show regional and/or distant metastasis. In the Year 1992 *734 patients* were admitted for gastrointestinal malignant neoplasms, *53* of them for primary liver tumor. *24* of these patients underwent hepatic resection. *170 of the 734* patients also had liver metastasis. The patients having multi-organ distant spread of the disease are candidates for systemic chemotherapy. The patients having liver metastasis only are treated by means of locoregional arterial cytotoxic infusion. In all cases the diagnosis was confirmed by histological examination. The vented B. Braun Implantofix arterial cannula with port was inserted via the pancreaticoduodenal artery at the time of the primary operation or during separate surgery. For some of the patients angiographic method was used with or without subcutaneous port. In the period from 1985 to 1994 *84* patients were treated via intra-arterial cannula. According to our analysis using the Kaplan Meyer formula the best survival i.e. *29* month could have been achieved at patients undergoing hepatic resection plus locoregional chemotherapy. The cumulative survival rate following any other method of treatment was less favorable, that means 11 to 18 months according to the method used.

1132 PCNA/Cyclin Defined Proliferative Activity in Colorectal Adenomatous Polyps

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Proliferative activity in 45 colorectal adenomatous polyps was evaluated with the use of immunochemistry and PCNA/cyclin monoclonal antibodies in alcohol fixed paraffin embedded sections. The size of polyps between various histologically classified groups of adenomas was also compared. All examined polyps were resected endoscopically from 40 patients. Proliferative activity was measured by the proliferation index.

No statistically significant differences in proliferation index between histologically classified groups of adenomas and between selected size groups of polyps were found.

Method using monoclonal antibodies to PCNA/cyclin in investigation of the proliferation activity in paraffin sections is recommended because of its technical and economical advantages.

1133 5-FU Modified Chemotherapy Following Surgical Resection for Large Bowel Cancinoma

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From 1982 to 1986, a randomized control study has been performed to investigate the chemotherapeutic effect of 5-fluorouracil (5-FU) regimen on resected colorectal carcinoma. 218 patients were randomly assigned to either 5-FU modified chemotherapy group or contral. 110 patients received modified chemotherapy of 5-FU " 3.2.1 " regimen. Totally the patients received 6 courses of treatment. The first course started on 14th day after operation. During the first year, 3 courses were given at an interval of 12 weeks. During the second year, 2 courses were given at an interval of 6 months. In the third year only one course was given. The patient's 5-year survival rate in this group was 80.6% with the rate in the stage B and C being 86.0% and 64.7% respectively, which were significantly higher than those in surgery alone ($P < 0.01$), and other surgery plus routine chemotherapy regimens (including 5-fluorouracil routine regimen, combination of chemotherapy with 5-fluorouracil and chemoimmunotherapy with 5-fluorouracil plus levamisolve) with P value being less than 0.05. We conclude that the modified chemotherapeutic regimen of 5-FU " 3.2.1 " has good efficacy and safety in the treatment of patients with colorectal cancer in clinical practice. The results also strongly suggest that the 5-FU modified chemotherapy is the best one at present.

1134 Fedotozine Versus Metoclopramide in Functional Dyspepsia: Results of a 6 Week Multicenter Therapeutic Trial

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Efficacy and safety of fedotozine (FZ), a peripheral κ agonist, were compared to those of metoclopramide (MC) in patients with functional dyspepsia. *Methods.* 381 patients were entered into a phase III, double blind, parallel group, multicenter trial and fulfilled the following criteria: presence in the last 3 months, and at least 3 times a week, of 2 or more post-prandial dyspeptic symptoms: epigastric pain, early satiety, fullness or epigastric distension, nausea or vomiting, feeling of slow digestion. An underlying organic disease was ruled out through medical examination, gastroduodenoscopy, upper abdominal ultrasound and routine blood tests. Patients completed a diary card daily and rated the overall intensity of their symptoms (main end-point) as well as the intensity of each dyspeptic symptom using a 0 to 4 verbal scale. A quality of life (QoL) questionnaire [1] was completed before and after the treatment period. At the end of a run-in period lasting 7 to 14 days, patients no longer meeting the inclusion criteria were excluded. 302 patients (172 females, 130 males, aged 45 ± 14 yrs, m ± SD) were randomized to receive either oral FZ, 30 mg tid (n = 152) or oral MC, 10 mg tid (n = 150) during 6 weeks. Intent-to-treat analysis was performed. In the absence of a significant difference (ancova), an equivalence test was carried out. *Results.* FZ and MC treatment groups were comparable before treatment. The overall symptom intensity score was similarly improved with MC (1.80 ± 0.56 to 1.28 ± 0.64) and FZ (1.79 ± 0.70 to 1.30 ± 0.71); p equivalence < 0.01. Score improvements for each dyspeptic symptom were also equivalent in both groups. Drug-related adverse events were significantly less common in the FZ group (12.0 vs 19.2%, p = 0.03), notably for CNS adverse effects (somnolence: 2.6 vs 8.7%, odd ratio: 3.5, p = 0.05). There were significantly fewer treatment discontinuations for adverse events in the FZ group (4.6 vs 12.7%, p = 0.01). Several items of the QoL questionnaire and multivariate analyses on all items showed a significantly greater improvement in the FZ group compared with the MC group (p < 0.05). *Conclusion.* After a 6 week treatment, efficacy of fedotozine is equivalent to that of metoclopramide in the symptomatic relief of functional dyspepsia complaints. Fedotozine is better tolerated than metoclopramide and has a better effect on patients' quality of life.

[1] Gerin P. et al. Fundam Clin Pharmacol 1992; 6: 263–276

1135 Is Combination of Neodym-Yag-Laser and Endocavitary Brachyradiation in Stenosing Esophageal Carcinoma Superior to Both Methods Uncombined?

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Introduction: Aim of all palliative therapy of inoperable esophageal carcinoma is to increase the quality of life by restoration or improvement of passage for oral nutrition. For this goal there exist different palliative procedures. Our work refers to the comparison of Nd-YAG-laser therapy and endocavitary afterloading respective the combination of both methods.

Methods: From 07/91 to 09/93 we divided randomly our patients with stenosing esophageal carcinoma in three groups. The indication for therapy was dysphagia, as consequence of which the caloric requirement could not be covered up. The patients with failure of the afterloading therapy were treated with combined therapy. Eighty four pts. (436 applications, mean 5.1, min 2 to max 9) were primarily treated with laser, 139 pts (488 applications, mean 3.5, min. 1 to max. 11) treated with afterloading and 52 pts. (122 applications, mean 2.3, min. 1 to max. 9) with the combination of both. 31% of the pts. were female, 69% male, the mean age was 68 years (37–89).

Results: The 52 pts. who were primarily assigned to afterloading but were treated further on in combination with laser therapy can be seen as therapy failures of the only afterloading therapy (37.4%). With comparable survival times of the three therapy groups (laser: 10.6 months, afterloading: 10.2 months, combination: 10.9 months) there was achieved a longer therapy interval with the combination of laser and afterloading (interval of laser application: 2.7 weeks, of afterloading 2 weeks and of the combination: 4.1 weeks). The complication of fistulation with lasertherapy was 2/84 pts. (2.38%), with afterloading 12/87 pts.: 13.80%).

Conclusions: In 37.4% of the patients where primarily an afterloading therapy failed a recanalisation was achieved with further laser application. In the group with the only lasertherapy all tumor stenoses could be opened primarily and permanently. Furthermore with the only afterloading therapy there was a six fold higher complication rate of fistula. The advantage of the combination therapy was the longer therapy interval.

1136 C3 Phenotypes and Cigarette Smoking in Patients with Duodenal Ulcer; Preliminary Results

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It has been reported an increased risk of Peptic Ulcer in people phenotypically C3FS and C3F [1]. In addition, the association of cigarette smoking with Duodenal Ulcer (DU) is known. In this study we looked for any relationship between cigarette smoking and C3 phenotypes in patients with DU in comparison with Healthy Controls (HC). 101 consecutive unrelative patients with DU (M: 74, W: 27, Mean age ± SD: 48.3 ± 15 years) and 95 unrelative HC (M: 60, W: 35, Mean age ± SD: 48.4 ± 16 years) well matched for socioeconomic status and area of origin were studied. Patients and controls were divided according to their smoking Habits in 4 groups: never smoked, ex-smokers (at least a year before), current smokers of 10–20 cigarettes/d, current smokers of more than 20 cigarettes/d. C3 phenotypes were determined as it was described [1]. "Statgraphics" was used for statistics. *Results:* C3 phenotypes

differed significantly between DU and HC (χ^2 = 12.59, p = 1.845 x 10^{-3}) due to the higher prevalence of "Ulcerogenic" phenotypes (FS and F) in DU patients (76% vs 53%); Smoking Habits differed significantly as well (χ^2 = 19.73, p = 0.0002) due to the higher prevalence of current smokers in DU patients (66% vs 37%). C3 phenotype distribution did not differ in smokers and non-smokers DU patients (p = 0.09) and HC (p = 0.06) although there was a higher prevalence of "ulcerogenic" phenotypes in non-smokers DU patients (86% vs 74%); in smokers. On the contrary, their prevalence in non-smokers HC was 47% (vs 61% in smokers). These results confirm the association of DU with C3F and C3FS phenotypes. In addition, there is a strong association of cigarette smoking with DU. It is interesting that there is a trend toward a higher prevalence of "Ulcerogenic" phenotypes in non-smokers DU patients.

[1] Archimandritis A. et al. Hum. Hered. 1992; 42: 198–200.

1137 Gastric Ulcer Short-Term Treatment: A Meta-Analytical Evaluation of Double-Blind Studies with Cimetidine vs Other H2-Blockers

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Gastric ulcer (GU) is less frequent than duodenal ulcer and studies involving a substantial number of patients are difficult to be performed. We aimed to establish whether newer H2-Blockers have improved GU short-term therapy.

We evaluated with a meta-analytical approach all studies appeared in Literature comparing cimetidine (CIM) with other H2-Blockers. Only double-blind trials were taken into account. Research of papers was done between August and September 1993 using both Medline and personal research.

We compared odds (Mantel-Haenszel modified method) with (1) a Fixed effects approach after Chi-square test for homogeneity computation and (2) a Random effect approach.

We found 8 papers reported results after 4 weeks: 5 compared CIM with ranitidine, 2 with famotidine and 1 with roxatidine.

Results:

Study no.	odds ratio	CI 95%
1	0.86	0.33–2.21
2	0.87	0.49–1.55
3	0.78	0.22–2.80
4	0.69	0.43–1.11
5	1.21	0.36–4.00
6	1.03	0.56–1.90
7	0.70	0.27–1.84
8	0.91	0.54–1.53
Cumulative	0.85	0.67–1.08
Homogeneity chi-square		0.975

In conclusion: newer H2-Blockers were proved to have comparable results when compared with CIM.

1138 Experience of 560 Ambulatory pH Recordings; Normal Range, Reliability and Patient Tolerance

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Oesophageal pH monitoring is performed regularly for the diagnosis and treatment of gastro-oesophageal reflux disease. The aim of this study was (1) to obtain a control range in asymptomatic subjects and to compare the results with those from other units and (2) to assess the reliability and tolerability of our technique.

Since 1986, 560 ambulatory pH recordings have been performed using a glass electrode (MI 506, Microelectrodes Inc) connected to a data storage and analysis system (Lectromed). Recordings were made over 22 hours under standardized conditions. Data was analyzed using 6 standard parameters at 5 pH levels between 3.0 and 5.0. A normal range was calculated using the method of Johnson and DeMeester from 20 asymptomatic controls [8 males, 12 females; mean age 39 yrs (range 18–62)].

The upper ranges of normal at pH < 4.0 were: total% reflux time <7.0, erect % reflux time time <9.0, supine % reflux time <10.0, total no. of reflux episodes <30, reflux episodes >5 mins <5, time of longest episode <50.0. Our results were towards the upper end of the range when compared with data from 11 comparable studies. There were 56 failed recordings (10%). 5 subjects (3 patients, 2 controls) were unable to tolerate the electrode (0.9%). Assessment at the standard level, pH < 4.0, proved of most clinical value.

In conclusion; there are wide variations in normal pH ranges defined by different units. The method used in this study was associated with a 10% failure rate but was well tolerated.

1139 Gastric pH Monitoring After Single I.V. Injection of Famotidine, Ranitidine, Cimetidine and Omeprazole: A Controlled Trial.

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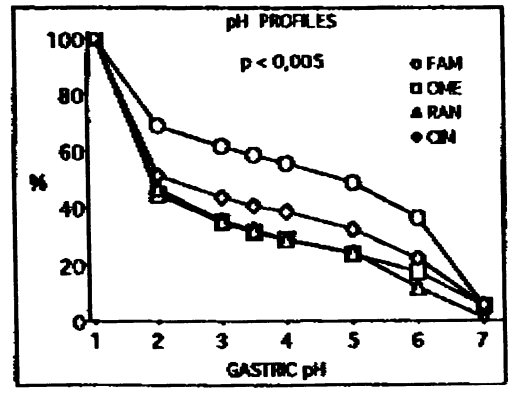
Aim: Treatment schedules for the intravenous (IV) use of antisecretory drugs are not clearly defined. We compared pH curves after a single IV injection of famotidine (F), ranitidine (R), cimetidine (C) and Omeprazole (O). Each dose was injected at the usual recommended unit range.

Methods: This randomised, double-blind, latin-square study was conducted in twelve healthy volunteers. In a fasting condition, pH monitoring (Proxima, France) was recorded for 1 hour (basal line) then 14 h, still fasting, after a single IV injection of F 20 mg, R 50 mg, C 300 mg, O 40 mg with a one week wash-out period between successive tests. Results are given in minutes (mean ± SD). Statistical analysis used ANOVA and Student t test.

Results: Time with pH values greater than 3.5 was significantly longer after F (516 ± 143) than after R (283 ± 235), C (355 ± 239) or O (270 ± 253) - p < 0.01 - with no period effect and no statistical difference between R, C and O. Total duration of the antisecretory effect was longer after F (635 ± 132) than after R (414 ± 205), C (405 ± 260) or O (393 ± 259) - p < 0.02 -. The four drugs were not statistically different for maximal pH (6.5 to 7), time for maximal pH appearance (112 to 183 min) or latency before pH increase 28 to 48 min). The pH profiles over 15 hours significantly favoured F (area under the curve, F: 110 ± 39, R: 54 ± 47, C: 75 ± 56, O: 59 ± 62, p < 0.005) (see figure).



Conclusions: Single first I.V. dose of 20 mg of famotidine give better results on gastric pH curves compared with usual dose of ranitidine, cimetidine or omeprazole. This difference is related to a longer pharmacodynamics activity.

1140 Time Course of Recurrence Following Duodenal Ulcer Healing with Pantoprazole or Ranitidine

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It was the aim of this multicenter, double-blind, one-year off-drug follow-up study to compare the time course of duodenal ulcer relapse in patients whose ulcers had healed on 2 or 4 weeks' treatment with either pantoprazole (PZ), 40 mg once daily, or ranitidine (RA), 300 mg once daily. Pantoprazole is a novel, selective proton-pump inhibitor. It is a potent inhibitor of gastric acid secretion.

Methods: 159 outpatients (pretreatment PZ: 114, RA: 45; 2:1 randomization) were routinely endoscoped after 3, 6, 9 and 12 months or whenever ulcer symptoms occurred on more than 3 consecutive days. Treatment with antacids was allowed for a maximum of 7 days for symptom relief. No other anti-ulcer drugs were permitted throughout the study. Laboratory tests (including serum gastrin after 3 months) were performed in addition.

