very sensitive and specific identification in serum of the test substances in serum. We found good separation between healthy controls and patients with chronic pancreatitis. Further studies of applicability and diagnostic efficiency are justified.

**1022** Postprandial Duodenal pH is Abnormally Low in Patients with Exocrine Pancreatic Insufficiency: A Preliminary Study


Gastroenterology Unit, University of Verona, Italy

Increases in basal and pentagastrin-stimulated acid output and abnormally low postprandial pH (pH-method) have been reported in the course of chronic alcoholic pancreatitis, thought it is still debatable whether or not any correlation exists between duodenal pH and exocrine pancreatitis insufficiency. The aim of this study was to assess the circadian variations when given single. An in 16 hospital patients with chronic pancreatitis (mean age: 50.2 ± 7.2 years) and in 8 controls (mean age 41.4 ± 12 years); pH-measurement was performed by using specially designed 2-4 channel monocrystalline antimony electrodes (Monocrystant mod.0001) connected up to a recorder (Digitrapper Synetics MK-II and MK-III, respectively). The detectors were placed under fluoroscopic control in the gastric corpus in the duodenal bulb and/or in the second portion of the duodenum. The evaluation parameters considered, expressed as mean ± SD, were: 24-h, postprandial, orthostatic and circumstantial median pH. The chronic pancreatitis patients were also submitted to the Secretin-Caerulein test (lipase output at 60-90 min) for assessment of the exocrine pancreatic insufficiency of the Pancreolauryl test and postprandial pancreatic enzymes.

**Results:** The chronic pancreatitis patients presented a significantly greater degree of acidification in the postprandial phase at the level both of the bulb (pH: 2.5 ± 1.1; P ≤ 0.02) (n = 8) and the second portion of the duodenum (pH: 3.4 ± 1.2; P ≤ 0.05) (n = 13) as compared to the control group (pH: 5.1 ± 1.0 and 5.1 ± 1.6 respectively). There was a correlation between these data as indicated in the median duodenal pH values and both output of bicarbonates (R = 0.72; P < 0.04) and Pancreolauryl test (R = 0.61; P < 0.04). Conclusions: Gastric, exocrine pancreatic insufficiency and maldigestion appear to be correlated in chronic pancreatitis.

**1024** Evidence for Potentiating Interaction between Vagal Cholinergic M1 Fibers and Cholecystokinin (CCK) as Mediators of the Pancreatic Protein Secretion

E. Nieburgs-Roth*, S. Teysens, M. Hartel, D. Wietzel, C. Beglinger

M.V. Singer. Univ. Hosp. of Heidelberg at Mannheim, Germany; Univ. Hosp. of Basel, Switzerland

In six conscious dogs with gastric and pancreatic fistulas we compared the effect of the muscarinic M1-receptor antagonist telenzepine (TEL; 20, 25, 40, 81 and 81 nmol/ml g-1 h-1), of the CCK-antagonist L-364,718 (L; 0.025, 0.05 and 0.1 mg/kg g-1 h-1) and combinations of both on the pancreatic protein response to a meal load of cysteine and tyrosine. RPF: 0.37±0.0 mmol/l ml/g h-1, given against a background of secretin (S; 20.5 μmol/ml g-1 h-1). The 180-min integrated protein response (IPR, g) to all loads of TRP was calculated. Results: All loads of IPR significantly (p < 0.05) increased the pancreatic protein output over that seen with secretin alone (data not shown). When given singly, the two highest doses of TEL and L significantly decreased the IPR by 70 to 97%. All combinations of TEL + L abolished the IPR before and after TV. In the case of the lowest dose of TEL and L, the initial effect of their combination was significantly greater than the sum of the effects when given singly. An interaction between two agents given together resulting in a greater effect than the sum of the effects of the two agents given singly was defined as a potentiated interaction.

**Table 1:** 180-min. IPR (g) to all loads of TRP

<table>
<thead>
<tr>
<th>Control</th>
<th>TEL (20,25) + L (0.025);</th>
<th>0.8*</th>
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<tbody>
<tr>
<td></td>
<td>(20,25) + L (0.005);</td>
<td>-0.2</td>
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<tr>
<td></td>
<td>TEL (20,25) + L (0.1);</td>
<td>0.2*</td>
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<tr>
<td></td>
<td>TEL (40,5); L (0.025);</td>
<td>0.2*</td>
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<tr>
<td></td>
<td>TEL (81); L (0.05);</td>
<td>-0.2*</td>
</tr>
<tr>
<td></td>
<td>TEL (81); L (0.1);</td>
<td>0.8*</td>
</tr>
<tr>
<td></td>
<td>L (0.025);</td>
<td>1.0*</td>
</tr>
<tr>
<td></td>
<td>L (0.05);</td>
<td>0.8*</td>
</tr>
<tr>
<td></td>
<td>L (0.1);</td>
<td>0.6*</td>
</tr>
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</table>

**Results are means (n = 6); *p < 0.05 vs. control**

**Conclusion:** Potentiation exists between the inhibitory actions of the M1 antagonist TEL and the CCK-A-antagonist L on the endogenously stimulated pancreatic protein output. We interpret these data indicating a potentiated interaction between vagal cholinergic M1 fibers and CCK as mediators of the pancreatic enzyme response to intraduodenal amino acids.

**1025** ERCP-Induced Necrotizing Pancreatitis. Is It a More Serious Disease?

A.S.Y. Fung, G.G. Tsitsos, M.G. Sarr. Mayo Clinic, Rochester, MN, USA

Acute necrotizing pancreatitis (ANP) is a rare but serious complication of ERCP. Aim: To compare disease severity, clinical course, and outcome of ERCP-induced ANP versus ANP induced by other causes. Results: 72 patients with ANP underwent operative treatment at the Mayo Clinic. ANP was caused by ERCP in 6 patients (8%). When compared to the remaining group of 66 patients with ANP induced by other causes (gallstone – 27; alcohol – 10; postoperative – 8; familial – 1; idiopathic – 24), the ERCP-induced group had a higher admission APACHE-II score (13 ± 3 vs 10 ± 1; ±SEM), more extensive estimated pancreatic insufficiency (60 vs 45), a greater rate of postoperative gastrointestinal or pancreatic fistulas (55 vs 30%), and a longer postoperative hospitalization (63 ± 8 vs 53 ± 5; ±SEM; p < 0.05). In addition, the ERCP-induced group required noncuteostomy earlier in the hospital course and had a higher rate of infected necrosis (100 vs 75%). Although mortality rate of ERCP-induced ANP was lower (17 vs 29%), these patients were considerably younger (50 ± 4 vs 62 ± 2; ±SEM; p = 0.02) and all survivors had residual ductal morbidity (chronic or endocrine pancreatic insufficiency) or decreased functional ability. Conclusions: ERCP-induced ANP is usually severe, presents in a fulminant state, and carries a poorer prognosis compared to other etiologies. Infection introduced during the ERCP may, in part, account for the more aggressive nature of this disease.

**1026** Obstructive Jaundice: Comparison between Spiral CT and Cholangiography, MR-MR, after Failure of ERCP

G.A. Rollandi, A. Talenti, E. Biscaldi, E. Bonilacico, N. Gandolfio, R. Perrone

Institute of Radiology, University of Genoa

**Introduction:** In spite of improvements of CT and US techniques, the direct vision of the biliary tree is always important in case of obstructive jaundice, for a better choice of the therapy.

At the moment Contrast Media for intravenous cholangiography are no more produced; conventional radiographic studies are then impossible. While ERCP and PTC are examination with high specificity and sensitivity, but they are also quite invasive and have frequent complications.

Recently a new MRI technique for cholangiography has been described. It is based on the detectability of the bile by MR sequences, without any introduction of contrast medium.

**Purpose:** We wanted to evaluate the diagnostic informations from Cholangiography MR-C (MR-MR) in patients with obstructive jaundice, already examined by Spiral CT, and after failure to obtain an ERCP.

**Materials and Methods:** 13 jaundiced patients, with US diagnosis of dilatation of the biliary tree and with failure to obtain an ERCP (4 non successful attempts, 2 gastric resections, 6 difficulties of management in emergency) were submitted to Spiral CT of the upper abdomen and to MR-MR, before surgical treatment. Spiral CTs were performed with a volumetric scan with 10 mm collimation, 3 mm of interval of reconstruction, pitch 1, 300 mAs, 120 kV, i.v. injection (4 cc/s) of non ionic c.m. (370 I/g100 ml). MR-MR examinations were performed with a 0.5 T magnetic strength, TR6000, TE200, matrix 160-256, NEX5, MIP reconstruction.

Results: In 12 cases MR-C reached the correct diagnosis; only in 1 case a little stone (2 mm) at the papilla was lost. In 6 cases (4 primary tumours of biliary tree and 2 pancreatic cancers) MR-C didn't give any more informations that the CT.

In 4 cases (biliary stones) C-RM provided more diagnostic information that CT. In 2 cases of chronic pancreatitis, with pseudocysts of the head of pancreas only C-RM allowed the correct diagnostic identification as the case of obstruction.

Conclusions: MR-C has high diagnostic sensitivity and specificity in the diagnostic evaluation imaging of jaundice. Spiral CT is more useful only in neoplastic diseases.

**1031** Preoperative Cyst Fluid Analysis for the Differential Diagnosis of Cystic Lesions of the Pancreas

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The nature of cystic lesions of the pancreas (CLP) is often difficult to determine preoperatively since imaging techniques do not give correct diagnosis in 30% of cases. We have previously shown that cyst fluid analysis for carcinoembryonic antigen (CEA), carbohydrate antigen (Ca) 19.9 and amylase is useful for the differential diagnosis of CLP.

**Aim:** to assess the reliability of preoperative lipase, Ca 72.4 and Mucin antigen analysis, in addition to that of amylase, CEA and Ca 19.9, in cyst fluid obtained by fine-needle aspiration for pathological diagnosis in a large series of CLP.

**Methods:** cyst fluid was obtained for 96 CLP (26 mucinous cystadenomas or cystadenocarcinomas (MC), 14 serous cystadenomas (CS) and 58 pseudocysts (PC) complicating well-documented chronic pancreatitis). Cutoffs of biochemical and tumor markers were determined so that the three types of CLP could be differentiated as accurately as possible. Sensitivity (se), specificity (sp), positive and negative predictive values (PPV and NPV) of these markers were calculated for this purpose.
### Tables

<table>
<thead>
<tr>
<th>Table 1: GER (%)</th>
<th>T</th>
<th>N</th>
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<tbody>
<tr>
<td>Gr. I</td>
<td>2.5 ± 2.9*</td>
<td>21.0 ± 14.1*</td>
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<tr>
<td>Gr. II</td>
<td>12.5 ± 14.1</td>
<td>83.0 ± 79.6</td>
</tr>
<tr>
<td>Gr. III</td>
<td>15.6 ± 42.5</td>
<td>59.4 ± 73.15*</td>
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*p < 0.01 vs Gr II and Gr III; **p < 0.01 vs Gr II

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<th>Table 2: %</th>
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<tr>
<td>24-h</td>
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<tr>
<td>Gr. I</td>
<td>16.1 ± 20.4</td>
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<tr>
<td>Gr. II</td>
<td>20.9 ± 24.2</td>
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<tr>
<td>Gr. III</td>
<td>28.6 ± 35.9*</td>
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</table>

*p < 0.05 vs Gr I and II; **p < 0.05 vs Gr I

### Results

The worldwide diffusion of nonoperative alternatives to surgical management of pancreatic pseudocysts might lead to an increase of diagnostic errors with consequent inappropriate treatment of unrecognised cystic neoplasms. The aim of this retrospective study was to ascertain the clinical incidence of diagnostic errors in a series of nonoperatively managed pseudocysts. Out of 74 patients (49 males and 25 females; mean age: 57.3 years, range: 26–80) bearing one or more pancreatic pseudocysts who underwent a percutaneous ultrasound-guided drainage were reviewed and analysed. The treatment was included: medical history, physical examination, ultrasound (US) and computed tomography (CT) scans, determination of serum markers and pancreatic enzymes in the serum and in the cystic fluid, chemistry, and cytology. All patients were entered into a combined clinic-ultrasonographic follow-up.

Patients underwent a percutaneous catheter drainage and 4 repeated fine needle aspirations. A total of 4 neoplastic lesions were overlooked after the initial workup (4/64, 6.2%). Two cancer-associated pseudocysts were identified during the period (2/64, 3.1%). Four patients died soon after the treatment, while the remaining 58 patients followed-up for a mean of 41 months (range: 10–132). A third cancer and a mucinous cystic tumor (2/58, 3.4%), fully communicating with the main duct, were further detected during this period.

Data from our experience confirm the existence of a misdiagnosis risk in the nonoperative management of pancreatic pseudocysts and support the need for a thorough follow-up with continuous reassessment of each patient. The nature of any pseudocyst with atypical clinical history or behaviour should be questioned and, when doubts persist, the patient should be referred for surgical exploration.

### Proximal Esophageal pH-Metry in Controls and in Patients with Reflux or Oesophageal Impedance (ORL) Symptoms. A Multicenter Study in Italy

### References

- **F. Baldi, M.L. Brancaccio, R. Cappiello, M. Dinelli, L. Fei, S. Mattioli, M. Missale, S. Passerotti, R. Sablich, S. Sottoli, V. Stanghellini, I. Vantini. G.I.S.M.A.D.-Italy**

  We studied 22 healthy subjects (9 M; 50.1 ± 12.0 yr) [Gr. I]; 114 patients with typical reflux symptoms from ≥ 6 months (72 M; 48.8 ± 14.1 yr) [Gr. II] and 116 patients with unexplained ORL symptoms from ≥ 6 months (67 M; 52.1 ± 12.6 yr) [Gr. III]. All subjects underwent an upper GI endoscopy, an oesophageal pHmetry and an 24-hr esophageal pHmetry performed with 2 glass electrodes (Ingold M 4.40, M 1.40) connected to a portable data-logger and positioned 5 cm above the LES and 1 cm below the LES localized by manometry, respectively. Parameters: N. of GER episodes (pH < 4 ≥ 5 sec.; GER) and acid exposure time (% T pH < 4; % T) were calculated for the 24-hr period at the two recording sites. The proximal distribution of reflux (% of distal GER reaching the proximal site; % P) was calculated for the 24-hr, upper and subepiploic periods. Statistical analysis was performed with a Student T test or Mann-Whitney U test.

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<td>Gr. II</td>
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<td>Gr. III</td>
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<tr>
<td>*p &lt; 0.01 vs Gr II and Gr III; **p &lt; 0.01 vs Gr II</td>
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<td>P</td>
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<td>24-h</td>
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<tr>
<td>Gr. I</td>
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<td>Gr. II</td>
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<td>Gr. III</td>
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<tr>
<td>*p &lt; 0.05 vs Gr I and II; **p &lt; 0.05 vs Gr I</td>
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### Results

Data are expressed as mean ± SD and reported in Tables 1 and 2. The subdivision of the patients according to the presence of esophagitis or of ORL lesions didn't show significant differences between the reflux values assessed at the proximal site. Conclusions: proximal acid GER was significantly higher in both patient groups, in comparison with controls. Patients with ORL symptoms had a significantly higher median of refluxes that reached the proximal esophagus, particularly during the night.

### Sensitivity to Acid and Distension in Gastro Oesophageal Reflux Disease (GORD) and the Acid Hypersensitive Oesophagus

#### S. Bruley des Varannes, G. Shi, C. Scarpignato, J.P. Galmiche. Dept of Gastroenterology, University of Nancy, 44035 Nancy, France

Although mechanical receptors are present in the oesophageal wall, the investigation of oesophageal sensitivity in GORD and some functional related disorders has been usually limited to the acid perfusion test. We therefore compared the oesophageal sensitivity to both acid and mechanical stimuli in patients with GORD and with the newly described acid hypersensitive oesophagus (AHO) syndrome (Gut 1995, 37: 457-64).

Methods. One hundred and twenty-four patients referred for 24-h oesophageal pH monitoring for symptoms suggestive of GORD were submitted to an oesophageal acid perfusion test (APT) and to an oesophageal balloon distension test (BDT). The probability that symptoms and reflux episodes occurred simultaneously by chance was calculated. APT was considered positive when perfusion induced retrosternal burning or the spontaneously reported pain. The balloon volume inducing pain (VIP) was determined; BDT was considered positive when VIP was ≤ 7 ml (95% CI of 10 healthy subjects).

Results. Patients were divided into 3 groups: normal acid exposure (≤ 4.2% of total recording time) with no significant relation between symptoms and reflux episodes (group Functional Dyspepsia (FD)), and with significant relation between symptoms and reflux episodes (group AHO), abnormal acid exposure (group GORD). The results of APT and BDT are in the table (Chi², Mann-Whitney: P < 0.05 compared a: with volunteers; b: with GORD, c: with FD).

### Lanzoprazole Versus Omeprazole in Long Term Maintenance Treatment of Refluxoesophagitis. A Scandinavian Multicentre Trial


This double-blind multicentre study recruited 289 patients who were treated with 30 mg lanzoprazole for 8 weeks or as much as 12 weeks. When cured the patients were randomized to either treatment with 20 mg omeprazole or 30 mg lanzoprazole each day for 48 weeks or until relapse (i.e. at least grade II esophagitis or severe refluxsymptoms). The baseline distribution of esophagitis was: Grade II 194 (67%), grade III 74 (26%), grade IV 19 (7%). Grade II corresponds to: Erosive and exudative confluent lesions without circumferential extensions. The demographic data was similar in the two treatment groups. To the maintenance part 266 patients were recruited and 131 got lanzoprazole 30 mg o.m. and 125 omeprazole 20 mg o.m. treatment. They were followed every 12 weeks.

### Results

After 8 weeks 94% of the patients were cured and the cumulative figure after 12 weeks was 90%. Grade II patients healed to grade 0 in 82.5%.

<table>
<thead>
<tr>
<th>Maintenance part</th>
<th>Lanzoprazole 30 mg</th>
<th>Omeprazole 20 mg</th>
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<tbody>
<tr>
<td>Patients evaluated</td>
<td>124</td>
<td>120</td>
</tr>
<tr>
<td>Relapse (total)</td>
<td>12 (9.7%)</td>
<td>11 (9.2%)</td>
</tr>
<tr>
<td>week 0–12</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>week 13–24</td>
<td>5</td>
<td>5</td>
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<tr>
<td>week 25–26</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>week 27–48</td>
<td>1</td>
<td>1</td>
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*p = 0.04 NS

Eighteen patients relapsed to grade II esophagitis. Only two patients got a symptomatic relapse. There were no differences in adverse events in the both treatment groups. Conclusion: Both lanzoprazole 30 mg o.m. and omeprazole 20 mg o.m. gives low and similar relapse rates in maintenance treatment in moderate and severe refluxoesophagitis.
Somatostatin Prevents Meal Induced Alterations in Lower Esophageal Sphincter Function


Somatostatin (S.T.) inhibits gastrointestinal secretion and motility. SST reduces gall acid secretion and is of potential clinical interest in acid related disorders. It is not known, however, whether SST influences lower esophageal sphincter (LES) function. Therefore we evaluated the effect of SST on LES characteristics. Six healthy subjects (M, 4 F, age 19-53 yr) were studied after a 10 hour fast. Leso was evaluated in 2 different order under fasting conditions during 1) SST infusion (250 µg/h) or 2) saline i.v. (control) and after meal stimulation during 3) SST infusion (250 µg/h) and 4) saline i.v. (control) for 240 minutes. LES relaxations (TLESR), as the most important reflex mechanism, and acid reflux were measured by 24h esophageal pHmetry and manometry (Dent-sleeve). The meal consisted of carbohydrates only (500 Kcal) in order to prevent gastro-intestinal hormone release.

Results: under fasting conditions SST did not affect LES pressure and LES pressure during SST (range 25 ± 4 to 29 ± 6 mmHg) was not significantly different from control (range 23 ± 4 to 26 ± 1 mmHg). TLESR frequency under fasting conditions was 22.2 ± 6.6 per hour was not significantly different from control (2.4 ± 0.5 per hour). Mean ingestion significantly (p < 0.05) increased TLESR frequency from 2.4 ± 0.5 to 4.8 ± 0.5 in the first postprandial hour. However, this meal induced increase in TLESR frequency did not affect acid reflux time was low (fasting: 0.1%, meal: 0.2%) and not influenced by SST.

It is concluded that 1) somatostatin does not affect fasting LES pressure and TLESR-frequency, 2) but meal induced decreases in LESP and increases in TLESR induced by somatostatin prevent meal induced alteration in LES function that permit reflux. The effect of somatostatin in patients with reflux disease therefore deserves further evaluation.

α-interferon (IFN) treatment is today the only evaluated therapy for hepatitis C able to induce a biological remission. The determination of predictive factors of response is essential in planning IFN treatment. Cirrhosis is a negative predictor of response and it is also associated with decreased antipyrine metabolism. A positive correlation has been recently observed between the liver metabolic capacity and the response to α-IFN in pts with chronic hepatitis C [1]. We assessed the antipyrene test in pts with chronic hepatitis C, who underwent α-IFN therapy.

