

the animal's treatment status. C. Ethanol blood clearance and hepatocellular necrosis: 20 rats were administered an LD50-IP dose of ethanol and thirty minutes afterwards saline or ZS (50 mcg/kg) were IP injected. Two animals from each group were hourly sacrificed in order to measure blood ethanol levels by gas chromatography and the extent of hepatocellular necrosis by a pathologist who was unaware of the animal's treatment status. **Results:** A. A reduction in mortality was observed in rats receiving ZS. The strongest protective effect was observed with a dose of 50 mcg/kg (36% vs 83%, $p < 0.05$). B. ZS shortened the narcotic period. The strongest effect was observed 4 hrs after intoxication (2.4 vs 1.9 Majchrowicz Index, $p < 0.05$). C. Finally ZS significantly decreased the extent of hepatocellular necrosis 3 and 5 hrs after intoxication (1% and 5% in ZS vs 20% and 15% in controls). Blood ethanol levels were lower with ZS than with saline. **Conclusions:** ZS in physiological dose was shown to have a protective effect on acute ethanol intoxication. The precise mechanism of action remains to be elucidated.

20 HLA-DPB1 and Susceptibility to Primary Biliary Cirrhosis

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Introduction: While the precise etiology of primary biliary cirrhosis (PBC) is unknown, several studies suggest that immune abnormalities and a genetic susceptibility participate in the disease pathogenesis. The search for candidate genes has been centered on the HLA class II region located on chromosome 6. HLA genotyping techniques enabled the recognition of a large series of DPB1 alleles and the association of several diseases with particular DPB1 alleles. Recently, an increased frequency of the allele HLA-DPB1*0501 in patients with PBC has been described in a Japanese population. Considering the known differences among allele frequencies of HLA class II genes between different ethnic groups, we determined the allele frequencies of the HLA-DPB1 gene among Caucasians with PBC and normal controls. **Methods:** 26 unrelated patients with the diagnosis of PBC based on standard clinical, histological and immunological criteria and 47 unrelated normal controls among a German population were included. Genomic DNA was extracted, the second exon of the DPB1 gene amplified by the polymerase chain reaction and hybridized with 25 sequence specific oligonucleotide probes (PCR-SSO method) to assign the HLA-DPB1 alleles on the basis of known sequence variations, according to the protocols of the XIth HLA workshop. **Results:** The HLA-DPB1*0301 allele was found to be positive in 50% (13/26) of patients with PBC and 13% (6/47) in the control population ($p < 0.001$), resulting in a relative risk estimate of 6.8 (95% confidence limits: 2.2–21.6). A higher frequency of the allele HLA-DPB1*0601 in patients with PBC (15% vs 2%) was observed, but did not result in a significant relative risk estimate, probably due to the low number of patients. No differences were observed comparing frequencies of other DPB1 alleles in our study group. **Conclusions:** These data demonstrate a significant association between PBC and the allele HLA-DPB1*0301 in a Caucasian population. This supports a strong contribution of HLA-DPB1 alleles to the genetic susceptibility to primary biliary cirrhosis.

21 Fructose Stimulates Liver Growth After Partial Hepatectomy

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Graft function and ATP synthesis are impaired in transplanted livers. Since fructose may be a better source for ATP synthesis than glucose, the effect of a 20% sucrose diet on liver regeneration was determined in 60 rats. A diet of 59% starch, 20% protein, 10% fat, 3% fiber, and vitamins and salts was fed for 1 week. 15 rats had partial hepatectomies and were fed the control diet; 15 had sham operations and this diet. 30 rats were fed a diet of 20% fructose, 39% starch, 20% protein, fiber, vitamins and salts for 1 day, and then 15 had partial hepatectomies, and 15 had sham operations. Liver samples were obtained 1, 2, 3, 4 and 7 days after operation, and were assayed for ATP, total lipid, triglyceride, protein, and DNA synthesis. Mitotic Index and fat vacuoles were determined by histology.

