-positive patients had been admitted to the Academic Medical Centre; 395 of these patients (29%) underwent general surgical treatment. Eighty-eight patients (6.6%) presented with multiple anorectal pathology (n = 211 different lesions). Fifty of these patients (57%; mean age 39 years, 48 male homo/bisexuals, 2 heterosexuals) were found to have perianal sepsis; seven patients (14%) had serious septic complications. Four of those patients had severe necrotizing gangrene for which multiple necrotectomies (n = 4), construction of a stoma (n = 4) and hyperbaric oxygen treatment (n = 2) were applied. Three other patients presented primarily with abscesses in the brain, the liver and the mediastinum, respectively. Later on, these abscesses turned out to be metastatic abscesses from a 'asymptomatic' perianal fistula. CD4+-lymphocyte count was significantly lower in patients with septic complications as compared with those with uncomplicated perianal sepsis (p < 0.05).

Conclusion: Atypical patterns of anorectal sepsis with rare and severe septic complications were encountered in 14% of the patients. In patients with septic complications immune status was significantly decreased. To prevent these septic complications perianal fistulas and abscesses should be adequately treated, even in HIV-infected patients with a very limited life-expectancy and/or patients suffering from diarrhoea and incontinence.



The Role of Concanavalin A-Binding Glycoprotein (CABG) in Cholesterol Crystallization in Native Human

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Many Con A-binding glycoproteins have been proposed to influence cholesterol crystallization in human bile. However, the importance of these factors in native bile has not been determined. It was the aim of this study to establish whether indeed CABG play an important role in cholesterol crystallization in native bile.

Methods: Human gallbladder bile specimens were obtained from 22 patients with gallstone disease during surgery by needle aspiration of the gallbladder and were processed immediately. From the samples two portions of bile were taken, to one of them Con A Sepharose was added and to the other portion Sepharose alone. After incubation the beads were sedimented and in the supernatant crystal observation time (COT) and crystal number were determined using standard techniques. IgA and haptoglobin content were determined by ELISA. Biliary lipids were measured using standard techniques.

Results: The efficacy of the Con A-Sepharose extraction procedure was $95\pm4\%$ for IgA and $99\pm1\%$ for haptoglobin. Con A did not bind significant amounts of bile salt, cholesterol or phospholipid. As described before (Jungst et al, Hepatol. 15:804, 1992), two groups of samples could be distinguished to slow nucleators (COT >4 days, n = 10) and fast nucleators (COT ≤4 days, n = 12). In the group of slow nucleators extraction of CABG did not affect COT (13.3 ±5.3 vs 12.1 ±5.4 days) and had no effect on number of crystals formed (0.6 vs 0.5 crystals/ μ l/day). In the group of fast nucleators extraction of CABG prolonged COT slightly (4.0 \pm 3.0 days vs 2.3 \pm 1.3 days, p = 0.03) but had a dramatic effect on the number of crystals formed (2.6 \pm 6.6 crystals/ μ l/day vs 118 \pm 273 crystals/ μ l/day, p = 0.01). Bile from fast and slow nucleators did not differ in IgA or haptoglobin content nor was there a difference in total protein content or CSI.

Conclusion: We have investigated for the first time the physiological importance of CABG. The fraction does not control crystallization in slowly nucleating biles despite the presence of putative promoters or inhibitors. Our data show that CABG are primarily involved in induction of the massive crystallization in fast nucleating biles.



Kica Breath Test Analysis to Detect Mitochondrial Toxicity in Patients with Chronic HBV Infection Treated with Lamivudine

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Lamivudine is a potent inhibitor of human hepatitis B virus (HBV) replication. After the occurrence of fatal liver failure in patients treated with FIAU, another nucleoside analogue, due to mitochondrial DNA toxicity, we started to evaluate toxicity in 20 patients exposed to Lamivudine. For early detection of mitochondrial dysfunction we used a paired 2-keto[1-14C] isocapoic caid (KICA) breath test. All patients were tested at the start and the end of treatment. The test was also performed in alcoholic patients (known for its damaged mitochondria) and 8 healthy controls. The reproducibility in con-

trol persons was measured by repeating the test at least one week apart. We analyzed the peak exhalation, the time to reach the peak exhalation, the area under the curve after 60 and 120 minutes and the half life of ¹⁴CO₂ appearance in breath. Normal controls showed a variation in peak exhalation and time to reach peak exhalation of 3.0 \pm 0.7% and 36.3 \pm 13.0 minutes respectively. Alcoholic patients showed an impaired KICA decarboxylation in the liver, as was expected resulting in a lowered peak exhalation and a lowered fraction of the dose exhaled in 1 and 2 hours. There were no differences between the healthy controls and the patients on Lamivudine. There were neither significant differences between the pre- and post-treatment breath analysis of the patients, nor between the different dosages of Lamivudine. If all patients were analysed with their start KICA as background control, no individual patient showed an abnormal KICA breath test at the end of treatment. In conclusion during treatment with Lamivudine, clinically as well as by KICA breath test analysis, no abnormalities were seen. Lamivudine does not affect the mitochondrial function as evaluated by the KICA test.

2239

Short mdash; and Long mdash; Term Outcome of Cisapride Treatment in Primary Care Patients with Symptoms of Gastro-Oesophageal Reflux (GOR)

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Data on GOR in primary care are scarce. This multi-centre trial in Dutch general practices studied the response and relapse of patients with symptoms of GOR, treated with cisapride (CIS).

<code>Methods.</code> 600 patients (=pts.) with complaints of GOR [mean (range) age: 52 (18–90) yrs; duration of complaints: 2.2 (0.02–40) yrs] were treated with CIS 4 \times 10 mg daily for 4 to 8 wks. To stimulate the general practice situation, discontinuation of previous anti-reflux medication and specific investigations were not mandator. Of the 195 pts taking H2-blockers, 120 discontinued medication, symptoms severity and overall response were rated at 2, 4, 8 wks. Pts. were followed up to 6 months.