Results: Life table analysis (according to Cutler & Ederer) of 159 patients gave estimated relapse rates of 45% after 3 months, and 55% after 6, 9 and 12 months for PZ. Corresponding relapse rates following treatment with RA were 52% after 3 months, 57% after 6 months and 63% after 9 and 12 months. There was no significant difference between the groups with respect to the time course of ulcer relapse (p > 0.05, Uleman's U-test). Gastrin serum levels had returned to pretreatment values in both groups 3 months after withdrawal of acute treatment.

Conclusion: This study indicates that relapse rates following acute treatment with pantoprazole are similar to those following treatment with the H_2-receptor antagonist ranitidine.

1141 The Proton Pump Inhibitor Pantoprazole Does Not Impair Safety Related Performance

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As new drugs potentially affect safety in every day life (e.g. traffic safety, safety at work, home, sports), investigations with the standardized test battery of the Vienna Test System WTS90 were performed before and after administration of 40 mg pantoprazole, the recommended dose for the treatment of peptic ulcer disease in comparison to placebo.

18 healthy volunteers (9 m/9 f) aged 19 to 58 years completed the placebo-controlled randomized double-blind crossover study, with once daily oral intake of pantoprazole 40 mg and placebo, respectively, for five days each. The safety related performance was investigated before drug intake and on days 1 and 5 of each treatment period. The two periods were separated by a wash-out of at least 7 days. Visual orientation, forced concentration, simple reaction time, choice reaction time, stress tolerance, vigilance and motor co-ordination were evaluated using the analysis of covariance.

Most of the performance tests revealed no difference between placebo and pantoprazole on days 1 and 5. Only two statistically significant results were obtained: one in favour of placebo with the vigilance test and one in favour of pantoprazole with the simple reaction time.

In conclusion, repeated administration of 40 mg pantoprazole once daily is not expected to impair safety in traffic or at work.

1142 The Efficacy of Hormonal Contraception is Not Affected by Pantoprazole Treatment

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Inhibitors of the gastric H^+/K^+-ATPase from the class of the substituted benzimidazoles may interact with the CYP450 enzyme system and alter the pharmacokinetics or pharmaco-dynamics of coadministered drugs. In particular, interactions with oral contraceptives are of importance, as this can result in contraception failure. Therefore, the aim of this study was to investigate whether pantoprazole, a new, selective proton pump inhibitor, affects the efficacy of a low dose hormonal contraceptive.

Seventy-three healthy, premenopausal women with normal gynaecologic histories participated in this open study lasting 4 menstrual cycles. *Cycle 1*, proof of ovulation: no treatment was given; serum progesterone concentrations were measured 7 days after onset of menstruation and 7 days before expected onset of next menstruation (women who did not ovulate were excluded). *Cycle 2 and 3*, proof of suppression of ovulation: a low-dose triphasic contraceptive agent was administered daily for 2 menstrual cycles (women who ovulated despite hormonal contraception were excluded). *Cycle 4*, to determine interaction: the contraceptive was administered daily together with 40 mg pantoprazole from day 1 to day 23. *Blood sampling:* During cycles 2, 3 and 4, serum progesterone was determined on days 21 and 23 of each cycle, and on the 7th premenstrual day, determined according to each subject's normal cycle length prior to contraceptive treatment. Serum progesterone concentrations of 10 nmol/L or higher were considered indicative of ovulation.

Nine subjects withdrew or were withdrawn. No ovulation occurred amongst the remaining 64 subjects during cycle 4, demonstrating lack of interaction.

In conclusion, pantoprazole does not affect the efficacy of hormonal contraception.

1143 Dyspepsia: Parameters for Cost Calculations

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One of the objectives of this project was to estimate the indirect costs caused by dyspepsia (DYS) and determine the direct costs of diagnosis and therapy at the primary health-care level, during a 3 months period.

Patients and Methods: All patients visiting their MD due to epigastric troubles were screened; if the troubles had at least 1 month of duration and no anamnestic or otherwise evident explanation for their symptoms, they qualified as dyspeptics. In dyspeptics with an increased risk of organic disease, an upper GI-endoscopy was performed. The rest of the dyspeptics, as well as those with negative endoscopy, were presumed to be "functional" and classified in subtypes. Functional DYS was treated with cisapride; therapy of organic DYS was chosen by the treating MD. At each visit (days 0, 7, 30, 60 and 90) pts. were asked how many days they had been unable to attend work due to their digestive symptoms in the previous week.

Results: The data of 662 pts. could be evaluated. The percentage of responders at end point was app. 80% in all subtypes. The mean values of the parameters recorded are shown in the following table:

Functional dyspepsia	Absences in days/week before	Absences in days/week during study	Prescriptions per patient	Endoscopies per patient
Non specific	0.23	0.06	1.35	0.20
Dysmotility	0.71	0.12	1.38	0.23
Reflux	0.52	0.17	1.62	0.26
Ulcer-like	0.78	0.11	1.68	0.65
Peptic lesions all pooled	0.75	0.24	2.44	2.00

Conclusion: Knowing the costs due to absenteeism (indirect costs), the costs of the therapies prescribed and of diagnostic procedures employed (direct costs), it is possible to translate the above data into monetary terms. In the Swiss price system, the gains obtained by reduced absenteeism are much larger than the direct costs of medical care.

1144 Endoscopic Biopsy Versus Polypectomy in Diagnosis of Gastric Epithelial Polyps

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The purpose of this study was to compare endoscopic biopsy and polypectomy as methods in diagnosis of gastric epithelial polyps. Although it is well-known that material obtained by polypectomy and its histopathological diagnosis is gold standard for diagnosis of gastric epithelial polyps, there are always no possibilities for endoscopic polypectomy especially in small endoscopic units, so we wanted to compare these two diagnostic methods.

In prospective study 36 polyps were first biopsied (3 biopsies from the polyps larger than 1 cm, and 2 biopsies from the smaller polyps), and then removed in toto. In 33 comparison between biopsy and polypectomy was possible.

Identical histopathological diagnosis was found in 24 cases (73%). Different diagnosis was obtained in 9 polyps (27%). In 3 cases we had under diagnosis: polypectomy showed 2 adenomas, and 1 adenoma with malignant transformation, while biopsy showed focal foveolar hyperplasia (FFH), hyperplasiogenous polyp (HGP), and chronic gastritis (CG). Over diagnosis was present in 1 case (polypectomy showed HGP and biopsy adenoma), which was result of technical problems. In another 5 cases the difference in diagnosis was not of any clinical consequence (polypectomy: 3 cases of HPG while biopsy: FFH in 1 case and CG in 2 cases, and polypectomy: 2 cases of FFH while biopsy showed HGP and CG). Three polyps could not be compared after the polypectomy (terminal damage after "hot biopsy" polypectomy, where biopsy was definitive diagnosis.

In conclusion we can say that polypectomy is supreme diagnostic method, but the biopsy can also show the true nature of gastric epithelial polyps in 73% of cases. This is fairly high percent of identical histopathological findings, and it is noteworthy to mention that in this group is included one early carcinoma and one carcinoma arised from adenoma.

1145 Prevention of Duodenal Ulcer Relapse During Long-Term Treatment with Sulglycotide. A Placebo Controlled Study

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Sulglycotide, a polysulphated glycopeptide, extracted from porcine duodenum and unabsorbable from the gastrointestinal tract, has been shown to be effective in the short-term treatment of duodenal ulcer [1], as well as in non-ulcer dyspepsia [2] and in the prevention of NSAIDs induced gastropathy [3].

The aim of the present study was to evaluate the effectiveness of sulglycotide maintenance therapy in preventing duodenal ulcer (DU) relapse. One hundred nineteen asymptomatic patients with healed DU were randomly allocated, in a double-blind fashion, for one year either to sulglycotide 200 mg t.i.d. (60 patients) or placebo (59 patients). Patients underwent clinical control every third month whereas endoscopy was systematically repeated at six and twelve months or beforehand, if relapse was suspected.

The cumulative relapse rate was 61% in the placebo treated group whereas the group treated with sulglycotide showed a relapse rate of 43% (Log rank test: $p < 0.05$). This results indicate that sulglycotide administration is effective as a maintenance treatment in preventing the relapse of duodenal ulcer.

[1] G. Bianchi Porro et al. Br Med J 1979; 2: 17–8
[2] L. Barbara et al. Am J Gastroenterol 1990; 85 (9): 1109–13
[3] G. Bianchi Porro et al. Scand J Gastroenterol 1993; 28:875–78

1146 Comparison of Hydrotalcite and Ranitidine in an Open, Randomized Study in Patients with Duodenal Ulcer with Regard to Ulcer Healing, Intragastric Bacterial Growth, Nitrate and Nitrite Content

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Healing of duodenal ulcer (DU) and pain relief was compared in 24 outpatients under treatment with an antacid (hydrotalcite, HT) or ranitidine (RA) after 2 and 4 weeks. The influence of both treatments on intragastric pH, bacterial growth (BG), nitrate- and nitrite content was also investigated.

Methods: 12 patients (pts) were treated with HT and 12 pts received RA. The recommended dose was 4 × 2 tablets (1 tablet = 500 mg) for HT and 1 × 2 capsules (1 capsule = 150 mg) for ranitidine. The pts were allowed to increase the dose up to the triple standard dose according to their symptoms. Endoscopy and a microbiological examination of gastric juice was performed at day 0, day 14, and day 28. The level of pain (0 to 6) was assessed by the pts using the paintrack-system.

Results: Endoscopic healing rates were identical in both groups (75 % after 2 weeks, 100 % after 4 weeks). Mean pain during the day was reduced from 1.26 ± 0.78 (first week) to 0.86 ± 0.84 (second week) under HT and from 1.02 ± 0.70 to 0.62 ± 0.62 under RA. Intragastric pH rose from 1.6 to 4.3 (median) under RA and was unchanged under HT (1.6) after 2 weeks. 7 pts in the HT-group and 10 pts in the RA-group showed an increased number of germs after 2 weeks. The median ratio day 14/day 0 of the total number of germs was 3.72 under HT and 7.60 under RA demonstrating an enhanced BG under RA. No significant changes were observed for the number of nitrate reducing germs (increase in 3 vs. 5 pts) and for the concentration of nitrate and nitrite. In pts with a high pH BG was not pronounced. The median daily dose was 7 tablets of HT and 3 capsules of RA in the first week.

Conclusions: The microbiological flora is influenced by treatment with RA even after two weeks. However, no change in the concentration of nitrate and nitrite was observed. HT and RA seemed to be equally effective in healing DU and relieving pain.

1147 G, PGA and PGC Basal Serum Levels Modifications during Omeprazole Long-term Therapy for Peptic Disease

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The aim of this study was to evaluate Gastrin (G), Pepsinogen A and C (PGA and PGC) basal serum level modifications during maintenance therapy with Omeprazole (OME) in 302 outpatients (aged 18–76) with peptic disease.

114 duodenal ulcer (DU), 94 gastric ulcer (GU), 94 reflux esophagitis (RE) pts, successfully healed in a short-term protocol, were enrolled in the follow-up study. They were randomly assigned to 12-month treatment with either OME 20 mg/day (DU = GROUP I; GU = GR II; RE = GR III) or OME 20 mg every other day (UD = GR IV; UG = GR V; RE = GR VI). Endoscopy, routine histology and G, PGA and PGC evaluation were performed on admission (TO), at 6 (T6) and 12 (T12) months or earlier, if pts had a recurrence of symptoms. Patients completed the study after 12 months or earlier, if a relapse occurred. *Statistical Analysis.* Wilcoxon Rank Sum test; a p-value < 0.05 was taken as significant. Data were expressed as Mean ± SD. *Results.* 214 outpatients completed the study. After 12 months, G, PGA and PGC levels were significantly decreased in all DU and RE pts (TO vs T6 vs T12) (G pg/ml; GR I 110.7 ± 51.2 vs 119.8 ± 89.7 vs 79.5 ± 46.6; GR IV 106.8 ± 55.3 vs 97.4 ± 75.1 vs 76.5 ± 30.2; GR III 124 ± 70.5 vs 110.1 ± 71.9 vs 105.6 ± 54.5; GR VI 112.8 ± 60.3 vs 107.2 ± 48.8 vs 81.9 ± 27.9; PGA ng/ml; GR I 261.3 ± 105.3 vs 164.1 ± 89.4 vs 135 ± 49.9; GR IV 259.5 ± 136.1 vs 157.7 ± 103.6 vs 147 ± 72.8; GR III 254.3 ± 131.1 vs 173.4 ± 76.6 vs 179.6 ± 54.5, GR VI 215.8 ± 161.2 vs 164.4 ± 91.3 vs 159.9 ± 27.9; PGC ng/ml; GR I 20.2 ± 10.1 vs 14.4 ± 8.5 vs 12.3 ± 6.4; GR IV 21 ± 14.7 vs 15.2 ± 13.1 vs 10.6 ± 7; GR III 15 ± 5.2 vs 6.5 ± 6.3 vs 7.3 ± 2.5, GR VI 12.9 ± 8 vs 7.4 ± 3.7 vs 6.9 ± 4.3).

In GU pts, only PGA levels were significantly decreased at the end of the study (TO vs T6 vs T12) (GR II 205 ± 130 vs 168 ± 90.5 vs 139 ± 89.4; GR V 256 ± 105 vs 148 ± 74.8 vs 128 ± 37.5). *Conclusions.* Our data showed a significant decrease in G, PGA and PGC levels in DU and RE, but not in GU, patients after 12 month therapy with OME, which may reflect the different physiopathology of these diseases.

1148 Duodenal Ulcer Maintenance Therapy with Omeprazole: A 12-month Follow-up Study

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This study investigated the efficacy of maintenance therapy with omeprazole (OME) in preventing duodenal ulcer relapse. *Study design.* 114 outpatients (aged 18–76) with endoscopically documented duodenal ulcer successfully healed in a short-term protocol were enrolled in the follow-up study. Patients were randomly assigned to 12-month treatment with either OME 20 mg/day (Group I; n = 56) or OME 20 mg/every other day (Group II; n = 58). Patients were seen at 3 and 6 months for clinical assessment; endoscopy was performed on admission (T0) and at 6 (T6) and 12 (T12) months or earlier, if they had a recurrence of symptoms. At each scheduled endoscopy, serological evaluation (Gastrin (G), Pepsinogen A and C (PGA and C) basal serum levels) was performed, and gastric biopsy specimens were taken for routine histology. Ulcer relapse was defined as symptomatic or asymptomatic endoscopically verified recurrence of ulcer. Patients completed the study after 12 months or earlier, if a relapse occurred. *Statistical Analysis.* Wilcoxon Rank Sum test, Chi-square test; a p-value < 0.05 was taken as significant. Data were expressed as Mean ± SD. *Results.* 89 outpatients completed the study. After 12 months, life table analysis showed that the cumulative proportion of pts in remission was 94.6% for OME 20 mg/day and 80.8% for OME 20 mg/every other day, respectively (p = 0.025, test Breslow and Mantel-Cox). At the end of the study, G, PGA and PGC levels were significantly decreased in both groups (T0 vs T6 vs T12) (G pg/ml; GROUP I 110.7 ± 51.2 vs 119.8 ± 89.7 vs 79.5 ± 46.6; GROUP II 106.8 ± 55.3 vs 97.4 ± 75.1 vs 76.5 ± 30.2; PGA ng/ml; GROUP I 261.3 ± 105.3 vs 164.1 ± 89.4 vs 135 ± 49.9; GROUP II 259.5 ± 136.1 vs 157.7 ± 103.6 vs 147 ± 72.8; PGC ng/ml; GROUP I 20.2 ± 10.1 vs 14.4 ± 8.5 vs 12.3 ± 6.4; GROUP II 21 ± 14.7 vs 15.2 ± 13.1 vs 10.6 ± 7). *Conclusions.* Both regimens are effective and safe in preventing duodenal ulcer relapse, with a significant lower relapse rate in OME 20 mg/day group.