Mitotic Index increased after partial hepatectomy, and fructose further increased mitosis by 3-fold 1 day after hepatectomy. Fructose decreased triglyceride levels and fat vacuoles in both sham and hepatectomy groups, but total lipid increased. ATP levels decreased slightly, but DNA synthesis and protein content was unchanged. Since 20% sucrose stimulated cell division after partial hepatectomy, fructose metabolism increased ATP utilization for energy requiring functions of liver regeneration. Low concentrations of fructose in enteral or parenteral nutrition may stimulate recovery of the transplanted liver.

22 Effects of Endothelin-1 on Systemic and Regional Hemodynamics After Intraportal and Centralvenous Injection

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Lung and liver are important in clearing endothelin-1 from the circulation. To compare the hemodynamic effects of endothelin-1 (ET-1) after first pass through the liver with first pass through the lungs, six piglets received 10 ml 10^{-6} ET-1 in the portal vein and centralvenously in randomized order. Cardiac output with thermodilution technique and blood gas analysis was performed to confirm baseline conditions prior to injections. Flow was measured continuously in the hepatic and renal arteries and in the portal vein with perivascular ultrasonic transit-time probes. Pressure was measured continuously in the aorta, in the pulmonary artery, in the portal and the superior caval veins. Heart rate, oxygen consumption and carbon dioxide production were determined every minute.

Central venous injection of ET-1 caused a larger reduction in portal vein flow (a difference of 295 ml/min \pm 66, $p < 0.01$), a larger increase in aortic pressure (45 mm Hg \pm 7, $p < 0.01$), a larger increase in heart rate (23 \pm 7, $p < 0.05$) and a smaller increase in portal vein pressure (3.5 mm Hg \pm 0.6, $p < 0.01$) than intraportal injection. The effects on hepatic and renal artery flows seemed to depend upon whether the animal received the central venous or the intraportal injection first. Given prior to the intraportal injection, the central venous injection caused a loss of the hepatic arterial buffer response. This response was intact when the intraportal injection preceded the central venous injection.

Thus, the hemodynamic effects of ET-1 given centralvenously is different from ET-1 given intraportally.

23 Symptoms and Quality of Life in Patients with Uncomplicated Duodenal Ulcer Disease

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Patients treated for duodenal ulcer (DU) disease in primary care have been suggested to have a milder "uncomplicated" disease compared to hospital outpatients. In cooperation with local primary care units we investigated untreated primary care patients with possible ulcer disease regarding endoscopic findings, symptoms, history and Quality of Life before endoscopy, during treatment and follow up. Patients were treated with effective acid inhibition during 2–8 w healing and at symptomatic relapse (2–4 w) for 12 months.

Quality of Life (QOL) was investigated with two earlier well established and validated questionnaires Psychological General Well Being Index (PGWB) and Gastrointestinal Symptom Rating Scale (GSRS). These questionnaires were filled out before endoscopy, day 15, 14 days after healing and at 6 and 12 months follow up.

1526 patients were investigated with endoscopy. A total of 393 DU were included, 57% males, 56% smokers, mean age 50 yrs. History of ulcer symptoms was <5 years in 35% and >20 yrs in 24%. During the last year 64% had 1–2 and 27% 3–5 symptomatic periods. In 16% this was the first verified ulcer episode. In another 33% their first ulcer had been verified within less than one year. Current symptoms were classified severe enough to partly or definitely inhibit normal work in 93% of patients. During follow up ($n = 305$) 31% had no relapse, 26% one, 23% 2–3 and 20% >3 relapses or constant symptoms.

QOL scores: PGWB showed a low degree of general well being at entry, the values returned to those found in a normal population after healing. Evaluation of the GSRS showed severe symptoms at entry with a reduction during follow up.

We conclude that our "uncomplicated" DU patients have symptoms and relapse pattern as described in hospital outpatients. General well being (QOL) is low in untreated patients.