Results. The response to CIS was rated excellent or good in 74% of the pts at treatment end (63% at wk 2, 76% at wk 4 and 84% at wk 8). The reflux symptoms day-time heartburn, night-time heartburn, acid and bitter regurgitation, retrosternal pain and cough fits at night were significantly reduced (p < 0.001): the total reflux symptom score decreased from 9.0 to 4.3 at wk 2, 2.7 at wk 4 and, 1.7 at wk 8 (p < 0.001). Within 6 months, symptoms recurred in 38% of pts: pts with recurrent symptoms had a longer period of complaints before trial entry and had a higher symptom score at end of treatment. Relapse rates in pts symptom-free at end of CIS treatment (survival analysis) were 6, 12, 20, 21, 26, 30% resp. at 1, 2, 3, 4, 5, 6 months. Upon symptom recurrence, one fourth of pts was referred for endoscopy; the other pts were again empirically treated. Pts receiving repeated treatment with CIS usually responded well.

Conclusions. Empirical treatment with cisapride is effective for GOR patients in primary care setting. Relapse rates in patients responding to treatment are low.

2241

Depressed Arterial Arginine Levels in Obstructive Jaundice are Prevented by Gut Endotoxin Restriction

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Arginine (ARG) is an important substrate for wound healing and adequate immune responses both of which are seriously depressed in obstructive jaundice where endotoxemia is present. We hypothesized that ARG metabolism is disturbed in obstructive jaundice and possibly related to gut derived endotoxemia. ARG metabolism and serum arginase activity was investigated in bile duct ligated (BDL) rats and the effect of gut endotoxin restriction by cholestyramine was evaluated. Male Wistar rats (n = 10 per group, 250-275 g) received the endotoxin binder cholestyramine (CH, 150 mg/d) or saline twice daily in the same volume. This treatment started on day 1 and was continued until the end of the experiment. On day 7 groups were randomized to receive a SHAM operation (SH) or bile duct ligation (BDL). This resulted in 4 groups i.e. SH-SAL, SH-CH, BDL-SAL and BDL-CH. On day 20 rats were subjected to a xyphoidectomy in order to mimick surgical trauma. Blood flow was measured at day 21 using radiolabeled microspheres and blood samples were drawn for ARG and arginase determination. ARG fluxes were determined by A-V differences and plasma flow over the target organs i.e. the gut, liver, and kidneys. CH had no effect on ARG organ handling in SH rats. In BDL-SAL rats significantly lower arterial ARG and higher serum arginase levels were measured compared to SH rats (p < 0.01 and p < 0.005). Lower ARG levels were present despite an increase in ARG release from the kidneys (p < 0.01). The changes in splanchnic ARG handling in BDL-SAL rats could not explain the decrease in ARG levels. CH treatment in BDL rats restored ARG to levels measured in SH rats by significantly reducing serum arginase activity and increasing net renal ARC production compared to BDL-SAL rats. (p < 0.05 and p < 0.05). It is concluded that ARG plasma levels were reduced in BDL rats as a result of high circulating arginase levels. Gut endotoxin restriction restored ARG levels to normal by reducing serum arginase activity and increasing net renal ARC production. Endotoxemia plays an important role in hypoargininemia in obstructive jaundice.

2245

Comparison Between Surgical-Medical Percutaneous Treatment of Hydatidosis

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Objective: to analyse and compare three different therapeutic methods.

Method: between January 1985 and January 1995 a total of 121 patients with hydatidosis of different organs (90% liver cyst) were treated with differing methods at the Armed Forces Hospital. Medically or drug therapy was used in 37 patients, 22 with Albendazole and Praziquental. 11 patients were treated with ultrasound guided percutaneous drainage, 72 patients had surgery.

Result: Group 1 — drug therapy: In this group 22 patients had Albendazole and 15 patients had a combination of Albendazole and Praziquental. In Albendazole 4 out of 22 patients (18%) showed disappearance of the cyst and in the combination group in 15 patients out of 34, 15 cysts (44%) showed disappearance. There was cyst recurrence in 2 patients after 2–3 years. Group 2 — in 11 patients, 13 cysts were treated with ultrasound guided percutaneous drainage and irrigation of the cyst with hypertonic saline. Procedure was well tolerated and the response was rapid and encouraging. The duration of the follow-up period ranged from 6 months to 10 years in the medically and surgically treated patients and in 3–16 months for percutanieous drainage group patients. Group 3 — in surgically treated patients, about 30% had recurrence and a second operation.

Conclusion: Percateous drainage method in accessible cases is found to be superior to other methods. Response to medical therapy occurs only in some cases, combination therapy is more effective and faster but the long term follow-up showed cyst recurrence. Surgery carries morbidity, mortality and recurrence rates and surgical indication are limited only is disseminated forms.

2252

ERCP in the Management of Biliary Echinococcus Cysts

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Objective: To report our own experience of 10 cases with hydatid cysts and endoscopic management outcome.

Subject: 10 patients with hydatid cysts in a period of 10 years.

Methods: after the confirmation by US, ERCP was performed followed by retrograde cholangiogram and retrograde cystogram through communication with the biliary tree. When sphincterotomy is performed daughter cysts are removed by basket and naso-biliary tune is inserted into proximal biliary tree close to the main cyst. Irrigation in head down position is performed.

Results: all the patients jaundice disappeared within four days and the main cyst was collapsed and calcified in a few months later. From the procedure itself there were no complications or allergic reactions.

Conclusion: in cases of rupture of hydatid cysts into the biliary tree, endoscopic management is the best method of treating these patients and it carries only the usual morbidity of ERCP.

2262

Human Pancreatic Elastase 1 Concentration in Faeces of Healthy Children and Children with Cystic Fibrosis

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Introduction: Determination of human pancreatic elastase 1 (E1) concentration in faeces is a reliable, non-invasive, new test of exocrine pancreatic function. Aim of this study was to determine the concentration of human pancreatic E1 in the faeces of children in order to estimate if the reference concentration (200 μ g E1/g faeces) of adults is also applicable to children. Secondly we studied if the determination of fecal E1 concentration is a suitable parameter for the diagnosis of cystic fibrosis (CF).