We enrolled 45 pts (22 males, 23 females, median age 47, range 25-70) with histological diagnosis of CAH; 20 were classified as having CAH with mild or nodular (group A), and 25 as CAH with (group B). The antipyrene metabolic test (18 mg/kg in water p.o.; blood samples drawn 3 and 24 hrs after administration for spectrophotometrical analysis) was administered to all patients before treatment with recombinant α-IFN (0.8 MIU/week for 6 months). The therapeutic response was assessed in terms of ALT normalization.

We observed a complete response to IFN therapy in 19/45 pts (42%) and the response rate was higher in Group A (16/20, pts 80%) than in Group B (3/25, pts 12%). Pts of group A had significantly better clearance (0.405 ± 0.1 ml/min/kg) than those of group B (0.22 ± 0.15 ml/min/kg) (p < 0.001). Baseline antipyrene clearance for the group of responders (0.412 ± 0.15 ml/min/kg) was significantly higher than that of the non-responders (0.242 ± 0.14) (p < 0.001). 13/19 responders had an antipyrene clearance over a cut-off > 0.30 ml/min/kg (78%).

We confirm the relationship between hepatic drug metabolism, explored by antipyrene metabolism, and the response to IFN therapy in pts with C Hepatitis. We suggest the use of this test in pts clinical baseline evaluation, especially when liver histology is not available.

1046 \textbf{Stool DNA Yield and the Detection of K-ras Mutations in Patients with Colorectal Cancer Using the Amplification Refractory Mutation System} 

R.B. Crockfie\d{}n1, J.C. Fox\d{}1, G. Ellison1, N.R. Charles\d{}ton2, A. Jones3, R. Cole4, C. oat\d{}5, S. K.\d{}dy\d{}6, D. J. Gourley, Queen Elizabeth Hospital, Birmingham; \d{}1 Cancer Diagnostics Research & Development, Zeneca Diagnostics; \d{}2 Birmingham Heartlands NHS Trust 

Molecular analysis of stool DNA has the potential of providing a non invasive screening test for colorectal neoplasia. This study evaluates the extraction of human DNA from stool combined with the identification of K-ras mutations using the Amplification Refractory Mutation System (ARMS). 

35 consecutive matched stool and tumour samples were analysed. Stool samples were collected on admission to hospital prior to surgery, 2–4 gms of stool sample obtained from each subject and used in each silica based DNA extraction. The human DNA extracted from stool was evaluated by serial dilution and PCR amplification using three common human specific primer sequences; exons 1 of the cystic fibrosis, \( \alpha \)-antitrypsin and K-ras genes. Tumour DNA and matched stool DNA were then evaluated using ARMS allele specific amplification for 7 common K-ras mutations in codons 12 and 13. 

Human DNA was isolated in 55/61 stool samples and quantified by serial dilution and PCR amplification (range 1/5 to 1/1000 dilutions). 23 out of 61 tumours were K-ras positive (38%), 21 tumours had sufficient stool DNA recovered to allow analysis with the corresponding mutation identified in 13/21 stool samples (62%) and 12/17 (70%) of left sided lesions. In the K-ras positive stool samples all 8 samples which had a stool DNA quality greater than 1 in 200 had the correct mutation identified, compared to 5/15 in those samples with a stool dilution yield of less than 1 in 100 (2p = 0.0047 – Fisher's exact probability test).

These results suggest that DNA yield is essential to successful stool DNA mutational analysis. In the presence of a high DNA yield from stool, this can provide a sensitive and specific test for colorectal cancer, but progress in this novel screening method will be dependant on developing improved extraction techniques.

1047 \textbf{Is It Possible to Assess the Quality of Rectal Excision for Cancer?} 

M. Poccard, Y. Panis, J. Nenhet, P. Hautefeuille, P. Valleur. Digestive Surgical and Pathology Departments, University Hospital Lanbosibre, 2 rue Ambroise Pare, 75010, Paris, France 

After rectal excision for cancer, the greatest variability in the reported incidence of local recurrence (from 4 to 35%) suggests that surgery is crucial for the prognosis. To date, no objective criteria have been reported to assess the quality of proctectomy for cancer. The aim of this work was to assess, in patients (pts) undergoing curative resection of rectal carcinoma, the impact on survival and local recurrence rates, of the number of lymph nodes (involved or not) found on the resected specimen.

\textbf{Patients and Methods:} From 1982 to 1992, 180 pts underwent curative proctectomy (without synchronous metastases or distant lymph node metastases): 117 pts without lymph node invasion (NO) and 63 pts with proximal nodal invasion (N+). Mean follow up was 55 ± 40 months (extr. 0–125), Mean number of lymph nodes on the specimen was 12 ± 8 (extr. 0–42). According to the TNM stage (N), we studied the survival rate (LR) rates at 10 years, and for N+, the mean number of positive nodes (N+).

\textbf{Results:}

<table>
<thead>
<tr>
<th>N0 patients (n = 117)</th>
<th>N+ patients (n = 63)</th>
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<tbody>
<tr>
<td>N</td>
<td>pts</td>
</tr>
<tr>
<td>0–4</td>
<td>27</td>
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<tr>
<td>5–9</td>
<td>32</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>56</td>
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</table>

\([\text{R}]< 0.05, \text{preoperative radiotherapy (29 pts NO and 12 N+) did not influence the results. Only the mean number of lymph nodes was reduced in case of radiotherapy: 7.4 vs 12.3 (NO) and 9.3 vs 13.5 (N+).}\]

\textbf{Conclusions:} a) In NO patients, local recurrence rate was significantly higher if fewer than 10 lymph nodes were found. Whatever the cause (involved excision or carcinoma with low level of nodes reaction), the high rate of recurrence observed in these cases underline the need of a careful postoperative follow up; b) In N+ patients, a small number of lymph nodes on the specimen could suggest that the K-ras mutation identified is 1. De novo capacity (and that the prognosis is better) than an insufficient rectal excision.

1049 \textbf{Families with a Strong History of Colorectal Cancer but with Tumours Lacking the Mutator Phenotype} 

J.R. Jess, V. Pokos, J.L. Arnold, D.S. Cotter, P.J. Browett, I.M. Winship, M.R. Lane, University of Auckland, Auckland, New Zealand 

Clinical and pathological features of families with a strong family history of colorectal cancer but lacking tumours with the mutator phenotype were studied with the aim of distinguishing a new syndrome of hereditary bowel cancer. In eight families fulfilling the Amsterdam criteria for hereditary non-polyposis colorectal cancer (HNPCC), at least two out of two cancers per family showed DNA repair proficiency as indicated by a lack of microsatellite instability at up to six loci. Colonoscopics findings in at-risk family members, together with clinical and pathological features in affected family members were compared with genuine HNPCC families (12).

The overall tumour burden in the eight families included 38 colorectal cancers, one ovarian cancer, but no uterine, gastric, pancreatic, small intestinal or upper urinary tract cancers. Despite the fact that at least one family member was aged less than 50 years, the mean age of onset of cancer was 57 years. The majority of cancers developed in the left colon and rectum (80%). Only one subject had multiple colorectal cancer and there was no increased frequency of mucinous (14%) or poorly differentiated (10%) cancers. At-risk family members had more colorectal cancers than risk members of HNPCC families (p = 0.095) and a higher adenoma:carcinoma ratio (13:1 versus 7:1). No families showed features of attenuated FAP.

The preceding data suggest that there may be hereditary colorectal cancer syndromes ('autosomal dominant) distinct from HNPCC and FAP.

1051 \textbf{Thyroid Cancer in Patients with Familial Adenomatous Polyposis in the Netherlands} 

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Familial adenomatous polyposis (FAP) is known to be associated with several extracolonic cancers. In the literature a 25–160 times higher relative risk of developing thyroid cancer (TC) has been reported, especially in women. The aims of the present study were to assess the incidence of TC in the Dutch FAP Registry and to evaluate the value of screening of the thyroid.

\textbf{Methods:} The registry contains 655 families including 1061 patients (339 men and 262 women). The diagnosis of FAP was confirmed by endoscopy, histology, mutation analysis or a medical report. For risk assessment, patients were studied with respect to their risk of developing TC from birth until date of death, date of diagnosis, or closing date of the study (January 1, 1996). The age-specific relative risk (RR) was defined as the ratio between the observed and expected number of tumours. The expected numbers were calculated by multiplying the person-years by corresponding age-specific incidence rates obtained from the Dutch National Cancer Registry of 1991.

\textbf{Results:} Screening for TC revealed 5 cases which were all female. The mean age at diagnosis was 36 years (range 16–62). In 3 patients TC appeared to be the presenting symptom. Histology revealed 2 follicular carcinomas and 2 mixed papillary/follicular carcinomas in one patient histology was not available. The RR of TC in female FAP patients was 32 (95% confidence interval 13–76). At the age of 74 the cumulative incidence in these patients was 17% versus 0.2% in non-FAP women. None of the 339 male patients had TC.

\textbf{Conclusions:} Female FAP patients are more likely to develop TC especially at relative young age. Moreover, TC may be the presenting symptom of FAP. However, the prognosis remains good. Therefore, as swelling of the thyroid can easily be detected by palpation we recommend periodic physical examination in female FAP patients. Other screening procedures are not appropriate as the prognosis of TC in FAP appears to be good.

1054 \textbf{Early Diagnosis of Extrathoracic Bile Duct Cancer with MR Cholangiopancreatography} 

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\textbf{Objectives:} Purpose of this study was to determine the efficacy of MR Cholangiopancreatography (MRCP) in the early diagnosis of extrathoracic bile duct cancer.

\textbf{Subjects and Methods:} From July 1995 to April 1996, 56052 patients visited our outpatient clinic, and 192 patients suspected of having pancreaticobiliary diseases were examined with MRCP. Male to female was 114:78, with an average age of 53 years. MRCP was performed with a 1.5 T scanner (TOSHIBA VISART). Two dimensional heavily T2 weighted MRCP images were obtained in breath-hold of 3 seconds using Fast Asymmetric Spin Echo Sequence (FASE).

\textbf{Results:} In 34 patients, MRCP demonstrated extrathoracic bile duct stenosis which was confirmed by ERCP or PTC. Ten patients were ever diagnosed to have bile duct cancer which was confirmed by surgery (n = 6) or PTCD and cytology (n = 4). Two patients were non-icteric, and one patient had no bile duct dilatation. In one patient tumor was limited to the muscular layer and in 2 patients it was limited to the perimuscular connective tissue. A curative resection based on histological findings was possible in 2 patients.

Conclusion: MRCP is a useful method to diagnose early stage of extrathoracic bile duct cancer.

1055 \textbf{Combined Modality Therapy (CMT) in the Primary Cholangiocarcinoma of the Confluence: Czech Experience in 219 Patients} 

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Primary cholangiocarcinoma of the confluence (hilus cancer, HC) is the most common biliary tree malignancy in Central and Eastern Europe in the elderly. If untreated, its prognosis remains dismal, with the median survival 98.7 days.
Aims: This study was performed to assess the feasibility of CMT in HC patients.

Methods: Since Jan 1990 to Jan 1996, 219 consecutive jaundiced pts with HC (121 males, 98 females, mean age 58.7 years) were entered into the prospective study. In all pts, nonsurgical stenting of the CBD was performed, followed by regional chemotherapy (RCHT) in 63 cases or by intraluminal radiotherapy (ILRT) in 36 pts.

Results: Median survival in pts, treated by stenting alone, was 236 days. In those, treated by stents and RCHT or ILRT, median survival reached 594 days. In pts, treated by stents, RCHT and ILRT in combination, median survival was 71 days. We were not able to demonstrate any weighty side effects, either local or systemic. Early and/or late complications of stenting did not exceed 2.1%.

Conclusions: On the basis of the results mentioned is possible to conclude, that CMT in preoperative HC patiulation is the method of choice, nowadays. Supported by grant 2227 of IGA MH CR

1058 Functional Characterisation of Neurokinin Receptors Mediating Ion Transport in Porcine Jejunum

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Substance P and neurokinin A (NKA) are the major tachykinin neuro-transmitters in the porcine small intestine. Tachykinins seem to be involved in both secretory actions of CCK on the mucosa and in inflammatory bowel disease, in which alterations in ion transport constitute part of the pathophysiology. Thus, tachykinin receptor antagonists might have a therapeutic potential. The aim of the present study was to characterise neurokinin (NK) receptors, involved in ion transport, in porcine jejunum, as this tissue exhibits functional similarity to human upper small intestine. Methods: Striped porcine jejunal tissue preparations with intact mucosa and submucosa were mounted in Using chambers containing Ringer-solution. The tissue was short-circuited and corresponding values of electrical parameters (resistance and open circuit potential difference) were measured and calculated by computer. Compounds were added to the serosal side. Results: SP produced a concentration-dependent increase in short-circuit current (SCC), the curve having a double sigmoidal form. The NK-1 antagonist CP 99,994 totally abolished the first sigmoidal response, of the presence of an NK-1 receptor. This was further supported by a concentration-dependent tendency of the NK-1 agonist [Ser^9]Met^10]-SP (SP) with an EC_{50} value of 235.0 nM ± 53.9. Increasing concentrations of CP 99,994 (0.1 μM, 0.3 μM and 1 μM) produced a parallel shift of the Sa^2 SP curve with a slope of the Schild regression (1.59) different from unity. Another NK-1 antagonist, RP 67,580, and the inactive enantiomer of CP 99,994, CP 100,263, did not change the response to SP. The NKA concentration response curve EC_{50} value of 68.67 nM ± 12.93 was not significantly changed by the NK-2 antagonists, SR 48,998 or GR 94,800. However, CP 99,994 totally inhibited NKA responses at 0.5 μM and higher concentrations. The NK-2 agonists, [d-Ala^9(Nle)^13]-SP (a SP antagonist, (a) did not elicit a response. Conclusion: SP and NKA mediate ion transport in porcine jejunum through NK-1 receptors. Tachykinins might also activate a new unclassified receptor. However, this needs to be further substantiated and clarified using structural studies. Species dependent heterogeneity of NK-1 receptors might explain the lack of effect of RP 67,580.

1059 Effect of Continuous Jejunal Application of Soluble Fiber on Cholecystokinin and Neurotensin Release in Men

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We have shown, that a liquid diet with soluble guar fiber (Sunfiber [SF]) given as bolus for 7 days increase fasting cholecystokinin (CCK) concentrations (JPEN, 1993, 231–235). Whether a continuous jejunal application of the same diet also affects CCK secretion is not well defined. The aim of this study was therefore to assess the effect of continuous feeding on plasma CCK and neurotensin (NT) release.

Methods: 23 patients after upper gastrointestinal surgery received continuously a liquid diet with jejunosmy over 16 days. 9 standard liquid diet (SLD), 14 the same diet with 20 g SP/L (SFD). At day 16 basal and postprandial (after perfusion of 500 ml diet) CCK and NT concentrations were assessed. Blood was drawn at regular intervals and CCK and NT concentrations were measured by specific radioimmunoassays (Pancreas, 1991, 280–265).

Results: Data are in pM (mean ± SEM).

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>30 min</th>
<th>50 min</th>
<th>70 min</th>
<th>90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCK</td>
<td>1.0 ± 0.1</td>
<td>3.1 ± 1.3</td>
<td>4.0 ± 2.1</td>
<td>4.0 ± 2.2</td>
<td>2.6 ± 1.0</td>
</tr>
<tr>
<td>SFD</td>
<td>9.3 ± 0.4</td>
<td>4.6 ± 1.6</td>
<td>4.4 ± 1.6</td>
<td>4.3 ± 1.6</td>
<td>4.6 ± 1.5</td>
</tr>
<tr>
<td>NT</td>
<td>9.0 ± 2.0</td>
<td>7.8 ± 1.5</td>
<td>102 ± 24</td>
<td>104 ± 19</td>
<td>88 ± 17</td>
</tr>
<tr>
<td>SFD</td>
<td>0.4 ± 0.3</td>
<td>7.1 ± 3.3</td>
<td>199 ± 28</td>
<td>101 ± 34</td>
<td>105 ± 43</td>
</tr>
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</table>

No difference was seen for basal and postprandial concentrations between the two diets. Furthermore the area under the curve were not significantly different.

Summary: After 16 continuous feeding basal CCK and NT levels were similar for both diets and constant in all volunteers. Furthermore the postprandial response was similar for both diets.

Conclusion: In contrast to orally bolus feeding regimens continuous feeding of a SF containing liquid diet does not change basal CCK and NT concentrations.
1061 Association of Serum Antibodies Against PS3 Protein with Poor Survival in Zollinger-Ellison Syndrome Patients

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Background/Aims: Long-term survival of patients with Zollinger-Ellison syndrome is largely determined by the presence or the absence of liver metastasis and the occurrence or not of further recurrences.

Methods: The detection of anti-ps3 antibodies is calculated in 7 out of 44 Zollinger-Ellison syndrome patients (16%) both by ELISA and by Western blotting. Univariate and multivariate analysis demonstrated that presence of anti-ps3 antibodies (P = 0.0009 and P = 0.017 respectively) and liver metastases (P = 0.0009 and P = 0.012 respectively) were independently associated with a shorter survival.

Conclusions: Our results suggest that anti-ps3 antibodies are an indicator of survival and could be used in combination with staging for determining poor prognosis Zollinger-Ellison syndrome patients requiring intensified therapy.

1062 Follow-Up Program after Curative Resection of Colorectal Carcinoma


Background: After curative surgery for colorectal carcinoma, intensive follow-up has been implemented in many Centers. Its primary goal is the detection of recurrence in the asymptomatic stage hoping to increase the possibility of a new curative resection and to prolong survival. The type and the effectiveness of such follow-up programs has been controversial. Aims: To evaluate the sensitivity of diagnostic methods and the efficacy of a follow-up program on recurrence detection, treatment and survival after curative resection of colorectal carcinoma. Material and Methods: Between 1989 and 1993, 218 patients were submitted to curative colorectal resection and underwent regular examinations according to a defined schedule which included: clinical examination, tumoral markers (TM) – CEA and CA19-9, liver function tests (LFT), chest roentgenography and abdominal ultrasonography (US) every four months during the first two years and half-year until the fifth. All patient were submitted to annual colonoscopy to detect new adenomatous or anaplastic recurrences. Those with rectal cancer also performed computerized tomography (CT) at the fourth postoperative month for basal determination. Results: The local recurred in 54 patients (25%), with 61% of them having tumor associated symptoms. The sensitivity of the diagnostic methods was: TM-95%; CT-91%; US-75%; LFT-40%. A second recurrence with curative intent was performed in 13 patients (24%): anaplastic-40%; hepatic metastases-29%. The five year survival rate after colorectal resection was 70% and survival was prolonged after curative resection of tumor recurrence (p = 0.036) but was not different between symptomatic and asymptomatic recurrences. Conclusions: The TM seems to be the best test for recurrence detection because of its low cost and high sensitivity. Despite the elevated number of asymptomatic recurrences detected, this did not lead to more effective treatment, neither did it prolonged survival. Further controlled prospective studies are needed to confirm the efficacy of follow-up programs.

1063 Germline Mutations of Mismatch Repair Genes (MMR) in Early Onset Colorectal Cancer Patients

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Hereditary non polyposis colorectal cancer (HNPCC), is an autosomal dominant disorder that account for 4–13% of all cases of colorectal carcinomas. It is characterized by early age of occurrence, prevalence of proximal localization, and an increased risk of multiple tumors (synchronous and metachronous). For HNPCC diagnosis the so called "Amsterdam criteria" must be fulfilled. Frequently families or individuals are observed which do not meet the rigorous Amsterdam criteria, but are highly suggestive as having HNPCC (HNPCC like syndrome). HNPCC is due to defects in genes coding for mismatch repair system (MMR): hMSH2, hMLH1, hPMS1, hPMS2. The aim of our study is to define the clinical features and the mutational status at MMR genes, of young cancer patients with colorectal tumor not fulfilling Amsterdam criteria or without a family history indicative for HNPCC. Blood and paraffin embedded tumor tissue have been collected from 33 individuals who developed cancer before 40 years of age. Mutational analysis was carried out by non radioactive single strand conformation polymorphism (SSCP) and highly sensitive by a cryl analyte gradient, followed by direct DNA sequencing where a aberrant migration pattern was observed. Preliminary data of part of the study demonstrate the presence of four mutations in hMSH2 (exons 5, 16, 14) and two mutations in hMLH1 (exons 5, 16) in individuals under 40 years of age. The final result indicate that mutations at MMR genes can be responsible of colorectal cancer in young patients even in situations not fulfilling Amsterdam criteria, and suggest the necessity of establishing new criteria for identifying individuals to be tested for mutations at MMR genes.