1149 Treatment of Functional Dyspepsia with Cisapride – Results of a German Multicenter Trial

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Aim: The aim of this study was to assess the efficacy and the tolerability of a low dosage of the prokinetic agent cisapride in the treatment of functional dyspepsia.

Patients and Methods: 8766 adult patients presenting to 1757 practitioners with mild, moderate or severe symptoms and found to have functional dyspepsia were treated for four weeks with cisapride 5 mg three times a day. Symptom severity was scored by patient visual analogue scales (VAS) and by doctors' assessment. For calculation of differences in each parameter between initial and final examination, an intent-to-treat analysis was performed.

Results: The low dose cisapride treatment resulted in a reduction in the total scores of all dyspeptic symptoms. For example, an improvement was documented in 78.6% of patients reporting fullness and bloating, in 73.6% of patients with abdominal distention and in 77.4% of patients suffering from epigastric discomfort. The treatment success showed no regional or sex-linked variations, but moderate and severe dyspeptic symptoms reacted remarkably better and independently of the underlying dyspepsia subgroup. Adverse events were reported in 8.3% of patients, mainly modifications of the frequency and consistency of stools.

Conclusions: The results of our study underscore the efficacy and the positive safety profile of low-dose cisapride in the treatment of all of the different categories of functional dyspepsia.

1150 Effect of Antacid Hydrotalcite (HT) on Gastroduodenal Lesions Induced by NSAID (Randomised, Double-Blind, Placebo-Controlled, Multicentre Trial)

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Aim: The purpose of this study was to define the effects of HT on NSAID-induced dyspepsia and gastroduodenal lesions. In addition, we investigated possible connections between the kind of NSAID and the severity as well as location of the mucosal damage, and connections between the efficacy of the study medication and the consumption of coffee, tobacco and alcohol.

Patients and Methods: The study involved 15 centres. 150 arthritic patients with a minimum of 4 weeks' NSAID treatment and endoscopically proven mucosal injury were randomly divided into two groups. While still on NSAID, each patient received two tablets of either HT or a placebo four times a day. Symptom severity was scored by patient visual analogue scales (VAS) and by doctors' assessment. For calculation of differences in mucosal injury scores between initial and final endoscopy, an intent-to-treat analysis was performed.

Results: After six weeks, mucosal damage was healed in 88% of the patients on HT, and in 66.7% of those on placebo (p < 0.001). HT clearly diminished abdominal diurnal and nocturnal pain. Endoscopy revealed most of the lesions to be located in the antrum, but no differences in NSAID ulcerogenicity. In regular coffee consumers, the healing process of gastric, but not duodenal lesions was retarded. However, no correlation was established between the efficacy of the study medication and smoking or alcohol consumption; indeed the latter even improved healing rates.

Conclusions: The data underscore the efficacy of hydrotalcite in the treatment of NSAID-induced gastroduodenal lesions and associated abdominal pain.

1151 Does Cigarette Smoking Influence the Recurrence of Peptic Ulcer Disease?

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Inhibitory effect of smoking on speed and rate of healing of peptic ulcer is well documented. However, opinions about impact of this habit for recurrence of gastric and duodenal ulcer are different.

Aim: The aim of the study was to evaluate the influence of cigarette smoking on recurrence of peptic ulcer disease.

Material and Method: One hundred patients with gastric and duodenal ulcer were studied within a period from 1 to 5 yrs. Out of 60 patients with gastric ulcer the 40 were smokers and the 20 non-smokers, whereas of 40 patients with duodenal ulcer the 25 were smokers and 15 non-smoking patients. The patients were randomly tested by means of endoscopic examinations, which were repeated at least two times a year regardless the symptoms and also in case of exacerbation of the disease. Anti-ulcer drugs were administered only for acute treatment of a new active ulcer. Occasionally taking of small amounts of antacids was allowed.

Results: In five years period of observation cumulative recurrence rate of gastric ulcer was 60% in smokers and 50% in non-smokers (N.S.). In duodenal ulcer group the cumulative recurrence rate was 80% in smokers and 73.3% in non-smokers (N.S.).

Conclusion: Cigarette smoking does not seem to affect the recurrence of gastric and duodenal ulcer significantly.

1152 Have Patients with Non-Ulcer Dyspepsia Responding to Treatment with Ranitidine a Characteristic Pattern of Gastro-Oesophageal Reflux?

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This study compares the gastro-oesophageal reflux pattern in patients with non-ulcer dyspepsia classified as responders or non-responders to treatment with ranitidine.

Patients and methods. Thirty-one patients (male/female: 20/11) with non-ulcer dyspepsia had a 24-h oesophageal pH monitoring performed. They were randomised to 6 weeks' double-blind alternating treatment with 150 mg ranitidine twice daily and placebo, 1 week of each alternative. After the treatment period the patients were classified as responders or non-responders based on improvement of symptoms. The gastro-oesophageal reflux patterns in the two groups were compared. The results are given as median with range in brackets.

Results. 6/17 (35%) of patients classified as responders, and 2/14 (14%) of patients classified as non-responders had pathological 24-h pH monitoring, defined as total time pH < 4: ≥ 4.5% (n.s.). Total time pH < 4 in the responders and non-responders were 2.6% (0.3–11.7) and 2.5% (0.1–21.5) respectively (n.s.). Nor were any statistically significant differences seen during upright or supine position, or in relation to symptoms. The total number of reflux episodes (pH < 4) and the number of short reflux episodes (<1 minute) in the responder group were 38 (16–102) and 25 (9–66) respectively, and in the non-responder group 23.5 (2–77) and 15 (2–47) respectively. The difference in number of short reflux episodes was statistically significant ($p < 0.05$).

Discussion. Although there was a higher proportion of patients with pathological gastro-oesophageal reflux among the responders than the non-responders, most responders had no pathological reflux. Thus, total reflux appears unsuitable to predict the effect of ranitidine. Numerous short reflux episodes have not previously been associated with non-ulcer dyspepsia. However, if this reflux pattern is the cause of symptoms in some patients with non-ulcer dyspepsia, it is plausible that ranitidine relieves these symptoms.

Conclusion. A high number of short gastro-oesophageal reflux episodes might be characteristic for patients with non-ulcer dyspepsia responding to treatment with ranitidine.

1153 Lack of Correlation Between the Macroscopic and Microscopic Views in Diagnosing Atrophic Gastritis

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Histological findings of Atrophic Gastritis (AG) is considered a pre-malignant stage in the development of epithelial malignancy. There is a difference of opinions as to whether it is possible to identify by macroscopic viewing which of the patients has AG.

The aim of this work is to investigate if there is a correlation between the macroscopic view (presence of submucosal capillaries is accepted as a sign of AG) observed in the course of the UGI endoscopy, and the histologic finding.

Hundred fifty patients who had come for a routine UGI endoscopy were examined consecutively. The endoscopist described the macroscopic view, during the UGI endoscopy, biopsy was taken from the antrum and body of the stomach for histological and bacteriological examination. The samples were blinded tested in Pathology and Bacteriology laboratories. Seventy four males and 76 females participated in the study. The average age was 57 years old (range from 10 to 91). Ten patients were found to have prominent submucosal capillaries and the endoscopist was sure about the diagnosis of AG. In none of these cases was AG in histology expected. On the other hand, 12 patients were diagnosed as having AG according to the histological findings while the endoscopist had no suspicion of AG being present. In the AG patients, the level of Helicobacter pylori (HP) was 25% as opposed to 51% in our study population.

In conclusion: According to our experience, the macroscopic view in UGI endoscopy cannot diagnose the presence of AG and the HP infection is lower in AG.

1154 The Efficacy of Different Doses of Ebrotidine (E), A Novel H_2-Receptor Antagonist in Duodenal Ulcer (DU) Healing

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We have shown that 800 mg of E nocte is as effective as 300 mg of Ranitidine nocte in DU patients. The objective of this study was to establish the efficacy of E (200, 400 and 800 mg) given in single nightly dose versus placebo.

DU patients from 5 centers were randomized into an endoscopically controlled double blind trial. Patients (n = 110) fulfilled the entry criteria and the protocol was completed. The endoscopy was performed at entry and after 2, 4, 6 and maximum 8 weeks duration of therapy. All groups appeared well matched for population demography, DU history and prestudy symptomatology. Cumulative healing rates at 6 and 8 week of treatment was 59.4% with placebo, while after higher doses of E (400, 600, 800 mg) reached 90–95%. The 200 mg of E group did not show any significant differences in ulcer healing when compared to the placebo group. However the difference between 400, 600 and 800 mg was not clinically or statistically significant, but the incidence of the degree of duodenitis was significantly lower with all 4 doses of E than with placebo. The number of epigastric night pain episodes diminished significantly for all E groups ($p < 0.0003$), but not for placebo group ($p = 0.046$). Ebrotidine increased moderately plasma level (measured after 4 week treatment) of gastrin (by 20.9 %) and lowered plasma PP (by 14.2 %). No important clinical or biochemical side effects were noted.

We conclude that E in single nightly doses of 400, 600 and 800 mg is highly effective in DU healing rate, however no significant differences between used doses in clinical end-points were noted.

1155 Histamine Levels in Whole Blood of Healthy Subjects and Those Suffering from Ulcer Disease Smokers and Nonsmokers

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Histamine is one of the important links in the etiopathogenetic chain of the ulcer disease. Negative effects of cigarette smoking on the healing, complications and recurrence of active ulcers is undeniable. Our aim was to establish histamine levels in whole blood of healthy persons, smokers and nonsmokers, as well as in the blood of smokers and nonsmokers suffering from ulcer disease, and the comparison of the results in the respective groups.

124 persons were examined. Histamine in whole blood was measured by radioimmunoassay using double antibody RIA (Pharmacia). The research was carried in standard conditions. Allergic patients were excluded from examination. Smokers did not smoke for 12 hours before blood sampling. Those treated with H-2 receptor antagonists did not take them for 4 days preceeding the test.

Statistical analysis of the results showed that histamine level was significantly higher in healthy smokers than in healthy nonsmokers; it was also higher in the blood of smokers suffering from ulcers than in blood of healthy persons. There were no significant differences in the histamine level of smokers and nonsmokers suffering from ulcer disease.

These preliminary reports seem to suggest that habitual cigarette smoking, disturbing histamine release irregardless of its origin, plays a role in pathogenesis of ulcer disease.

1156 Juxtapapillary Duodenal Diverticula and Clinical Characteristics

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In order to explore the relationship between duodenal diverticula and biliary stone disease and pancreatitis, we reviewed 1291 endoscopic retrograde cholangio-pancreatography (ERCP) procedures. A total of 46 patients were found to have diverticula with an incidence of 3.7 percent, being significantly higher in elderly group aged 60 years or older ($P < 0.01$) and no sex difference was noted. The occurrence of duodenal diverticula increased with age. Patients with duodenal diverticula were older, had mote gallbladder stones, more common bile duct stones, had undergone cholecystectomy more frequently and experienced more frequently common bile duct stone recurrence after cholecystectomy. The incidence of chronic pancreatitis was higher in patients with juxtapapillary diverticula than in patients without diverticula ($P < 0.01$). These result show a significant association between juxtapapillary duodenal diverticula and gallstone disease and pancreatitis.

1157 Late Results Duodenal Ulcer Treatment by Truncal Vagotomy and Pyloroplasty

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The aim of this study was evaluation of changes in gastric mucous after surgical treatment of duodenal ulcer. The material consists of 28 patients who have had 15–29 years ago bilaterally truncal vagotomy and pyloroplasty. These patients, meantime one to 13 years after surgery underwent investigations based on generally accepted clinical examination and gastric mucous biopsy.

Postoperative duodenogastric reflux was investigated by gastroscopic findings and after following 14 years by 99mTc-HIDA scintigraphy. In the first as well as in the second histological investigation all patients presented inflammatory changes in gastric mucous in the form of glandular atrophy, chronic inflammation and active gastritis. After the lase of the time an increasing atrophy and frequency of intestineal metaplasia in gastric mucous was observed. These histological features were strongly associated with the presence and intensity of duodenogastric reflux.

Our results in 28 patients indicate that truncal vagotomy and pyloroplasty is favourable in the duodenal ulcer treatment but creates circumstances of duodenogastric reflux which leads to atrophic changes and intestineal metaplasia in gastric mucous.

1158 Triage, Probatory Therapy with Cisapride and Follow Up in Functional Reflux and Dyspepsia

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One of the objectives of this project [OMEGA-Project] was to determine the efficacy of a probatory therapy at the primary health-care level, both at the end of therapy and after a 2 months follow up in different types of functional dyspepsia.

Patients & Methods: All patients visiting their MD due to epigastric troubles were screened; if the troubles had at least 1 month of duration and no anamnestic or otherwise evident explanation for their symptoms, they qualified as dyspeptics. In dyspeptics with symptoms indicating an increased risk of organic disease, an upper GI-endoscopy was performed. The remainder of the dyspeptics, as well as those with negative endoscopy, were presumed to be "functional dyspeptics" and classified in subtypes as reflux-like, ulcer-like, dysmotility-like and non specific. All four subtypes received a probatory therapy with cisapride (15–40 mg/day) during 1 month and were followed up for additional 2 months. Persistence or relapse of symptoms led to a post-endoscopy. "Responders" are pts. with $\sum$ score-reduction of > 66% and "relapse" if $\sum$ symptoms score returned to >50% of baseline.

Results: Out of 1033 patients screened, 662 complied with the definition of dyspepsia; after endoscopy of 120 patients, 612 were admitted to the therapeutic trial. The distribution of the different subtypes and the main results are summarised in the following table:

Data at end point

	N pts.	Resp.	Non resp.	Relaps
Reflux-l.	184	82%	11%	7%
Ulcer-l.	72	81%	14%	5%
Dysm.-l.	187	86%	10%	4%
Non-spec.	169	79%	16%	5%

Conclusion: Cisapride provided a high response rate in all subtypes. The relapse rates reported two months after the end of active therapy are small and indicate the persistence of therapeutic benefit which should be confirmed in adequately controlled trials. No severe ADEs were registered.

1159 Non Aspirin Non Steroidal Anti-Inflammatory Drugs (NSAIDs) and Ulcer Complication, a Case-Control Study of Risk Factors

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NSAID use is associated with an increased risk of ulcer complication with an odds ratio (OR) about 3 to 4. The risk for the individual NSAID user is small but the widespread use of these drugs results in a large number of ulcer complications.

Aim: to identify risk factors for the development of ulcer complication in association with NSAID use.

Methods: CASES: consecutive NSAID users admitted with an ulcer complication over a three year period. CONTROLS: NSAID users without ulcer complication identified by a pharmacoepidemiologic database as a random sample of all NSAID users in the area. Cases were interviewed at hospital and controls were send a questionnaire with identical questions. To evaluate the effect of each factor multiple logistic regression analysis was performed and the adjusted OR was calculated with its 95% confidence interval (CI).

Results: 94/118 cases were interviewed and 323/540 controls answered the questionnaire. Analysis showed no differences between included and excluded patients. Analysis was performed for two clinical situations:

(1) For patients considered to start NSAID treatment risk factors were: high age: 60–75 year: OR 3.5 (CI: 1.8–7.0), >75 year: OR 8.8 (CI: 4.3–18.1), male sex: OR 1.7 (CI: 1.0–3.0), ulcer history: OR 2.5 (CI 1.2–5.1), steroid treatment: OR 2.0 (CI: 0.8–4.6), smoking: OR 1.6 (CI: 0.9–2.7), alcohol use: OR 1.8 (CI: 0.9–3.6).