Patients: In this study 145 newborns, 204 babies and children (1 month-14 years) with normal pancreatic function and 86 CF patients (1 week-30.5 years) were included.

Methods: Human pancreatic E1 concentration was determined immunologically with an ELISA (ScheBo*Tech, Wettenberg, Germany). Chymotrypsin activity was determined enzymatically (Boehringer Mannheim, Germany).

Results: The concentration of E1 in meconium was 63.9 μ g/g \pm 3.6 (mean \pm SEM, n = 145). During the first month after birth the E1-concentration increased to 586.1 μ g/g \pm 65.4. After this rapid initial increase after birth, we only found a further slight increase of E1-concentration with age. ($r^2 = 0.087$, linear regression analysis). This increase was not observed with chymotrypsin activity ($r^2 = 0.00072$). Fecal chymotrypsin activity correlated only weakly with fecal E1 concentration ($r^2 = 0.031$).

Day to day variations (10 days) of individual patients (n = 8) were acceptable with the pancreatic E1 (CV = 24%, range: 3–32%). In comparison chymotrypsin activity varied with CV = 69% (range: 27-84%).

With the cut-off concentration of 200 μ g E1/g the sensitivity for the diagnosis of CF was 89.5% with a specificity of 99%.

Conclusion: The results show that the determination of fecal E1 in healthy children and children with CF is a reliable, easy-to-perform, non-invasive parameter of the exocrine pancreas function with high sensitivity and specificity. In contrast to other indirect pancreatic function tests, the E1 determination is not interfered by substitution therapy.

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2263

Study of EGF on Hepatic Tissue PGE₂ in Rats Using Acute Hepatic Failure Model

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[Aim] We reported that the administration of EGF kept the hepatic blood flow and protected hepatic cell necrosis in animal model of acute hepatic failure. The volume of hepatic tissue PGE2 that participate with hepatic cell regeneration and cytoprotection was measured. [Method] EGF was administrated at 20 µg/kg.Bw.iv, on male SD rats about 250 g in weight (injection group, n = 10). After 30 minutes, D-galactosamine (D-gal) was injected at 1 g/kg Bw ip. Instead of EGF, the same volume of saline was administrated before D-gal injection. The volume of hepatic tissue blood flow (HTBF) and hepatic tissue PGE₂ were measured by semiconductor laser Doppler flowmeter and PGE method (RIA) before D-gal injection (n = 5), and after 48 hours. [Result] In non treatment group, serum ALT and HTBF were 51.6 ± 12.31 U/I and 460 ± 54.9 my. In EGF non injection group on acute hepatic failure model, those were 43.0 ± 5.9 and 473.6 ± 49.6 at 0 hour, 7614 ± 1536 and 220.0 ± 23.7 at 48 hours. In EGF injection group, those were 39.4 \pm 6.8 and 630.0 \pm 76.5 at 0 hour, 5200 \pm 1812 and 296.8 \pm 30.7 at 48 hours. Serum ALT at 48 hours in injection group was significantly (P < 0.05) lower than that corresponding value in non injection group. HTBF at 48 hours in injection group was significantly (P < 0.01) higher than that in non injection group. Hepatic tissue PGE2 was 0.26 ± 0.06Pg/w.w.mg in non treatment group. In EGF non injection group, those were 0.19 \pm 0.13 at 0 hour, and 28.16 \pm 10.23 at 48 hours. In EGF injection group, those were 0.94 \pm 0.20 at 0 hour, and 6.96 \pm 2.98 at 48 hours. That value at 0 hour in injection group was significantly (P < 0.001) higher than that in non injection and non treatment group. However, that value at 48 hours was significantly (P < 0.01) lower than those groups. [Conclusion] The results suggested that PGE2 was relative to liver damage and was induced by hepatic cell damage, because cytoprotection and maintaining hepatic blood flow of EGF were not induced by PGE₂.

2264

Treatment and Prevention of Relapse of Oesophagitis Grade I-II with Omeprazole and Cisapride: Comparison of Two Treatment Approaches

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The aim of this open study was to evaluate the efficacy of (1) cisapride addon to omeprazole in healing grade I–II oesophagitis and (2) cisapride maintenance treatment in preventing relapse.

Methods: Patients (pts) with endoscopically proven oesophagitis grade I (n = 120) or grade II (n = 105) were randomized to receive 8 wks of healing treatment with omeprazole 20 mg od (= OM) followed by 12 mo without maintenance treatment, or to 8 wks of combined treatment of omeprazole 20 mg od plus cisapride 5 mg tid (= OMCIS) followed by 12 mo of maintenance treatment with cisapride 5 mg tid (CIS). Only pts healed after acute treatment were included in 12-month follow-up.

Results. With OM, 88% of pts were healed, vs 94% with OMCIS. Endoscopic relapse rates at 3, 6 and 12 mo were resp. 20–31–40% in the Gradelpts 48–85–96% in Grade-I pts healed on OM without further maintenance treatment (p = 0.04 - p < 0.001 - p < 0.001). For grade II, they were resp. 20–39–52% versus 39–78–95% (p = 0.056 - p < 0.001 - p < 0.001).

Conclusions. Continued treatment with CIS — after initial healing on omeprazole plus cisapride — is a beneficial treatment strategy in patients with grade I and grade II oesophagitis: although acute add-on treatment results only in a minor increase in healing rates, the continuation of cisapride after acute healing allows significant reduction of the high relapse rates observed after stopping healing treatment with omeprazole.

2265

Interferon-alfa 2b Plus Indomethacin Combined Therapy for Chronic Hepatitis C: A Pilot Study

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In vitro and in vivo studies have demonstrated that Indomethacin (IN), a NSAID which inhibits cyclooxygenase pathway in arachidonic acid metabolism, augments antiviral and immunomodulatory effects of IFN-alfa (IFN). The likely results of IFN + IN combination may be increased efficacy of IFN, better cost-effectiveness, and more side effects due to synergism. To clarify these hypotheses 15 pts with chronic hepatitis C diagnosed by anti-HCV (ELISA2) and HCV-RNA (PCR) positivity and liver biopsy were given IFN (Intron-A 3 MU/d/tiw) and IN (oral, 75 mg/d/tiw, one hour before IFN inj.) for 6 months. Pretreatment ALT levels were greater than 2Xupper limit of normal (range 97–199 IU/L) in all pts. Therapy was discontinued in 3 pts due to non-compliance in 2 and adverse effect which was not typical for IFN in 1. Other 12 patients completed 6 months therapy without any important adverse reaction. A group of 20 pts treated by IFN alone (Intron-A 3 MU/d/tiw for 6 months) was assessed as historical control.