24 Pain and Quality of Life in Acute Duodenal Ulcer (DU): Effect of Ranitidine

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The effect of antisecretory drugs on the sensory and affective components of DU pain, and on the quality of life of DU patients, have not been studied so far. **Patients (pts) and methods:** 101 pts with epigastric pain and DU at endoscopy (diameter at least 5 mm) were included in this multicentre prospective study. All were treated with effervescent ranitidine 300 mg per day for 4 weeks. The following parameters were assessed: a – disappearance of DU pain by self-

evaluation and on a visual analogic scale (VAS) from 0 to 100; b – evolution of sensory and affective components of DU pain, by the QDSA questionnaire (validated French version of the Mac Gill Pain Questionnaire); c – quality of life before (D0) and after (D28) treatment, evaluated by the Nottingham Health Profile (NHP). *Results:* 95/101 pts (59 M, 36 F, aged 47 ± 14 years) completed the study. DU pain had been present since 20 (2–180) days and judged as mild (8%), moderate (62%) or severe (30%) by the patients. DU healing rate was 86% at 4 weeks. 1–49.5%, 66% and 87% of the pts were free of DU pain during daytime after 7, 14 and 28 days, respectively. Corresponding figures for nighttime were 80, 88 and 97%, respectively. Median time to disappearance of DU pain was 8 days.

2-Scales of DU pain

	D0	D2	D8	D14	D28
VAS [0–100]	59 ± 2		32 ± 2*	20 ± 2*	13 ± 2*
Sensory QDSA [0–36]	13 ± 0.7	7 ± 0.6*	4 ± 0.6*	3 ± 0.5*	2 ± 0.5*
Affective QDSA [0–28]	11 ± 0.7	6 ± 0.6*	2 ± 0.4*	2 ± 0.4*	2 ± 0.3*

3-NHP:	Physical aspects (0–100)			Affective aspects (0–100)		
	Pain	Motility	Tone	Emotions	Sleep	Social isolement
D0	26 ± 3	10 ± 2	39 ± 4	29 ± 2	34 ± 3	9 ± 2
D28	6 ± 1*	5 ± 1*	17 ± 3*	13 ± 2*	21 ± 3*	4 ± 1**

*p = 0.01 (vs D0); **p = 0.001 (vs D0).

Conclusion: Using for the first time complementary scales measuring different aspects of DU pain, the effect of ranitidine is significant from the second day of treatment on sensory and affective components. A significant improvement in quality of life is observed after 4-week treatment.

25 Prognosis of Benign Gastric Ulcers. A Retrospective Study

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The relationship between gastric ulcer (GU) and malignancy is a matter still open to debate. Clinical presentation of gastric cancer often imitate peptic ulcer disease and a misdiagnosis of GU at first endoscopic procedure often occurs. In order to determine the frequency of malignant outcome of GU considered as benign at first endoscopic/histologic evaluation, we have reviewed the outcome of 506 benign GU followed up at least until one year from healing.

From January 1981 to December 1991, 1255 GU were detected in our GI unit and defined according to the endoscopic appearance as benign (903/1255, 71.9%) or possibly malignant ("suspicious") (352/1255, 28.1%). Eight or more biopsies were taken from the four quadrants as well as from the base of the ulcer or from its scar. Dysplasia was observed in 170/1255 GU (13.5%) (116 mild, 32 moderate, 22 severe), gastric malignancy was diagnosed in 256/1255 GU (20.4%).

The general guide-line was to follow-up the patients with repeated endoscopies and biopsies at intervals of 4 to 6 weeks until complete healing and then at the 3th, 6th and 12th month. A follow up of at least one year after healing has been performed in 506 GU (40.3%); 391 GU (31.1%) were lost to follow up, and 102 GU (8.2%) are yet regularly controlled.

During follow up 38 malignancies were detected (34 adenocarcinomas and 4 lymphomas). The endoscopic appearance and the grade of dysplasia at first observation of these 38 neoplasias is shown in the table below.

Apparently benign GU		Apparently malignant GU
12	No dysplasia	13
7	Dysplasia	6
1	Low	1
1	Moderate	4
5	Severe	1
19	Total	19

Our data confirm that:

- (1) misinterpretation of GU and therefore delayed diagnosis of gastric carcinoma may occur even in an accurate follow up for GU;
- (2) the macroscopic suspicion of malignancy of GU by experienced endoscopist involves a new immediate examination if negative bioptic specimens occur;
- (3) even patients with apparently benign GU should be followed up with repeated endoscopies; in our opinion procedures should be performed every three months for at least one year after complete ulcer healing and should be carry out with multiple directed biopsies from the edge and the base or the scar of the lesion;
- (4) the finding of dysplasia requires a more careful patient follow up.