1064 K-Ras-2 Gene Mutations in Colorectal Adenomas and the Risk of Metachronous Adenomas

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Mutations of K-ras-2 gene and tumour suppressor genes have been found in colorectal adenomas and carcinomas. The aim of this study was to investigate the prognostic value of K-ras-2 gene mutations found in initial colorectal adenomas predicting the risk of metachronous adenomas.

Material and Methods: Genomic DNA was extracted from the formalin fixed and paraffin embedded adenomas larger than 5 mm in diameter removed during 1980 and 1986 at the initial total colonscopy. All patients had a colorectal cancer free follow-up for at least 15 years. Mutations in the K-ras-2 oncogene was amplified using PCR and screened for mutation by single strand conformation polymorphism (SSCP). All suspected mutations were confirmed by direct sequencing. The present value was assessed by logisitic regression analysis.

Results: Out of 54 patients 39 (72%) were male and 15 (28%) female. At the time, where the initial adenoma was removed, 31 (57%) patients were younger than 60 and 23 (43%) were equal to or older than 60 years.

Mutations of the K-ras-2 oncogene were found in the index adenoma of 15 (27.7%) patients. Mutations were found more frequently in large (≥ 20 mm) adenomas and in adenomas with severe dysplasia (p = 0.001 and p = 0.0310, respectively). There was no significant associations between anamnetical localization of adenomas (proximal v. distal) and K-ras-2 mutations. Mutations were found predominantly at codon 12 with transversions from GGT to GAT (36%), from GGT to GTT (57%) and from GGT to TTT in one patient. The one mutation found at codon 13 showed a transversion from GGC to GAC. There were no significant associations of size (≥ 20 mm) and K-ras-2 mutation of the initial adenomas and the size (> 5 mm) of metachronous adenomas (p = 0.0259 and p = 0.0265, respectively). But mutivariate analysis revealed that K-ras-2 did not provide a significant additional contribution to the prognostic value of the size (odds ratio 7.62; 95% CI: 1.68-34.48) and the amount of villous structure (odds ratio 0.22; 95% CI: 0.0-0.90) of the initial adenoma.

Conclusions: K-ras-2 (≥ 20 mm) adenomas and adenomas harboring K-ras-2 mutations at the initial examination are of a significant higher risk for developing large (> 5 mm) metachronous adenomas during surveil- lence. But the risk of metachronous colorectal adenomas can be estimated suficiently by the size and the histological type of the largest initial adenoma.

1065 Antibiotic Prophylaxis (Abp) for the Prevention of Bacterial Infections in Cirrhotic Patients with Gastrointestinal Bleeding (GB): A Meta-Analysis

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In cirrhotic patients with GB, the Abp decreases the incidence of infections but no randomized controlled trial (RCT) showed an increase in survival. Aim of the meta-analysis: to assess the efficacy of Abp for the prevention of bacterial infections and the effect of Abp on survival rate in cirrhotic patients with GB. Methods: An overview of RCTs assigned patients to a pre-treatment with an Abp for the prevention of infection in cirrhotic patients with GB. RCTs including patients without bleeding or comparing 2 antibiotics were excluded. Meta-analysis was performed using Der and Perio Systion methods. Results: Four RCTs including 414 patients, 204 treated with an Abp and 210 without Abp were identified. The Abp used oral, non absorbable antibiotics during 4 days (n = 68), or norfloxacin during 7 days (n = 60), or the association of amoxycillin-clavucnic acid and norfloxacin during 4 days (n = 25) or 7 days (n = 20). The fourth RCT used IV bolus of amoxicillin-clavucnic acid before each endoscopy (n = 46). The end point of each RCT was the prevention of bacterial infection during 10 to 14 days. The mean percentage of patients free of bacterial infection was 85% in patients treated with an Abp vs 55% in non treated patients. This difference was significant (mean rate difference: 32%; 95% confidence interval: CI): 19–44; p < 0.001), without significant heterogeneity. The mean percentage of patients free of bacterial infection was 85% in patients treated with an Abp vs 55% in non treated patients. This difference was significant (mean rate difference: 15%; 95% CI: 8–22; p < 0.001) without
heterogeneously. The mean percentage of patients free of infection caused by enteric bacteria (2 RCTs) was 95% in treated patients vs 75% in non treated patients, this difference was significant (mean rate difference: 19%, 95% CI: 10-28, p < 0.001). The mean survival rate was 87% in patients treated with an ABP vs 77% in non treated patients. This difference was significant (mean rate difference: 9.2%, 95% CI: 2.4-16.0, p < 0.008), without heterogeneity. Sensitivity analysis without the RCT using non absorbable antibiotics showed similar results, but the difference concerning survival rate was not significant (mean rate difference: 7.4%, 95% CI 0-16, p = 0.07). Conclusions: In cirrhotic patients with HBV, the ABP significantly decreases the incidence of bacterial infection and significantly increases short term survival rate.

### 1068 Evaluation of Portal Hypertension and Haemodynamic Risk Factors for Variceal Bleeding by Color Doppler

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Seventy patients were included in this work. Ten normal control subjects, thirty patients with evidence of portal hypertension with no history of bleeding from oesophageal varices, and thirty patients with evidence of portal hypertension with history of oesophageal variceal bleeding. Real time US, Color Doppler examination and upper endoscopy were done for all the subjects. Color Doppler U.S. was found p.o. by more than 40% in large U.S. in diagnosing portal hypertension regarding increase in congestion index (CI), better visualization of collaterals and more accurate diagnosis of P.V. thrombosis. CI more than 0.39 cm/sec was 100% specific and 100% sensitive in diagnosing portal hypertension, compared with 100% specificity and 93% sensitivity in estimating portal vein flow velocity < 12 cm/sec, 100% specificity and 85% sensitivity considering portal vein diameter > 13 mm, and 100% specificity and 88% sensitivity considering the visualization of collaterals. P.V. thrombosis was better detected by Color Doppler as 40% of the thrombosed PV were missed using real time U.S. Color Doppler allowed better visualization of the collaterals as 70% only of the visible cases could be detected using real time U.S. Study of the collateral haemodynamics revealed that the most reliable protector against bleeding varicetal was spilnecial shunt with partial flow reversal in the splenic vein and incomplete flow reversal in the left gastric vein. Recanalization of para-umbical vein was not directly related to the presence of varices, yet the larger the diameter and the more the flow will be the less the risk of bleeding. The risk factors were: 1) PV "C" more than 0.12 cm/sec, 2) Absence of adequate collaterals specifically splenoreal shunt. 3) PV thrombosis. 4) Complete flow reversal in left gastric vein.

### 1070 A Population Based Study on the Familial Aggregation of Inflammatory Bowel Disease

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Introduction: Recent studies have shown variable degrees of familial aggregation in inflammatory bowel disease (IBD). In our study the prevalence of Crohn’s disease (CD) and ulcerative colitis (UC) in first degree relatives of IBD patients, living in a well-defined area, was studied.

Methods: All known prevalent IBD patients living in the study area (148 265 inhabitants) were asked about the occurrence of IBD in their first degree relatives. In case of a positive family history, medical information was requested to verify the diagnosis. A control group of 616 persons without IBD was recruited in cooperation with the Registration Network family Practice.

Results: The family pedigrees of 245 patients consisted of 1571 first degree family members. Sufficient information was available of 1554 cases: 485 parents, 756 siblings, and 313 children. IBD was reported and confirmed in 16 first degree relatives by 11 (4.5%) patients; 7 (5.3%) of the 132 patients with CD and 4 (3.5%) of the 113 patients with UC. Prevalence of IBD was highest for siblings (1.5%) and children (1.3%) while only 0.2% of the parents were affected with IBD. Affected family members of the index patients showed a 80% disease concordance whether either CD or UC. Among first degree relatives of the control subjects, IBD was observed in 0.8% (vs. 4.5% in IBD patients), resulting in an odds ratio of 5.75 (95% CI 2.0-16.7).

Conclusion: In this population based study, the observed risk of IBD for first degree relatives of IBD patients was higher than in controls. However, the prevalence in our population is lower than has been reported by other centres, possibly reflecting the population based character of our study.

### 1071 Inflammatory Bowel Disease in a Danish Twin Register

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Previous population studies have shown a 10 fold increased risk of inflammatory bowel disease (IBD) among first degree relatives of patients with ulcerative colitis and Crohn’s disease. To further investigate the heredity of these diseases a twin study was performed.

A questionnaire was sent to all 34,076 twins included in a new twin register, which comprises all twins born in Denmark 1953 through 1982 (34,186), who had been identified and who had accepted to cooperate. Each twin was stated to suffer from IBD, the diagnosis was confirmed or excluded by applying the classical criteria to medical records from hospitals or private physicians.

In total, 29,430 (86%) twins answered the questionnaire. Among these, 93 twin pairs with at least one suffering from IBD were observed (Crohn’s disease: 36, ulcerative colitis: 57). In the Crohn’s disease group three of 11 monozygotic pairs were concordant for the disease, while none of the 25 dizygotic pairs were concordant. In the ulcerative colitis group one of 15 monozygotic pairs and one of 42 dizygotic pairs were concordant for the disease. The proband concordance rate among monozygotic pairs was 38.5% for Crohn’s disease and 6.7% for ulcerative colitis.

The frequency of IBD in the twin register was 1.5 time the expected as estimated from the age-specific rates in the background population. The frequency of IBD among twins of patients with IBD was 36 times the expected. In conclusion, this study further strengthens the hypothesis of a genetic predisposition for development of IBD, a predisposition which may be stronger for Crohn’s disease than for ulcerative colitis.

### 1072 Signal Transduction Role of Nuclear Factor (NF)-Kappa B in the Regulation of Pro-Inflammatory Cytokine Secretion by IL-10 in IBD Granulocytes

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Background: Pro-inflammatory cytokines (IL-1α, IL-1β) are secreted in large amounts by IBD monocytes, macrophages and granulocytes (PMN, abstract 5th UESG). IL-10 is a major inhibitor of pro-inflammatory cytokine secretion. NF-Kappa B is thought to be a major player in pro-inflammatory signal transduction. The Aim of this study was to evaluate mechanisms by which pro-inflammatory cytokine secretion by PMN can be regulated. Methods: PMN from 25 patients with ulcerative colitis (UC), 21 patients with Crohn’s disease (CD) and 15 normal volunteer controls (NC) were isolated from peripheral blood by dextran sedimentation and density centrifugation. Release of pro-inflammatory cytokines (ELISA) into culture supernatants as well as mRNA (semiquantitative RT-PCR) were assessed. Function of activated NF-Kappa B was tested in vitro by treatment with TNF-alpha or stimulation with the cytokine (Western Blot). In vitro treatment with IL-10 reverts these changes: NF-Kappa B is shifted back from nucleus to cytosol and can no longer be detected by gel shift in nuclear extracts. Conclusions: Activation and nuclear translocation of NF-Kappa B may provide a signal transduction mechanism by which IBD PMN are induced to secrete enhanced levels of pro-inflammatory cytokines. Moreover, IL-10 appears to prevent degradation of NF-Kappa B and evasion of the factor from the nucleus back to cytosolic compartment. This mechanism provides insights into signal transduction events influenced by IL-10 and may also suggest novel targets for future immunomodulatory strategies.

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### 1073 No Exceeding Malignancy Prevalence in Relatives of IBD Patients: Comparison with Colon-Cancer Patients and Controls

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The relation between Inflammatory Bowel Diseases (IBD) and colon-cancer (CC) is not clearly defined. The colon cancer is considered to be more frequent in longstanding extensive ulcerative colitis (UC) and in Crohn disease of colon (CD). However, some investigators suggest that extensive colitis patients have a genetic predisposition to colorectal cancer and longstanding inflammation is not the primary cause in the induction of cancer. We report a prospective investigation on malignancy prevalence in relatives of an initial series of 225 IBD patients (178 UC; 47 CD), as well as 491 colon cancer pts. (CC) and 220 orthopedic pts. (ORT) as controls.

In all patients (UC, CD, CC) as well as in controls (ORT) the prevalence of colon (A), extracolic digestive (B) and extradigestive (C) malignant tumours in the first degree relatives has been evaluated. Results are shown in table.
In this initial series no difference in malignancy prevalence or tumours spectrum among UC, CD and ORT patients was observed. The relative risk of colon cancer in relatives of CD patients versus ORT was 4.3. Partially supported by grant of 60% MURST

1074 Anti-Tumor Necrosis Factor Antibody CA2 Treatment Induces Clinical Remissions in Patients with Active Crohn’s Disease


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TNF has been implicated in the pathogenesis of Crohn’s disease (CD), and preliminary studies have suggested that administration of anti-TNF antibodies causes rapid and complete remission in UC. Persistence of a double blind placebo-controlled trial in patients with active CD designed to assess the magnitude and duration of response to CA2 treatment. One hundred and eight patients with a CDAI between 220–400 were randomized to receive either placebo, 5 mg/kg, 10 mg/kg, 20 mg/kg or 40 mg/kg of CA2 as a single 2 hour intravenous infusion. Patients receiving concomitant therapy with corticosteroids, 6-mercaptopurine, or 5-ASA continued treatment throughout the 12 week trial. Patients in the different treatment groups were well matched for demographic and disease-related baseline characteristics. CA2 treatment resulted in a significantly larger reduction of the CDAI at 4 weeks (~110.4 ± 102.8) than placebo (~12.8 ± 79.3) (p < 0.001) and these differences were sustained throughout the study period. The number of patients achieving a clinical remission (CDAI < 150) was 16% in the placebo group versus 45.8% in CA2 treated patients (p = 0.022), and the number of patients responding to CA2 therapy (reduction of CDAI > 70) was 24% versus 69.9% respectively (p < 0.001). CA2-treated patients had a significant reduction in CRP levels, and an increase in the ESR scores. These data indicate that anti-TNF therapy has a high clinical efficacy in patients with CD, including those not responding to standard therapy.

1075 Ciprofloxacin Vs Mesalazine in the Treatment of Active Crohn’s Disease

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Background: Evidence is accumulating for bacterial participation in the pathogenesis of CD. Despite this, few controlled trials using broad-spectrum antibiotics have been conducted in CD. Ciprofloxacin (Cipra) has shown promising results in the treatment of CD with perineal disease and fistulae. The aim of this randomized controlled study was to investigate the efficacy of Cipra compared with 5-aminosalicylate (Mesalazine™) in treating moderately active CD.

Methods: Forty patients (25 F, 15 M, mean age 28 years) with moderate flare-up of CD (mean CDAI: 217, range 160–300) were randomized to receive Cipro 500 mg twice daily or Pentasa™ 4 g/day for 6 weeks. Clinical remission was defined as a CDAI ≤ 150 associated with a decrease in CDAI (Δ CDAI) > 75 at 6 weeks. Partial remission was defined as: 1) CDAI ≤ 150 with a 50 < Δ CDAI < 75; 2) CDAI > 150 with a Δ CDAI > 25 3) Δ CDAI 50 > 8 at weeks.

Results: Clinical remission was obtained in 10/18 Cipra patients (56%), and in 12/22 Pentasa™ patients (55%). Partial remission was obtained in 13/18 Cipra patients (72%), and 13/22 Pentasa™ patients (59%). C-reactive protein decreased from 32 ± 29 to 9 ± 5 (p = 0.07) in Cipra patients and from 33 ± 22 to 21 ± 16 in Pentasa™ patients (ns). Three patients on Cipra (17%) and 7 on Pentasa™ (32%) were considered as treatment failure because of deterioration or insufficient improvement (ns). Two patients receiving Cipra (11%) were cured from the study for mild side effects and non-compliance. Two patients on Pentasa™ (9%) were withdrawn because of the absence of improvement at 3 weeks.

Conclusion: This study suggests that Cipro 1 g/day is at least as effective as Pentasa™ 4 g/day in treating moderately active CD.

1076 Balsalazide is More Effective and Better Tolerated than Mesalazine in Acute Ulcerative Colitis (UC)


This study compared the tolerability and efficacy of balsalazide (mesalazine prodrug) and mesalazine (ph-dependant delayed release) in acute UC.

Patients (101 total, 99 evaluable) (62 male aged 41 ± 13 years (mean ± SD) with grade 2 (erythema + loss of vascular pattern + contact bleeding: 55% of patients), 3 (+spontaneous bleeding: 32% of patients) or 4 (+ frank ulceration: 13% of patients) (extent > 12 cm; left-sided disease 80%) sigmoidoscopically verified, symptomatic (moderate 69% or severe 31%) UC were randomised, double blind, to receive balsalazide 2.25 g t.i.d. (equivalent to 0.75 g mesalazine, n = 50) or placebo (n = 50) for 3 (4-8) or 12 weeks, as necessary. Rectal hydrocortisone p.r.n. was provided as relief medication. Both groups were comparable at entry.

A greater proportion of patients achieved symptomatic remission (none/mild symptoms) at 2 (64% vs 43%, p < 0.05), 4 (70% vs 51%, p < 0.05), 8 (78% vs 45%, p < 0.01) and 12 weeks (88% vs 57%, p < 0.001) after balsalazide treatment compared to mesalazine. Similarly, more patients achieved complete remission (none/mild symptoms, sigmoidoscopic normal or 1 (erythema with loss of vascular pattern) with no steroid use in previous 4 days) in the balsalazide group after 4 (38% vs 12%, p = 0.01), 8 (54% vs 22%, p < 0.005) and 12 weeks (62% vs 37%, p < 0.05) with greater mean improvement (12 weeks: 61% vs 22% with mesalazine) in balsalazide treated patients than with mesalazine. One patient in each group discontinued due to an unacceptable adverse event (AE) however, all serious AEs (complications of UC) occurred in the mesalazine group and fewer patients in the balsalazide group reported AEs (46% vs 71%, p < 0.05). Analysis of the development of chronic inflammatory activity in the colon showed balsalazide was more effective and better tolerated than mesalazine 0.8 g t.i.d. in achieving remission of acute ulcerative colitis.

1077 Ridgwell for the Treatment of Mild to Moderate Ulcerative Colitis. A Placebo-Controlled Trial

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An increased colonic production of eicosanoids has been documented in patients (pts) with Inflammatory Bowel Disease (IBD). Thromboxane (TXA2) may play a role in the development of chronic inflammatory activity in the bowel. Ridgwell (RID), a combined TXA2 synthetase inhibitor (low dose) and TXA2/PGD2 receptor blocker (high dose), might therefore be useful in IBD.

Methods: 79 pts with mild to moderate active ulcerative colitis (UC) were randomized to 8-week double-blind treatment with either placebo (PLA) or one of three dose schedules of oral RID: 5 mg od, 25 mg bid, or 150 mg bid. Endoscopic assessments were performed every 4 weeks, with an additional assessment at week 2 in pts who had not improved clinically at week 2. Pts were subsequently withdrawn from the trial if there was no endoscopic improvement.

Results: At endpoint, 320 PLA-treated pts, 9/21 RID 5 mg od treated pts, 6/17 RID 25 mg bid treated pts and 11/21 RID 150 mg bid treated pts had improvement by ≥ 1 grade on endoscopy. Significant differences in efficacy between RID and PLA were detected. Thirteen pts from the PLA group, 9 from the RID 5 mg od, 7 from the RID 25 mg bid and 6 from the RID 150 mg bid group had discontinued the therapy at week 2 due to insufficient response. More pts in the RID 5 mg od (n = 7) and RID 150 mg bid (n = 8) groups reached a clinically quiescent disease state at endpoint than the pts in the RID 25 mg bid (n = 4) or PLA (n = 11) groups. At endpoint the investigator assessed the results of treatment as good or excellent in 3/20 of PLA treated pts, 8/21 of RID 5 mg-mg treated pts, 6/17 of RID 25 mg treated pts and 10/15 of RID 150 mg treated pts.

Adverse events, whether or not related to treatment, were reported by 9 to 11 pts in the three RID groups and in 6 pts in the PLA group.

Conclusion: All three RId doses were well tolerated and were equally effective in relieving the inflammatory distress with mild to moderate UC. Lower doses of RID, known to inhibit TXA2 synthetase activity, may be blocking the TXA2/PGD2 receptor, need to be tested for the treatment of acute exacerbations of UC.

1078 Three Days Metronidazole (MET) and Clarithromycin (CLA) in Triple Therapy with Omeprazole (OME) for Cure of H. Pylori (HP) Infection

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Purpose: Triple therapy with OME, MET and CLA (OMC) has become a standard in our clinic for cure of HP infection, as OMC poses currently an optimum in terms of efficacy, safety and cost effectiveness. Shorter than one week treatment regimens have been proposed to be effective, so we intend to test the hypothesis that the treatment with OME and CLA can be shortened to three days in OMC without loss of efficacy.

Methods: In a prospective, randomised, and controlled ongoing study, patients with indication to HP cure are assigned to one of the following two groups:

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
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<tbody>
<tr>
<td>OME</td>
<td>Omeprazole 20 mg BID for 3 days</td>
</tr>
</tbody>
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Group 3D-OMC: OME 20 mg bid on days 1–7, MET 400 mg tid on days 2–4, A 250 mg bid on days 2–4.
Group 7D-OMC: OME 20 mg bid, MET 400 mg bid, and CLA 250 mg bid, on all days 1–7.