Results: Complete response defined as normal ALT level at the end of 6 months therapy was obtained in 8 (67%) pts. One had partial response with a decrease in ALT level greater than 50% of initial value while only 2

pts (18%) did not respond to combined therapy. HCV-RNA became negative in 4 of 8 complete responders. In control group the rate of complete and partial responders and non-responders was 35% (7/20), 45% (9/20) and 20% (4/20) respectively. Relapse rate was 38% (3/8) and 43% (3/7) in complete responders of IFN + IN group and historical controls respectively in the first 6 months after treatment. Although complete response was more frequent (67%) in combined therapy group than in controls (35%), the difference did not reach significance (p 0.05).

Conclusion: The results indicate that IFN + IN combined therapy is associated with increased efficacy of IFN as complete response was more frequently achieved. Larger and controlled trials are necessary to assess the real effectiveness of IFN + IN combined therapy in chronic hepatitis C.

2266

Increased Levels of TNF- α GM-CSF, ECGF and TGF- β mRNA in the Mucosa of Patients with Ulcerative Colitis

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Cytokine dysregulation may play a crucial role in the pathogenesis of inflammatory bowel disease (IBD). In this study, we analysed the cytokine mRNA patterns of the affected and not affected colonic mucosa of patients with Crohn's Disease (CD) and with ulcerative colitis (UC) compared to that of normal mucosa

Total RNA was extracted from colonic biopsies of patients undergoing colonoscopy. A semiquantitative RT-PCR was carried out using oligon-uoleotide primers for IL-1 to IL-8, IL-10, TNF- α and - β , IL-1R, IL-1RA, IL-2R, IFN- γ , TGF- β , GM-CSF, and ECGF. The intensity of the PCR product was quantified by laser densitometry scanning. For statistical analysis a Mann-Whitney U test was performed.

Statistically significant results were obtained for IL-3, TNF-a, GM-CSF, ECGF, and TGF- β . No significant differences in the cytokine mRNA expression could be found in the mucosa of CD patients. However, the UC specimens contained significantly more mRNA for IL-3, TNF-a, GM-CSF, ECGF, and TGF- β . In the affected mucosa particularly TNF-a and TGF- β mRNA was increased while in the not affected mucosa higher levels of GM-CSF and ECGF mRNA could be detected. IL-3 mRNA was increased in both affected and not affected colonic mucosa of IBD patients compared to normal mucosa.

The significantly enhanced expression of the proinflammatory cytokines GM-CSF anf TNF-a in the gut of patients with UC indicate the special role of these cytokines in the pathogenesis of UC, particularly as GM-CSF mRNA is increased in histologically affected mucosa of UC patients, too. The role of the significantly higher expression of TGF- β mRNA is not completely clear, but it is known, that IL-6 production by fibroblasts can be augmented by TGF- β .

2267

Place of Adjuvant Radiotherapy in the Management of Rectal Cancer

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After curative surgery, the prognosis and the patterns of failure of colon and rectal cancers are quite different. The overall 5 year survivals are respectively 55% and 45% with a median time to the diagnosis of recurrence of 18 and 13 months. Liver and peritoneal metastases account for 60% of the recurrences of colon cancer whereas local failures (LF) represent about 10%. On the contrary, LF, liver and lung metastases are equally distributed and account each for 30% of rectal cancer failures. These figures explain why adjuvant treatment should be adapted to the site of the primary.

The aims of adjuvant treatment in rectal cancer are both survival and local control, keeping acute and late toxicity to an acceptable level.

The postoperative approach permits to select patients on the basis of the pathological findings. None of the four randomized published trials demonstrated that a 50 Gy postoperative dose is able to decrease significantly the LF rate in Dukes B and C patients. Increasing the dose seems inappropriate for multicentric trials and will certainly conduct to an increased acute and late toxicity.

Combined postoperative radiotherapy and chemotherapy produced a benefit in some studies at the expense of a high rate of acute toxicity and treatment interruption in about 20–30% of the patients. Moreover, the treatments induced unacceptable high rate of late toxicity after sphincter sparing procedures.

On the other hand, moderate dose, in the 25–35 Gy range, preoperative irradiation significantly reduced LF in four large randomized trials totalling more than 3000 patients. This reduction in LF had the same magnitude for all Dukes' stages (50 to 65%). Furthermore in the latest report of the Stockholm 2 trial, a definite increase in overall survival was observed in patients treated by preoperative irradiation.

The comparison of the therapeutic ratio issued from the post or preoperative adjuvant therapeutic approach, definitely favours the pre-operative irradiation. The next step is to evaluate in selected patients (T3-T4 resectable stages), the optimal integration of chemotherapy with preoperative irradiation and whether post operative chemotherapy should be added. These two questions are addressed in the current EORTC 22921 protocol. Beside the main goal of this trial, increase in overall survival, the evaluation of sphincter function and quality of life have also been selected as a new end point in this trial.

2268

New Strategies for the Treatment of Type 2 Diabetes: Focus on the Metabolic Syndrome

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Type 2 diabetics still suffer from a shortage of life expectancy of 5–10 years with atherosclerotic cardiovascular diseases as main cause of death. As shown in prospective studies dyslipidemia, hypertension, smoking and poor glucose control are the major independent modifyable risk factors for coronary heart disease and early death. Android obesity and hyperinsulinemia at least enhance the level of risk factors. This cluster of risk factors that we called metabolic syndrome acts as a vicious cycle for both deterioration of diabetes and accelerated development of atheroslcerotic lesions. Therefore correction of overweight, improved health behavior with respect to nutrition, aerobic physical activity and cessation of smoking are the primary measures to reduce insulin resistance and level of risk factors resp.