26 The Natural Course of Peptic Ulcer Disease and Its Predictors

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Little is known about the natural course of peptic ulcer disease (PUD) today. A follow up study was therefore attempted in 728 patients with an endoscopic diagnosis of peptic ulcer in 1980–1984. The average follow up was 7.2 (range 6–10) years. Of the 183 patients that died during the follow up period, 14 died because of PUD (1.9%), seven during the first month. A telephone interview was performed in 441 patients. No ulcer like symptoms or other manifestations of PUD during the follow up period were reported by 15%, 10.9% had experienced one or more bleeding episodes, 0.7% had had perforation and 17% had been operated. The operated patients reported significantly (p < 0.01) less symptoms and a smaller use of histamine 2-receptor antagonists (H₂RA) during the last two weeks prior to the interview than those not operated. The majority (72%) of the unoperated patients had had ulcer like symptoms during the follow up period, on an average for 16.2 weeks per year, and during 4.9 of these weeks the symptoms had been severe. More than one third (36%) of the unoperated patients stated that the symptoms had had a significant negative impact on their lives. About half (51%) of the unoperated patients had used H₂RA, on an average for 20.4 weeks per year and 18% reported long term treatment. Age and age at onset of disease, family history, the use of non-steroid anti-inflammatory drugs and alcohol, bleeding and the presence of another chronic disease, were found to be significant independent predictors of the clinical course. Their predictive values alone or combined, however, were not impressive. This study shows that at least half of the patients with PUD have a benign course. In more than one third of the patients, however, the course is still burdened with much symptoms and complications.

27 Gastric Ulcer and Malignancy: Predictive Value of Endoscopy and Dysplasia

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Little information exists about the misinterpretation of gastric ulcer (GU) at first endoscopic/histologic examination. It is also unknown the exact percentage of apparently benign GU that are instead ulcerated malignant lesions. The aim of our study is to define the predictive value of endoscopy and dysplasia in the evaluation of GU at first diagnosis.

The records of 32353 upper GI endoscopies (Jan 1981–Dec 1991) have been reviewed. In this period 1255 GU have been detected in 1135 patients (716 M; 419 F; mean age 59.3 yrs, range 17–96). The mean GU incidence and prevalence have been 4.1 ± 0.6% and 6.9 ± 0.7% per year respectively.

According to endoscopic appearance 903 (71.9%) GU were considered as benign and 352 (28.1%) as "suspicious"; in 256 (20.4%) GU a malignancy was histologically detected.

A follow up for at least until one year after healing has been performed in 506 GU; 121 showed dysplasia (86 mild, 21 moderate, 14 severe) and 385 did not. During follow up 38 new gastric cancers have been detected.

Predictive value of endoscopic appearance (EA) and severe dysplasia (SD) at first diagnosis is shown in a 2 × 2 table:

	CANCER		SD	CANCER		
	yes	no		yes	no	
EA						
malignant	228	36	264	6	8	14
benign	66	432	498	25	460	485
	294	468	762	31	468	499

Sensitivity (Sens), specificity (Spec), positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy (ACC) and the likelihood ratio (LR) of EA and SD are shown in the table below:

	Sens	Spec	PPV	NPV	ACC	LR
EA	77.6%	92.3%	86.4%	86.7%	86.6%	10.1
SD	19.3%	98.3%	42.3%	94.8%	93.4%	11.3

Our data show that the endoscopic evaluation of GU from an expert endoscopist is comparable to the prognostic value of SD. This is stressed by similar LR values. Difference in PPV reflects the low prevalence of SD in our series (2.8%).