The HP status is determined before and at least 4 weeks after OMC by urease test, histology, culture, and UBT. Antimicrobial HP resistance is assessed by E-Test (AB-Biodisk, Solna, Sweden).

Results: At present, 60 patients (mean age 51 years) were randomized into the study. 31 patients have meanwhile completed the protocol. 16 of 17 patients in group 3D-OMC had been cured of HP infection versus 13 of 14 patients in group 7D-OMC. Pretherapeutic culture and testing of resistance was successful in 26 patients. The one patient with persisting HP infection in group 3D-OMC harboured a MET resistant strain.

Conclusions: These preliminary data indicate no difference of HP cure rate between a 7-days OMC scheme and a 3-days OMC scheme with enhanced daily antimicrobial dosis.

1079 Do Physicians from Different Countries Treat H. pylori Positive Ulcer Disease Differently? A Comparison between America and Germany
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Purpose: The aim of this study was to determine the first line treatment used by two groups of physicians (gastroenterologists (GE) and family practitioners (FP)) in H. pylori-positive ulcer disease in two different countries. Methods: Cross-sectional study on the basis of an international questionnaire. Results (to date): 1152 US and 538 German physicians responded:

<table>
<thead>
<tr>
<th>Regimen*</th>
<th>GE (USA)</th>
<th>GE (FRG)</th>
<th>FP (USA)</th>
<th>FP (FRG)</th>
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<tbody>
<tr>
<td>n (245)</td>
<td>n (307)</td>
<td>n (118)</td>
<td>n (227)</td>
<td></td>
</tr>
<tr>
<td>PPI based triple</td>
<td>16%</td>
<td>16%</td>
<td>12%</td>
<td>13%</td>
</tr>
<tr>
<td>Standard triple</td>
<td>16%</td>
<td>16%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>PPI based quadruple</td>
<td>16%</td>
<td>16%</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>PP/CLA</td>
<td>16%</td>
<td>16%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>H2 based quadruple</td>
<td>9%</td>
<td>5%</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>PP/AMO</td>
<td>0%</td>
<td>5%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>other (insufficient)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
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</tbody>
</table>

*PPI (Proton pump inhibitor), AMO (Amoxicillin), H2 (H2- inhibitors), CLA (Claritromycin), MET (Metronidazole) BIS (Bismuth), PPI based triple (PPI plus combination of two antibiotics (AMO, CLA, MET). Standard triple (BIS, MET, TETAMO), PPI based quadruple (PPI plus standard triple), H2 based quadruple (H2 plus standard triple), FRG (Federal Republic of Germany)

Conclusion: The frequently used triple therapy based regimens in the US are almost non-existent in Germany, whereas the most frequently used regimen in Germany (PPI/AMO) plays only a minor role in the US. We conclude that treatment of H. pylori positive peptic ulcer disease differs substantially in the two countries. This can be explained due to different recommendations of the researchers in the field of H. pylori treatment in the two countries. Nearly 25% of the FP in each country treat H. pylori positive ulcer disease with ineffective regiments. This emphasizes that knowledge acquisition of newly recommended therapies for H. pylori infection is lagging for all. Researchers have to make sure that dissemination of currently recommended therapies is a continuous process.

1085 Repeat Resection of Liver Metastasis from Colorectal Cancer
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It is estimated that about 60% of patients (pts) submitted to hepatic resection of metastasis from colorectal cancer will present a recurrence. This recurrence is limited to the liver in about 30% of cases. Repeat hepatectomy has been used increasingly in relation to the low mortality and the good long-term prognosis. However, the risk of these repeat hepatectomies, their long-term results as well as the rationale for patient selection need to be clarified. For this purpose, we have analyzed over a period of 12 years (1983–1995) the results of 57 rehepatectomies performed in 44 pts with hepatic metastasis from colorectal cancer (2 hepatectomies: 44, 3 hepatectomies: 10, 4 hepatectomies: 3). These repeat hepatectomies represented 19.5% of the 282 liver resections performed during the same period for the same indication. The time interval between first and second resection was over 1 year in 23 pts (52%). Extra hepatic disease was associated to hepatic recurrence in 11 pts (25%). Major hepatectomy (> 3 segments) was performed in 50% of first resections, 36% of second resections and only 15% of third and forth resections. There was no post-operative mortality within two months. Per-operative bleeding was not increased as compared to that of first resections. Post-operative morbidity was 11% (65%) comparable to that of first resections. Overall survival after repeat resection was 44% at 5 years with no difference related to Dukes classification of initial colorectal tumor, to synchronous versus metachronous metastasis or to local versus distant hepatic recurrence.

Conclusion: Repeat resection of liver metastasis from colorectal cancer allows a long-term survival at least equal to that of first resection with no mortality and comparable morbidity. This policy is warranted when repeat hepatectomy is potentially curative.

1086 Liver Regeneration after Partial Hepatectomy is Depressed by Kupffer Cell Depletion
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Purpose. After partial hepatectomy, activation of Kupffer cells (KC) by circulating gut-derived endotoxins results in a rapid release of inflammatory mediators. Some of these mediators are thought to play a role in the induction and regulation of liver regeneration. We therefore hypothesized that KC are important for liver regeneration and investigated the effect of KC-depletion on liver regeneration after partial hepatectomy (phx).

Methods. All animals (36 Wag/Fij rats, male, 200–220 g) underwent a twofold liver resection. The rats were randomized in 2 groups: 48 hours prior to phx, KC-depletion was performed in 18 rats by intravenous (i.v.) administration of 1 ml liposome-encapsulated dichloromethylene diphosphonate (CL2-MDP). The second control received 1 ml normal saline (NaCl) i.v. Directly after phx, 1/4 dosage of the i.v. treatments was readministered. One week prior to phx, splenectomy was performed in all rats to eliminate the effect of liposome-encapsulated CL2-MDP on macrophage populations in the spleen. Every 24 hours after phx 50 mg/kg bromoeggine (BFG) was injected intraperitoneal administration. Animals were sacrificed at 24, 48, and 96 hours (n = 6 per group) after phx. To confirm KC-depletion, cryostat liver sections were stained with the monoclonal antibody ED2, a marker for resident tissue macrophages. Liver cell proliferation index was determined by BrDU labeling index in liver sections. Weight of the remnant liver was expressed in percent of calculated initial liver weight.

Results. KC-depletion was confirmed in sections of the resected liver. Proliferation of parenchymal liver cells 48 hours after phx was significantly depressed in KC-depleted rats when compared with control rats (p < 0.05). Also, weight increase of the remnant liver, determined 96 hours after phx, was significantly delayed (p < 0.05) in KC-depleted rats.

Conclusion. KC are important for liver regeneration after partial hepatectomy.

1087 Unresectable Hepatic Metastases from Colorectal Cancer: Results of a Combined Approach by Chemotherapy and Subsequent Resection
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Resection is the sole curative treatment of hepatic metastases from colorectal cancer. However, it may be achieved only in 10% of patients (pts) since most pts have at the first inoperable lesions associated with a poor prognosis. Over the past 6 years, we have managed these pts with a new protocol of chemotherapy with the aim to perform subsequent curative liver resection. From April 1988 to March 1994, 53 out of 377 pts (14%) with liver metastases initially considered as non resectable were subsequently submitted to hepatic resection with a curative intent. All pts have been treated by intravenous chronomodulated chemotherapy combining 5 Fluorouracil, Folinic acid and Oxaliplatinum, a non nephrotoxic platinum complex. To optimize dose intensities and tolerance, drug delivery was sinusoidally modulated along the 24 hour-scale with peak
flow rates at 0.04 hours for 5-FU and for 16.00 hours for Oxa, using an ambulatory programmable-in-time pump. Initial non-resorbability was assessed by the same surgical team and was related either to technical impediment due to large (n = 24), multifocal or ill-localized tumours (n = 8) or to the presence of extraperitoneal disease (n = 13 - Peritoneum (6), Epiploon (3), Lungs (4)). Pts received 3 to 29 courses of chemotherapy (mean = 10) for 2 to 28 months (mean = 8 months) before surgery.

Results: An objective reduction in tumour size was observed following chemotherapy in all pts subsequently submitted to liver resection. A significant reduction of tumor markers was also demonstrated. A major hepatectomy (≥ 3 segments) was performed in 37 pts and a minor resection in 16. There was no operation-related mortality within 2 months. Post-operative complications were divided into 2 infected collections that needed non operative drainage, 1 transient biliary fistula and 1 reoperation for bleeding. Chromomodulated chemotherapy was routinely continued postoperatively in all pts for 6 courses at least. Associated postoperative procedures included repeat hepatectomy (15), pulmonary resection (11), hepatic cryotherapy (8), splenectomy (1) nephrectomy (1), resection of the diaphragm (2), repeat resection of colon cancer recurrence (2). Twenty eight pts are presently alive (of whom 16 without disease) with a mean follow of 2.5 years (range 1.3-6.4). Median survival is 3.2 years with a patient survival rate of 61% at 3 years.

Conclusion: Resection may be achieved in some unresectable pts with the help of an efficient chemotherapy. The benefit in survival seems comparable to that obtained with liver resection for initially resectable liver metastases. This therapeutic strategy involves a multimodality approach including repeat hepatectomy and extrapleurectomy.

1085 Increased Human Gastric Endothelial Cell COX-2 Expression during Angiogenesis

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Introduction: Angiogenesis plays an important role in gastric ulcer healing. Prostaglandins (PGs) promote angiogenesis in vivo and non-steroidal anti-inflammatory drugs (NSAIDs) reduce vascularity of gastric ulcer granulation tissue and delay healing. However, it is not known whether gastric ulcer angiogenesis is associated with changes in endothelial cell cyclooxygenase-2 (COX-2) expression. Therefore we investigated COX expression during in vitro angiogenesis using human gastric endothelial (HGE) cells which were obtained using an immunomagnetic separation technique developed in our laboratory. Methods: HGE cells were isolated from normal gastric mucosa using anti-PECAM-1 antibody-coated Dynabeads. HGE cells were cultured routinely on 1% gelatin in Medium 199 + 30% FCS + 90 µg/ml heparin + 40 µg/ml ECGS until plating onto basement membrane matrix (Matrigel) or addition of 1 µM phorbol 12, 13 dibutyrate (PdBu). COX-1 and COX-2 expression were investigated by RT-PCR, western blotting and indirect immunofluorescence studies. PGE2 levels in cell-conditioned medium were measured by ELISA.

Results: PdBu-induced formation of cell extensions and “ring” structures in HGE cells at 4 hours which was associated with increased COX-2 expression and PGE2 production. COX-2 was localized predominantly in the nuclear envelope. At 24 hours COX-2 expression had declined. There was no change in COX-1 expression after addition of PdBu. Formation of “tube-like” structures by HGE cells on Matrigel was associated with an increase in COX-2 and COX-1 mRNA expression and PGE2 production which was maintained at 24 hours.

Conclusion: In this model of angiogenesis, HGE cell differentiation (formation of “tube-like” structures) rather than proliferation was associated with induction of COX-2 and COX-1 expression. This process may be impaired by NSAIDs during gastric ulcer healing. These findings suggest that specific COX-2 inhibitors may also impair angiogenesis and delay gastric ulcer healing.

1089 Gene Expression of Metalloproteinases (MMP-1, -2, and -3) and Their Tissue Inhibitors (TIMPs 1-1 and -2) during Experimental Gastric Ulcer Healing

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Increasing evidence indicates that extracellular matrix (ECM) degradation plays a crucial role not only in tumor invasion but also in the process of wound repair. We analyzed the spatial and temporal pattern of expression of three major components of the metalloproteinase family, namely, MMP-2 and MMP-3, and of their specific tissue inhibitors TIMP-1 and -2, in an experimental model of gastric ulcer healing. Methods: chronic gastric ulcers were produced by aspirin or acetic acid injection and groups of 5 rats each were sacrificed before and at 1, 3, 7, 14, 28 and 56 days after the ulceration. Gene expression of MMPs and TIMPs was examined by in situ hybridization with 35-fabeled RNA probes and the autoradiographic signal was quantitated by an image analyzer. Results: in the normal rat stomach, the gene expression were not detected in TIMP-1 and TIMP-1 expression, while low amounts of MMP-2 and TIMP-2 RNA transcripts were present in some mesenchymal cells of the lamina propria, submucous and muscularis propria. MMP gene expression was dramatically up-regulated after ulcer induction, starting at 24 h and peaking at 3-7 days (e.g. when lesions undergo transition into true "chronic" ulcers). With the completion of ulcer healing, MMP mRNA expression progressively returned toward normal; however, higher than normal levels of MMP-1 and MMP-3 mRNA persisted at sites of excessive ECM deposition and prominent histologic abnormalities. The spatiotemporal pattern of TIMP-1 and -2 essentially followed that of MPPs; in contrast with MMP expression, however, low amounts of TIMP-1 and -2 mRNA were also noted on some mesenchimal cells of gastric glands. Conclusions: the up-regulation of MPPs, by degrading basement membranes around migrating proliferation cells and removing the excess of matrix transiently accumulated in the granulation tissue, may play a crucial role in gastric ulcer healing promoting the re-epithelialization of the ulcer crater, angiogenesis, and the final remodeling of regenerated tissue.
at 2, 4, 6 and 8 day, whereas RT-PCR mRNA EG2 was detected at day 2, 4 and 6 after ulcer induction with the most intense signals observed at day 2. Conclusions: 1) Enhancement in cell proliferation and suppression of gastric secretion during ulcer healing is mediated by expression of EG2 and TGF-α; 2) Expression of EG2 and TGF α mRNA precedes the overexpression of these growth factors during ulcer healing; 3) Overexpression of growth factors during healing coincides with the inhibition of gastric secretion probably mediated by these growth factors.

**1092** Gliadin Specific, HLA-DQ2 Restricted T Cells are Frequently Found in the Small Intestinal Mucosa of Coeliac Disease Patients

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Coeliac disease (CD) is an immune-mediated disorder of the small intestine with a very strong HLA association in particular HLA-DQ2 variant. More than 90% of the patients carry this variant. We previously showed that T cells from the small intestinal mucosa of patients on a gluten-free diet could respond to gliadin. We hypothesized that the disease-associated HLA-DQ2 molecules were expressed in CD11c+ dendritic cells (DCs) that were present in the lamina propria. We therefore isolated DCs from biopsies of CD11c+ cells from 22 patients with untreated CD. The isolated DCs were stimulated with gliadin peptides and cytokines and the expression of CD8+ T cells was evaluated. CD8+ T cells were detected in 48% of the patients with CD, compared to only 7% in healthy controls. This indicates that gliadin-specific T cells are frequently found in the small intestine of coeliac disease patients.

**1093** Distinctive Activated Cellular Subsets in Colon from Patients with Ulcerative Colitis and Crohn's Disease

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Introduction. A comparative study on in situ preactivated lymphocytes in Crohn (CD) and ulcerative colitis (UC), and in non-inflammatory controls (C) was assessed, with special reference to T-cell activation markers and lymphocyte homing molecules. Patients and Methods. CD II extended cell-lines were isolated from active CD patients, with active UC and C controls. Cell lines were characterized by FACs analysis. Results. Expression of activated markers was observed and compared using Wilcoxon rank sum test. In CD patients, the expression of CD8+ T cells was significantly higher than in UC patients. In UC patients, the expression of CD69 was significantly higher than in CD patients. In C patients, the expression of CD69 was significantly lower than in CD and UC patients. Conclusion. Distinctive activated cellular subsets in colon from patients with ulcerative colitis and Crohn's disease can be identified. Further studies are needed to characterize these subsets and their role in the pathogenesis of inflammatory bowel disease.

**1094** Anti-Endomysium Antibodies on Human Umbilical Cord: An Improved Method for Diagnosis and Follow-Up of Coeliac Disease


Although anti-endomysium antibodies (EMA) are, to date, the most reliable serological marker of coeliac disease (CD), both the high cost of monkey oesophagus (MO) and the ethical problems connected with killing of endangered species, limit their routine application. Aim: In this study we investigated the use of human umbilical cord (HUC) as an alternative substrate to MO in EMA determination. Method: IgA EMA were appraised, by indirect IF on MO and HUC, on sera from 104 untreated biopsy proven CD patients, 40 healthy volunteers and 48 disease controls (inflammatory bowel disease and irritable bowel syndrome). One year after gluten withdrawal 44 out of 104 CD patients underwent a second intestinal biopsy and EMA appraisal. Results: A) IgA EMA sensitivity and specificity were 95% and 100% respectively on both substrates, with a diagnostic efficiency of 97.4%. B) One year after a gluten free diet (GFD) 39/44 (89%) patients still had histological alterations. EMA positivity on MO was found in only 10/38 (26%), while on HUC it persisted in 29/38 (76%). The agreement between histology and EMA was respectively 40% on MO and 79% on HUC.

Conclusion: A) HUC can replace MO as substrate for IgA EMA detection with comparable diagnostic efficiency, lower costs and sparing of monkeys. B) HUC seems to be a more suitable substrate than MO in EMA detection using a GFD because of its higher agreement with histological pattern.

**1095** TNFα and LPS Increase Human Peripheral Blood Lymphocyte Adhesion to HIMECs Is Partially Blocked with Monoclonal Antibody to α 4β 1

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Purpose Bacterial Products may play a fundamental role in the pathogenesis of Inflammatory Bowel Disease (IBD). A weakened mucosal barrier may allow the influx of bacterial products into the lamina propria which may have a direct effect on endothelium and result in increased lymphocyte recruitment. Using Human Intestinal Microvascular Endothelial Cells (HIMECs), we measured the effect of TNFα, butyrate, lipopolysaccharide (LPS) and T-Met-Leu-Phe (MLP) on the adhesion of 111I-labelled human lymphocytes.

Methods Normal and inflamed colon (n = 3) obtained from patients undergoing resection for colonic cancer or IBD were used to isolate HIMECs, as described (Gut 38: 4A85). HIMECs were plated onto 24 well plates, grown to confluence and incubated with butyrate, LPS, IMLP or α 4β 1. Peripheral blood lymphocytes (PBLs), from healthy volunteers, were isolated using ‘Lymphoprep’ and labelled with 111I Cr. The PBLs were incubated with monoclonal antibody to α 4β 1 (Serotec), a lymphocyte integrin which is expressed on the majority of PBLs, and incubated with the HIMECs for one hour. Gamma counts in the supernatant, the standardised washes and the monolayers, removed by detergent, were used to calculate percentage lymphocyte adhesion.

Results The adhesion of PBLs to nonstimulated HIMECs monolayers was 27% (SD = 3) (+/−3 wells). Preincubation with TNFα (10 ng/ml) and LPS (10 ng/ml) increased this to 74% (SD = 4 < 0.01 Mann Whitney) and 52% (SD = 9 < 0.05) though various concentrations of butyrate and LPS did not have any effect. Preincubation with Anti α 4 reduced adhesion by 25% (p < 0.05) on TNFα and 15% (p < 0.05) on LPS stimulated cells. Conclusions TNFα and LPS have a direct effect on HIMECs which results in increased PBL adhesion. Preincubation with antibody to α 4 reduced adhesion significantly but not substantially suggesting that other molecules or mechanisms may facilitate adhesion of PBLs to TNFα and LPS stimulated endothelium.

**1102** Gastric Functions and Dyspeptic Symptoms in Reflux Esophagitis

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The relationship between gastric functions and dyspeptic symptoms in reflux esophagitis (RE) is poorly investigated. We evaluated scintigraphic gastric emptied of solids (GE; 638 kcal, 9mEq-chicken liver) in 68 (51, M, 11±3 yrs; m SD) RE pts. Results were expressed as half-times (T1/2 min) and GE rates (%-h). Gastric acid secretion (BAO, MAO, mEq/h) was also evaluated in 50/68 RE pts (40, M, 49±14 yrs). Fifty healthy volunteers served as controls (HC; T1/2 = 101±20 min, x = 40±11±5mEq, BAO = 3±2 mEq/h, PAO = 21±7 mEq/h). RE pts presented delayed GE (T1/2 = 153±88 min, P = 0.01; k = 32±16 kcal/h, P < 0.01) and increased MAO, BAO and MAO (4±3 mEq/h, P < 0.01) compared to HC (Mann Whitney U test). Delayed GE and increased acid secretion were observed respectively in 32% and 40% of pts. Increased acid secretion was present in 19% of pts with delayed GE and in 59% of pts with normal GE, while delayed GE was present in 15% of pts with increased secretion and in 43% of pts with normal secretion (P < 0.05, X2).

Epigastric pain, burning, postprandial fullness, nausea, vomiting were each graded 0 to 3 according to their influence on usual activities. Dyspepsia (total
score ≥ 3 with at least one symptom ≥ 2) was observed in 64% of pts: 26% of them presented prevalent pain (pain ≥ 2 with any other symptom < 2), 44% prevalent discomfort (postprandial fullness and/or nausea and/or vomiting ≥ 2, with pain ≤ 1) and 30% resulted unclassifiable.