In NIDDM insufficiently controlled by intensified health education alone antihyperglycemic oral drugs such as alpha-glucosidase-inhibitors (acarbose) and biguanides (metformin) reduce blood glucose and improve insulin sensitivity without weight gain and risk of hypoglycemia. Sulfonylureas should be prescribed if failure of insulin secretion develops, -early in type IIa, late in type Ilb diabetes. Metformin is more effective in subjects with high fasting blood glucose due to excessive gluconeogenesis. Acarbose is preferentially used in cases with strong postprandial hyperglycemia. In the failure of monodrug therapy all oral antidiabetics can be combined using their complementary mode of action, Insulin treatment is indicated in acute complications and when with oral antidiabetica HbA_{1C} cannot be lowered below 7–8%. Drug treatment must be individualized based on relevant insulin secretion capacity, patient's health status and psycho-social situation. The target levels of glycemic control must be defined with respect to life expectancy, associated risk factors and primary and secondary prevention of complications. Recently published data have shown that strict glucose control is essential for both to prevent detioration of diabetes and late complications resp.

2271

Glycemic Status and Pancreatic Changes in Patients with Fibrocalculus Pancreatic Diabetes and Chronic Calcifi Pancreatitis

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Fibrocalculus pancreatic diabetes (FCPD) is a subclass of malnutrition related diabetes mellitus (MRDM), as suggested by the WHO Study Group of Diabetes Mellitus, affecting mainly young subjects in the tropical countries. The etiology is still uncertain. The most crucial question regarding its etiology is whether diabetes in FCPD cases is just a progression from chronic calcifi pancreatitis (CCP) with involvement of endocrine pancreas of FCPD and CCP are altogether distinct entities with incidental coexistence. To help in answering this question fasting and 2 hour postprandial blood glucose and serum fructosamine levels were compared between 13 nondiabetic CCP and 11 newly diagnosed FCPD cases. ERCP of 9 of the CCP and 4 of the FCPD cases were also compared. Blood glucose and serum fructosamine were determined by enzymatic-colorimetric methods, and ductal changes in ERCP were scored by the criteria of Axon et al. FCPD patients showed about 4 times higher blood glucose values, both at fasting (CCP: 4.5 \pm 0.4, FCPD: 18.0 \pm 3.1, mmol/l M \pm SEM) and 2 hour after 75 g oral glucose load CCP: 7.0 \pm 0.6, FCPD: 26.1 \pm 3.2, mmoM, M \pm SEM). Serum fructosamine was also about 3.5 time higher in the FCPD subjects (CCP: 255 \pm 17, FCPD: 874 \pm 77, umoM, M \pm SEM). The percent of subjects showing mild, moderate and severe changes of chronic pancreatitis were 22, 22, and 56 respectively in CCP and 0, 25 and 75 respectively in FCPD cases. Frequency distribution diagrams clearly showed that both blood glucose values and serum fructosamine clustered at the lower end in case of CCP and they are clearly demarcated from FCPD where clustering is seen at the higher end. In contrast, regarding ERCP findings patients of both groups clustered at the group showing severe pancreatic damage. The results suggest that there is no correlation between the degree of pancreatic damage and the development of the diabetic state. Thus, diabetes in FCPD is probably a primary disease which is complicated by the incidental coexistence of chronic fibrocalculus changes in the pancreas.

2275

Increased Colonic Production of Butyrate from Dietary Fiber (Plantago) in Patients with Former Colonic Cancer

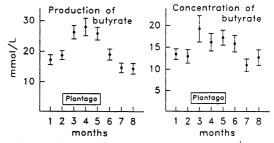
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Colonic fermentation of dietary fiber produces butyrate and other short-chain fatty acids (acetate end propionate). Numerous reports have shown that butyrate possesses antineoplastic properties against colonic cancer cells in vitro and a few studies have indicated it to occur in animals too. Two human studies have shown that the relative production of butyrate from dietary fibre is diminished in patients with former colonic cancer or adenomas.

Seventeen patients operated for colonic cancer who had no signs of recurrence at the time of entry were treated with the fiber plantago ovate seeds 10 g b.i.d. for 3 months. Eight fecal samples were obtained from every patient:

two before treatment (no 1 and 2), three during the 3 months of treatment (no 3, 4 and 5) end three samples 1, 2 and 3 month after treatment had stopped (no. 6, 7 and 8; Figure).

The production of butyrate from plantago added to fecal homogenates increased significantly in samples obtained during the 3 months of fiber treatment in comparison with pre- and post-treatment periods (p < 0.00001; Figure, mean \pm SE). Fecal concentrations of butyrate also increased in the 3 months patients were treated with plantago (p < 0.0001; Figure).



In conclusion, oral treatment with plantago adapted the colonic flora to produce increased amounts of butyrate from a given amount of plantago and increased the concentration of butyrate in faces. Production and concentration of butyrate returned to pretreatment levels within 1–2 months after the treatment with fiber was stopped. Therefore, it is possible to reverse a decreased production of butyrate in colonic cancer patients by a continuous intake of plantago, which may be advantageous for fiber used in cancer prophylaxis.

2280

Role of Helicobacter pylori Eradication in Duodenal Ulcer Healing and Relapse

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It has been shown that concurrent administration of omeprazole and appropriate antibiotics not only heal duodenal ulcer but also eradicate H. pylori. In this study we compared the ulcer healing rate and H. pylori eradication rate of the following two treatment regimens: (A) omeprazole (Losec) 20 mg b.d. + amoxicillin 750 mg b.d. for 2 wks. (B) omeprazole (Losec) 20 mg b.d. + bacampicillin 800 mg b.d. for 2 wks. 43 patients with H. pylori associated duodenal ulcer proven endoscopically were randomized to the above two regimens. Endoscopies were performed 4 wks after cessation of treatment to assess ulcer healing and H. pylori eradication. Of 35 patients with healed ulcers followed endoscopically for 6, 12 and 18 months to assess ulcer relapse. The ulcer healing rates were 81.8% (18/22)in group A, and 81.0% (18/21)in group B. H. pylori eradication rates were 59.1% (13/22) and 42.9% (9/21) in group A and B respectively. None of 22 patients with H. pylori-negative had relapsed at 6 months, the cumulative relapse rates were 9.1% (2/22) at 12 months and 22.7% (5/22) at 18 months, however, 21 patients with H. pylori positive were 53.8% (7/13) at 6 months and 100% (13/13) at 12 months. There were significant differences between patients with H. pylori-negative and patients with H. pylori-positive (p < 0.005).