28 Peptic Ulcer Perforation; Impact on Long-Term Survival

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Previous studies on long-term survival of peptic ulcer patients have shown conflicting results because of uncertainty about the ulcer diagnosis, selection of ulcer patients for study and use of inappropriate methods for calculating expected survival. We studied survival during 38 years follow-up in all patients (n = 1098) treated for perforated peptic ulcer in the Bergen area of Norway 1952–1990. Patient survival was estimated by the Kaplan-Meier method, and expected survival calculated from population mortality data. The effects of age, birth-cohort and calendar year on relative mortality was analysed by Cox regression models. Overall patient survival was significantly lower than expected for 30 years after perforation due to excess mortality the first and second year, after which observed and expected survival curves were parallel. Survival was relatively lower in patients with gastric as compared to patients with duodenal perforations, and in patients treated by suture as compared to patients treated by resection. Excess mortality increased with age at perforation and year of birth, and decreased over the study period.

Conclusion: Survival in ulcer perforation patients was significantly lower than expected for 30 years after perforation due to initial excess mortality. In certain patient groups, however, life-expectancy was substantially lower than expected.

29 Gastric Leakiness in Patients with Atrophic Gastritis

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Atrophic corpus gastritis is associated with an increased risk of malignant neoplasia in the stomach and possibly other digestive organs. An abnormal permeability of the gastric mucosa to carcinogenic substances could contribute to this risk.

Methods: Recovery in six hour urine of polyethylene glycols (mol wt 414–766) was studied both after oral and duodenal load in patients with atrophic corpus gastritis (n = 18) and controls (n = 9). The difference in recovery after oral and duodenal load was used as an approximation of gastric absorption.

Results: Urinary recovery of polyethylene glycols after oral load was somewhat, although not significantly, higher in atrophic corpus gastritis patients than in controls. In atrophic corpus gastritis recovery after oral load was higher than after duodenal load for mol wt 502–546, while there was no such difference in the controls.

Atrophic corpus gastritis patients with atrophy also in the antrum (n = 7) had significantly higher recovery after oral load and higher calculated gastric absorption than controls for molecular weights 458–590 and 414–546, respectively.

Conclusion: Patients with atrophy both in the corpus and antrum showed an increased gastric absorption of small polyethylene glycols. This indicates that there is an abnormal gastric permeability to small hydrophilic substances, such as nitrosamines, in atrophic gastritis.

30 Patients with Functional Dyspepsia have Impaired Accommodation of the Gastric Fundus to a Soup Meal

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Objectives: Patients with functional dyspepsia (FD) have demonstrated a wider gastric antrum both fasting and after a soup meal compared with healthy controls (C). We hypothesize that the abnormal filling of the antrum is caused by an impaired adaptive function of the gastric fundus. The purpose of this study was to evaluate the size of the fundus of patients with FD and C after a soup meal using a novel method based on ultrasonography. **Methods:** Fasting individuals were scanned in a sitting position, leaning slightly backwards, after a 4 min ingestion period. Ultrasound images were obtained by a 3.25 MHz transducer which was positioned in the epigastrium and tilted cranially. To evaluate the stability of the method and to determine which measures of the fundus to apply in further studies, one C was examined on 6 consecutive days. The same person was also examined with CT including 3-dimensional, digital reconstruction of the images, in order to verify the anatomical sections obtained by ultrasound. The fundal area in a standardized sagittal section and the maximal diameter in a frontal section were chosen as repeatable measurements. 20 patients with FD and 20 C, comparable with respect to gender, age and smoking-habits, were scanned after drinking 500 ml meat soup (Toro) with the addition of 15 g animal fat

(170 kcal totally). The ultrasound scanner (CFM 750 Vingmed Sound) provided images 2.5, 5, 7.5, 15, 20 and 25 min after the ingestion period and the volunteers were asked to score total symptoms (1–9) provoked by the meal. **Results:** This ultrasound method proved low day-to-day variation and the selected ultrasound sections were congruent with CT images. Patients with FD revealed a significantly (p < 0.05) smaller sagittal area from 7.5 to 25 min and shorter frontal diameter from 5 to 25 min compared with C. FD patients suffered more symptoms (mean: 2.9) in response to the soup than C (mean: 0.9), (p = 0.002). **Conclusions:** The ultrasonographic method is stable and is capable of monitoring the size of the gastric fundus. Patients with FD have smaller size of the gastric fundus after a soup meal compared with C, and more symptoms are induced by the meal among patients.