(2) For patients considered to continue NSAID treatment risk factors were high age, male sex, ulcer history and smoking. Furthermore dyspepsia was a risk factor: OR 2.1 (CI: 1.0–4.2), especially NSAID-related dyspepsia: OR 8.9 (CI: 4.1–19.2). For patients treated less than 3 months OR was 4.6 (CI: 2.3–8.9) (reference group: patients treated ≥1 year).

Conclusion: Risk factors for development of ulcer complication in association with NSAID use were high age, male sex, ulcer history and dyspepsia, especially NSAID-related dyspepsia. Risk decreased with treatment time beyond 3 months.

1160 Simultaneous Intake of Antacids Has No Influence on the Pharmacokinetics of the Gastric H^+/K^+-ATPase Inhibitor Pantoprazole

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Pantoprazole is a new selective proton pump inhibitor for the treatment of gastric acid related diseases. High healing rates and rapid pain relief have been established in patients (Müller et al., Z Gastroenterol 1992; 30: 771–5). Although concomitant intake of antacids is not necessary, patients might employ self-medication. Therefore, the aim of this study was to investigate whether concomitant intake of an antacid influences the pharmacokinetics of pantoprazole.

In a randomized two-period crossover study 24 healthy subjects (median age: 28 years, median body weight: 63 kg) were given 10 mL Maalox® 70 and 40 mg pantoprazole p.o. simultaneously (Test) and 40 mg pantoprazole p.o. alone (Reference). Serum pantoprazole concentrations were determined by HPLC over 24 h.

Both treatments were well tolerated. Lack-of-interaction was statistically handled as an equivalence problem (Steinijans et al., Int J Clin Pharmacol Ther Toxicol 1991; 29: 323–8), with AUC and C_{max} being the confirmative characteristics. The pharmacokinetic results of pantoprazole-Na are summarized in the following table:

Variable	Ref.	Test	Equivalence ratio Test/Ref.	
	Geom. mean (N = 22)		Point estimate	90%-conf. interval
AUC (mgxh/L)	5.84	5.96	1.02	0.95–1.09
C_{max} (mg/L)	3.13	3.18	1.02	0.89–1.16
$t_{1/2}$ (h)	1.22	1.22	1.00	0.95–1.06

There is no interaction between pantoprazole and antacids, i.e. concomitant intake of antacids does not affect the therapeutic efficacy of pantoprazole.

1161 Pantoprazole in the Elderly: No Dose-Adjustment

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Pantoprazole is a new inhibitor of the gastric H^+, K^+-ATPase. Since the pharmacokinetics of drugs may be altered in the elderly due to a number of factors, including changes in volume of distribution, liver enzyme activity or blood flow, pantoprazole was investigated in this population subgroup.

N = 16 healthy elderly subjects (age >65 years) were given once daily 40 mg pantoprazole p.o. for 7 days and 30 mg i.v. for 5 days in a randomized crossover study. Blood samples were frequently taken on days 1 and 7 (p.o.) and 1 and 5 (i.v.) for pharmacokinetic analysis.

Median values of the pharmacokinetic characteristics AUC, C_{max}, $t_{1/2}$, Cl and $V_{d\,area}$ of pantoprazole-Na after repeated administration are given in the following table:

	AUC (μgxh/mL)	Cmax (μg/mL)	$t_{1/2}$ (h)	Cl (L/h/kg)	$V_{d\,area}$ (L/kg)
i.v. 30 mg	4.98	3.94	1.47	0.0775	0.162
p.o. 40 mg	6.58	3.25	1.35	–	–

The pharmacokinetic characteristics were comparable after single and repeated dosing. Ratio analysis of the pharmacokinetic characteristics in elderly subjects and the corresponding values in healthy young subjects following repeated administration yielded point estimates of 1.13 for Cl (i.v.), and 1.35 or 1.22 for AUC or C_{max} (p.o.), respectively.

As the pharmacokinetic characteristics of pantoprazole in the elderly are comparable to healthy young subjects, pantoprazole may be safely administered to elderly patients without dose-adjustment.

1162 Influence of Ranitidine and Diclofenac on Angiogenesis and Mucosal Cell Proliferation in Human Chronic Gastric Ulcer

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Angiogenesis and the proper cell proliferation of gastric mucosa are believed to play a significant role in the healing process of chronic gastric ulcer. Reparation mechanisms that occur in the granulation tissue in the ulcer base are relatively well known contrary to these that take place in the ulcer margins. The purpose of this study was to assess the influence of ranitidine and diclofenac on angiogenesis and mucosal cell proliferation in the mucosa adjacent to the ulcer.

Patients and methods: Endoscopic biopsies were taken from the edge of gastric ulcer in 6 patients on longstanding diclofenac therapy, 15 patients on ranitidine therapy and 15 control patients. The ulcers were 8–12 mm in diameter and at least 2 mm in depth. Histological sections were tested for factor VIII – a specific vascular endothelial cell marker. Proliferation index of gastric mucosal epithelial cells in the margins of ulcer was assessed using mouse monoclonal anti-PCNA antibody.

Results: Number of capillaries in the mucosa of the margins of gastric ulcers in the group of patients taking ranitidine as well as in the group taking diclofenac was similar to the vascularity in the control group. PCNA defined proliferation index of epithelial cells in the margin of gastric ulcers was also similar in the three groups of patients.

Conclusions: The number of capillaries in the mucosa adjacent to the ulcer does not seem to be influenced by ranitidine and diclofenac. The proliferation index in the gastric mucosa adjacent to the ulcer is also not influenced by ranitidine or diclofenac. Our results do not exclude the possibility that these drugs may influence the number of capillaries in the granulation tissue at the bottom of the ulcer.

1163 Are Histamine H2 Antagonists Arrhythmogenic? The Effect of Two H2 Antagonists in Patients with Ventricular Arrhythmias

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Frequently patients with cardiac arrhythmias have concomitant peptic ulcer disease. In some studies histamine H2 receptor antagonists had proarrhythmic or negative inotropic effects on the heart. This study investigates the effects of roxatidine and ranitidine on ventricular ectopy in patients known to have ventricular arrhythmias.

37 Patients (pts) entered a randomized placebo controlled double blind crossover study comparing the effect of roxatidine 150 mg BD and ranitidine 300 mg BD to placebo. The concomitant therapy including antiarrhythmic medication was kept unchanged during the study. Three stages of 12 days on medication with the study drugs or on placebo were each followed by a 7 day wash out period. 48 Hour Holter ECG recordings were performed prior to and at the end of each stage. 30 Pts completed the study.

Ischaemic heart disease was present in 16 of the pts, 4 pts had valvular heart disease and the remaining 10 were either hypertensive and had no structural heart disease. 6 Pts had an LV ejection fraction of 40% or lower. 10 Pts took anti-arrhythmic therapy: 5 amiodarone, 4 amiodarone and another antiarrhythmic and one each on mexilitene and quinidine.

Results: Compared to pts on roxatidine more pts receiving ranitidine or placebo developed >10 ventricular ectopics per hour (VE10), or developed an 100% increase in the number of ventricular ectopics beats (VEB). No pts developed sustained ventricular tachycardia or cardiac failure.

	n	VE10 Less	VE10 More	50% Less	100% More VEB
Placebo	31	11	15	2	3
Roxatidine	31	9	9	3	2
Ranitidine	30	6	10	3	4

Conclusions: Roxatidine and ranitidine did not increase the number or severity of ventricular ectopy significantly compared to placebo in these patients. No patient developed serious drug-related cardiac side effects during this study.

1164 Blood CA 19-9 Levels and Correlation to the Histopathology of Gastric Ulcers

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50 patients with gastric ulcers were evaluated by endoscopy and histopathology. There were 32 males and 18 female patients whose average age was 55.4 (41–74). We looked for a correlation between CA 19-9 and the endoscopic and histopathologic diagnoses of the lesions. The endoscopic appearances in 13 patients were evaluated as malignant and in 11 of these patients histopathologic approval was obtained. The lesions detected in the surrounding mucosa were intestinal metaplasia (7 pts), atrophic gastritis (11 pts), and superficial gastritis (10 pts). Median CA 19-9 levels were 19.4 U/ml in benign ulcers while 24.5 U/ml in malignant ulcers. CA 19-9 levels were significantly high in patients who had malignant ulcers with hepatic metastasis. As a result CA 19-9 levels increased markedly in patients with malignant ulcers and hepatic metastasis.

1165 Endoscopic Findings in Patients with Symptomatic Relapse of Duodenal Ulcer

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Relapses of duodenal ulcers are not rarely presented with dyspeptic symptoms. However, it isn't clear if recurrence of these symptoms is necessarily associated with the relapse of the ulcer.

Patients – Methods: Sixty two patients with dyspepsia and endoscopically confirmed duodenal ulcer and no history of previous gastric surgery or NSAID's use, received an 8 week course of an H2 antagonist (ranitidine). New endoscopy, after completion of therapy, revealed healing of the ulcers in all patients and treatment was then discontinued. Follow-up lasted for one year and they asked to return immediately if there had been recurrence of their presenting symptoms.

Results: Forty seven (76%) patients relapsed and a new endoscopy was performed. Only 30 (64%) of them had duodenal ulcer recurrence. Of the remaining 17 (36%) no macroscopic abnormality was observed in 13, but 4 had minimal changes of the duodenal bulb. There were no differences in the age, alcohol consumption and smoking among those with and without recurrent ulcer.

Conclusions: This study shows that recurrence of dyspeptic symptoms is not frequently associated with the presence of an active duodenal ulcer disease.

1166 Omeprazole in the Maintenance Treatment of Duodenal Ulcer: A Prospective Randomized Controlled Trial Comparing Two Treatment Schedules

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Omeprazole the first proton pump inhibitor of gastric acid secretion is undoubtedly superior to H2 receptor antagonists in duodenal ulcer (DU) healing and pain relief however long term safety of this drug in the prevention of duodenal ulcer relapse is being questioned. After the encouraging reports [1,2] of efficacy and safety of Omeprazole in the prevention of DU relapse, a

prospective randomized controlled trial comparing the efficacy and safety of Omeprazole 20 mg daily and Omeprazole 20 mg three days a week (Fri, Sat, Sun or weekend therapy) in prevention of DU relapse was conducted.

Materials & method: 65 patients (M/F 50/15 age range 20–65 years, mean age 32 years) with completely healed duodenal ulcer (with Omeprazole) documented by endoscopy were randomized to receive either Omeprazole 20 mg daily before breakfast (Group A 32 pts) or Omeprazole 20 mg before breakfast Fri, Sat, Sun (Weekend therapy, Group B 33 pts). Both groups were comparable for age, sex, cigarette smoking, duration of ulcer disease etc.

Patients on chronic NSAID therapy, those with bleeding ulcer or pyloric stenosis, previous gastric surgery, concomitant gastric or prepyloric ulcer, complicating medical illnesses (i.e. Kidney or liver failure) likely to make the evaluation of drug difficult, pregnant and lactating women were excluded from the study. Laboratory evaluation (CBC, BUN, Creatinine, liver function tests, serum calcium, Urinalysis ECG) were carried out on entery, and at 3, 6, 9 and, 12 months or earlier if clinical situation demanded. Patients were seen and endoscoped after 3, 6, 9, 12 months or earlier if there were recurrence of symptoms. Those with endoscopically proven relapse or those who completed 12 months follow up were considered to have completed the trial.

Results: Of these 65 patients 60 completed the study (Group A 30 pts, Group B 30 pts) as 5 patients were lost to follow up. Endoscopic proven relapse of 0% at 3, 6, 9 and 12 months in Group A and 3.3%, 10%, 13.3%, 16.5% at 3, 6, 9 and 12 months respectively in Group B was noted. No clinical biochemical or hematologic side effect was noted in either group.

Conclusion: (1) Omeprazole 20 mg daily and Omeprazole 20 mg weekend therapy for 12 months were both safe and effective in prevention of DU relapse. (2) However Omeprazole 20 mg daily was definitely superior to weekend therapy.

[1] Digestion 1990; 47 (Supp1): 64–68
[2] Gastroenterology 1991; 100: 663–9

1167 "Ulcer Like" Dyspepsia: How Predictive are the Classical Symptoms? The Lesson from the Dyspepsia Project 3 (DP3)

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A recent working team report [(WTR), Gastroenterology Internat 1991; 4; 145–160] classified functional dyspepsia in "dismotility-like (DL)", "ulcer-like (UL)", and "unspecified" (UNS) forms. According to other teams, another subgroup should be added ["reflux-like (RL) dyspepsia]" (Lancet 1988; 1: 576–579). During May 1992 and March 1993 (spring and winter phases of DP3), the clinical history and examination of all dyspeptic patients coming for the first time at 14 outpatient GI Clinics have been registered on a computerized standardized questionnaire (N = 408). For each of 17 main symptoms, intensity, frequency, and influence on quality of life were also recorded, using a visual analogue scale. After an upper endoscopy, ultrasonography and double contrast barium enema being performed, the final diagnosis resulted to be: organic dyspepsia 39% [among which 9% oesophagitis, 4% gastric ulcers, 10% duodenal ulcers (DU), and 8% acute erosive gastritis or duodenitis]; DL 28%; UL 17%; RL 11% and UNS 2%. The "weight" of each symptom in favor of a diagnosis was calculated as a function of the likelihood ratio. The more predictive "guide" symptoms in favor of UL (weight >0.3 with a SD <0.3) resulted in descending order:

	UL%	nonUL %	weight	SD
* pain ameliorates with food	43	18	0.8	0.2
* fasting pain	21	14	0.4	0.3
pain lasts 30'-2 hours	33	22	0.4	0.1
* epigastric pain	95	68	0.3	0.04
* pointing sign	49	36	0.3	0.1
acidity ameliorates with antacids, H2 antag, ome	36	29	0.2	0.2
* pain ameliorates with antacids, H2 antag, ome	43	34	0.2	0.2
use of antacids	31	26	0.2	0.2

Conclusions: symptoms proposed for UL by WTR (*) are present in 21–95% of patients: pain ameliorating with food has a greater predictive value, while the other symptoms have a lower weight, due to their relatively elevate frequency among non UL dyspeptic patients. An overlap between UL and the other forms of functional dyspepsia interested 28% of UL patients. No symptoms could be used to discriminate between UL and DU.