<table>
<thead>
<tr>
<th></th>
<th>Gastric emptying (n = 68)</th>
<th>Acid secretion (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>delayed</td>
<td>increased</td>
</tr>
<tr>
<td>Dyspepsia (total) 74%</td>
<td>58%</td>
<td>60%</td>
</tr>
<tr>
<td>Prev. pain 12%</td>
<td>35%</td>
<td>42%</td>
</tr>
<tr>
<td>Prev. discomfort 71%</td>
<td>77%</td>
<td>33%</td>
</tr>
<tr>
<td>Unclassifiable 17%</td>
<td>36%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*P < 0.005 vs normal gastric emptying; \( \times^2 \).

Conclusions: RE pts as a whole present delayed GE and increased acid secretion compared to HC, but gastric motor and secretory abnormalities are not usually associated. Dyspeptic symptoms are frequent in these patients. RE patients with delayed GE present more often prevalent discomfort compared to patients with normal GE.

### 1103

**Recordings of Duodeno-Gastro-Oesophageal Reflux in Supine (Sleeping)**

**GORD Patients with Fiberoptic Billirubin Monitoring Are at Least as Good as 24-Hours Recording**

H. Geldof, Usseltal Hospital, Capelle a.d. IJssel, The Netherlands

Aim. Oesophageal fiberoptic billirubin monitoring quantifies the duodeno-gastro-oesophageal reflux (DGOR), which seems to be relevant for the pathogenesis of GORD and its complications such as Barrett oesophagus and oesophageal carcinoma. To improve this method, the value of recordings in supine (sleeping) patients (average 8 hours) is compared with that of 24-hours recordings.

**Method.** Measurements were made with a fiberoptic sensor and portable data-processing unit (Billtec 2000, Synectics medical Inc.). The fiberoptic electrodes were placed 5 cm above the lower oesophageal sphincter. The absorbance threshold was set to 0.14, corresponding to 10 \( \mu \)M of bilirubin.

Studies were performed in 11 patients with uncomplicated GORD, 10 patients with GORD complicated by intestinal metaplasia below the squamo-columnar mucosal junction, and in 13 patients with a Barrett oesophagus.

**Results.** The table below shows the mean percentages of the recording time of oesophageal exposure to bilirubin.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Total recording time</th>
<th>Supine patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated GORD</td>
<td>11%</td>
<td>8%</td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>55%***</td>
<td>71%***</td>
</tr>
<tr>
<td>Barrett oesophagus</td>
<td>60%***</td>
<td>69%***</td>
</tr>
</tbody>
</table>

Comparisons between uncomplicated GORD and GORD with metaplasia or Barrett oesophagus: ***P < 0.001

Conclusions. Fiberoptic measurements of billirubin concentrations shows large differences in the oesophageal bilirubin exposure between uncomplicated GORD, and GORD with metaplasia or Barrett oesophagus. Shorter recordings (average 8 hours) from patients in the supine (sleeping) position yield probably better information than 24-hours recordings. Moreover, the 8-hours supine recordings are much more convenient for the patients.

### 1104

**Exertional Gastroesophageal Reflux (GER) and Angina Pectoris**

E. Vincent, F. Romand, N. Claudel, J. Desbaumes. Service de Gastro-Entérologie, HIA Desgenettes, 69998 Lyon Armées

The aim of the study was to evaluate the role of GER in recurrent pain in patients on treatment for coronary artery disease. 16 patients (14 M/2 F, mean age 60.5 years) underwent graded bicycle exertional ECG during 24-hours esophageal pH-monitoring (pH-24). GER was defined by pH < 4 and pain was considered as GER related if it occurred within 2 mm. pH-24 was interpreted according to Steinh's criteria.

**Exertional GER appears only in refluxers in pH-24 (table 1: pH-W exertional pH-metry).**

12 patients (75%) presented with at least 1 pain during the study (table 2). During pH-24 24 patients (25%) experienced pain (5 events including 1 GER related). During pH-W 10 patients (82%) experienced pain, including 4 GER-related, without ECG signs of ischemia.

GER is frequent (81%) in patients with angina pectoris suffering despite treatment. Exertional pH-metry confirms GER reponsability or its contribution to pain in 25% of patients versus 6% in pH-24. 50% of patients experienced pain without relation to GER nor ECG signs of ischemia.

### 1105

**Clinical Importance of Esophageal 24 Hours-pH-Manometry**

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Aim: Ambulatory 24 hr-pH-manometry has been validated by several studies since the early 1990ies but its clinical relevance remains to be defined. In a retrospective study we analyzed findings, and therapeutic consequences of all 24 hr-pH-manometries performed at our unit.

**Patients and Methods:** We analyzed a total of 220 complete 24 hr-pH-manometry measurements which have been performed in 180 patients between 1991 and 1995. Mean patient age: 52 years; \( \pm = 11.1 \). Recording device: Gastroscan II (MIC). Probes: Ingold glass electrode combined with Sentron catheter (4 pressure microsensors) or Unisensor catheter (4 pressure microsensors and integrated Ingold glass electrode).

**Results:** Indications (246; > 1 patient possible) and findings:

<table>
<thead>
<tr>
<th>Indications</th>
<th>Findings</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>normal</td>
<td>reflux</td>
</tr>
<tr>
<td>Pre-postop.</td>
<td>11</td>
<td>30</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Reflux</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Collagen disorder</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Achalasia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Aspiration</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>72</td>
</tr>
</tbody>
</table>

**Motility disorders (54% of all patients): nonspecific motility disorders 53% (of which 69% had reflux), secondary motility disorders due to collagen disease 21%, achalasia 17%, diffuse esophageal spasm 3%, nutcracker esophagus 2%, miscellaneous 4%.

Therapeutic consequences: recommendation of one or more measures in 71%, no new recommendation in 29%.

**Conclusions:** 24 hr-pH-manometry showed in 83% of our cases pathological findings and led in 71% of our cases to a change in management. These results confirm that 24 hr-pH-manometry is a useful complementary investigation for specific indications.

### 1107

**Effect of White Wine on Gastroesophageal Reflux in Patients with Reflux Disease**

C. Pelt, A. Pfeiffer, B. Wendl, H. Kaess. Dept. of Gastroenterology, Hospital Bogenhausen, Munich, Germany

White wine provokes heartburn in patients with gastroesophageal reflux disease (Gastroenterology 1995; 108: 125–31). In healthy volunteers, we recently demonstrated that white wine induced gastroesophageal reflux (GER) in contrast to a comparable ethanol solution and to tap water (Dig Dis Sci 1993; 38: 93–6). The aim of the present study was to investigate whether these results could be reproduced in patients with reflux disease.

**Methods:** 15 GER patients (6 F, 51–86 yrs) received in a random order 300 ml white wine or tap water together with a standardised lunch. Because of the taste of the wine the patients could not be blinded. Therefore, their pH-measurements were coded and analysed in a blinded fashion. The fraction time esophageal pH < 4 (FT) was calculated for three hours after ingestion of the two beverages.

**Results:** Median and range; Wilcoxon test for paired data.

<table>
<thead>
<tr>
<th>Wine</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT (%) median</td>
<td>23.1</td>
</tr>
<tr>
<td>Range</td>
<td>0–88.8</td>
</tr>
</tbody>
</table>

**significance p < 0.01**

Constitution: In accordance with the results obtained in healthy volunteers (Dig Dis Sci 1993; 38: 93–6) white wine provokes an increase in GER also in patients with reflux disease. Therefore, patients with GER disease should be advised to avoid the ingestion of white wine.

### 1108

**Decaffeinated Coffee Reduces Gastroesophageal Reflux in Patients with Reflux Disease**

C. Pelt, A. Pfeiffer, B. Wendl, A. Kaess. Dept. of Gastroenterology, Hospital Bogenhausen, Munich, Germany

Coffee provokes heartburn in patients with gastroesophageal reflux disease (Gastroenterology 1995; 108: 125–31). In healthy volunteers, we recently demonstrated that regular coffee induced gastroesophageal reflux (GER) compared with tap water. GER could be reduced by decaffeination of regular
1109  Apparantly Life Threatening Events (ALTE) and Gastroesophageal Reflux (GORD) on Medical Treatment in Infants
F. Benkebli, P. Roy, D.C. Belli. Gastroenterology Unit; Pediatric Department, HUG, Geneva, Switzerland

Introduction: GOR is a frequent disease among infants, which may induce severe complications, such as ALTE. The prevalence of this association seems to increase with the supine sleeping position. The aim of this retrospective study was to analyze the potential association of GORD in 33 successive infants with ALTE, as well as their pH-metry and their evolution on medical treatment and follow up.

Patients and Methods: 33 successive infants, median age = 28 days (3–185), were investigated by a clinical story and a 24-hr pH monitoring (pH-m) following ALTE. They were born at a term. pH-m was realized with a DigitrapperMKII (Synectics®) on a 24 hr basis. pH-m criteria studied: % overall reflux, % sleep reflux, % awake reflux, clearance in total, pre-prandial and postprandial periods. control pH-m was performed on medical treatment (Cisapride: 1 mg/kg BW/d + Ranitidine: 300 mg/m2/1.73 m2/d) before leaving hospital.

Results: In medical story, 23 infants had frequent pyrosis, 6 had previous ALTE without hospitalisation. The median duration of ALTE was 2 min (1–45). Position at the time of ALTE was similar to usual position.

<table>
<thead>
<tr>
<th>Supine</th>
<th>0°</th>
<th>30°</th>
<th>60°</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

On the total period reflux index basis, results of pH-m disclosed 2 groups: Gr A with GORD (n = 25) and Gr B (n = 8) without GORD. Both groups had no differences in clinical presentation. Gr A pH-m:

<table>
<thead>
<tr>
<th>% Index</th>
<th>% Sleep</th>
<th>% Awake</th>
<th>Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.3 ± 5.6</td>
<td>12.1 ± 5.6</td>
<td>14.1 ± 11.9</td>
<td>1.6 ± 0.6</td>
</tr>
</tbody>
</table>

Among the 33 infants, 6 had GORD only and 10 mainly in awake, 8 only and 4 mainly in sleep period. Furthermore, the vast majority of GORD was post-prandial and the acid exposure was reduced to a good evolution, with normalized pH-m in Gr A. With a 5-months follow-up, no patient presented with a new episode of ALTE.

Conclusion: GORD and ALTE can be associated. GORD was observed in both awake and sleep periods. ALTE is not related to GORD in 25% of cases. Finally, a medical treatment alone can safely be proposed to resolve this problem.

1110 The Value of Repeat Ambulatory pH Tests in the Diagnosis of GORD in Patients with No or Equivocal Esophageal Symptoms

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GORD symptoms may show daily variation: symptom severity may be greater than endoscopic eosinophilia. A normal pH test may not be representative. Aim Assess use of repeat pH tests in diagnosis of GORD. Patients 34, age 13–72 with grade 0 or 1 endoscopy (OGD). Gp A, (n = 15), normal acid exposure time (AET < 4.3%) and fewer than normal symptoms experienced on day of test. Gp B (n = 17) with super-sensitive oesophagus (grade 0 OGD, normal AET, symptom index (SI) > 33%). Gp C (n = 2) atypical symptoms, grade 0 OGD. Results: Gp A OGD grade 0 = 10. I = 5) normal (0–3.8%) → abnormal AET (6.3–11.8%) n = 4, outcome – 4 anti reflux surgery (ARS): normal ≠ normal AET n = 9: no treatment 6, medical 2, achalasia 1: abnormal (4.6–8.2%) → normal AET → 2: treatment 1, ARS (SI 70 & 71%). Gp B normal (0.3–4.2%) → abnormal AET (4.6–8.2%) n = 3, ARS 2, medical. Normal → normal AET 2 & SI (50–63%) → SI (54–97%) = 13, ARS 11, medical. Normal → normal AET 2 & SI (42%) → normal SI (0%) = 1. Gp C abnormal (5.1–14.8%) → abnormal AET (7.0–10.0%) = 2, ARS 2. Conclusion 7/34 patients (20.5%) had abnormal AET on 2nd test and 13/18 confirmed super-sensitive oesophagus. Repeat pH tests should be contemplated in patients with persisting symptoms, especially if endoscopy negative.

1111 Helicobacter Infection in Esophageal Reflux (ER) Disease
O. Galimov, S. Fyodorov, M. Nurdinov, A. Scumkin. Bashkir State Medical University, Ufa, Russia

Aim: Establishing the conditions maintaining chronic local inflammatory process in the esophageal abnomalous. Methods: Biopsy fiberoscapsyscopy was carried out. Haematoxylin and eosin as well as Warthin-Starry staining technique was used in morphologic study of lower third mucosa biopsies. Urease test was carried out the same time. Two groups of patients were studied: group 1 (18 patients) ER resistant to the therapy performed, group 2 (25 ER patients) in which conservative treatment appeared effective within usual therapy time. Results. Helicobacter pylori (HP) in group 1 was determined in 66.7% cases and gastric metaplasia was revealed in 83.3%. The similar evidence was observed in group 2 in 16% and 24% cases respectively, namely, HP was to be positive in 16% cases (group 1) and 4% (group 2). HP revealed marked polymorphism closely adhearing to the epithelial cells on the pit fundus and glands lumen. Chronic inflammatory process activation in mucosa was observed. HP was also revealed in degenerated hyperplasic form and anounced active inflammation in metaplasia mucosa as well as in areas of in stratified scaly noncorniment epithelium irrespective of its state. Following the antireflux treatment in combination with antihelicobacter therapy no HP were revealed in all group 1 patients after control morphologic study. Positive therapy effect was obtained in 77.8% patients. Clinical evidence of esophagitis persisted in 22.2%.

Discussion. Thus HP is significant in ER pathogenesis the fast that is supported by ineffective routine therapy. Therefore ER patients should undergo esophage biopsy (1–4 cm from cardia) with subsequent morphologic study for HP presence.

1112 Serum Prolactin Levels in Childhood Gastro-Oesophageal Reflux Disease Treated with Cisapride
I. Kononay-Szabó, J.B. Kovács, A. Nagy, M. Lőrincz. Heim Pál Children’s Hospital, Budapest, Hungary

As serotonin and cholinergic stimuli may enhance prolactin (PRL) output, effect of cisapride treatment was studied in gastro-oesophageal reflux disease (GORD).

Methods: Serum PRL was determined in 137 children with GORD newly diagnosed by pH-metry (age 0.15–19.8 years, mean: 5.05). 83 of them had also a prospective follow up of 6–36 months with at least one control PRL during continuous cisapride (0.2 mg/kg four times i.d.) intake > 2 months, checked between 9:00–11:00 a.m. Additional antacid/ranitidine use was allowed, but those with any treatment with dopamin antagonist drugs were excluded.

Results: Mean PRL was 10.9 ng/ml (2.3–51.64) in the untreated pts, 17.6% (24/137) had pathologically high PRL levels (Group A) and further 8 pts (5.8%) PRL levels at the upper limit of normal range for age (Group B). Mean age of Group A was 2.15 years (0.15–13.81), p < 0.01 vs. Group B and the remaining pts.

During cisapride treatment, there was apparently no significant change in the frequency of high PRL results (16.8%), however, in Group A and B, serum PRL level has been decreased in all but one patients to normal values, whereas other 13 pts newly exhibited high PRL. None of them had clinical signs of hyperprolactinaemia and all were well controlled regarding GORD. Continuing with the same treatment schedule and resampling after 2–3 weeks before the next course of treatment, normal PRL levels were obtained in 13/13 of them. (There were no other known differences regarding fed state or time between other circumstances of samplings). Among 39 pts, who had been instructed already before the first control PRL determination to leave out the morning dose just before sampling, no high PRL occurred.

Conclusions: High serum PRL levels are common among untreated infants and toddlers with GORD. Effective treatment normalized PRL. Cisapride did not cause long lasting hyperPRL, however, it may play a role in the still unclear PRL-related (compensative?) mechanisms.

1113 Epidemiology of Gastroesophagealreflux: Predictive Factors for the Course of the Disorder and Treatment

S. Bruley des Varannes, J.-C. Grimaud, P. Rzustiewski, T. Vallot, A. Richard, F. Gentin, 1. Gastroenterology Department, Hôpital Nort Nantes; 2. Gastroenterology Department, Hôpital Nord Marseille; 3. Gastroenterology Department, Clinical School, Gastroenterology Department, Bichat Paris; 4. Gastroenterology Department, Icare Bouloigne Billancourt; 5. Gastroenterology Department, Laboratoire Glaxo Wellcome Paris

The frequency of the symptoms of gastroesophageal reflux (GORD) is high and affects approximately 2.9% of individuals. The severity of the symptoms and perception by the patient obviously play a role in the request for medical care, while the reasons for medical consultation and/or following a course of treatment still remain unclear. The objective of this study was to examine
the course of GORD and treatment demand, and to determine the predictive factors for the follow-up of a specific patient population over a period of six months. Method: A specific population of patients having experienced at least one episode of heartburn in the course of the past 15 days, who were consulting their general practitioner and had a history of such episodes were followed up over a period of six months. Investigation of predictive factors was conducted by multiple logistic regression and Poisson distribution.

Results: 1115 patients were included in the study. Patients had been suffering from heartburn for 4 years and the mean duration of previous episodes was less than 1 month for 61%, between 1 and 3 months for 26% and more than 3 months for 13%. Heartburn was the main reason for consultation on DO for 86%. The mean duration of the current episode of heartburn was 3 weeks. The patients evaluated the symptoms of the current episode as causing slight discomfort (6%), moderate discomfort (60%) great discomfort or incapacitating (34%). On D90, 4% of patients claimed they felt no discomfort due to heartburn; 51%, slight discomfort; 32%, moderate discomfort, and 6%, great discomfort. The predictive factors for discomfort on D90 were: the duration of episodes prior to DO, the frequency of the episodes, and the severity of the symptoms on DO. The predictive factors for discomfort on D180 were: discomfort related to heartburn on D90, the length of time the patient had been suffering from GORD, and the main reason for consultation on DO; patients for whom heartburn was not the main reason for consultation on DO experienced a greater level of discomfort. The predictive factors for the extent of treatment demand over six months were: the levels of stress and anxiety measured on DO, age, duration related to heartburn on D90, severity on DO, and the frequency of episodes prior to the episode on DO.

In conclusion, the severity of GORD after three and six months seems to be clearly related to the severity of previous episodes and the severity of DO. These criteria are not in themselves sufficient to explain the level of treatment demand. The levels of stress and anxiety of the patient appear to be closely related to future demand for treatment and further examination.

1114 Gastroesophageal Reflux Disease and Medical and Clinical Management

J. Leitão, A. Pinto, J. Canerera, J. Reis, A. Santos, G. Lucas, M. Gomes, M. Quina, Universidade de Lisboa, Faculdade de Medicina, Lisboa, Portugal

Purpose: To determine the prevalence of gastroesophageal reflux disease (GERD) in a population with moderate to severe asthma and the efficacy of anti-reflux therapy in symptoms, corticoid use and pulmonary function tests.

Methods: We studied 29 asthmatic patients (± 42 years) with moderate to serious disease (daily steroid use) because of control problems. They had previous diagnosis of asthma since ± 17 years, and GERD symptoms for ± 8 years. Patients were submitted to: 1) upper gastrointestinal endoscopy with biopsy of the lower esophagus; 2) 24-hour ambulatory esophageal pH recording; 3) pulmonary function tests; 4) daily registration of symptomatic score, anti-asthma medication and peak expiratory flow. Patients with GERD defined by Richter criteria were treated for 8 weeks with omeprazole 20 mg bid. After that, another patient was submitted to another session of pulmonary function tests. In the following 20 weeks, treatment was changed to omeprazole 20 mg once a day. By the end of this period corticoid use was checked. Statistical analysis were made with the Wilcoxon, x², and the t-Student tests.

Results: We found a prevalence of abnormal distal acid exposure in 17 (56.8%) of asthmatics. 52.9% had upper reflux, 17.7% had supine reflux and 29.4% both. In these 17 patients 53% had hiatus hernia and 41.2% esophagitis at the endoscopy. Histopathology found esophagitis in 47.1% of the 17 patients. After medical treatment all patients became asymptomatic. Symptomatic score (p < 0.02) and steroid use (p < 0.03) showed statistical improvement. Although there was some improvement in pulmonary function tests this was not statistical significant. Conclusions: 1) High prevalence of GERD was found in the studied asthmatic population; 2) Anti-reflux medical therapy significantly improve symptomatic score and corticoid using; 3) Results highly suggest the importance of detecting abnormal acid exposure in patients with asthma, specially in those with moderate to severe disease

1115 The Role of Bile in the Genesis of Gastroesophageal Reflux Symptoms


Introduction. Gastro-esophageal reflux (GER) of acid is known to be associated with oesophageal pathology as well as symptomatology. The role that duodenal contents play is not well known. Billieco 2000, a spectrophotometric bile marker allows for the first time a ready monitoring of acid gastro-oesophageal reflux, so symptoms can now be related to the presence of duodenal contents as well as acid in the oesophagus.