31 Nutrient-Specific Modulations of Gastric Mechanosensitivity in Patients with Functional Dyspepsia (FD)

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Recently we demonstrated that infusion of lipid into the small intestine of FD patients induced dyspeptic symptoms and increased the mechanosensitivity of the stomach. To test whether these effects are specific to lipid, the AIM of this study was to compare the effects of intraduodenal lipid with an isocaloric glucose solution on symptoms and gastric mechanosensitivity in FD patients.

Methods: Twelve FD patients were allocated to two groups (A and B, n = 6), matched for sex and age. After an initial infusion of 0.9% saline, group A received a duodenal infusion of a glucose solution (1 kcal/ml), while group B received a 10% lipid emulsion (1 kcal/ml) at a rate of 1 ml/min. Fifteen minutes after starting the infusions of both saline and nutrients, repeated distensions of the stomach were carried out with an air-filled bag, at a rate of 100 ml/min. Intragastic pressure was continuously recorded, and subjects were asked to report the sensations of epigastric fullness and discomfort, and any other gastrointestinal symptoms, like nausea or bloating.

Results: The pressure-volume profiles of the stomach during distensions were similar during lipid and glucose infusion, and both were significantly lower than those during saline. The table shows the threshold volumes for fullness and discomfort in both subgroups during saline (SI) and lipid (LI) or glucose (GL) infusions. Data are expressed as mean ± SEM.

	Group A		Group B	
	SI	LI	SI	GL
Fullness	362 ± 57	197 ± 23*	366 ± 76	407 ± 53#
Discomfort	442 ± 57	278 ± 32*	490 ± 71	691 ± 77#*

* significantly different from SI, # significantly different from LI, p < 0.05.

During lipid infusion, four patients experienced symptoms of severe nausea and abdominal bloating; these symptoms were exacerbated by the gastric distensions and two patients vomited. During glucose infusion, three patients complained of abdominal bloating and slight nausea, two of them reported hunger at the end of the test, none of them vomited.

Conclusions: Our data suggest that lipid but not isocaloric infusion of glucose increases the gastric mechanosensitivity in patients with functional dyspepsia.

32 No Effects of Omeprazole in Treatment of Non-Ulcer Dyspepsia

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Upper dyspeptic symptoms are from time to time referred to as "acid-related" and as a consequence often attempted treated with different kinds of anti-ulcer drugs. To test the possible role of acid in generating dyspepsia we treated non-ulcer dyspeptic patients with omeprazole.

Design: 85 consecutive patients were included in the study following esophago-gastro-duodenoscopy to exclude organic disease. The patients were stratified according to whether they had a positive (24 pts) or a negative (61 pts) CLO-test, and they received either placebo or Omeprazole (40 mg daily) (double-blind design) for 4 weeks. On the day of inclusion the symptoms of the patients were evaluated in four groups (i.e. epigastric pain, regurgitation, heartburn, and nausea) on an ordinal scale from 0 to 3. It was, furthermore, attempted to group the patients clinically, according to the Colin-Jones criteria.

After treatment the symptoms were reevaluated and the patients were asked whether their symptoms were aggravated, unchanged, ameliorated, or had disappeared.

Results: 74 patients (36 treated with Omeprazole, 38 with placebo) were evaluable at the end of the study. Although there was a tendency towards higher scores in global assessment after 4 weeks treatment in the Omeprazole treated group this was not significant (p = 0.11 by Wilcoxon-test). Di-

viding the patients according to the criteria of Colin-Jones gave very small groups and offered no further information. The effects of the drug on individual symptoms, likewise, did not reach significance.

Conclusion: Our results do not support a role for gastric acid production in generation of functional upper dyspepsia and do not warrant prescription of Omeprazole to patients suffering from non-ulcer dyspepsia.