The study has shown: (1) The ulcer healing and H. pylori eradication of the group A were similar to that of the group B; (2) The patients with unhealed ulcers were H. pylori positive, suggesting that H. pylori influenced the healing of duodenal ulcer; (3) When patients were analysed according to post-treatment H. pylori status, it was seen that most relapses occurred in those remaining H. pylori positive, relapse was uncommon in those rendered H. pylori negative, suggesting that H. pylori is a very important factor in the relapse of duodenal ulcer disease.

2283

Effect of Alpha-interferon Plus Octreotide on Metastasized Gastrointestinal Endocrine Tumours

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Preliminary data suggest an antiproliferative effect Of combined therapy with octreotideplus alpha-interferon on gastrointestinal endocrine tumours. 16 patients with metastasized endocrine gastroenteropancreatic tumours (6 patients with non-functional tumours, 3 patients with gastronome, and 7 patients with carcinoid-syndrome) revealing tumour progression during octreotide monotherapy (3 \times 200 $\mu g/die t.i.d)) were treated with the combination of alpha-interferon (3 <math display="inline">\times$ 5 Mio.IU per week) plus octreotide (3 \times 200 $\mu g/die t.i.d.). Follow-up examinations were performed every 3 months.$

Results: 9 out of the 16 patients exhibited progression of tumour growth after 3 months and dropped out. 7 patients (44%) responded to this therapy. In 5 patients, inhibition of tumour growth during combined therapy lasted for 6–47 months (median duration 23 months) and was thereafter followed by tumour progression again. In one patient, standstill of tumour growth maintained for 6 months now. One patient had a partial regression now continuing 34 months. Inhibition of tumour progression was not necessarily parallelled by respective changes in peripheral blood hormone levels. In 7 out of the 10 patients with functional tumours, serum gastrin and urinary 5-

hydroxyindoleacetic acid significantly decreased in the first 3 months of dual therapy. However, this effect was not maintained until the end of the observation period. Most patients with functional tumours experienced improvement of hormone-related symptoms

Conclusions: The combination of alpha-interferon and octreotide is superior to octreotide monotherapy in metastasized endocrine gastrointestinal tumours. These results stimulated us to a prospective controlled study to evaluate the beneficial effect of the combination of alpha-interferon and octreotide in metastasized endocrine gastroenteropancreatic tumours.

2285 Prevalence of Gallstones in a Siberian Population: Comparison of Autopsy Study and Cross-sectional Ultrasonographic Study

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The aims of the study were 1) to estimate prevalence of gallstones in a Siberian population and 2) to compare two approaches for this estimation.

Representative sample of 842 males and 876 females (25-64 years), who lived in one of the typical districts of Novosibirsk, was investigated using ultrasonography of the gallbladder. Autopsy protocols (401 males and 338 females aged over 24 years) were analyzed in one of the main hospitals of Novosibirsk (1989-1993). In both studies presence of gallstones and previous cholecystectomy were recorded.

Prevalence of gallstone disease shown in the table as per cent at year

	25–34	35-44	45-54	55-64	AAP	
Men						
US	0.91	0.91	2.93	4.33	1.85	
AS	0.00	0.00	3.78	5.88	1.82	
Women						
US	5.94	7.11	9.52	18.22	9.53	
AS	0.00	9.09	4.71	20.93	7.73	

US, ultrasonographic study; AS, autopsy study; AAP, age-adjusted prevalence in 25-64

These data consistent with those of Jorgensen et al. (1994) that results of estimation of gallstones prevalence by these two methods are reasonably similar When done in the same area during the same time period.

In the present study the prevalence of gallstones in male population of Novosibirsk appeared to be twice as low that in the West European countries (Wales, Netherlands, Denmark), while in females these figures were about the same. The explanation of this fact is unclear, because factors formerly shown to be associated with gallstone disease (smoking, high intake of animal fat and proteins and deficiency of dietary fibers) are widespread among Siberian citizens. On the other hand, antilithogenic factors such as high physical activity, low body mass index and high alcohol consumption are usual for Siberian

2286

Chronic Viral Hepatitis in Western Siberia: Epidemiologic and Clinical Data

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Immunoenzyme assay of viral infections markers (HBV, HCV, HDV, CMV) was performed in 238 residents of large industrial centre of Western Siberia (as a facultative fragment of WHO "MONICA" programme), in 200 donors also resided in Novosibirsk, and in 164 patients with gastrointestinal pathology (including 62 with chronic hepatitis and liver cirrhosis).

Overall prevalences of these markers in population and donors were similar: HBs Ag — 1.3% and 2%, HBc Ab — 10.5% and 0%, HCV Ab — 3.8% and 2.5%, HDV Ab (Ig M) — 0% and 0.02%, CMV Ab (Ig M) — 1.2% and 4.8%, HBs Ab — 7.2% and 15.0%.

The viral infection markers were found in 31% of patients with gastrointestinal pathology (in 72% with hepatic pathology). Anti-HCV occurred more frequently (44%), in one third of cases in association with HBs Ag and anti-HBc (Ig M). On the whole HBV markers were detected in 24% of cases, in a half together with anti-HDV (Ig M).