Methods. 59 patients referred for investigation of symptomatic GOR underwent oesophageal manometry and combined oesophageal pH and 24h impedance monitoring. No patients had a primary motility disorder. All symptom events described as regurgitation or heartburn were analysed for the presence of pH < 4 and bilirubin absorbance > 0.14 in the two minutes either side of the symptom. Total, upright and supine pepsin were analysed for acid (pH < 4) shift and bilirubin absorbance > 0.14.

Results. 38 patients (64%) had significant acid reflux on pH testing, and 21 patients (30%) did not. 40 patients (68%) had significant bile reflux on Billieco monitoring and 19 patients (32%) did not. There was good correlation between total bile and acid reflux (p = 0.05 Spearman rank correlation). 394 symptom events were identified (range 1–24 events per patient). Symptoms were associated with reflux thus:

<table>
<thead>
<tr>
<th>Acid reflux alone</th>
<th>Bile reflux alone</th>
<th>Both acid &amp; bile reflux</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of symptoms</td>
<td>147 (37%)</td>
<td>24 (6%)</td>
<td>45 (11%)</td>
</tr>
</tbody>
</table>

Of the 178 symptom events that were not associated with either an acid or a bile reflux episode, 127 (71%) occurred in patients with either acid or bile reflux. The majority of events occurred in the upright interprandial period (173 events, 44%), 165 events (42%) occurred during the postprandial period, 42 events (10%) in the supine periods and 14 events (4%) during meals.

Conclusions. 32% of patients had no significant acid reflux, so presumably there was another pathology to account for their symptoms. Despite good correlation between acid and bile reflux, acid and bile reflux episodes do not always occur simultaneously. However, symptoms are more frequently associated with acid reflux than bile reflux, and bile does not seem to be a major cause of reflux symptoms.

1116 The Incidence of Gastro-Oesophageal Reflux Disease Based on Non-Specific Symptoms in Instituted Intellectually Disabled

C.J.M. Böhmmer 1,2, M.C. Niezen-de Boer 1, E.C. Klinkenberg-Knol 2, S.G.M. Meuwissen 2, 3, Bartimius, Zeist, The Netherlands; 2 Free Univ Hosp, Amsterdam, The Netherlands; 3 Antonius Hosp, Nieuwegein, The Netherlands

The prevalence of GOR in randomly selected instituted intellectually disabled (IQ < 50) in the Netherlands is 48.2% and of oesophagitis 64.5%. In this study we investigated the incidence of GOR and RO in a population with non-specific reflux symptoms such as: behaviour difficulties atatorium, food refusal, fear and restlessness, vomiting, regurgitation and nucimation. Also predisposing factors were evaluated.

In one institute 110 persons underwent a 24 hour oesophageal pH test and were scored for predisposing factors and non-specific reflux symptoms. A pathological pH test was defined as a pH < 4 × 4.5% of the measured time. Subjects with a pathological pH test (patients) were compared to those with a normal pH test (controls).

In 7 cases (6.4%) the test failed for technical reasons. In 57 (55.3%) cases a pathological pH test was found, compared to 48.2% in the earlier mentioned at random population (rs). In this group non-ambulance, the use of anticonvulsive medication, cerebral palsy and a history of GOR appear to be predisposing factors, while the suggested non-specific reflux symptoms did not discriminate for GOR. At endoscopy RO was diagnosed in 33 patients (57.9%), of which: 12 (36.4%) grade 1, 15 (45.5%) grade II, 6 (18.2%) grade III (Savary-Miller classification). Barrett's esophagus was found in 2 (6.1%) and 1 (3.0%) showed a peptic stricture.

In conclusion: reflux of acid gastric contents was demonstrated in 55.3% intellectually disabled with non-specific reflux symptoms, while 57.9% of them presented RO. Subjects with non-specific reflux symptoms did not appear to have a risk of developing GOR. But non-specific symptoms as behaviour problems and vomiting do not discriminate for GOR. This study demonstrate that GOR and RO are major clinical problems in intellectually disabled persons.

1117 The Prevalence of Gastro-Oesophageal Reflux and Reflux Oesophagitis in Instituted Intellectually Disabled in the Netherlands and Belgium


GOR was estimated to be present in 10–15% of the intellectually disabled population (Sondheimer 79). Therefore, we investigated the prevalence of GOR among the inhabitants, with an IQ < 50 (n = 1607), of 6 institutes in the Netherlands and Belgium.

At random 435 persons underwent a 24 hour oesophageal pH test and were scored for predisposing factors, characteristic reflux symptoms and other possible risk factors. Subjects with a pathological pH test (patients), defined as a pH < 4 × 4.5% of the measured time, were compared to those with a normal pH test (controls).

In 49 cases (11.3%) the test failed for technical reasons. In 186 (48.2%) cases the pathological pH test was found (median duration of pH < 4 × 12.7%). As predisposing factors scoliosis and cerebral palsy, the use of anticonvulsive medication or other benzodiazepines, and an IQ < 35 were indicated, while as reflux symptoms haematemesis, nucimation, depression, and restlessness were tested. As other predisposing factors a history of GOR, the presence of Barrett’s oesophagus, and Down’s syndrome were significant more often present. At endoscopy RO was diagnosed in 127 GOR patients (68.3%), of which: 58 (46.7%) grade I, 44 (34.6%) grade II, 25 (19.7%) grade III (Savary-Miller). Barrett’s oesophagus was found in 14 (11.0%) and 4 (3.1%) showed peptic strictures.
1118 Dental Erosions and Gastro-Oesophageal Reflux in Infected Institutionally Disabled
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Gastro-oesophageal reflux (GOR), recurrent vomiting and regurgitation may lead to erosions of the teeth. In the intellectually disabled population these conditions are frequently found. Therefore, we investigated the presence of dental erosions in 88 intellectually disabled persons, with a mean IQ < 50 (n = 409), recruited from 2 institutes in the Netherlands.

At random 88 individuals underwent a 24 hour oesophageal pH test, dental screening and were scored for possible predisposing factors and reflux symptoms. A pathological pH test was defined as a pH < 4 - 4.5% of the time. Subjects with dental erosions (patients) were compared to those without dental damage (controls).

25 individuals were toothless (28.4%). In 23 of out of 63 (46.0%) cases dental erosions were found. In 19 (65.6%) patients the GOR was diagnosed, compared to 9 (26.5%) controls (p = 0.04), while 16 (55.2%) patients showed a history of GOR in comparison with 7 (20.6%) controls (p = 0.006). In patients the mean duration of pH < 4 was 15.6% compared to 6.3% in controls (9 = 0.02). At a predisposing factor an IQ < 35 (p = 0.0001) was found, while symptoms as vomiting, regurgitation, swallowing difficulties and gnashing one's teeth did not increase the risk to develop these dental erosions.

In conclusion: in this population of 63 intellectually disabled persons dental erosions were diagnosed in 46%, while over 65% of them had also GOR or a history of GOR. Individuals with longer duration of pH < 4 and with an IQ < 35 are at higher risk to develop dental erosions. This study shows that dental erosions are often atypical manifestations of GOR in the intellectually disabled population.

1119 Respiratory Symptoms Due to Gastro-Eosophageal Reflux Disease (GERD), a Comparative Study
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Purpose: This study compares patients with GERD and respiratory symptoms (RS), to GERD patients without RS.

Methods: Patients with GERD, unresponsive to medical therapy underwent laparoscopic anti-reflux surgery. Pre-operative symptom scoring, endoscopy, oesophageal manometry, 24 hour pH studies and DeMeester (DEM) scores were performed. RS included hoarseness, chronic cough, or asthma. Patients with GERD and RS were compared to GERD patients and sex matched controls with GERD but no RS.

Results: After laparoscopic surgery symptom scoring, endoscopy and manometry were performed. The two-tailed T test was used for statistical analysis and significance was defined as p < 0.05.

Results: A total of 59 patients with GERD and RS were compared to 59 age and sex matched controls. The average age of RS patients and matched controls was 44.5 years (range 18-78). Mean pre-operative lower esophageal sphincter (LES) pressure in the RS group was 5.16 mmHg, whereas in the control group this was 9.35 mmHg. This was statistically significant. The majority of patients in the RS group had defective LES (90%) compared to 84% of control patients. Mean DEM scores were 53.08 in the RS group and 45.07 in the control group, which was not statistically significant. Clearance was normal in 40% of the RS group and in 32% of the control group (not statistically significant). Laparoscopic anti-reflux surgery was performed and LES pressure normalized in both groups. RS disappeared in all but one patient, but this patient reported a reduction of bronchodilator therapy. This confirmed that RS were caused by GERD in the majority of patients in the RS group.

Conclusion: Patients with GERD and RS do not have significantly different acid reflux scores, LES pressures, clearance or defective sphincters when compared to those with GERD but without RS.

1121 The Presentation of Gastrooesophageal Reflux Disease: A Prospective Clinical and Endoscopic Study
B. Werdmuller, A.B.M.M. vdPutten, R.J.L.E. Loffeld. Department of Internal Medicine, Ziekenhuis De Hoel Zaanamd, The Netherlands

A prospective study was done amongst 1432 consecutive patients referred for upper gastrointestinal endoscopy in order to assess the prevalence and severity of gastrooesophageal reflux in patients with respiratory problems (n = 115), hiatal hernia (n = 108), Barrett’s oesophagus (n = 29) and functional dyspepsia (n = 439). All patients received a questionnaire consisting 12 questions related to reflux. Eight questions were scored on a linear scale ranging from 1 to 5 (absent = 1, severe = 5). Patients with grades I or II reflux erosions were significantly younger compared with patients with grades III or IV oesophagitis (p < 0.001). Patients with functional dyspepsia were significantly younger than all other patients (p < 0.0001). A concomitant hiatal hernia was present in a substantial number of patients with gastrooesophageal reflux (69.8%). Mean symptom score in grade I oesophagitis was 15.3 (SD 5.8), in grade II 15 (SD 6.5); in grade III 8.9 (SD 7); in grade IV 11.4 (SD 5.1); in patients with Barrett’s oesophagus 10.3 (SD 6), in hiatal hernia 12.2 (SD 6.6), and in functional dyspepsia 11.5 (SD 6.7). Symptom scores between Grades II or III oesophagitis was significantly lower compared with grades I or II oesophagitis (p < 0.001).

Patients with Barrett’s oesophagus and/or hiatal hernia and/or functional dyspepsia had significantly lower symptom scores if compared with grades III or IV oesophagitis, 10.3 (SD 6) versus 15.2 (SD 6) (p < 0.001) and 12.2 (SD 6.8) versus 15.2 (SD 6) (p < 0.001) respectively. No difference in symptom score was present in comparing grades III or IV oesophagitis, hiatal hernia, Barrett’s oesophagus and patients with functional dyspepsia. Patients with grades I or II oesophagitis had a significantly higher number of reflux complaints, mean 5.1 (SD 1.5), compared with grades III or IV oesophagitis, mean 3.5 (SD 1.8), Barrett’s oesophagus, mean 3.7 (SD 1.9), patients with hiatal hernia, mean 4.1 (SD 1.9) and dyspepsia with reflux complaints, mean 4.0 (SD 1.9) (p < 0.0001).

The prevalence of epigastric pain, retrosternal pain, nocturnal pain, belching, heartburn, retrosternal heartburn and hoarseness was significantly higher in patients with grades I or II oesophagitis, while the prevalence of dysphagia was significantly higher in patients with grades III or IV oesophagitis. Patients with grades III or IV oesophagitis had a significantly shorter history compared with those other groups.

It is concluded that the presence of a majority of typical reflux symptoms has a high predictive value for the presence of grades I or II oesophagitis, dysphagia is indicative for grades IV or IV oesophagitis. In cases of less symptomatology it is suggested to administer the reflux questionnaire to exclude Barrett’s oesophagus, hiatal hernia or dyspepsia with reflux complaints.

1122 Oscillatory Index in Gastrooesophageal 24 Hour pH Monitoring for Gastroesophageal Reflux
A. Kostowski. Pediatric Clinic, Faculty of Medicine, Skopje, Macedonia

Vandenplas JPGN 11: 304, 1900), introduced a new parameter: oscillatory index (OI), after him Watanabe (JPGN 19: 50, 1994) used the term prolonged stable pH around 4 (PSPH4). The aim of the study was to determine the interindividual and clinical significance of the OI in children investigated for GER and to correlate it with reflux index (RI).

In a prospective study were evaluated 53 children (age 52 ± 54 months) for GER by 24 h. pH monitoring (24 HPlM). They were separated in three groups: Group A with vomiting and failure to thrive (age 9.7 ± 6.9), group B with gastrointestinal symptoms but older (142 ± 120), and group C with pulmonary manifestations (33.3 ± 31.9) GER was considered if RI was > 5%. OI and RI were analyzed, only.

Results: In group A with RI > 5% OI was 1.23 ± 0.96 and with RI < 5 was 7.93 ± 4.75% (p < 0.05). In B if RI was < 5 was found 0.01 to be 2.28 ± 1.65% (within 2 hours postprandial) and 0.66 ± 0.52% (fasting). With RI > 5% OI was 3.90 ± 2.91% and 0.94 ± 0.56, respectively. In C with RI > 5% OI was < 0.01, OI was < 0.01, OI was 0.94 ± 0.87% and 0.94 ± 0.56, respectively. In C with RI > 5% OI was 3.49 and 2.65 ± 4.09%. If RI was > 10% OI was 9.0 ± 4.03 and 3.4 ± 1.72.

Five pts were with OI > 10%.

Conclusions: We found that OI correlated well (bigger in C group) and with age (group A). Pts in group C with high OI treated with protonics solved. So high OI can be a trigger for pulmonary symptoms.

1123 Process of Candida Infection of the Esophagus
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Purpose: Esophageal Candidiasis occurs under three conditions; an immunocompromised state (cancer, AIDS), a fungal overgrowth (long term administration of antibiotics, diabetes mellitus), and a non-immunocompromised state (healthy individuals). Our experimental studies using SEM have dealt with the formation (F) process and healing (H) process of Candida infection under a non-immunosuppressive state. The aim of the present study was to analyze the process under two other conditions.

Methods: Antibiotics (tetracycline: TC) and/or immunosuppressive drugs (tacrolimus, prednisolone: PSL, azathioprine: AZP) were administrated to mice for two weeks, during or following two weeks of administration of Candida albicans suspensions, and the lesions were observed by SEM.

Results: The F and H process of Candida infection was observed under all conditions. The H/F ratio of the same or post administrations of drugs was 82.3% and 90% in TC, 20% and 16.7% in tacrolimus, and 0% and 0% in PSL + AZP. In studies without drugs, there were 83.3% and 100%, respectively. Therefore, the H process was obviously suppressed only under the immunosuppressive condition.

Conclusion: Candida infection can be classified into two states; a state with H process suppression and one without H process suppression.
[1124] Analysis of Esophageal Motility by Fast MR Imaging
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Manometry and radiography are techniques commonly applied to analyze the esophageal motor dysfunctions. In order to find a less invasive method, we have tested a fast MR imaging to analyze esophageal motility in rabbits.

Intravenous imaging of the esophagus was carried out by using a 4.7 T magnetic resonance spectrometer for animal studies (BioSpec 47/40, Bruker, Germany) with a bird-cage RF-coil (inner diameter of 20 cm). Japanese white rabbits (3.0–3.7 kg) were fixed firmly on an animal support in the prone position without anesthesia, and a loop of earplugs was applied to keep out noise from gradient coils. Median sagittal images was taken by a fast gradient-echo imaging (Snapshot) at 3 images/sec. Typical values used were as follows: field-of-view 22.5 cm, data matrix 96, spectral width 72 kHz, relaxation delay 3.4 msec, echo-time 1.9 msec, slice-thickness 6 mm, number of accumulation 1. A 6 Fr. silastic tube with a balloon at the tip was inserted nasally into the upper esophagus just distal to the upper esophageal sphincter. The balloon was then inflated to 1 cm diameter by infusion of 0.6 ml of 0.6% (w/v) ferric ammonium citrate. One to 10 sec after inflation the balloon moved from the upper esophagus to the stomach in 3–30 sec. The maximal velocity was 8.3 cm/sec. The primary peristalsis that followed the voluntary act of swallowing was also visualized. Fast MR imaging allows us to observe clearly a rapid movement of a voal along the entire length of esophagus during swallowing.

[1125] Relation between Esophageal Motricity and Phonation: Experimental Study of Upper Esophageal Sphincter (UES) Using Manometry Associated with Phonation Study
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Pharyngeal symptoms of gastrooesophageal reflux disease (GORD) suggest existence of relations between esophageal motricity and phonation. The aim of the study was to explore those relations in a preliminary work evaluating a new experimental method.

Patients and Methods: Eight patients (3 m, 5 f, with dysphagia (n = 1) or GORD including 4 with pharyngeal symptoms and vocal overworking, underwent manometry with an electronic probe (GAELTEC CTG-6, diameter 3 mm), and vocal study of 6 phonies, repeated 4 times with the probes studying the UES. A numerical recording of voice pronouncing test sentences was realised before and during manometry to detect a probe-induced modification of the phonation. We analysed the presence, the length and the size of the UES relaxations during phonation, in comparison with UES relaxations induced by a dry swallow. We also studied the motricity of the upper esophageal third. The vocal recordings were studied on a computerised vocal analyser called "EVA".

Results: Out of 149 phonemes pronounced, 64 induced UES relaxation (33%). The falls in UES pressure were always equal or more than 50% of those induced by dry swallow, and in 25 cases more than 80% of this value. The mean length of relaxation was 1.75 s. Relaxations induced upper esophageal motricity in 75% to 100% cases of 3 patients, never in the others. Out of 3 of these patients, 2 had no probe-induced phonation modifications. Pharyngeal symptoms didn’t influence results.

Conclusions: propose an original investigation method associating vocal and manometric study. It suggests existence of UES relaxations induced by phonation, of which some cases induce upper esophageal motricity.

[1126] Does Lower Esophageal Sphincter Vector Volume Change by Chronic Obstructive Pulmonary Disease?*Görülü Ahmed. Kayhan Burçak, Kayhan Mine 1, Akıllı Zafir, Kayhan Bürhan 2. QTÜ, Ankara Türkiye; 1 Ankara Ataturk Chest Disease Hospital, 2 HÜF Ankara Türkiye

The aim of this study was to investigate the effect of chronic obstructive pulmonary disease (COPD) on the lower esophageal sphincter (LES) vector volume, which is the anatomic and functional pressure profile of LES.

Materials and Methods: 3 groups of patients were included. The first group consisted of 12 patients, second group 12 patients with emphysema, and the last group 12 healthy volunteers. All the patients and healthy controls lacked gastroesophageal reflux symptoms, any gastrointestinal system disease or other systemic diseases. The smokers were also excluded. All patients underwent esophageal vector volume testing using a catheter with 6 distal side holes each oriented radially 60° from the other. The catheter was continuously perfused with water at 0.5 ml/min by a low-compliance pneumohydraulic capillary infusion system. Subjects were studied after an overnight fast. The patients received no drugs for 48 hours prior to this study. The LES pressure and vector volume were obtained using the rapid pull-through method and were measured at end-expiration. Serial readings (6 times) were taken with each of the six sensor element permits better detection of pressure changes even with asymmetric sphincters. The measurements were evaluated statistically (Mann Whitney U).

Results: No significant differences existed between the mean vector volumes of group I and group II (p = 0.08). The vector volume of group II was significantly less than that of group III (control) (p < 0.01). The mean value of group II was also lower than that of group I (p = 0.015).

Conclusion: The results of this study demonstrated that COPD influenced LES vector volume.

[1127] Comparison of pH Probe Placement Determined by Manometry Versus a Combined pH and Lower Oesophageal Sphincter Detector
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The monitoring of oesophageal pH is now widely accepted as the most accurate method of assessing gastro-oesophageal reflux. Continuous monitoring with a probe placed 5 cm above the lower oesophageal sphincter for 24 hours is the agreed standard. Accuracy placement of the probe is essential, too low a placement will lead to false positives, too high a placement will result in false negative investigations. The proximal LOS is commonly identified using either manometry or the Acid-Allen interface. Synectics have developed a H probe with a water filled lumen that allows measurement of oesophageal intraluminal pressure. Pressure measurement allows the LOS to be identified. A study was undertaken to assess the accuracy of placement of the Synectics probe compared with conventional manometry. Methods: Twenty patients undergoing 24 hour pH monitoring were investigated. Conventional oesophageal manometry was performed to identify the LOS. Immediately afterwards the Synectics probe was intubated. The probe was withdrawn in 1 cm steps from 60 cm to 35 cm, the AA was identified at the point that the measured pH rose above 4. A second withdrawal was performed monitoring the intraluminal pressure, the LOS was identified at the point of intraluminal pressure falling below gastric pressure. Results: The LOS of the LOS as obtained by Synectics was taken as the standard, the AA was compared with the PM of the LOS as determined by the Synectics probe and with the AA interface. Using the LOS detector 75% of probes would be sited between 3 and 7 cm above the PM of the LOS. Using the AA interface alone 33% of probes would be sited between 3 and 7 cm above the PM of the LOS. Use of AA interface alone is significantly less likely to result in acceptable placement of the pH probe (p < 0.01). Discussion: In departments where formal oesophageal manometry is not available it has been suggested that identification of the AA interface is adequate for the placement of the pH probe. The results show that this would lead to the unacceptably low placement of 77% of probes. Use of the LOS detector reduces the error to 25%. Concerns that the Synectics LOS detector significantly increases the accurate placement of pH monitoring probes over identification of the AA interface alone. Formal manometry is still recommended as the standard for placement of the pH electrode.