33 Effects of Fedotozine in Chronic Idiopathic Dyspepsia: A Double Blind, Placebo Controlled Multicentre Study

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Safety and efficacy of fedotozine (F), a peripheral κ agonist, were assessed versus placebo (P), in a double blind multicentre study conducted in France by hospital and private gastroenterologists. **Methods.** 367 dyspeptic patients were entered in the study. They were defined by the presence, in the last 3 months and at least 3 times a week, of 2 or more post-prandial symptoms: early satiety, fullness/epigastric distension, nausea/vomiting, impression of slow digestion for more than 2 hours after meals, epigastric pain. An underlying organic disease was ruled out through medical examination, gastroduodenoscopy, upper abdominal ultrasound and routine blood biochemistry and hematology. At the end of a run-in period where all patients received placebo for 1 to 2 weeks, 305 were found to have persistent dyspeptic symptoms and were randomized in 2 parallel groups: F 30 mg or P, 1 tablet tid for 6 weeks. Patients completed a diary card daily. Using a fixed point scale with 5 possibilities they were asked to rate the overall intensity of their symptoms (main efficacy end-point) and the intensity of each individual symptom. They also rated their quality of life (QoL) before and after treatment using the Subjective Quality of Life Profile questionnaire [1]. The protocol was approved by the Nantes academic hospital ethics committee and written informed consent was systematically obtained. The mean over the 6 week treatment period for each self-assessed parameter was evaluated using covariance analysis, the covariate being the mean before treatment. **Results.** The improvement with F was greater than with P after analysis of the 163 patients who complied with the protocol. This beneficial effect was significant for the main efficacy end-point (overall intensity, $p = 0.017$), for the 2 most frequently reported symptoms (slow digestion $p = 0.031$, post-prandial fullness $p = 0.027$) and for nausea ($p = 0.038$). For the patients having completed both questionnaires, F significantly improved also the QoL compared to P ($p = 0.01$, discriminant analysis). Safety profile was very good. **Conclusion.** Fedotozine had a significantly greater beneficial effect than placebo with regard to the self-assessed overall dyspeptic syndrome and some individual symptoms in those patients who complied with the protocol. Quality of life was also significantly improved. Fedotozine had an excellent safety profile.

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

34 Placebo-Controlled Trial of Cisapride and Nizatidine in Unselected Patients with Non-Ulcer Dyspepsia

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Patients in most trials of medical treatment of non-ulcer dyspepsia (NUD) have been selected groups referred for endoscopy. This could have lead to a selection-bias of non-responders explaining the negative outcome of most controlled treatment trials in NUD.

Aim: to assess the effect of cisapride (CIS) and nizatidine (NIZ) in an unselected group of patients with NUD who consult their general practitioners (GP) and to determine whether symptom subgrouping provides a useful basis for choice of medical therapy in this patient group.

Design: Consecutive patients who consulted their GP with dyspepsia were invited to an interview and endoscopy. Patients with no abnormalities at endoscopy were eligible. Patients with a history of peptic ulcer, NSAID use and use of ulcer drugs except antacida within 4 weeks were excluded. Prior to endoscopy symptoms were classified by the clinician as: reflux-like (R), dysmotility-like (D), ulcer-like (U) or idiopathic/unclassifiable (I). 330 patients were randomized to double-blind treatment with CIS 10 mg tid, NIZ 300 mg at night or placebo (PLA) for two weeks. Randomization were stratified in accordance to symptom groups. Symptoms were assessed at entry and at day 14.

Results: 109 patients received CIS, 111 NIZ and 110 PLA. 20, 15 and 16 patients were excluded because of poor compliance or side effects. At entry the groups were comparable with regard to clinical variables and symptoms. 23% of patients were classified as R, 46% as D, 13% as U and 18% as I. Symptomatic response (symptoms resolved/improved) was found in 55 (62%) of patients on CIS (therapeutic gain CIS vs PLA: 0.1%, 95% CI -14% to +14%) and in 52 (54%) of patients on NIZ (therapeutic gain NIZ vs PLA:

-8%, 95% CI -22% to +7%). The response was unrelated to subgroups of dyspepsia: effects of CIS, NIZ and PLA, respectively, in R: 57%, 60%, and 74%, in D: 61%, 55%, and 55%, in U: 67%, 50%, and 60% and in I: 67%, 50%, and 64%.