1168 Functional Dyspepsia and Prokinetic Agents: Which Symptoms are Predictive of a Clinical Response? A Preview of Dyspepsia Project 3 (DP3) Report

M. Koch, A. Dezi, A. Ciaco, L. Capurso, E. Camarri, A. Greco, R. Caprilli, G. Frieri, G. Riegler, P. Esposito, M.C. Parodi, P. Cognein, G. Dobrilla, M. Comberlato, A. Franze', A. Bertelè, R. Galeazzi, G. Novelli, F. Pacini, A. Dei, A. Russo, G. Aprile, A. Saggioro, Costa, M. Valentini, M. Sozzi, S. Gullini, S. Gamberini, G. Minoli, V. Terruzzi, A. Tittobello, S. Passaretti, C. Scarpignato. *GI Units of Rome, Italy; GI Units of Grosseto, Italy; GI Units of L'Aquila, Italy; GI Units of Napoli, Italy; GI Units of Genova, Italy; GI Units of Bolzano, Italy; GI Units of Parma, Italy; GI Units of Ancona, Italy; GI Units of Firenze, Italy; GI Units of Catania, Italy; GI Units of Mestre, Italy; GI Units of Aviano, Italy; GI Units of Ferrara, Italy; GI Units of Como, Italy; GI Units of Milano, Italy; Chair of Pharmacology, Parma, Italy*

During May 1992 and March 1993 (spring and winter phases of DP3), the clinical history and examination of all dyspeptic patients coming for the first time at 14 outpatient GI Clinics have been registered on a computerized standardized questionnaire (N = 408). For each of 17 main symptoms, intensity, frequency, and influence on quality of life were also recorded, using visual analogue scales (VAS). After an upper endoscopy, ultrasonography and double contrast barium enema being performed, the final diagnosis resulted to be: organic 39%, dismotility-like (DL) 28%; ulcer-like (UL) 17%; reflux-like (RL) 11% and unspecified 2% dyspepsia. All functional patients were given cisapride (30 mg/day). A functional dyspepsia index (FDI) was calculated as a function of all VAS scores in each subject at 1, 2 and 3 months of follow-up. A clinical response was defined as a reduction in FDI >90% in comparison of baseline value. At 3 months, 78% of DL, 75% of RL and 66% of UL patients responded to the drug. Initial symptoms were "weighted" according to their frequency among responders and non-responders (likelihood ratio). The more predictive "guide" symptoms in favor of a clinical response to the prokinetic agent (weight >1.0 with a SD <0.7) resulted in descending order:

	responders %	non responders %	weight	SD
DL dyspepsia				
post prandial fullness	32	3	2.5	0.5
early satiety	40	3	2.5	0.5
discom. due to distension	35	3	2.3	0.5
epigastric pain	37	8	1.5	0.3
RL dyspepsia				
pyrosis	37	4	2.2	0.5
eructation	31	8	1.4	0.5
acidity	37	11	1.2	0.4
epigastric pain	37	12	1.1	0.4
UL dyspepsia				
acid. amel. with antacids	30	2	2.8	0.6
pyrosis amel. with antacids	21	2	2.5	0.7
acidity	61	7	2.2	0.3
pyrosis	26	4	1.8	0.5

Conclusions: a "response" to cisapride is to be expected in about 70% of DL or RL, but also in about 60% of UL patients. A prediction of response to the drug could be done on the basis of clinical symptoms. The accuracy of the prediction rule should be confirmed in a randomized clinical study.

1169 "Dismotility Like" Dyspepsia: How Predictive are the Proposed Symptoms? The Experience of the Dyspepsia Project 3 (DP3)

M. Koch, A. Dezi, A. Ciaco, L. Capurso, E. Camarri, A. Greco, R. Caprilli, G. Frieri, G. Riegler, P. Esposito, M.C. Parodi, P. Cognein, G. Dobrilla, M. Comberlato, A. Franze', A. Bertelè, R. Galeazzi, G. Novelli, F. Pacini, A. Dei, A. Russo, G. Aprile, A. Saggioro, Costa, M. Valentini, M. Sozzi, S. Gullini, S. Gamberini, G. Minoli, V. Terruzzi, A. Tittobello, S. Passaretti, C. Scarpignato. *GI Units of Rome; GI Units of Grosseto; GI Units of L'Aquila; GI Units of Napoli; GI Units of Genova; GI Units of Bolzano; GI Units of Parma; GI Units of Ancona; GI Units of Firenze; GI Units of Catania; GI Units of Mestre; GI Units of Aviano; GI Units of Ferrara; GI Units of Como; GI Units of Milano; Chair of Pharmacology, Parma*

Functional dyspepsia is usually classified in "dismotility-like (DL)", "ulcer-like (UL)", and "unspecified" (UNS) forms [working team report (WTR), Gastroenterology Internat 1991; 4; 145–160]. According to other teams, another subgroup should be added ["reflux-like (RL) dyspepsia]" (Lancet 1988; 1: 576–579). During May 1992 and March 1993 (spring and winter phases of DP3), the clinical history and examination of all dyspeptic patients coming for the first time at 14 outpatient GI Clinics have been registered on a computerized standardized questionnaire (N = 408). For each of 17 main symptoms, intensity, frequency, and influence on quality of life were also recorded, using a visual analogue scale. In all patients, a final diagnosis was achieved, among a list of 13, after an upper endoscopy, ultrasonography and double contrast

barium enema being performed. The final diagnosis resulted to be: organic dyspepsia 39%; DL 28%; UL 17%; RL 11% and UNS 2%. Overlap between DL and UL or RL interested 28% of DL patients. The "weight" of each symptom in favor of DL was calculated as a function of the likelihood ratio. The more predictive "guide" symptoms in favor of DL (weight >0.3 with a SD < 0.3) resulted in descending order:

	DL%	nonDL%	weight	SD
symptoms are due to gas excess	46	22	0.7	0.1
*early satiety	61	38	0.6	0.1
*pain/discomfort for epig. distens.	71	41	0.5	0.1
*post-prandial fullness	77	45	0.5	0.1
started after alimentary abuse	16	10	0.5	0.3
abdominal distension	37	24	0.4	0.2
symptoms invite to release belt	25	17	0.4	0.2
metheorism	45	32	0.3	0.1
sympt. ameliorate with antispasm.	11	8	0.3	0.3
*vomiting	12	9	0.3	0.3
*nausea	46	34	0.3	0.1

Conclusions: symptoms that define DL according to WTR (*) were present in 12–77% of patients: however, they were present also in 9–45% of other forms of dyspepsia. So, their predictivity in favor of DL is reduced (LR < 0.6). An overlap with other functional forms of dyspepsia interests only 28% of patients.

1170 Comparison of the Efficacy and Safety of Ebrotidine and Ranitidine in the Treatment of Duodenal Ulcer (DU)

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Ebrotidine (E), a novel H_2-receptor antagonist, that contains a N-sulfonyl formamidine group instead of 2-nitroethendiamide of ranitidine (R) and shows unique gastroprotective and anti-Helicobacter pylori effects. This study was designed (1) to determine the DU healing rate with E at 200, 400, 600 and 800 mg or placebo (P) given in nightly dose of 4 wk duration in total of 240 DU patients and (2) to compare E (800 mg nocte) with equimolar dose of R (150 mg nocte) on DU healing in randomized, parallel and controlled clinical trial with a maximum duration of 8 wk.

In first trial, the most significant results were obtained with higher E doses (400, 600 or 800 mg) which increased healing rate after 4 wk treatment to 90–95% compared to 55% achieved with P. The difference in healing rate between 400, 600 and 800 mg was not clinically or statistically significant but the incidence of the degree of duodenitis was significantly lower with all 4 doses of E than with P. The efficacy of E at 200 mg was not different from that of P group. In second trial, 4 visits (weeks 0, 4, 6 and 8) were made. DU patients treated with E (N = 150) showed similar healing rate to that in R treated patients (N = 148), reaching at 4 wk 66.7% and 70.1%, at 6 wk 80.4% and 85.4% and at 8 wk 86.7% and 90.9% with E and R, respect. Both drugs were similarly affective in the improvement of ulcerous dyspeptic symptomatology. The incidence of side-effects was low and insignificant. Both drugs increased moderately plasma levels (measured after 4 wk treatment) of gastrin (by 20.9% for E and 21.4% for R) and lowered plasma PP (by 14.2% for E and 16.2% for R). Both tobacco and alcohol influenced adversely DU healing, the values being more significant for R than for E.

We conclude that E in single nightly dose of 400–800 is as effective in DU healing as R at 150 mg but E is superior than R in treatment of smoking DU patients.

1171 Comparison of Gastroprotective and Inhibitory Activities of Ebrotidine and Ranitidine in Humans

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Ebrotidine (Ferrer, Barcelona Spain) is a novel competitive antagonist of H2-receptors characterized by the presence of N-sulphonyl formamidine substructure and a remarkable gastroprotective activity.

This study was designed to compare the effects of various doses of ebrotidine (200, 400 and 800 mg) and equimolar doses of ranitidine (75, 150 and 300 mg) on gastric acid secretion in response to pentagastrin (2 μg/kg-h) in 8 subjects of group A and on acute gastric lesions induced by 50% of 100 ml ethanol sprayed on the mucosa via an endoscope on 24 subjects of group B. Ebrotidine in doses used inhibited dose-dependently pentagastrin-induced acid secretion being equipotent with ranitidine and resulting in the significant reduction (by 60–80%) in pentagastrin-induced acid output for at least 6 h on administration of 400 or 800 mg ot ebrotidine. Pretreatment for 3 days with ebrotidine or ranitidine in randomized, cross-over study reduced dose-dependently the endoscopic score of ethanol-induced gastric damage and deep hemorrhagic lesions caused by ethanol. The mucosal score at a dose of 800, 400 and 200 mg per day averaged 0.75 ± 0.14 and 1.0 ± 0.18 and 3.20 ± 0.26, respectively. In ranitidine-treated subjects, ethanol caused widespread endoscopic lesions (score = 2.4 ± 0.32) and deep hemorrhagic lesions in histological examination at all doses of ranitidine used.

We conclude that ebrotidine is equipotent with ranitidine in gastric acid inhibition but, unlike ranitidine, it shows a remarkable and dose-dependent gastroprotective activity that deserves consideration for the treatment of acute gastric damage and peptic ulcerations in men.

1172 Comparison of 24-h Intragastric pH and 24-h Gastrin Profiles During Therapy with the Proton Pump Inhibitors Pantoprazole and Omeprazole

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Proton pump inhibitors are a new drug class which is increasingly employed in the treatment of acid peptic diseases. In the present study, the effect of a new proton pump inhibitor, pantoprazole, on intragastric pH and 24-h gastrin output was compared to the longer available omeprazole. *Methods:* Seven healthy volunteers of both sexes (3 females, 4 males; age 24–31 years) were studied separately on the final day of 7-day treatment courses with 40 mg pantoprazole and 40 mg omeprazole taken as a single morning dose. Intragastric pH was recorded by means of a glass electrode (Ingold) and a solid state recorder (Synectics). Serum samples were obtained in 1-h intervals (2-hourly in the night) for gastrin determinations (RIA). All subjects were hospitalized, a strict protocol included identical meals. *Results:* Pantoprazole was equally effective in inhibiting acid secretion as omeprazole (see table). Pantoprazole appeared to be slightly more effective during the night period whereas results from pH recordings during the day time were identical. 24-h gastrin output was slightly but significantly lower in subjects treated with pantoprazole. *Conclusions:* Pantoprazole and omeprazole given at the same dose for 1 week are effective inhibitors of gastric acid secretion though pantoprazole appeared to be slightly more effective during night time. The lower gastrin levels over the 24-h period despite the marginally more pronounced acid inhibitory effect during pantoprazole therapy requires further investigation.

medians	Pantoprazole	Omeprazole
24-h pH/day pH/night pH	4.2/4.3/3.4	4.0/4.5/1.7
pH > 4: 24-h/day/night (%)	54/62/40	50/62/25
24-h gastrin output (pg/ml x 24 h)	1683*	3537

*p = 0.0469 versus omeprazole (Wilcoxon signed rank test).

1173 Incidence and Risk Factors for Duodenal Ulcer Disease. A Retrospective Cohort Study

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The aim of this study is to assess the incidence of peptic ulcer (PU) in a group of dyspeptic subjects and to determine some of the main risk factors for duodenal ulcer (DU), assessed before disease occurrence.

We studied a cohort of 621 consecutive patients of both sex with non-ulcer dyspepsia who had been subjected to esophago-gastro-duodenoscopy and gastric drainage from 1978 to 1982 in our Institute. Subjects who had died (29 subjects) or emigrated (23 subjects), who refused to collaborate (43 subjects), were withdrawn from the study. Later, all the 526 subjects (265 males and 261 females), equal to 84.7% of the total historical cohort, who entered the study were reexamined using anamnesis for gastric ulcer (GU) and/or DU diagnosis.

Results: Forty-eight incident cases of peptic ulcer (PU) (41 duodenal ulcer patients, 6 gastric ulcer patients and 1 combined gastric and duodenal ulcer patient) were found. All these cases were verified by means of the medical documentation available. The incidence rate per 1000 person-year was 1.0 for gastric ulcers (GU) and 6.7 for duodenal ulcers (DU). The male/female ratio was 2:1 both for GU and DU. The relative risks for DU associated with the secretion of gastric acid, cigarette smoking, familiarity for PU, and sex were assessed. Gastric acid secretion was assessed before the occurrence of ulcer disease: OR = 2.3 (95% C.I. 0.8–6.3) and 3.5 (95% C.I. 1.4–9.0) in the II and III tertile of Basal Acid Output (BAO), compared respectively to the I tertile; OR = 2.6 (95% C.I. 0.8–8.3) in the II tertile and 7.0 (95% C.I. 2.3–20.7) in the III tertile of Maximal Acid Output (MAO) compared to the I tertile. Cigarette smoking: OR = 2.4 (95% I.C. 0.7–7.2) and 4.4 (95% C.I. 2.2–8.8) in smokers with a consumption of less than 10 cigarettes per day and in those smoking 10 or more cigarettes per day, compared respectively to non-smokers. The presence of PU cases among first-degree relatives was found to be a risk factor for DU only in the cases where one or more siblings had peptic ulcers: OR = 4.3 (95% C.I. 1.8–10.4); as regards sex, the relative risk in females compared to males was 0.4 (95% C.I. 0.2–0.9). The Multiple Logistic

Regression model did not modify the associations of DU with MAO, cigarette smoking and familiarity, while there were no associations between sex and BAO. *Conclusion:* The results of our study confirm the influence of gastric acid secretion, cigarette smoking and familiarity in the pathogenesis of DU.

1174 Main Digestive Diseases Diagnosed for the First Time in a Rural District

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Detailed questionnaires (13 questions with 2–7 alternatives, referring to the possibility of digestive diseases, out of 72 questions in total) were filled in by physicians.

Dyspeptic complaints had 500 persons from questioned 1316 rural adult residents. Persons with dyspepsia (345 female and 155 male) with average age 45 ± 0.7 years) underwent ultrasonography (Sal - 32B, "Toshiba") and oesophagogastroduodenoscopy (GIF-D3 "Olympus").

Duodenal ulcer was found in 43 (8.6 ± 1.3%), gastric ulcer in 19 (3.8 ± 0.9%), gallstones in 41 (8.2 ± 1.2%) and hiatal hernia in 54 (10.8 ± 1.4%) dyspeptic persons. Taking into account that patients were often unsure about having had hiatal hernia in past history and in several cases other diseases were diagnosed we were not able to distinguish cases of hiatal hernia detected for the first time. We would like to emphasize that about ½ of duodenal (21 cases) and gastric ulcers (10 cases) were diagnosed for the first time in the person's life. More than ¾ gallstones (35 cases) were detected for the first time.

In conclusion, we found peptic ulcer and gallstones in a rural community of Estonia more frequently than it was known by medical care units data.