Chronic viral hepatitis C had a number of peculiarities. As usual, there were no anamnestic data about acute hepatitis. However, in a half of cases previous operations and parenteral administration of drugs took place. Usually activity of process was not marked, jundice was absent, progression of disease was slow. Among extrahepatic manifestations various skin affections were the most frequent (in 64%). Splenomegaly occurred often but without hypersplenism. Arthropathies were also often, however, mialgia, ophtalmopathia, thireoiditis, ovarian sclerocystosis, pulmonary fibrosis were seen in single cases

Superinfection (HDV), as well as association with CMV was accompanied by significant increase of hepatitis activity and rapid progression into hepatic

Thus, viral infection is the main cause of chronic liver diseases in Western Siberia. This fact should be taken into account in clinical practice and demands more strict control of donor blood and its derivatives in relation to wide range of viruses

2287

Life-threatening Food Allergy in a Child Treated with

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A 7-month-old girl was transplanted for biliary atresia. Family history was unremarkable except for asthma in her mother's childhood. Prior to liver transplantation (LT) she had been on a normal diet supplemented with MCT. After LT she was given a protein hydrolysate. Immunosuppression comprised FK506, prednisone and azathioprine. She was well until 5 months after, LT, when she had three episodes of severe angioedema with generalized urticaria, responsive to high dose steroids. She was then hospitalized in ICU for a severe attack of asthma, responsive to steroids and epinephrine. Giant urticaria appeared after contact with latex. The child was supposed to drink only protein hydrolysate, but it was discovered that each episode followed an accidental ingestion of cow's milk. Total IgE were elevated (190 kIU/I), so were specific IgE (PAST) against casein, egg yolk, peanut, and latex. After the last episode she was given a mixture of aminoacids (Neocate*, SHS), and other nutrients were reintroduced one by one on hospital supervision. Latex was excluded from the environment. Despite all this, she was readmitted several times for asthma, and once in ICU where she needed mechanical ventilation. The triggering allergen was not always discovered. She also developed eczema. At age 17 months, she is treated with oral steroids, ketotifen, sodium cromoglycate, and nebulizations of salbutamol and steroids. The liver tests have always been normal. FK506 blood level has been maintained between 5 and 7 ng/ml. Severe allergic reactions to cow's milk are not rare in children, but they usually do not occur after such a long period of tolerance. It is also uncommon to see so many allergic manifestations despite adequate treatment and eviction of allergens. FK506 may have a vet unknown effect on the immune reaction leading to these anaphylactic manifestations. We are testing this in vitro in lymphocytes from normal and allergic subjects by studying proliferation and cytokine production (particularly IL4) with and without FK506. With the results, we may switch the child to cyclosporine.

Case Report-Giant Cell Hepatitis and Severe Aplastic **Anemia**

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Recent reports suggest that non-A non-B non-C viruses might not be uncommon etiologic agents of hepatitis-associated aplastic anemia. We describe a seven years old boy who developed severe aplastic anemia after an episode of subacute cholestatic hepatitis, apparently syncyntial giant cell hepatitis. Personal history was nonrelevant (drugs or toxics excluded) and extensive aetiological evaluation non contributive (virologic and metabolic studies, autoantibodies). However, a positive serology for a paramyxovirus agent (syncytial respiratory virus) was demonstrated, compatible with acute infection, in absence of any clinical evidence. Percutaneous liver biopsy showed diffuse hepatic necrosis, mainly in centrolobular area, giant-cell hepatocytes and marked cholestasis. Ultrastructural examination of liver tissue couldn't be performed. Clinical course was favourable concerning hepatitis, in parallel with a progressive haematological worsening. Bone marrow biopsy was profoundly hypocellular, confirming severe aplastic anemia. Growth factors therapy (recombinant GM-CSF and erythropoietin) didn't affect haematological parameters, so immunossupressive therapy was started. No recovery occurred yet after a 2 weeks course of antithymocyte globuline (ATG) followed by a second course of methylprednisolone plus cyclosporine (1 month). Bone marrow transplantation from a partially HLA-identical sibling is actually under consideration.

Post infantile giant-cell (syncyntial) hepatitis has recently been reported. eventually related to a paramyxovirus, and carring a poor prognosis. The association of these two features-giant cell hepatitis and aplastic anemia (a potentially fatal complication of hepatitis) — may be a rare eventuality in childhood. In the present case, potential contributory role of a "paramyxoviruslike" agent, though an interesting possibility, remains speculative, deserving further confirmatory evidence.

2310 Protective Effects of Verapamil on Hepatocyte **Function Following Warm Ischemia**

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Verapamil (VER) has recently been shown to attenuate hepatocellular necrosis following warm ischemia and reperfusion (IR). To more fully evaluate the protective effects of VER on liver IR injury we measured the effect of a single dose of VER on cellular efflux of glutathione and bile flow (a sensitive marker for hepatocellular function and ATP content (J. Surg Res. 46: 99, 1989). Cell injury was assessed by the release of liver enzymes.

Methods: 20 male Sprague-Dawley rats (250-300 g b.wt) underwent pentobarbital anesthesia, had abdominal laparotomy, femoral vein and bile duct cannulation. Rats were randomized to receive either an infusion of VER (n = 12) (0.3 mg/kg) or NaCl (n = 8) over 30 minutes prior to 60 min of partial liver ischemia. Normothermic ischemia was induced in the median and left lobes

by clamping of the proper hepatic artery and portal branches for 60 minutes, leaving the blood supply intact to the right lobe. Liver enzymes (ALT, LDH) and bile output (μ I/g liver/min) were measured immediately prior to as well as 1 and 24 hrs after reperfusion of the liver. Assay of biliary and plasma glutathione was done as described by Baker.

Results: Data are presented as mean \pm SD. Basal bile flow in controls 2.17 (0.42) and VER 1.91 (0.33) decreased during postischemic period in both groups, however, was significantly higher in VER group reaching after 24 h 1.67 (0.73) compared to 0.43 (0.37) in controls, p = 0.01 using variance analysis with repeated measures. Concentration of liver enzymes LDH and ALT decreased significantly during reperfusion in VER versus controls (p < 0.01). Concentration of total glutathione in bile at 24 h after reperfusion was significantly higher in the group treated with VER compared to controls. GSSG in the plasma was significantly lower in the VER group compared to controls (p = 0.01). A significant correlation between ALT, LDH, and bile flow (p = 0.001, r = 0.76) at 24 h after ischemic insult was demonstrated. Efflux of total glutathione into the bile was significantly correlated with bile excretion during 60 min of reperfusion (p = <0.001, r = 0.84).