Conclusion: effects of a 2-week course of CIS or NIZ in unselected patients with NUD were not superior to effects of PLA. Symptom grouping was not predictive of response to therapy.

35 Endoscopic Ultrasonography and Computed Tomography in Diagnosis and Staging of Pancreatic Tumors: Comparison with Surgery

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Purpose: The aim of this prospective study was to compare the effectiveness of endoscopic ultrasonography (EUS) and computed tomography (CT) in diagnosis and staging of malignant pancreatic tumors (MPT).

Patients and methods: From January 1990 to May 1993, EUS or CT suspected 67 MPT. Among them, 38 underwent surgery. The procedure included tumor diagnosis (D), lymph node metastases (LNM) and vascular involvement study. The final results, surgically and histologically assessed, were: pancreatic carcinoma: $n = 29$, ampullary carcinoma: $n = 4$, pancreatic metastase: $n = 1$, cystadenocarcinoma: $n = 1$, malignant endocrine tumor: $n = 1$, cholangiocarcinoma with pancreatic involvement: $n = 1$. There were 23 LNM, 19 venous involvement (VI), and 9 arterial involvement (AI).

Results: EUS and CT sensitivity (Se) and specificity (Sp) were determined by reference to operative and histologic findings.

		D	LNM	VI	AI
EUS	Se %	95	57	68	55
	Sp %	97	86	93	100
CT	Se %	65	35	26	66
	Sp %	97	100	100	100

In MPT diagnosis, there was one false-positive in both techniques. In LNM diagnosis, there were 10 false-negative EUS findings explained by micrometastases in 6 cases. In VI diagnosis, there were respectively 6 and 14 EUS and CT false-negative findings. In AI diagnosis, there were respectively 4 and 3 EUS and CT false-negative findings.

Conclusion: (1) EUS is more accurate than CT in MPT diagnosis, detection of metastatic lymph nodes and venous involvement. (2) Results of EUS and CT are similar in detection of arterial involvement.

36 Safety of Linear Array Endoscopic Ultrasonography in Upper Gastrointestinal Malignancies

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Endoscopic ultrasonography (EUS) has been performed for almost a decade with increasing evidence of its capacity in the pretherapeutic staging and assessment of resectability in upper gastrointestinal malignancies (UGIM). Despite the widespread use of EUS only estimates of the risk related to the EUS examination has been reported and most materials are based upon retrospective series. Therefore, prospectively we recorded the number of complications during or immediately after EUS examination of patients with UGIM.

Materials and results: One hundred thirty-two consecutive patients with UGIM were referred for pretherapeutic staging and assessment of resectability. Forty-six patients had esophageal cancer, 56 patients had gastric cancer and 30 patients had pancreatic cancer. EUS was performed using a forward oblique viewing linear array echoendoscope. The examination time varied from 4 to 55 minutes (median 25 minutes). Five to 15 mg (median 10 mg) of diazepam was used during the examinations. Analgesic (Pethidine), 20 to 40 mg (median 25 mg), was administered together with sedatives when dilatation was performed. In 128 patients (97%) a complete EUS examination was performed without any complications at all. Twenty patients (15%) presented with a non-traversable tumor stenosis. EUS of the area oral to the stenosis gave sufficient information in 7 cases, but in 13 patients EUS of this area was inconclusive and dilatation was attempted. All patients were dilatated using the balloon method, but three of these patients needed bougienage in general anaesthesia in order to perform a complete dilatation. No complications were seen during or after EUS following balloon dilatation, but two patients with severe tumor stenosis in the esophagus suffered a small perforation related to the dilatation and EUS procedure. Both patients, however, recovered uneventful on a conservative regimen. In 8 patients the water-filled-stomach method was necessary in order to obtain a reliable EUS image of the tumor and in two of these cases (25%) a combination of overfilling and tumor stenosis resulted in nausea and vomiting. The examination was completed in both