1175 Lymphocytic Gastritis and Associated Small Bowel Disease: A Diffuse Lymphocytic Enteropathy?

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Introduction: Lymphocytic gastritis (LG) is a condition of unknown aetiology. Described as "transient" it has been associated with coeliac disease and H. pylori (HP) infection. 22 patients [mean age 52.3 (23–88) years; 12 male] diagnosed as having LG were investigated to determine its natural history and association with small bowel disease and HP. *Results:* 3 patients had just been diagnosed as having LG. 15 had the condition after a mean of 13.9 (range 2–38) months involving the antrum alone in 3, antrum and body in 7, body alone in 6 and gastric remnant in 2. Gastroduodenal (GD) intra-epithelial lymphocytes (IELs) were T-cells, predominantly of T-suppressor (CD8) type. Median (quartile) duodenal (2nd part) IELs were increased in LG [19% (14.6–22.8)] compared to age-sex matched controls with chronic gastritis [9.5% (7–11)] ($p < 0.001$; Mann Whitney). 4 patients had duodenal villous atrophy. 4 patients no longer had LG after a mean of 29.3 (10–70) months but had increased GD IELs. Antrum = 17% (8–19) [Controls = 7% (5.3–8) $p < 0.01$]. Body 14% (14–29) [Controls 6% (3.3–8) $p < 0.01$]. Duodenum = 17 (14–20) [Controls = 9.5% (7–11) $p < 0.01$]. On histology HP were absent in 18/22 patients but HP serology was positive in 11/22, borderline in 1, and negative in 9. There was no difference in seropositivity when compared to controls; (14/18 seropositive, 1 borderline, 3 seronegative). 10/19 patients with LG tested had abnormal Lactulose/Mannitol (La/Ma) absorption (vs 0/22 controls with chronic gastritis). The patients with villous atrophy, were seropositive for IgA endomysial antibody. There was no difference in seropositivity to anti-gliadin IgA, IgG, and IgM when compared to controls. *Conclusion:* The persistence of LG with time, the association with increased duodenal IELs, and abnormal small intestinal permeability suggests LG may be a manifestation of a diffuse gastroenteropathy related sensitivity to gluten or some other agent.

1176 Control of Gastric pH with Ranitidine in Patients with Crohn's Disease Receiving Total Parenteral Nutrition (TPN). Comparison of Two Intravenous Regimens

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Background: We have reported that intragastric hyperacidity was sustained during TPN for nutritional therapy for patients with Crohn's disease. This study was underwent whether intravenous H2-blocker regimen might have inhibitory effect on sustained intragastric hyperacidity induced by TPN and NPO. *Materials and Methods:* Eleven patients with Crohn's disease in remission receiving TPN underwent continuous intragastric pH monitoring before and during ranitidine administration. Patients were randomized to receive 200 mg/day (group 1) or 400 mg/day (group 2) ranitidine in continuous infusion. The pH was monitored throughout a 24-hr period with a gastric probe. *Results:* Basal mean 24-hr gastric pH was 2.13 ± 0.22 in group 1 and 1.91 ± 0.32 in group 2 ($p > 0.05$) and mean pH > 3 holding time was 46 ± 35 min in group 1 and 42 ± 30 min in group 2 ($p > 0.05$). After ranitidine administration, mean pH was 3.28 ± 0.41 in group 1 ($p < 0.0005$) and 3.36 ± 0.46 in group 2 ($p < 0.005$) and pH > 3 holding time was 546 ± 191 min ($p < 0.005$) in group 1 and 524 ± 167 min in group 2 ($p < 0.005$). There were no differences in mean pH and pH > 3 holding time between the two groups during ranitidine administration, however, plasma ranitidine concentration was significantly higher in the latter group. Conclusion: These data indicate that continuous infusion of standard dose of ranitidine exerted a maximum inhibitory effect on sustained intragastric hyperacidity induced by TPN and NPO, however, it did not achieve to maintain intragastric pH levels at or above 3.5, which is considered a desired therapeutic goal.

1177 Faecal Calprotectin-Shedding After Short-Term NSAID Treatment

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Inflammation and mucosal damage in the GI-tract lead to an increased concentration of faecal calprotectin. We have studied faecal calprotectin shedding in association with short-term NSAID treatment and the correlation to mucosal damage assessed by endoscopy.

Material and method: 22 healthy male volunteers participated in two randomised, blinded, cross-over studies. Median age was 22 years (range 20–30).

Treatment regimens consisted of indomethacin 50 mg bid or naproxen 500 mg bid for 14 days in the first study (n = 17) and lornoxicam 8 mg bid or naproxen 500 mg bid for 7 days in the second study (n = 18).

Faecal calprotectin was analysed quantitatively by enzyme immunoassay. In the second study, endoscopic assessment of gastroduodenal changes was performed before and after each treatment period.

Median with 95% confidence intervals were used as location parameters. Non-parametric tests were used throughout in the analyses.

Results: The overall basal calprotectin shedding was 4.9 mg/l (1.2–17.0 mg/l).

Reproducibility of the method was tested by investigating 13 persons twice. There was no significant difference between test I and test II neither before nor after one week of naproxen treatment.

The reproducibility of the method's results was tested by determining baseline shedding level in 2 groups (n = 22 and n = 50). There was no significant difference between the two groups.

To test the method's stability, we analysed basal calprotectin shedding 4 times in 13 persons. There were no significant differences between any of the results of these tests.

Results of the faecal calprotectin shedding tests after NSAID treatment (medians with 95% C.I.);

	1 week of treatment	2 weeks of treatment
Naproxen	8.0 mg/l (5.0–25.0)**	10.0 mg/l (6.0–22.0)**
Indomethacin	9.0 mg/l (5.0–27.0)**	6.0 mg/l (3.0–13.0), p = 0.07
Lornoxicam	7.4 mg/l (5.0–12.3), p = 0.23	

The p-values denote significant increase from baseline calprotectin shedding, ** $p < 0.01$.

Shedding of calprotectin correlates well with the endoscopic assessment of duodenal lesions ($p < 0.05$), while the correlation to gastric changes did not reach statistical significance.

Conclusion: This study indicates that the inflammatory changes induced by NSAIDs are detectable even in a short-term setting, and seem to be correlated to endoscopic changes.

1178 Upper G.I. Tract Lesions Associated with Arterial-Chemo-Embolization of Liver Neoplasm

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Transcatheter-Arterial-Chemo-Embolization (TACE) is an useful therapeutic procedure for the treatment of HCC and liver metastases. This procedure may cause many side effects. Acute cholecystitis, pancreatitis, gastritis and duodenitis were reported.

Objective: To evaluate the upper gastrointestinal tract mucosal morbidity (incidence and prevalence) associated with TACE.

Design: Perspective, observational study with internal comparison.

Setting: Gastroenterology Unit in a Hospital with Interventional Radiology facility, in Bologna, Italy.

Patients and Events: 14 male patients, scheduled to undergo 19 TACE, who agreed with the protocol were enrolled between February 2nd and October 27th 1993.

Intervention: Upper-GI-Endoscopy exams were performed within the 5 days before and within 24 hours after TACE; a third examination was proposed within 6 days.

Measurements: Mucosal lesions were classified in four degree of severity (G1-G4). Prevalence Pre-TACE, Prevalence and Incidence Post-TACE of lesion G3 (slight or moderate mucosal erosions) or G4 (severe mucosal erosions, ulcer) were considered. Relative Risk (R.R.) was estimated with Prevalence Odds Ratio, frequency distribution per tract was described.

Results: Upper GI endoscopy before TACE found out mucosal lesions G3 or G4 in 26.3%; after the prevalence of G3-G4 was of 78.9%. Relative Risk. estimated with Prevalence Odds Ratio results of more than ten fold (10.5) The post-TACE examination showed new G3-G4 lesions in of 73.7%. New G3-G4 lesions were found in oesophagus 5.3%, stomach 57.9, duodenum 47.4%. In 1 case the second portion of the duodenum was involved. 6 patients underwent a third Upper GI Endoscopy 5 or 6 days after TACE, ameliorate mucosal conditions were found in all.

Conclusions: Erosive and ulcerative lesions of upper GI tract follow TACE, involve most frequently the stomach. They may be due to ischemic phenomena. It is not to exclude a direct chemotherapic effect.

1179 Predictors of Intractable Gastric Ulcer, Analysis of Local Factors and Intragastric PH Metry

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Background: The relationship between the inhibition of intragastric acidity and healing rate in duodenal ulcer has been established. However, factors influencing healing rate of gastric ulcer have not been elucidated clearly. This study was undertaken to clarify the relative importance of various factors associated with healing. *Materials and methods:* In 48 cases of gastric ulcers, 24 hrs intragastric pH monitoring was performed before and after medication. All patients have an ulcer larger than 10 mm and mean age was 54.9 ± 13.0 years. The healing rate of gastric ulcer was evaluated by endoscopy before and eight weeks after commencement of treatment. Various factors as follows were analyzed by univariate and multiple logistic regression analysis; Background (age, sex, life style, drugs, etc, 8 items), radiographic and endoscopic findings (size, location, depth, fold convergency, surrounding overhanging mucosa, etc, 16 items), and pH > 3 or 4 > holding time etc, (18 items). *Results:* The healing rate was 70.8%. The significant factors of intractable gastric ulcer were pH > 4 holding time less than 1000 minutes (relative risk 54.6), an ulcer locating on the angle (RR24.5), and surrounding overhanging mucosa (RR20.9). Predictive rate of being intractable at 8 weeks was 42.6%, 24.8% and 21.5% respectively. However, it was 87.9% in combination of two of the three factors, and increased to 100% in combination of all of the three. *Conclusion:* We concluded that both inhibition of intragastric acidity and gastric local factors were important predictors of the healing of gastric ulcer.

1180 Low Carbonic Anhydrase VI Concentration in Saliva may Predispose to Acid-Peptic Diseases

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Saliva is known to contain factors that protect the alimentary canal mucosa against acidity. Since carbonic anhydrases regulate the acid-base balance in various biological fluids, we studied here the concentration of carbonic anhydrase isoenzyme VI secreted into the saliva from patients with gastrointestinal disorders.

A sensitive time-resolved immunofluorometric assay (DELFIA) was used to measure salivary carbonic anhydrase VI concentrations from 48 voluntary patients undergoing gastroscopy and from 29 healthy male controls. The saliva samples were collected during paraffin stimulation.

The intra-assay coefficient of variation (CV) in one assay was 5.1% and the interassay CV, determined in five assays, was 5.3%. The mean analytical recovery was 93%. The enzyme concentrations were found to be significantly lower in patients with verified acid-peptic disease. The mean concentrations were 6.9 ± 0.8 μg/ml (n = 29) in controls and 2.6 ± 1.3 μg/ml (n = 10), 3.2 ± 1.0 μg/ml (n = 20) and 0.5 ± 0.2 μg/ml (n = 9) in patients with oesophagitis or oesophageal ulcer, gastritis and gastric ulcer, respectively.

The results suggest that low salivary concentrations of carbonic anhydrase VI are associated with acid-peptic diseases. Thus, the enzyme swallowed in the saliva, together with salivary and/or locally produced HCO_3^-, may have an important role in neutralizing the gastric juice and thereby in protecting the oesophageal and gastric mucosa from acidity.

1181 Decrease of Surgical Management of Duodenal Ulcer (DU) in Romania After Introducing Potent Antiulcer Drugs

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Concerning the Western countries, it has been reported a decrease of hospital time and surgical treatment for DU since introducing and using highly efficient antiulcer drugs (pirensepin, H2 - receptor antagonists). In Romania, these drugs became available beginning with 1985–1986. Nowadays they are currently used, although some of these drugs are not available even at present (omeprazole). The present study was carried out to demonstrate that in Romania too, it can be ascertained a decrease of surgery for DU since these drugs are used.

The study has been based on the operation notes of the surgical operations performed in the last decade, in the 3rd Surgical Clinic (an abdominal surgery unit). To make a comparison, we chose three time periods: 1982–1983 when these drugs were not used, 1987–1988 when the drugs became available, for the treatment of DU and 1992–1993 when the drugs were currently used. From the operation notes, sex and age were recorded for all patients. For those who underwent surgery for DU, the postoperative diagnosis and the surgical procedure performed, were also recorded. The frequency of operated DU (expressed as percent from the all cases of operations per year) was calculated for each sex and age decade. For statistical comparisons, the chi - square test was used.

Surgery for DU decrease progressively and significantly from 7.2% in 1982, 5.8 in 1983, 4.5% ($p < 0.01$) in 1987, 4.4% ($p < 0.01$) in 1988, 3.2% ($p < 0.001$) in 1992 to 3.5% ($p < 0.001$) in 1993. The ratio between men and women operated for DU was constantly 3.5/1. There is a decrease in the number of operated DU in men as follows: in the age decade 20–29 years, from 17.6% in 1982 to 14.4% in 1993; in the age decade 30–39 years from 20.1% in 1982 to 15.2% in 1993; in the age decade 40–49 years from 15.4% to 10.1% in 1993 and in the age decade 50–59 years from 8.8% in 1983 to 3.4% in 1993. Concerning the women, there is decrease too, as follows: in the age decade 30–39 years from 2.8% in 1982 to 0.3% in 1993, in the age decade 40–49 years from 6.4% in 1982 to 1.4% in 1993, and in the age decade 50–59 years from 2.4% in 1982 to 0.8% in 1993. The spectrum of complications has changed too. While stenosis and penetration were significantly more frequent in 1982 (32.2%, 49.9% respectively) as compared to 1993 (13.8%, 27.7% respectively) ($p < 0.01$, $p < 0.01$ respectively), the free perforation predominates (33.6%) in 1993, as compared to 1982 (18.6%) ($p < 0.01$).

With the medical treatment available, especially the H2 blockers for our country too, it has ascertained a significant decrease of surgery for DU.

1182 Cigarette Smoking, Alcoholic Abuse, Coffee Consumption and Gastric Metaplasia in the Duodenum

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Informations on gastric metaplasia in the duodenum are poor and strictly related to few observations.

In this multicenter trial the possible correlations between presence of gastric metaplasia and life-style of dyspeptic patients were analyzed. 759 consecutive patients referred for dyspepsia to an endoscopy room were studied. All were strictly investigated for cigarette smoking and recorded as positive for more than 5 cigarettes per day; alcoholic abuse was defined as more than 40 g of alcohol per day and coffee consumption more than two cups per day. Two biopsies, taken from the proximal bulb, 2 centimeters from the pyloric area on the anterior and posterior wall, were stained with Alcian blue-PAS and classified according to Wyatt's criteria. 396 (52.17%) patients were positive for gastric metaplasia and 363 (47.83%) negative. Chi-squares either uncorrected or Yates corrected were significant for cigarette smoking ($p < 0.001$) or alcoholic abuse ($p < 0.01$) but not for coffee consumption ($p < 0.5$). Stratified analysis showed a Mantel-Haenszel Summary Chi Square = 10.87 and a p value = 0.00097, with a Relative Risk of developing metaplasia of 1.16.

We conclude that cigarette smoking and alcohol abuse may have a role in the development of gastric metaplasia in the duodenum.

[1] Wyatt J.I. et al. Gastric epithelium in the duodenum: its association with Helicobacter pylori and inflammation. J. Clin. Pathol. 1990, 3: 981–986.