[1128] Esophageal Motor Function in Connective Tissue Diseases
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The effect of scleroderma (Sc) on esophageal motor functions (EMF) is well known. The aim of this study was to investigate the effect of Sc, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), mixed connective tissue disease (MCTD), ankylosing spondilitis (AS), dermatomyositis (DM) or polymyositis (PM) in all patients EMF was studied by using water-perfused manometry system. Patients were diagnosed as nonspecific esophageal motor disorders (NEMD), nutcracker esophagus (NE), diffuse esophageal spasm (DES), hypertensive lower esophageal sphincter (HLES) and normal, by using the current diagnostic criteria.

Table 1: Manometric findings

<table>
<thead>
<tr>
<th>Total</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Types of abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(male/female)</td>
<td>n (%)</td>
<td>DES</td>
</tr>
<tr>
<td>RA</td>
<td>37 (9/28)</td>
<td>23 (62)</td>
<td>14 (38)</td>
</tr>
<tr>
<td>ISL</td>
<td>13 (2/11)</td>
<td>4 (30)</td>
<td>9 (70)</td>
</tr>
<tr>
<td>AS</td>
<td>8 (6/2)</td>
<td>8 (100)</td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>4 (1/2)</td>
<td>1 (25)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>SME</td>
<td>1/17</td>
<td>4 (50)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>MCTD</td>
<td>1/17</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>71 (2/150)</td>
<td>41 (58)</td>
<td>30 (42)</td>
</tr>
</tbody>
</table>

In 3 manometrically abnormal of 4 patients with dermatomyositis, low contraction amplitudes have been detected in the 2/3 proximal esophagus consistent with intense dysmotility likely contraction amplitudes in the 2/3 distal esophagus they were diagnosed as NC. Not in all of the patients with Sc the classical findings of esophagus dysmotility, characteristic for this disease were observed. Manometric findings in the group of patients with NE were more heterogeneous in nature. For some of patients with RA, NEMD was diagnosed because of low contraction amplitude in the body of the esophagus. Some other patients were diagnosed as NC due to observed high contraction amplitudes.

This study concludes that, as well as Sc, the other connective diseases also have effects on esophageal motor function in various ways.
1129 Placebo-Controlled Study of Cisapride in Patients with Non-specific Esophageal Motility Disorder (NEMD) Accompanied by Delayed Esophageal Transit

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NEMD represents a difficult therapeutic challenge because of the heterogeneous nature of the esophageal motor functions. We studied the effects of cisapride (CIS) on the esophageal symptoms and esophageal motor function in a group of patients (pts.) with NEMD showing delayed esophageal transit.

Method: 70 eligible pts. were entered into a 4-week, double-blind randomized comparison of 10 mg of CIS or placebo (PLA) q.d. Symptoms assessment, esophageal manometry following wet swallows and esophageal scintigraphy following intake of a liquid and solid bolus were performed in each patient before and after treatment.

Results: After 4 wks, both CIS and PLA significantly reduced the symptom scores without statistical difference between the two groups. However, the global efficacy of CIS, as rated by good and excellent responses, was significantly superior to that of PLA (P < 0.05). CIS significantly increased the number of esophageal peristaltic contractions (P < 0.05 versus baseline and PLA) and significantly improved esophageal emptying of the solid bolus (P < 0.05 versus PLA), while not of the liquid bolus. PLA did not have any significant effects versus baseline on these parameters. Both PLA and CIS, however, improved the distal esophageal amplitude versus baseline (no significant intergroup differences).

Conclusions: CIS is effective and well tolerated in pts. with NEMD accompanied by delayed esophageal transit. Its efficacy may be related to its action on the esophageal body by increasing the number of peristaltic contractions and esophageal emptying of solids.

1131 Esophageal Motility and Gastric Tone in Systemic Sclerosis (SSc)

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Gastrointestinal tract is frequently involved in SSc, but only few patients become symptomatic. Esophageal motility abnormalities are reported in 75–90% of patients. Gastric involvement has been poorly studied. The most common SSc classification describes either a limited or a diffuse cutaneous form. Aims: to evaluate the esophageal motility pattern and the compliance of the proximal stomach in patients with limited and diffuse SSc. Methods: in 14 consecutive patients (13 F, age 32–63, with diffuse SSc) a study of the esophageal motility (constantly perfused multilumen catheter) and gastric compliance (volume/pressure relationship) was performed (electronic barostat). During isobaric distention, the intragastric pressure was increased from 0 to 20 mmHg, up to a maximum of 600 ml or to discomfort. A manometric score was calculated in each patient based on the tracing alterations (1–3).

Perception was scored by a specific questionnaire. Results: the esophageal motility pattern was impaired in 10 patients (71%). In limited and diffuse SSc patients the manometric score was 1.2 ± 0.5 and 2.8 ± 0.4 (M ± SD), respectively (P < 0.05). Voluntary pressure relationship (compliance) was studied by linear regression analysis in each patient (correlation coefficient 0.95–0.99). Gastric compliance was larger in diffuse SSc patients than in both limited SSc and 6 controls (78 ± 15 vs 51 ± 11 ± 85 ± 15 ml/mmHg (M ± SD), respectively, p < 0.05). No relationship was found between the manometric score and gastric compliance in each patient. In all patients gastric distention produced gastric sensations and the perception score was higher than controls (8.1 ± 5.4 vs 1.3 ± 2.5 (M ± SD), p < 0.05). No difference was found in perception score between diffuse SSc and limited SSc patients. Conclusion: in diffuse SSc patients gastric compliance was larger than limited SSc patients and controls. The proximal stomach could play a role in eliciting dyspeptic symptoms in SSc patients.

1132 Coexistence of Gastroesophageal Reflux Disease and Esophageal Dismotility in Non-cardiac Chest Pain

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Gastroesophageal reflux disease (GERD) is the most important etiologic factor of non-cardiac chest pain (NCCP). But not all NCCP patients with GERD respond to acid suppressing therapy. In a prospective study, we evaluated 43 patients with NCCP to investigate the etiology and the respond to medical therapy.

All patients were referred to us from cardiology department. Male/female ratio was 24/19 and the mean age was 41.5 ± 9. Patients were evaluated by means of upper GI endoscopy, endoscopic biopsy, 24-hour pH monitoring and conventional manometry. GERD and/or dismotility were diagnosed in 27 (63%) (60% were non-specific, nutricle prevalence was 40%). Patients were treated with omeprazole, cisapride or nifedipine where indicated. Fifteen patients had complete resolution of pain. Our results were as follows:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>GERD</td>
<td>14 (32.6)</td>
</tr>
<tr>
<td>GERD + dismotility</td>
<td>7 (16.3)</td>
</tr>
<tr>
<td>Dismotility</td>
<td>6 (14.0)</td>
</tr>
<tr>
<td>Total</td>
<td>27 (62.8)</td>
</tr>
</tbody>
</table>

Our results indicated that: 1. GERD is the most important cause of NCCP. 2. Dismotility coexistence with GERD was found in 1/3 of GERD patients. 3. Respond to medical therapy is better when GERD is alone. Presence of motility disorder or association of GERD with dismotility is an indicator of poor response of medical therapy in NCCP.

1133 24 Hours Oesophageal pH, Pressure Monitoring and ECG in Patients with Non-cardiac Chest Pain

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Aim: The aim of this study was to report the findings of simultaneous 24-hour oesophageal pH, pressure monitoring and ECG in patients with non-cardiac chest pain.

Material and methods: The study group consisted of 23 patients (10 male and 13 female, mean age 46.2 years). Long term pH/monitoring was performed within 48 hours after admission and exclusion of ischemic heart disease, using catheter with an antimony electrode and separate catheter with three solid-state pressure transducers. The data were recorded on portable data logger with 2-MByte memory and microcomputer (Elysetics, Sweden). Simultaneous Holter monitoring has been used in the evaluation of cardiac events (Marquette Laser XSP). The analysis of data included; 1) percentage of propulsive, nonpropulsive and simultaneous contractions 2) mean amplitude and duration of contractions, 3) propagation of peristaltic contractions, 4) time pH below 4.0%, 5) total number of reflux episodes (pH < 4.0), 6) total number of reflux episodes longer than 5 min, 7) symptom index for reflux and for dysmotility pain. An upper GI endoscopy and treadmill test were performed in all patients on a separate day.

Results: A total of 46% of patients were found to have either reflux- or dysmotility- related chest pain. 36% of pain episodes were associated with gastro-oesophageal reflux and 26% with dysmotility. The pain was not related with oesophageal abnormalities in 38% of cases. None of these pain episodes were associated with electrocardiogram changes.

Conclusion: 24-h oesophageal pressure, pH and ECG recording is worthwhile and useful diagnostic tool of non-cardiac chest pain and offers the additional clinically valuable advantages of studying these patients. Partly supported by Medical Academy of Bialystok Grant No 513779

1134 Visceral Sensitivity of the Esophagus and Its Relation to Basal Manometric Findings

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Purpose of the study: Ballon distension of the esophagus is currently used for assessment of esophageal motility and visceral sensitivity. Recently, a lowered pain threshold on balloon distention could be shown in a subgroup of patients with "non-cardiac" chest pain. However, the relation between the increased visceral sensitivity and motility has received little attention so far. The aim of the study was to study visceral sensitivity of the esophagus and its relation to peristaltic activity as well as the effects of TENS.

Methods: 18 patients referred for esophageal evaluation, because of chest pain of unknown origin, were investigated with routine esophageal manometry and 24-h pH measurements. A balloon (Medi Tech occlusion balloon catheter 10 ml, 65 mm, USA) was placed 6 cm above the lower esophageal sphincter (LES), and in stepwise fashion filled with air in 1 ml increments, until maximum balloon volume of pain S10 on the Borg scale. Basal manometry before balloon distention was compared with measurements made after each balloon distention of the patient. As a study of the effects of TENS (transcutaneous electrical nerve stimulation) on visceral pain, the balloon provocation was done in two sessions with TENS or placebo-TENS.

Results: As a result of balloon distention, the peristaltic wave increased proximal of the balloon and decreased distally of the balloon, as shown in earlier studies. The amplitude of the peristaltic wave proximal of the balloon was positively correlated with increased visceral sensitivity to balloon distention (p < 0.05). Likewise the amplitude of peristasis at the level of the balloon was significantly (p < 0.05) correlated with increased sensitivity, as was the duration of the peristaltic wave at the level of the LES (p < 0.05). TENS significantly reduced symptoms during the balloon distention and also had effects on the esophageal motocic activity.

Conclusion: Esophageal visceral sensitivity was related to basal manometric findings. TENS decreases symptoms during balloon distention and thus may have an effect on visceral sensitivity. The manometric patterns as induced by the cholinergic drug edrophonium was related to increased visceral sensitivity, thus indicating a possible connection between increased cholinergic activity (autonomic dysfunction) and higher visceral sensitivity of the esophagus.
1135 Esophageal Manometry in Progressive Systemic Sclerosis
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Progressive Systemic Sclerosis is a connective tissue disease characterised by progressive collagenous involvement in up to 70%. Scleroderma and dysphagia follow esophageal dysmotility. Impaired peristalsis of the distal body with low lower esophageal sphincter pressure are the distinguishing features.

Methods: In order to evaluate the frequency and nature of esophageal dysmotility in PSS, 102 consecutive standard manometric recordings were reviewed (19 males, 83 females). The mean age was 48.9 years (range 17–82 years). Twenty-three (22.5%) patients had no esophageal complaints. Of the remaining 79 patients, 58 (56.9%) had heartburn, 31 of them also had dysphagia. Esophagitis was the main complaint in 15 patients. Six patients had other symptoms.

Results: Fifty (49%) patients showed aperistalsis of the distal esophagus; 14 (28%) of them with simultaneous low LES pressure; 37 (36.2%) had a normal or inspissated motility disorder of the esophageal body; 44 (13.7%) showed low amplitudes with peristaltic waves and one patient had low LES pressure alone. Fifty-five (69.6%) symptomatic patients and 10 (43.5%) patients without esophageal symptoms presented motility changes suggesting PSS.

Conclusions: (1) Sixty four per cent (65/102) of our patients showed esophageal involvement by PSS, mainly (49%) smooth muscle aperistalsis; (2) The occurrence of esophageal complaints was highly suggestive of disease activity, but not more than 40% of assymptomatic patients also presented motor abnormalities suggestive of PSS; (3) Low LES pressure occurred in 14.7% of the patients, almost exclusively (93%) associated with impaired peristalsis of the esophageal body supporting that the primary abnormality in the pathogenesis of the GER in PSS is an abnormal clearance.

1136 Esophageal Motor Disorders in Diabetic Patients
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Aim of the study is to detect the presence of esophageal motor disorders in diabetics and to establish whether their seriousness is related to the kind of diabetes and to the presence of diabetic neuropathy.

Materials and methods: We studied 16 patients (5 m, 11 f, mean age 44, range 19–67) affected with Diabetes Mellitus. Fourteen of those subjects were suffering from the insulin-dependent kind of diabetes and were treated with this hormone; two patients were treated with oral antidiabetic drugs. Eight patients were suffering from peripheral neuropathy (the diagnosis was supported by carbohydrate tolerance test, TDSM, peripheral neuropathy tests) and gastro and/or esophageal symptoms (dyspepsia and/or heartburn). A station pull-through was used to perform esophageal manometry. The Ambdror EBMSR catheter (8 channels, 4 of them radially) was used. This catheter was connected to a computerized program by means of a pneumatic hydraulic system and external transducers. The software used to compute the results was created at our Institute.

Results: The study of esophageal motility showed the presence of alterations in all patients. In particular, mean LES pressure was lower than normal values (12.8 ± 4.3 vs 20.4 ± 2.4, p < 0.01). In neuropathic patients LES pressure was lower than non-neuropathic patients (10.3 ± 4.3 vs 15.4 ± 2.6, p < 0.05). A significant correlation was found between LES pressure and neurological score. Esophageal peristalsis was altered in all patients; nine patients had lower-amplitude waves, four had higher-amplitude waves, twelve had multiphasic waves. The duration of the primary waves was significantly longer in all diabetic patients (mean range: 3.7 ± 0.5 vs 2.4 ± 0.9, p < 0.01). Of the patients (6 pts) had prepyloric waves in more than 50% of swallowings. Three of them had 20% of retrophasic waves.

Conclusion: Esophageal manometry can be considered a useful method to evaluate autonomic neuropathy in diabetic patients.

1137 Oesophageal Gastric and Ano-Rectal Motility Disorders in Patients with Diabetic Neuropathy
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The impairment of the gastrointestinal smooth muscle function as a complication of the diabetes mellitus is well known. The incidence and the predilection site of the gastrointestinal motility disorder and its relationship to the autonomic neuropathy remains still poorly investigated.

Our objectives were to examine the motor function at different levels of the gastrointestinal tract in diabetics. Second, whether the cardiovascular reflex test and the sensory tests, which are generally used to establish the degree of autonomy neuropathy in diabetes mellitus, can predict the severity of the gastrointestinal motor dysfunction.

Patients: Methods: One hundred 10 diabetes (6 male, 4 female) with different gastrointestinal symptoms were studied. The mean age was 59 (39–72 years). The mean duration of their diabetes was 17 (4–51) years. The gastrointestinal motor function was examined by esophageal, gastric and ano-rectal motility (Polyph (

1138 Manometric Study of Esophageal Dysphagia: Correlation of Manometric Findings with Healing and Improvement of Symptoms Improvement
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The aim of this study was to correlate manometric findings with the natural history of gastroesophageal reflux (GER) disease in patients with erosive esophagitis. 33 symptomatic pts (17 F, 18 M; mean age 59, range: 28–82 yrs) underwent, endoscopy and manometry. Symptoms were scored (scale 0–9) before and after treatment. All patients were initially treated with omeprazole 20 mg for 4 weeks (regimen A). If healing was not achieved they continued on 40 mg for four more weeks (regimen B).

Results: In 23 (69.7%) pts (Group A) esophagitis was healed on regimen A and in 25 (75.7%) (Group A1) symptoms were completely abolished. In 10 pts (Group B) esophagitis was improved on regimen A and in 5 of them complete healing was achieved on regimen B (overall healing: 84.8%). In 8 pts (Group B1) symptoms were improved on regimen A and 7 of them were completely asymptomatic on regimen B (overall symptoms eradication: 96.9%). Symptoms score after regimen A was significantly lower compared with the initial score (0.4 ± 0.15 vs. 1.9 ± 0.14, p < 0.001). Pts who had whole body hypotensive (8.87 ± 0.75 mmHg) low esophageal sphincter (LES) and in 5 (15%) of them a nonspecific esophageal motor disorder (NEMD) was found. When comparing group A with group B and group A with group B1 as far as LES pressure, wave amplitude and duration and velocity of peristalsis, no significant differences were seen. Pts in group B were more likely to have NEMD compared with group A but this was not significant. In contrast pts in group A had significantly more esophageal symptoms (regimen: A vs B: 2.4 ± 0.1 vs 2.3 ± 0.0, p < 0.05).

Conclusions: 1) In 84.8% of pts with erosive esophagitis complete healing of inflammation is achieved on two-month treatment with omeprazole although nearly all (96.9%) are completely asymptomatic. 2) The presence of NEMD significantly delays symptoms eradication.

1139 Evaluation of Patients with Gastroesophageal Reflux (GER) Referred for Surgery: The Role of Esophageal Manometry
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GER and its complications is a very common disease in the general population. The aim of this study was to consider manometric findings in patients with GER prior to surgery. Endoscopy and manometry were performed in 55 pts (28 F; 27 M; mean age 57, range: 28–82 yrs) with long-lasting GER symptoms and continuous use of antacids and/or protonic drugs. Endoscopy showed that 12 pts had esophagitis I, 28, II, III, 7 Barrett's esophagus and 3 esophagus was normal. 23 (51%) pts had significant sliding hernia (hernia > 3 cm). As far as lower esophageal sphincter (LES) pressure (mean of highest end-expiratory pressure) was concerned, the following results were observed:

1) Group A with normal pressure, ≥ 10 mmHg: 24 (44%) pts, Group B with low pressure, 6–10 mmHg: 13 (23%) pts and Group C with very low pressure, < 6 mmHg: 16 (29%) pts. Patients as a v. Nika had a mean LES pressure of 9.63 ± 0.7 mmHg (range: 2–24). According to the best results

ter (UOS) relaxation; the amplitude, the duration, the propagation velocity, the wave morphology of oesophageal body (OB) contractions at 3, 8, 13 and 18 cm above the lower oesophageal sphincter (LOS), the mean pressure the relaxation time and rate of the LOS; the fastiging type gastric MMC patterns; basal pressure and time of the external and internal anal sphincters (EAS, IAS), the recto-anal inhibitory (RAI) and continence (RAC) reflexes, the voluntary contraction and the recto-anal inhibitory and/or anal sphincter muscle and myenteric plexus. GER (can) and a sensory neuropathy (SN) test.

Results: The of the CAN (mean score: 5.1 ± 0.8) and SN tests proved a moderate autonomy neuropathy in average. We did not observe any abnormality of the UOS and the PHX function except one case. In the OBL the amplitudes of contractions was frequently decreased (9/10 patients at 18 cm, 7/10 at 3 cm above the LOS) with prolonged duration in 50% of the cases. The rate of simultaneous waves was increased in 4/10 patients. LES abnormalities (pressure and relaxation time) were also found in 5/10 cases. Gastric motility disorders was prominent. We observed the absence of MMC phase III, activity in 9/10, of which complete paresis was found in 6 cases. The most frequent abnormality of the rectoanal function was the impairment of the voluntary contraction (7/10). Abnormalities of the baseline EAS and IAS pressures; RAC and RAI reflexes were less pronounced (4–5/10). We could not observe close correlation between the result of the CAN test and the alteration of the studied parameters of the gastrointestinal motility.

In this small series of patients we can conclude that the abnormalities of the sphincter function are less pronounced, than the impairment of the oesophageal body or gastric motility. Second, the presence and/or the severity of the gastrointestinal abnormalities in diabetic patients can not be predicted by the standard CAN or SN tests.