Conclusions: (1) 60 min of liver IR results in significant hepatocellular injury and dysfunction 24 hr after reperfusion; (2) VER significantly attenuates not only hepatocyte injury but also preserves overall liver function as reflected by preservation of bile flow; (3) Correlations between liver enzymes, biliary glutathione and production of bile is a important pathophysiological link of hepatocytic function and injury.

2311

Prospects of T-cell Immunotherapy of Cancer by Vaccination of MHC Class I Binding Peptides

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Immunotherapy of tumors by adoptive transfer of cytotoxic T cells (CTL) is now feasible in experimental murine systems (1-3). These CTL recognize peptide sequences of defined length presented in the groove of MHC class I molecules. Effective eradication of large tumour masses requires coadministration of IL-2. Tumour escape strategies are numerous, but in various instances can be counteracted by defined measures. Initiation of CTL responses against poorly Immunogenic non-virus-induced tumors (the majority of human cancer) requires novel strategies to overcome T cell inertia. Rather than wait-and-see whether tumor specific CTL (against unknown antigens) can be cultured from tumor infiltrating lymphocytes we propose an alternative strategy in which CTL are raised against target molecules of choice including differentiation antigens of restricted tissue distribution (autoantigens) or mutated/overexpressed oncogene products. The various steps proposed include 1) Identification of target molecules of choice 2) Identification in these target molecules of MHC allele specific peptide motifs involved in peptide binding to MHC molecules 3) Evaluation of actual binding of such peptides to specific MHC class I molecules 4) In vitro CTL response induction by such peptides, presented by highly efficient antigen presenting cells such as processing defective cells, carrying empty MHC class I molecules, loaded with a single peptide or dendritic cells. Both types of cells are capable of primary CTL response induction in vitro 5) Adoptive transfer of tumor specific CTL generated in vitro or, more convenient, vaccination with immunodominant peptides. These various steps have now been taken for several viruses, viral induced tumors and other types of tumors and the first indications that this strategy is useful have been obtained.

2312

Influence of Sulphasalazine, Olsalazine and Sulphapyridine on the Intestinal Cell Kinetics in Rats

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Our aim was to study the influence of sulphasalazine (SASP), olsalazine (OLZ) and sulphapyridine (SP) on cell kinetics in the small intestine and colon in rats.

Groups of conventional male AGUS rats were given 200 mg/kg SASP, 80 mg/kg OLZ, 125 mg/kg SP per day dissolved in drinking water for ten days. The control group was given water only. All rats were killed 2 h after injection of a metaphase blocker and the proliferative activity of the mucosa in the jejunum, ileum and colon was examined in histological sections by means of the cumulative mitotic index (MI) and the total number of cells in the left column of 30 well-oriented crypts and villi.

The MI in the jejunum, ileum and colon increased and also did the numbers of crypt cells in the jejunum and ileum of the rats treated with SP (p < 0.05 vs. controls). In contrast SASP and OLZ increased the MI only in colon (p < 0.05 vs. controls).

The results suggest that SASP, SP and OLZ have a selected proliferative action on the mucosa in the intestinal tract.

2315

Acetaminophen Hepatoxicity: Protective Effects of Prostaglandin E-1 in the Rat

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The aim of this study was to determine 1) whether PG protects the liver from the acute hepatotoxicity of acetaminophen (AA) and 2) whether this protection is mediated by nitric oxide (NO). Male Sprague-Dawley rats were divided into 7 groups as follows: the first group received normal saline; the second group received AA 1.6 g/kg by gavage; the third group received AA followed by PG 200 μ g/kg; the fourth group received AA followed by N-acetylcysteine (NAC) 1 g/kg; the fifth group was pre-treated with L-NAME prior to the administration of AA + PG; the sixth and seventh groups received only NAC or PG respectively. After 24 h, all animals were sacrificed; blood samples were drawn for the determination of AST, ALT, malone dialdehyde (MDA), NO₃ and NO2. The livers were snap frozen and stored at -80°C for the determination of NO synthase (NOS), except for a small specimen that was saved for histologic evaluation. AA-treated animals showed a profound elevation in both AST and ALT suggesting acute hepatocellular necrosis which was subsequently confirmed histologically. PG attenuated significantly (p < 0.001) the AA-induced liver injury as also did NAC, the classic AA antidote. Furthermore, PG restored the NOS levels which were depleted by AA. By contrast, pretreatment of the animals with the NOS-inhibitor L-NAME almost abolished the protective effect of PG. In conclusion: 1) PGE-1 attenuates the AA-induced liver damage in the rat. 2) The hepatoprotective effect of PG is mediated by the generation of endogenous NO.

2316

Colorectal Cancer Screening Compliance Enhanced by Personal Computer (PC) Based Multimedia Patient Education

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The potential reduction in morbidity and mortality from colorectal cancer achieved using endoscopic screening has been supported by numerous studies. The ultimate degree of success depends largely on the extent and regularity of compliance exhibited by patients. Participation in colorectal cancer screening is frequently limited by ignorance of modern technology, exaggerated fears of pain and suffering, and a lack of motivational understanding of the goals.

Preventative medicine efforts and screening elsewhere demonstrated improved compliance can be achieved using direct advertising and patient education. Automation can limit practitioner time consumed in teaching efforts, while ensuring uniform, complete presentation. A PC based, variable platform, interactive multimedia educational kiosk was created to fill these needs. Pre- and post-participation confidential questionnaires were used to assess subject attitudes and factual retention. Results were then used to further educate screening candidates and refine counselling presentations.

Computer assisted colorectal cancer screening counseling was well accepted by both medical practitioners and patient users. Many patients who stated they were inclined to refuse screening in questioning prior to education became motivated to participate in screening afterwards. Post-test factual retention was excellent in the majority of patients. Subjects who had participated in previous screening efforts rated the current computer aided counseling as generally superior to past oral instruction.

We conclude that computer based multimedia education is a significant advance in motivating and instructing our patients about the need for colorectal cancer screening.