1183 Factors Affecting Persistence of Symptoms in 1,052 Ranitidine-Treated Elderly Ulcer Patients

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It has been recently described persistence of ulcer symptoms as the most important factor suggesting slow healing peptic ulcer in patients over 65 yrs of age, while ulcer size were proved important only for duodenal ulcer (DU); alcohol, NSAID and antiplateled drug use have all an additional role. In order to ascertain how these factors may influence persistence of ulcer symptoms, we evaluated them and sex, age of onset of ulcer disease, smoking habit, alcohol consumption, complications, family history of ulcer disease, ulcer site for GU, ulcer size, ulcer healing after 4 weeks) by a multivariate analysis (Cox's models). All patients were treated with ranitidine 300 mg/daily and endoscopically evaluated after 4 and 8 weeks. Of the 1,052 subjects entered the study, 319 were gastric ulcer (GU), 699 DU and 34 GU + DU. After 4 weeks 79/215 GU resulted unhealed, as well as 138/497 DU. After 8 weeks there were 20 GU and 15 DU still in active phase. Factors affecting persistence of ulcer symptoms are reported in the following table:

	odds ratio	CI 95%	Wald test
GU & DU, as a whole:			
ulcer healing	4.59	3.30–6.37	p = 0.0001
esophagitis	2.38	1.63–3.47	p = 0.0001
hypoglicemic agents	1.98	1.03–3.78	p = 0.042
GU:			
ulcer healing	4.63	2.62–8.16	p = 0.0001
cigarette smoking:			
YES	1.57	0.82–3.00	
NO	0.37	0.15–0.94	p = 0.018
DU:			
ulcer healing	5.07	3.37–7.63	p = 0.0001
esophagitis	2.47	1.58–3.85	p = 0.0001

Conclusions: Ulcer healing is the most important factor in maintaining the persistence of ulcer symptoms in ranitidine-treated elderly patients. The presence of esophagitis (in DU) and cigarette smoking (in GU) must be also taken into account, while concomitant hypoglicemic treatment have a weak role, resulting statistically significant only when patients are considered as a whole.

1184 Does Tolerance Develop in Duodenal Ulcer Patients Treated with a Bedtime Dose of Roxatidine or Ranitidine for 28 Days?

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Conflicting data have been published on the development of tolerance to the antisecretory effects of H_2-receptor antagonists in healthy subjects and in duodenal ulcer patients in remission. To further clarify this matter, we performed a prospective pharmacodynamic study in a large group of patients with active duodenal ulcer using the well-established once daily dosing schedule of H_2 antagonists. Forty-eight patients (29 male and 19 female, mean age 53 years, range 21–65) with endoscopically-proven duodenal ulcer were recruited in four gastroenterological departments. Twenty-four-hour intragastric acidity was measured continuously in them before, on days 1 and 28 after receiving an oral bedtime dose (h 22:00) of either roxatidine 150 mg or ranitidine 300 mg, given in randomized and single-blind fashion. They underwent a first gastric pH-metry with glass electrode lasting for 48 hours (the first day in basal conditions and the second day while on the first day of treatment) within two days of the endoscopic diagnosis of ulcer. A second 24-hour gastric pH-metry was performed before the endoscopic control at 4 weeks of therapy. Acidity data were expressed as mean pH (±sd) values for the whole 24-hour period, evening, night and daytime. These findings were compared by means of two-way ANOVA and p values were corrected for multiple testing.

Results. Eight patients did not complete the study for various reasons. 82% of ulcers healed after 4 wks therapy. Mean pHs are reported in the table:

Time	Roxatidine 150 mg			Ranitidine 300 mg		
	day 0	day 1	day 28	day 0	day 1	day 28
17:00–16:59	1.7 ± 0.2	3.6 ± 0.5	3.8 ± 0.5	1.7 ± 0.2	3.7 ± 0.6	3.6 ± 0.5
17:00–21:59	1.8 ± 0.5	1.8 ± 0.6	2.1 ± 0.5	1.8 ± 0.5	1.8 ± 0.6	2.0 ± 0.6
22:00–07:59	1.4 ± 0.4	4.9 ± 1.0	5.2 ± 0.7	1.7 ± 0.5	4.9 ± 0.9	5.3 ± 0.8
08:00–16:59	1.8 ± 0.3	3.1 ± 0.9	3.0 ± 0.6	1.7 ± 0.4	3.3 ± 0.8	2.6 ± 0.7

Gastric pH was significantly higher ($p < 0.001$) in all time periods, but the evening, on days 1 and 28 than before the study with both H_2-receptor antagonists. Neither roxatidine nor ranitidine induced the development of tolerance after 28 days of therapy. There was no difference in pharmacodynamic data between the two active treatments. *Conclusion.* In patients with florid duodenal ulcer the antisecretory effect of both roxatidine and ranitidine does not decrease after one month's treatment and this sustains the good healing rates obtained in short-term antiulcer therapy with these drugs.

1185 Novel Oral Medication Delivery System for Famotidine

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A rapidly dispersing famotidine wafer that dissolves on the tongue without water is a novel alternative to other H_2-antagonist dosage forms. Benefits include use by patients who dislike tablets and capsules and by those who have difficulty swallowing.

We examined the absorption and tolerability of a new 40 mg famotidine wafer (FW) and the marketed 40 mg famotidine tablet (FT) in a 2 period crossover study (N = 18 healthy men) with the following mean results:

	AUC (ng·hr/ml)	Cmax (ng/ml)
FW	1096.43	161.10
FT	1049.33	168.10
FW v FT (as FW/FT)[1]	1.04	0.96
90% C.I.	(0.95, 1.14)	(0.85, 1.08)

[1] Log transformations with comparisons as geometric mean ratios.

Based on AUC and Cmax, FW and FT are bioequivalent. All subjects attained EC_{50} for inhibition of gastric acid secretion of 10 ng/ml within 2 hr postdose for FW and FT. The mean famotidine plasma concentration reached the EC_{50} for FW and FT within one-half hour.

In a second trial, FW as 40 mg, 20 mg, or placebo b.i.d. was evaluated for safety and tolerability in 192 volunteers in randomized, double-blind fashion for 14 days. The incidence of adverse experiences was similar in the three treatment groups.

In a third trial, 447 subjects reported FW (single 40 mg dose) to be preferred to tablets by 75% of subjects when asked to consider method of administration and flavor.

It is concluded that similar systemic exposure, excellent tolerability, palatability, and preference make FW a clinically acceptable and convenient dosage form.

1186 No Interaction Between Famotidine and Theophylline in COPD Patients

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Three previous investigations examined the influence of famotidine on the pharmacokinetics of theophylline in chronic obstructive pulmonary disease (COPD) patients. Two trials indicated no effect and one study suggested a substantial effect. In light of the conflicting results and design limitations in these studies, this trial was conducted.

The effects of famotidine (40 mg BID), cimetidine (800 mg BID), and placebo treatments on theophylline pharmacokinetic parameters in COPD patients were compared. This was a randomized, three-period crossover study in which each subject first underwent a 7 day theophylline washout period, and thereafter received three single intravenous doses of theophylline (5 mg/kg infused over 30 min) during the study. Each of the experimental treatments was administered orally every 12 hr for 9.5 days (19 doses). Theophylline was infused 1 hr after the 17th dose of each treatment. Blood samples (14) were collected beginning immediately prior to the start of each infusion, and for 30 hr after the end of each infusion. Plasma samples were assayed for theophylline by fluorescence polarization immunoassay. Pharmacokinetic parameters were estimated, and treatment effects on each parameter were compared.

Fourteen COPD patients (10 males; 4 females) completed all three periods of the investigation and the mean results (±sd) are as follows:

Treatment	Clearance (L/hr/kg)	Half-life (hr)	vs Placebo
Placebo	0.045 (0.02)	7.8 (4.0)	
Famotidine	0.046 (0.02)	7.8 (3.6)	$p > 0.20$
Cimetidine	0.033 (0.01)	10.8 (4.1)	$p < 0.05$

We conclude that relative to placebo, cimetidine significantly decreased theophylline clearance and prolonged its half-life; famotidine treatment at the highest clinical dose had no effect on either of the theophylline pharmacokinetic parameters in COPD patients.

1187 On-Demand Therapy in Preventing Symptomatic Duodenal Ulcer Relapse – Famontidine vs. Placebo

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The aim of this prospective, double-blind, multicenter study was to compare the efficacy of free access of Famotidine (Fam) or placebo in preventing symptomatic ulcer relapse. Ten Scandinavian hospitals participated and the patients were recruited from a duodenal ulcer healing study. The patients had Fam 40 mg/d ad libitum or identical placebo tablets. Clinical visits were scheduled at 4, 8 and 12 months and the patients were contacted by telephone at 2, 6 and 10 months.

Totally 237 patients were included, 149 men and 88 female, 119 patients had Fam ad libitum and 118 patients had placebo. Three patients were excluded due to adverse events, eight patients dropped out due to protocol violation and five patients were lost to follow-up giving 221 patients eligible for statistical analysis.

Recurrent ulcer disease symptoms were reported by 32/112 patients (29%) in the Fam group and 68/109 patients (62%) in the placebo group. Upper endoscopy showed duodenal ulcer recurrence in 23/112 patients (21%) and 39/109 patients (36%) in respective groups. The average time to relapse was 400 days and 256 respectively. Epigastric pain, heart-burn and nausea were the predominant symptoms. There was a significant difference in the overall evaluation of symptoms and occurrence of diurnal pain in favour of Fam. Following an open treatment period with 40 mg Fam/d and endoscopically verified ulcer healing 40/62 patients with ulcer relapse were reincluded in the follow-up study. Totally 38 patients had a number two relapse with endoscopically verified relapse in 29 patients, 6/10 in the Fam group and 23/28 in the placebo group. During the 12 months follow-up period significantly more patients reported restrictions in social life and daily activities due to ulcer symptoms.

Conclusions: Free access to a H2 receptor antagonist showed significant reduction in symptomatic and endoscopically verified relapses compared with placebo therapy.

1188 Superiority of Omeprazole Over Cimetidine or De-Nol in Healing of Gastric Stump Ulcer

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Aim of the study: To compare the rate of gastric ulcer healing with omeprazole, cimetidine or De-Nol in patients who had undergone partial gastric resection.

Material and methods: 104 patients with ulcer in the gastric stump (after Billroth I or Billroth II partial gastric resections) were divided into three comparable groups (according to age, sex, duration of ulcer disease, smoking habits and ulcer size) and were treated in the comparative short-term trial with omeprazole (Losec, 20–40 mg/day), cimetidine (Tagamet, 1000 mg/day) or colloidal bismuth subcitrate (De-Nol 4 × 5 ml/day). The ulcer healing was controlled endoscopically after 2, 4, and 6 weeks of treatment.

Results:

Drug	n	B I	B II	Healing rate %		
				2	4	6 weeks
Omeprazol	26	19	7	69.2*	88.4*	88.4
Cimetidine	54	32	22	46.2	68.5	75.9
De-Nol	24	20	4	25.0	54.1	75.0

* Difference significant in relation to cimetidine and De-Nol groups.

All kinds of treatment were more effective in patients who had been operated with Billroth I procedure.

Conclusion: Omeprazole appears to be superior to cimetidine and De-Nol in gastric remnant ulcer healing. According to multifactor pathogenesis of ulcer in gastric stump, the mechanism of omeprazole effect is not clear.

1189 The Effect of a Combined Therapy of Cisapride and Ranitidine Compared to Both Monotherapies in the Treatment of Uncomplicated Gastric Ulceration (GU)

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A randomized, double-blind multicenter study (20 SCUR-centers in Sweden and Norway) including 193 patients with symptomatic benign uncomplicated GU was conducted to evaluate the combination of cisapride and ranitidine compared to the two drugs as monotherapies regarding ulcer healing and symptom relief.

There were no statistically significant differences in the healing rate between the combination and the monotherapies at 4 and 8 weeks in the Intention-to-treat as well as in the Per-protocol analysis.

Epigastric pain, nausea and vomiting improved in all treatment groups. At the end of treatment the ranitidine group was significantly better than the combination group with regards to epigastric pain ($p = 0.01$) and vomiting ($p = 0.05$).

Assessment of general well-being done by Visual Analogue Scale and overall assessment of ulcer symptoms showed no differences between the combination and the monotherapies, whereas the patients global evaluation was in favour of ranitidine compared to the combination ($p = 0.04$).

Thus, in this study there seems to be no benefit in the addition of cisapride to ranitidine with regard to endoscopic healing or symptom improvement in patients with gastric ulcers.

1190 Effect of a 28-Day Therapy with the H2-Receptor Antagonist Famotidine on Blood Levels of Alcohol and Gastrin in Healthy Human Subjects

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The effects of prolonged administration of H2-receptor antagonists (e.g. 28 day therapy simulating treatment for duodenal ulcer) on blood alcohol levels (BAL) have not been reported. In short term studies (up to 8 day therapy) cimetidine and ranitidine but not famotidine (Dig. Dis. Sci. 33, 767–8, 1988) raised BAL. The *aim* of this study was to elucidate in a randomized, placebo controlled study on 10 female (n = 4) and male (n = 6) fasted healthy human volunteers the effect of a 28-day therapy with famotidine (40 mg once daily at 18:30 hr) or placebo on blood levels of alcohol and gastrin after a daily consumption of 500 ml of beer. On day 1, 7 and 28 of the study blood levels of alcohol and gastrin were determined at 15 min. intervals 30 min. before and 2 hrs after ingestion of beer at 19:00 hr. BAL was determined enzymatically, plasma gastrin by a specific radioimmunoassay. *Results:* On each test day, BAL peaked within 30 min. and did not reach basal levels 2 hrs after ingestion of beer (500 ml). On day 1, 7 and 28 famotidine did not significantly ($p < 0.05$) alter either the peak or the 2 hr integrated blood alcohol response (IBAR; g × min.) to beer as compared to placebo. Whereas basal plasma levels of gastrin were not significantly altered by famotidine, the 2 hr integrated plasma gastrin response (IPGR; pM × min.) to beer was significantly higher with famotidine as compared to placebo.

Peak blood-alcohol levels (g/l), the 2 hr IBAR (g × min.) and the 2 hr IPGR (pM × min.) to beer during the therapy with famotidine or placebo. (N = 10; means).

	Peak BAL		Integrated BAR		Integrated PGR	
	Famotidine	Placebo	Famotidine	Placebo	Famotidine	Placebo
Day 1:	0.28	0.26	25.0	24.5	3769*	174
Day 7:	0.26	0.27	25.1	23.9	2923*	238
Day 28:	0.25	0.29	22.6	25.6	2972*	57

* $p < 0.05$ vs placebo.

The *new findings* of the present investigation are, that (1) a 28-day therapy with famotidine does not alter either the kinetics of absorption or the peak blood alcohol levels after social consumption of beer; (2) with the beginning of the therapy with famotidine an exaggerated postprandial release of gastrin is seen.

1191 Gastrin – The Mediator of Tolerance of the Intragastric Acidity During a Long-Term Therapy with the H2-Receptor Antagonist Famotidine (F) in Healthy Human Subjects (HS)?

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A decrease of the inhibitory effect of different H2-receptor antagonists (i.e. cimetidine and ranitidine) on gastric acid output after repetitive dosing has been reported. The mechanism of tolerance remains unclear; gastrin being a good hormonal candidate as a mediator of this response. The *aim* of this study was to elucidate in a randomized, placebo (P) controlled study the effect of a 28-day long therapy with F (40 mg/nocte at 18:30 hr) or P on the ig. pH. PH-Metry, using combined glass electrodes, was performed on day 1, 7 and 28 between 18:30 hr and 9:00 hr in 10 healthy fasted female (n = 4) and male (n = 6) HS. Plasma gastrin was determined by using a specific radioimmunoassay. *Results:* The daily oral therapy with F significantly ($p < 0.006$) increased on day 1, 7 and 28 the ig. median-pH by 308%, 171% and 164%, resp., as compared to P. After 7 and 28 days of F the median 24 hr pH was significantly ($p < 0.03$) lower than on day 1. Baseline values (pH < 2.0) were reached at 9:00 hr the next morning at day 7 and 28, but not on day 1. There was no significant difference in the ig. pH measured on day 7 and day 28. Plasma levels of gastrin were not significantly altered by F as compared to P.

Intragastric 14.5 hr-median-pH and plasma gastrin levels (pM) in response to orally given famotidine in comparison to placebo. Results are medians with the interquartile distances () of 10 subjects for ig. pH and means ± SEM for plasma gastrin.

Table: Intragastric 14.5 hr-median-pH and plasma gastrin levels (pM) in response to orally given famotidine in comparison to placebo. Results are medians with the interquartile distances () of 10 subjects for ig. pH and means ± SEM for plasma gastrin.

	Intragastric pH		Plasma gastrin	
	Famotidine	Placebo	Famotidine	Placebo
Day 1:	4.0 (3.1–5.8)#	1.3 (1.1–1.5)	31.4 ± 2.7	31.5 ± 2.5
Day 7:	2.4 (2.0–4.7)*#	1.4 (1.1–1.6)	34.0 ± 2.8	29.6 ± 2.5
Day 28:	2.3 (2.0–3.7)*#	1.4 (1.2–1.4)	26.9 ± 2.0	28.1 ± 2.9

*$p < 0.03$ lower than day 1; # $p < 0.006$ vs P.

We *conclude* that (1) within 7 days of treatment with famotidine tolerance of the intragastric acidity occurs by an as yet unknown mechanism; (2) as gastrin levels remained unchanged, gastrin is probably not involved in the development of this tolerance; 3) this finding might have implications for the treatment with famotidine of peptic ulcers.

1192 Sucralfate Gel in Prevention of NSAIDs-Induced Gastroduodenal Lesions in Arthritic Patients

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used in arthritic patients (AP). There is a need to define strategies to reduces their risk of damaging gastrointestinal (GI) mucosa.

Aim: to evaluate the ability of sucralfate gel (Gastrogel) (SG) in the short term prevention of gastroduodenal lesions in AP receiving NSAIDs.

Methods: following rheumatologic examination and full informed consent 171 AP underwent upper GI endoscopy before starting standard NSAID therapy. Patients free of erosions or ulcers (≤2 according to modified Lanza grading scale) were eligible for the study. Patients received diclofenac 200 mg/day or naproxen 1 g/day plus either SG or placebo (P) bid in a randomized double blind study. Repeat assessment of GI symptoms and endoscopy were performed after two weeks.

Results: one hundred and seven patients (M/F: 18/89, mean age 55.2 ± 9.7) with osteoarthritis (n = 56) or with rheumatoid arthritis (n = 51) were randomly allocated to receive SG (n = 53) or P (n = 54). Ten patients (3 SG and 7 P) were lost to follow up. The table shows the prevalence of endoscopic findings at control endoscopy (≤2 = according to Lanza scale, AE = antral erosion, DE = duodenal erosion, PU = ulcer)

	≤2	AE + DE	PU
SG	31 (62%)*	15 (30%)*	4 (8%)*
P	8 (17%)*	26 (55%)*	13 (28%)*

*$p < 0.05$.

Upper GI symptoms were more frequently in the P group compared to SG group: heartburn 51 vs 30% ($p < 0.05$), epigastric pain 49 vs 28% ($p < 0.05$) and dyspepsia 28 vs 24% (NS). Minor side effects (nausea) were reported in 6 patients receiving SG and in 2 receiving P. An unexplained difference was found in the ulcer incidence between the two centers [MI 32% (SG 22%, P 42%); BO 8% (SG 0%, P 18%)].

Conclusion: sucralfate gel may reduce the frequency of early gastroduodenal lesion in arthritic patients receiving NSAIDs.

1193 Variants of Ulcer Disease of the Duodenum

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Purpose. To consider the possible reasons for lowered effectiveness of antisecretories in the course of long-term therapy of duodenal ulcer disease (DUD) patients.

Methods. 281 DUD patients underwent clinical and endoscopic examination, immunological (IgA, M, G in blood, T- and B-lymphoc. count), microbiological (H. pylori), RIA (serum gastrin, somatostatin, bombesin, histamine, pepsinogen I, PG E2) studies and mucosa biopsy specimens' morphometry (G- and somatostatin-producing cells).

Results. Two variants of DUD were distinguished: (1) with hypergastrinemia and/or G-cells hyperplasia, (2) with normogastrinemia and normal count of G-cells. The I-st was inclined to occur after antacids and antisecretories prolonged treatment and provided less response to them. Besides that, women with DUD were more sensitive to H2-blockers than men, whereas omeprazol's therapeutic results among men and women were just the same. Increased basal and/or stimulated gastric acid secretion and gastrin and pepsinogen I high levels in blood usually preceded ulcer disease exacerbation.

Discussion. The mentioned complex examination including the G-cells is desirable when taking a decision about operation and its type. Patients of the I-st variant need higher doses of antisecretories, simultaneous administration of the latter with mucosa protectors and anti-Helicobacter agents. Omeprazol may be the drug of choice. The changed response to therapy may be caused by receptors' alterations and G-cells' hyperplasia as a compensatory reaction.

1194 Antisecretory Responses During 72H Continuous Infusions of Omeprazole & Ranitidine

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The antisecretory efficacy of prolonged continuous infusions of omeprazole and ranitidine has not been assessed previously, but is important for their use in stress-related bleeding. The cross-sensitivity to these drugs is also unclear. Omeprazole and ranitidine continuous infusions were compared in a double-blind, randomised, placebo-controlled, cross-over study in 12 healthy volunteers. pH-feedback-controlled infusions (Gastrojet®; target pH of 5) of omeprazole (2–12 mg/h), ranitidine (2–24 mg/h) or placebo and continuous pH-measurements continued for 72 h after loading doses of 80 mg, 50 mg or placebo, resp. The between-study washout was 2 weeks.

Results: the median % time of pH > 4 (range), the mean drug doses (range) used on days 1 and 3 (24 h periods) of infusions and the numbers of subjects with better pH-responses to each drug are shown:

	Day 1		Day 3	
	omeprazole	ranitidine	omeprazole	ranitidine
%pH > 4	93 (88–95)*	67 (56–78)	97 (94–99)*	43 (31–51)
better response (n of subjects)	10	2	12	0
doses (mg)	236 (145–300)	503 (333–589)	134 (84–216)	542 (498–574)

*$p < 0.001$ omeprazole vs ranitidine.

Summary & Conclusions: The antisecretory effect of omeprazole increases in the first 3 days of continuous infusion, while dosing requirements decrease. The efficacy of ranitidine decreases, despite higher doses. Initially some subjects had a better efficacy with ranitidine, but this advantage was lost due to tolerance. Omeprazole continuous infusions maintain prolonged antisecretory efficacy better than ranitidine.

1195 The Effect of Single Dose of Ranitidine, Famotidine and Omeprazole on Intragastric pH in Duodenal Ulcer Patients

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Aim: To compare the effects of a single dose of ranitidine (RAN), famotidine (FAM) and omeprazole (OPZ) on intragastric acidity in duodenal ulcer (DU) patients (pts).

Methods: 45 pts (30 male, 15 female, mean age 44.7 years) with endoscopically proven acute DU were randomized into 3 treatment groups receiving post evening meal per orally: Zantac (RAN) 300 mg (n = 15), FAM 40 mg (n = 15), OPZ 20 mg (n = 15). Intragastric pH was measured by the system for 24-hour pH-monitoring (Synectics Medical, Stockholm, Sweden). The latency period (the time between drug intake and following increase of pH ≥ 4), the duration of action of a drug (the time with gastric pH ≥ 4 after onset of action of a drug) and % of time with gastric pH ≥ 4 for 24 hr were calculated.

Results:

Signs	Treatment groups		
	RAN	FAM	OPZ
Latency period (min)	219 ± 53	227 ± 60	393 ± 54
Duration of action (min)	511 ± 70	491 ± 64	315 ± 45
% of time with pH ≥ 4 for 24 hs	40 ± 4	41 ± 4	26 ± 2

Conclusions: (1) The latency period, the duration of action and % of time with gastric pH ≥ 4 of RAN and FAM were similar and significantly different from that of OPZ.

(2) The 24-hour pH-monitoring may prove useful in the individualized treatment and timing for drug administration in pts with DU.

1196 Gastrozepine and Triple Therapy in the Treatment of H_2-Bloker Resistant Duodenal Ulcer Disease

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Aim: To investigate the efficiency of combination of M_1-selective receptor antagonist gastrozepine and triple therapy (Denol + amoxicillin + metranidazole) in the treatment of Helicobacter pylori (HP) positive duodenal ulcer (DU) patients (pts) resistant to 8 weeks treatment of ranitidine 300 mg/d.

Methods: 38 pts with endoscopically proven DU (diameter was not less than 5 mm) randomized into 2 groups receiving: Group A (n = 20) Gastrozepine (100 mg/d for 2 weeks then 50 mg/d for 2 weeks) + De-nol (colloidal bismuth subcitrate) 480 mg/d for 4 weeks combined with amoxicillin 500 mg g. i. d. and metronidazole 250 mg g. i. d. for the first two weeks (triple therapy). Group B (n = 18) omeprazole 20 mg/d for 4 weeks and amoxicillin 500 mg g. i. d. for 2 weeks. The pts were rescoped 4 weeks, 6 and 12 months after the end of the treatment. HP was sought by histology and biopsy urase test. Eradication was defined as all tests negative at 4 weeks post treatment.

Results are summarized below:

Group	Healing DU (%)	Eradication HP (%)	Relapse DU (%)
A (n = 20)	80	70	15
B (n = 18)	88.9	66.7	27.8

Conclusion: There results indicate, that type of combined triple therapy with Gastrozepine is as effective as Omeprazole with amoxicillin in healing resistant DU, in HP eradication and in prevention of DU relapse. It is a good alternative in HP positive DU pts resistant to H_2-bloker.

1197 Sucralfate Treatment in Oral Aphthous Ulcers

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In this study, sucralfate was given to 11 patients with oral aphthous ulcers, the youngest one being 16 and the oldest, 45 years old. 7 of the patients (63%) were females and 4 (37%) were males. One had Ulcerative Colitis and another Behçet's Syndrome in relation with aphthous ulcers. No definite disease to result in aphthous ulcers was diagnosed in other patients. The patients, whose frequent history of aphthous ulcers had been taken for a minimum of the last one year were entered into this trial.

The patients were told to dissolve 1 gram sucralfate tablets in water and to gargle the prepared solution every morning and night, keeping it in mouth for at least three minutes each time. No other medicine was used during the treatment. At the end of the 15th day, in 8 patients out of 11 (72%), aphthous ulcers had completely disappeared. The patients with Behçet's Syndrome and Ulcerative Colitis were among the recovering patients. Sucralfate was thought to be effective in the treatment of oral aphthous ulcers. No research has been done on this subject before. We expect vaster studies on this subject to support this method of treatment.

1198 Evaluation of the Duodenogastric Reflux Using 99mTc-HIDA in Patients After Gastrectomy

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Duodonogastric Reflux is an often postoperatory complication in patients who had gastrectomy. The symptoms are various.

We studied 30 patients (13 males and 17 females). All of them had undergone a surgical operation on stomach, 24 had symptoms and 6 were asymptomatic. All of them were assessed by endoscopy.

Method: The patient must be fasting for 3–4 hours before the examination. With the patient in supine position and the callimator over the abdominal area 5 mCi 99m-Tc-HIDA (Amersham U.K) injected i.v. Sequential views of 120 sec are taken for 45 min. 100–150 ml of milk was administered orally 20 min. after the i.v. injection. Finally, a small quantity (200 μCi) of 99 mTc pertechnetate in 100 ml of water was administered orally to outline the stomach area.

Results: From the 24 symptomatic patients 19 had a typical Duodenogastric reflux radiopharmaceutical imaging in the stomach. The other five symptomatic patients with no imaging in the stomach had a long time imaging of common bile duct and delayed passage of radiopharmaceutical to the duodenum and probably this was the reason of their symptomatology. Two of the asymptomatic patients had a low grade of duodeno-gastric reflux.

Conclusions: Hepatobilliary scanning with Tc-99m HIDA is an excellent low risk high diagnostic value examination of Duodenogastric Reflux in patients after gastrectomy.

1199 The Effect of Long Acting Somatostatin Analogue in the Prevention of Post ERCP Pancreatitis

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To assess the effectiveness of long acting somatostatin analogue, sandostatin, in the prevention of post ERCP pancreatitis a double blind randomised trial was carried out. A total number of 172 consecutive patients undergoing ERCP were randomised to receive either octreotide 100 μgr subcutaneously 30 minutes before the procedure (84 pts) or isotonic sodium-chloride (88 pts). The same premedication (butyloscopolamine, midazolam) and contrast media (sodium diatroziate 30%) was used in all patients and the comparison of age, sex and indication for ERCP showed no significant differences between the octreotide and placebo groups. Serum amylase levels were measured before premedication and ERCP, and 180 min and 12 hours after the procedure.

Results. Cannulation of the papilla failed in 11 patients (6%). The pancreatic duct was visualised in 152 pts (87%). Common bile duct stone was the most common finding in ERCP, observed in 24 pts (28%) in the octreotide group and in 20 (22%) in the placebo group. Normal ERCP was found in 32% and 34% of the pts respectively. Endoscopic sphincterotomy underwent 42 pts (24%) and biliary duodenal endoprosthesis was placed in 8 pts. There was no difference between the two groups regarding the number of therapeutic procedures.

No statistical difference was observed between the two treatment groups in the mean serum amylase activity at baseline, 3 and 12 hours after ERCP. Hyperamylasemia was observed in the 57% of the patients in the octreotide group and in the 50% in the placebo group. There was also no significant difference between the number of patients who developed pancreatitis (3 and 4 patients respectively).

Conclusion. The results of this study suggest that octreotide may be ineffective in the prevention both of hyperamylasemia and pancreatitis following ERCP.

1200 Endoscopic Finding of Colonic Polyps in Acromegalic Patients

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Acromegalic patients constitute a high risk group for adenomatous colonic polyps [1]. We report preliminary data (3 months) concerning a prospective endoscopic study of patients with certain acromegaly.

Eight consecutive acromegalics (2 women and 6 men with a mean age of 55.4 years) were observed. Intestinal symptoms were never shown by patients but in one (sporadic blood after motion). No patient presented high risk for colorectal cancer. Six patients had acromegalic history from 15–20 years; two from 8–10 years. All patients had GH-secreting adenoma of the hypophysis. Colonoscopy was always performed till to the coecum. Any polyps identified were resected and submitted to histology.

Colonic polyps were revealed in 7 patients (87.5%). Nine polyps were found: 8 in the recto-sigmoid tract and 1 in the right colon; 7 were smaller than 0.8 cm., 2 were larger than 1 cm. Synchronous polyps were observed in 2 patients (in 1 case 2 hyperplastic polyps of the sigmoid and in 1 case 2 tubular adenomas in the rectum and ascending colon). Histology documented 3 hyperplastic polyps, 5 tubular adenomas and 1 tubulovillous adenoma. The tubulovillous polyp was detected in a patient with 18 years diagnosed acromegaly.

In conclusion we underline the high prevalence of colonic polyps in acromegalics (87.5% in our serie) and confirm the adenomas' prevalence in this group (66.6% in our serie). The accepted hypothesis of colorectal tumor development [2] suggest endoscopic screen for polyps in this patients, independently from symptoms.

[1] J. M. Raymond Gastroenterology 96 (sup.) A411, 1989
[2] B. Vogelstein New Engl J Med. 319: 525–532, 1988

1201 Gastric MALT Lymphomas – With Special Reference to the Endoscopic Appearance of the Initial Lesion and Its Pronostic Significance

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In 1984, Isaacson and Wrigth introduced a new concept for extranodal malignant lymphoma arising from Mucosa Associated Lymphoid Tissue (MALT). The cells of these lymphomas share the specific homing patterns that are characteristic of MALT derived lymphocytes and this accounts for their slow