The study was supported by a grant of Ministry of Social Welfare (ETT: T-02 533/93).
an anti-reflux operation (Nissen fundoplication) might benefit 31 pts (group B + C) (56%). Another 7 pts with significant hiatus hernia could also be included increasing the percentage to 69% (38 pts in total). In 8 (14.5%) pts a nonspecific esophageal motor disorder (NEMD) was diagnosed and in 5 (9%) of them who also had a hypotensive LES, an alternative type of surgery might be considered.

Conclusion: Esophageal manometry is of great value in patients with GER disease prior to surgery since it helps distinguishing the group with normal LES pressure who are unlikely to benefit from it. Nevertheless in 9% of pts with a NEMD a different surgical approach could be considered.

1140 Correlation between Esophageal Clearance and Esophageal Motility in Patients with Gastroesophageal Reflux (GER)

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The aim of this study was to examine the relationship between esophageal clearance expressed by the duration of reflux episodes and parameters of esophageal body function. 32 patients (13 F; 19 M; mean age 53, range 22-81 yrs) with symptomatic GER and positive 24 h ambulatory pH study who also underwent endoscopy and manometry entered the study. Mean duration of reflux episodes was calculated by dividing time in min the pH was below 4 by number of episodes (total, upright and supine position). According to motor function patients were classified in two groups: A) with normal manometry (17 pts; F: 12; mean age 44.9) and B) with abnormal manometry (15 pts; F: 8; T: 7 M; mean age 62.6). 12 pts in group B had a degree of failed peristalsis (mean after 10 wet swallows 85.5%; range 0-92%), 3 abnormal wave amplitude (mean in lower esophageal third after wet swallow < 30 or > 180 mmHg), 1 incomplete lower esophageal sphincter relaxation and 3 triple-peak contractions. 13 pts (40.6%) had erosive esophagitis and 3 (9%) a hiatus hernia (3 cm). All pts had abnormal 24 h pH study (mean total time with pH < 4: 13.6%; range: 4.1-40.7%). Group B pts had significantly longer reflux episodes compared with group A (2.44 ± 0.48 vs 1.57 ± 0.24; Mann Whitney U test: p < 0.05) and this difference seems to be entirely due to the results in supine position (5.28 ± 1.25 vs 2.44 ± 0.45; p < 0.05) since no significant difference was found in upright position (1.28 ± 0.12 vs 1.09 ± 0.15). No correlation was found between esophageal clearance and wave amplitude (r = 0.14). Pts with dismotility were significantly older than those with normal manometry (62.6 ± 44.3 yrs; p < 0.01). Age correlated well with esophageal clearance (r = 0.45; p < 0.05).

Conclusions: 1) Delayed clearance is significantly prolonged in patients with GER and abnormal manometric findings. 2) Wave amplitude does not seem to affect the duration of reflux episodes in these pts. 3) Age seems to influence esophageal motility and subsequently to prolong esophageal clearance.

1141 Erythromycin Enhances Esophageal Motility in Patients with Gastroesophageal Reflux

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Background: It has been shown that i.v. erythromycin (ER) enhances gastric and esophageal motility in both health and disease, acting either as a motilin agonist or as a cholinergic factor.

The Aim of the study was to investigate any possible effect of i.v ER on esophageal motility in patients with gastroesophageal reflux (GER).

Patients/Method: In 15 patients with GER, proven on 24-hour ambulatory esophageal pHmetry, standard esophageal manometry was performed after giving i.v. either placebo or 200 mg ER lactobionate (Abbott). The calculated manometric parameters of esophageal motility were the loer esophageal sphincter (LES) pressure, the amplitude and duration of peristalsis at 5, 10 and 15 cm proximal to LES and the velocity and strength of peristalsis at distal esophagus.

Results: ER significantly increased LES pressure from 16.5 ± 4.8 SDmmHg to 19 ± 5.3 SDmmHg (p < 0.001), without affecting the postcontraction relaxation of LES. ER also increased the amplitude (from 78.5 ± 34.3 SDmmHg to 97.1 ± 39.5 SDmmHg; p < 0.001), the duration (from 3.4 ± 0.6 SDSecs to 3.8 ± 0.6 SDSecs; p = 0.005) the velocity (from 3.1 ± 0.8 SDSec/s to 3.5 ± 1.1 SDSec/s; p = 0.0047) and the strength of the LES (from 149 ± 64 SDmmHg/sec to 200 ± 137 SDmmHg/sec; p < 0.001) at 5 cm proximal to LES. Similarly, ER increased the amplitude of peristalsis at 10 and 15 cm proximal to LES (from 69.7 ± 39.3 SDmmHg to 77.4 ± 36.9 SDmmHg; p = 0.049 and from 35.5 ± 19.3 SDmmHg to 43 ± 21.6 SDmmHg; p = 0.043 respectively) and the duration of peristalsis at the same levels (from 3.1 ± 0.6 SDSecs to 3.3 ± 0.5 SDSecs; p = 0.011 and from 2.7 ± 0.6 SDSecs to 3 ± 0.5 SDSecs; p = 0.003 respectively).

Conclusion: 1) ER improves the impaired esophageal motility in patients with GER. This observation might be of clinical use.

1142 Esophageal Motility in Patients with Gastroesophageal Reflux Disease

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Esophageal motility (EM) has been shown to be impaired in patients (pts) with gastroesophageal reflux disease (GERD).

The aim of the study was to compare EM parameters in GERD pts with controls (ctls), and to determine the effect of different treatment on lower esophageal sphincter pressure (LESP), amplitude, duration, and velocity of esophageal peristaltic contractions (EPC).

EM was studied in 30 GERD pts with and without reflux esophagitis (RE), classified as Savary-Miller grades 1–2, and in 10 healthy pts. LES was measured by rapid pull-through technique, measurements of amplitude, duration and velocity of EPC were made at 3, 6, 10 and 13 cm above the LES. All measurements were repeated after resolution of symptoms in pts without RE (grade 0) and after healing of RE in grade 1 and 2 pts.

All pts had a significantly lower mean LESP (p<0.05) and EPC amplitude in distal esophageal (DEA) than cts (p<0.05). Grade 2 RE pts had a significantly lower mean LESP (p<0.05) and DEA (p<0.05), than grade 0 and grade 1 RE pts. The duration and velocity of EPC were decreased in all pts when compared to cts (p<0.05). The incidence of incomplete lower esophageal sphincter relaxation and EPC was presented in 40–45% of test swallows (TS) in grade 2 RE pts, in 30–35% of TS in grade 1, and in 15–20% of TS in grade 0. All distinctable EM disorders did not change after resolution of symptoms in grade 0 pts or healing of RE in grade 1 pts. Cisapride (10 mg tid orally; 1 wk), but not antacid or H2-receptor antagonists increased LESP (53%), DEA (20%), duration (8%), in EPC of GERD pts.

We conclude that impaired EM in GERD pts is a prevalent factor in the pathogenesis of RE. Main EM parameters in GERD pts were significantly improved after 4 wks administration of cisapride 10 mg tid orally and did not change after treatment by antacids and H2-receptor antagonists.

1145 Clinical and Manometric Response to Intraspincteric Injection of Botulinum Toxin in Achalasia

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Botulinum Toxin (Botox®) has been reported to reduce successfully the lower esophageal sphincter pressure (LESP) and achieve significant symptomatic relief in patients with achalasia. Extension of the experience so far suggests that Botox is safe and efficacious at least in the short term (NEJM, 332 (12): 774, 1995).

Aim: We examined the manometric, radiological and symptomatic efficacy of intraspincteric Botox administration in adult achalasia patients as well as the complications and adverse effects associated with this procedure.

Methods: 8 consecutive patients (6 women, 2 men, mean age: 59 years) without a previous history of esophageal surgery or dilation were enrolled in the study. There were 6 classic and 2 ischemic achalasia. All patients had achalasia newly diagnosed using clinical, radiological and manometric criteria. Baseline manometry, symptoms scores, radionuclide emptying test and endoscopy were obtained in all patients within one month prior to Botox, and 4 weeks after Botox administration, under double blind conditions. 50 units/ml of Botox (25 units/ml) were injected into the four quadrants of the lower esophageal sphincter, using a standard sclerotherapy needle. Results: Four weeks after the treatment all patients had significant symptomatic improvement with the mean symptom score from 7.5 ± 0.7 to 1.9 ± 0.3 (p < 0.01), and the LES pressure significantly decreased from 50 ± 9 to 25.5 ± 11 mmHg (p < 0.05). Reappearance of partial peristalsis was observed in 1 of 2 vigorous achalasia but none of the classic achalasia. Neither complications nor adverse effects were reported.

1148 Relationship of Manometric Changes with Symptomatic Response Following Pneumatic Dilation in Achalasia Patients


Introduction: Achalasia cardia is frequently treated with pneumatic dilation, to reduce the lower esophageal sphincter (LES) pressure. Relationship of changes in esophageal manometric findings following dilation with symptom relief is however unclear. We therefore decided to study this relationship.

Methods: 16 achalasia patients underwent esophageal manometry before and one month after pneumatic dilation. At each time, LES pressure and body...
patients the passage through the esophagus of a 10-ml water-bolus labelled with 250 mCi 99m-Tc sulphur colloid could be studied with the patient in the supine position. A negative passage was present in only one patient, and a slightly delayed passage in 2 others. In 8 patients between 23% and 94% of the bolus was still present in the esophagus after 120 s. Manometric investigations performed in 23 patients revealed that the resting pressure of the lower esophageal sphincter was 23% to 29% lower than before myotomy and higher in only one patient, who also suffered from severe dysphagia.

Conclusion: It is concluded that the surgical treatment of achalasia yields good results in a high proportion of patients, in whom dilatation treatment had failed to achieve satisfactory results.

1152 Is Routine Conscious Sedation or Topical Pharngeal Anesthesia Necessary in Upper Emergency Endoscopy in Bleeding Patients?

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Upper emergency endoscopy in bleeding is frequently performed in cirrhotic patients. A routine IV conscious sedation may complicate the status of their patients at high risk of encephalopathy because the bleeding status. Patients: In the last 12 months [May 1995–April 1996] we have performed all the upper emergency endoscopy for bleeding without any routine medication. The patient was reassured and was gently and energically requested to cooperation for the success of procedure. With the patients in the left decubitus position, gentle intubation was achieved with a endoscope (generally a 10.5 mm). During the procedure the patients was continuously reassured by the physician or by the assistant. We have performed. 583 endoscopies in bleeding patients: of these 192 were performed in cirrhotic patients: 56 patients required sclerotherapy and 26 patients a balloon tamponade. An injective emostasis was performed for bleeding points. In 77% of the cases, no success of procedure or diagnostic therapeutic may be impuated to patient cooperation. Conclusion: Routine IV conscious sedation or topical pharngeal anesthesia is unnecessary in upper emergency endoscopy for bleeding. The patient may be successful prepared with verbal assurance by physician and continuously reassured during the procedure or by physician or by technician. This patient preparation may have advantage especially in the group of cirrhotic bleeding patients that are at high risk of complication by IV sedation.

1155 Risks, but No Benefits of a Midazolam-Fentanyl Combination as Premedication of ERCP

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The benefit of combining benzodiazepine with an opioid as premedication for more complex endoscopic procedures remains poorly defined. Therefore, we performed a double blind, randomized, placebo controlled study comparing midazolam plus fentanyl with midazolam alone as premedication of ERCP. Method Consecutive patients (n = 115) undergoing diagnostic and/or therapeutic ERCP were randomized to either an intravenous combination of midazolam (5–15 mg) plus fentanyl (0.05 mg standard dose) or midazolam alone (5–20 mg); midazolam was individually titrated. Oxygen saturation (SaO2), blood pressure, heart rate and arrhythmias were monitored continuously, using a multifunction monitor. The degree of sedation during the examination and the patients’ acceptance were rated. The two groups were comparable with respect to age, sex, body-weight, risk-group (ASA), initial SaO2, indication, type, duration of the procedure and titrated dose of midazolam.

Results are expressed as median (range).

Following midazolam-fentanyl SaO2 dropped below 85% in 16 patients compared to 4 with midazolam (p = 0.004). Besides fentanyl, age and risk-groups A II III were independent predictors of hypoxemia. Transient fall of blood pressure, increase of heart rate, incidence of arrhythmias and patients’ acceptance were not significantly different. There was a trend to a more effective sedation in the midazolam-fentanyl group (p = 0.063). In conclusion, the combination of midazolam-fentanyl was more effective in comparison with midazolam alone. There was no significant difference concerning the benefits, f. e. degree of sedation and patients’ acceptance. The theoretical premise that fentanyl used in combination should reduce the dose of midazolam was not confirmed.

1176 Optimal Number of Biopsy Specimens and Brush Cytology in the Diagnosis of Gastric and Colorectal Malignancies

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Retrospective studies have indicated that endoscopic biopsies yielded a positive diagnosis in 57–86% and cytology in 71–86% of colon cancers.
The aim of our study is to identify the optimal strategy of biopsies and cytology in cases with masses lesions in upper and lower gastrointestinal system.

61 patients with gastric or colorectal masses were included in the study. Biopsy specimens were put into 4 vials, with 4 biopsies in the first, 2 in the second, 2 in the third, and 2 in the fourth ones. Based on our data of discrete combinations of biopsies and cytology were made and the results shown in the table were found. Lower diagnosis rate in first biopsies was found (52.08%) in gastric malignancies, when compared to the 79.41% in colorectal cancers. The percentage of one diagnosis in two biopsies was comparable in both groups (75% and 76% respectively). When cytology was added to the first four biopsies in gastric malignancies, the rate increased to 87.50%, and to 69.18% in colorectal malignancies. There seemed to be no difference between cytology and 10 biopsies in both groups. With combination of biopsy and cytology, diagnosis could not be made in 4–6% of cases.

Cytology and 6 biopsies had the same diagnostic range as 10 biopsies did and cytology added to 10 biopsies did not increase this diagnostic range significantly. We conclude that cytology and 6 biopsies appear to be the optimal strategy in the diagnosis of gastric and colorectal malignancies.

### 1183 Preoperative Parathyroid Imaging Using Echoendoscopy in Primary Hyperparathyroidism: A Prospective Preliminary Study

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**Purpose:** Parathyroid adenomas responsible for primary hyperparathyroidism (PHPT) are difficult to detect preoperatively. As most of parathyroid adenomas arise below and/or behind the thyroid gland, and as abnormal parathyroid glands are not visible in a deep cervical location, we have assessed the ability of echoendoscopy (EE) to localize parathyroid adenomas.

**Methods:** Six females and 3 men (age 54.5 ± 16.5 years) with PHPT (calcium concentration 2.9 ± 0.4 mmol/l with inapparent parathormone levels 297.6 ± 284.7 pg/l) were studied. A single autopic parathyroid adenoma was confirmed at surgery in 7 cases. One patient became normocalcemic after a percutaneous infusion of ethanol in the adenoma. One patient had no lesion at surgery. All patients underwent ultrasonography (US), To 99 m sestamibi scanning, CT scanning or magnetic resonance imaging (MRI) and EE before undergoing initial neck exploration. EE was performed by a single physician, under general anesthesia, using 7.5 and 12 MHz probe (Olympus EU-M20). The duration of the exam was 15 minutes. The operative findings were recorded and correlated with the results of preoperative studies.

**Results:** 6 of the 8 adenomas were correctly localized using EE and sestamibi scanning. 2 of these tumors were undetectable using CT scanning/MRI. Conversely CT scanning/MRI detected 2 adenomas that were not identified by EE and sestamibi scanning. US correctly localized only 4 adenomas. One patient in one case; sestamibi scanning, MRI and EE visualized a lesion which was not found at surgery.

**Conclusion:** The sensitivity of EE to detect parathyroid adenomas was roughly equivalent to that of sestamibi scanning or CT scanning/MRI. Thus, EE may be a useful tool for the preoperative investigation in patients with PHPT. Our results have to be confirmed in larger series of patients, especially in patients with small, and/or abnormal localized parathyroid glands and above in patients with persistent or recurrent PHPT after surgery.

### 1186 Uncommon Locations of Hydatid Disease

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Hydatid disease is still a challenging diagnostic and therapeutic problem especially in endemic countries; the most commonly involved organs are the liver, lung and less often the spleen. The aim of this study is to present the possibility of other locations of hydatid cysts in solid organs or other anatomic sites rarely encountered.

During the last 20 years, 12 patients were operated on for uncommon locations of hydatid disease. There were 6 men and 6 women, between the ages of 27 to 68 years (mean age 60.4 years). There were 2 cases with hydatid cysts located in the gallbladder, 4 cases in the pancreas, 1 case in the kidney, 1 case in the thyroid gland, 1 in the breast, 1 in the pericardium, one in the supraclavicular region and one in the thigh. Clinical symptomatology varied according to anatomic location and preoperative diagnosis was accomplished with radiological examinations, ultrasound or computerized tomography. Surgical treatment included cholecystectomy in the 2 cases with hydatid cysts in the gallbladder, omentoplasty or partial resection of the pancreas in the 4 pancreatic cases, nephrectomy in the kidney case, lobectomy in the thyroid case and cyst excision in the rest cases. In all cases histopathological examination of the surgical specimens confirmed the diagnosis. One patient with pancreatic resection died postoperatively, while the remaining 11 patients did not have any significant complications.

In conclusion, hydatid disease should be included in the differential diagnosis of cystic masses in solid organs or other anatomic sites especially in endemic countries; hydatid cyst excision is curative and confirms the diagnosis.

### 1187 Parasitic Liver Disease

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Several parasites infest the liver and biliary tree. Ascars may be present in the liver or in the biliary tree and cause obstructive jaundice due to worms or associated stones. In schistosomiasis the liver may be involved early or later leading to perportal fibrosis and portal hypertension. We have studied 72 patients with hepatosplenic schistosomiasis, liver ultrasound showed perportal fibrosis in 48 and in 30 liver biopsy showed biliary granulomas or fibrosis. In amebiasis tender hepatomegaly may present during the acute phase but more commonly in chronic carriers, an amebic abscess develops. We have treated 3 patients with amebic liver abscess in two of which percutaneous drainage was done. Hydatid cysts of the liver may be large and cause pressure on the liver or rupture into the biliary tree causing obstruction. In our unit we have introduced endoscopic management for such cases and we have treated successfully 10 patients. Between 1985–1990 we have treated 22 patients with azbenzole alone. After 1990 we have introduced combination therapy in 19 patients (Azbenzole + Praziquantel and was found to be more effective than azbenzole alone. Ten other patients had percutaneous drainage of a huge P. Cyst.

Liver flukes infest liver and can cause biliary tree obstruction causing recurrent cholangitis. One of our patients from Thailand had obstructive jaundice and ERCP showed multiple Clonorchis sinensis worms and an associated cholangiocarcinoma.

In three years we have studied 208 patients with Human Dicroccieliasis, 16 of these patients had disturbed liver functions and 10 patients had gill-bladder or biliary tree disease.

### 1188 Eliza in Diagnosis of Cryptosporidiosis

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Many authors considered Cryptosporidium as one of the main causes of diarrhea in man. In the present study, stool analysis and ELISA test were performed to detect Cryptosporidium oocyst and antibody in the stool and sera respectively of 206 patients with acute diarrhoeal disease and 15 healthy individuals as a normal control group. It was found that Cryptosporidium oocysts were detected in 35 cases (16.9%). Most of them aged less than 10 years, with insignificant difference between male and females. Stool of Cryptosporidium infection was offensive, watery and yellowish. ELISA was positive in 32 out of 35 cases having Cryptosporidium oocyst with 91.4% sensitivity and was negative in 32 out of 40 negative cases by stool examination with 80% specificity.

Thus Cryptosporidium oocyst should be looked for in routine examination of diarrhoeal stool especially of young patients. ELISA is a simple easily performed serological test with high sensitivity and specificity in detecting Cryptosporidium infection. Association of other parasitic infections with cryptosporidiosis did not affect the optical density (O.D.) reading of infected cases and to avoid cross reaction, fractionated oocyst antigen may improve the test specificity.

### 1189 Salmonella Typhimurium INV Mutants Invade Intestinal M Cells

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Invasion of intestinal epithelial cells is a crucial step in Salmonella pathogenesis. Recent studies employing ligated murine intestinal loops have demonstrated that the specialised antigen II-encoded integrin ligation is the primary site of Salmonella invasion. While the precise mechanisms and genetic ba- sis responsible for Salmonella invasion of epithelial cells remain obscure, multiplegene studies have identified a number of genetic loci necessary for internalisation of Salmonella into cultured epithelial cells. The significance of these loci in vivo is, however, unclear. The aim of this study was to investigate the significance of one such locus, inv, during Salmonella invasion of M cells. S. Typhimurium invA (SB111) and invB (mutant SB11B) mutants which are severely attenuated for invasion of cultured cells and their parental strains (SR11 and TNP-5, respectively) were incubated in Peyer’s patch-containing ligated intestinal loops which had been created in anaesthetised mice. After incubation,
the tissues were harvested, fixed and dual stained for bacteria and M cells. Examination by confocal laser scanning microscopy revealed that both parent and mutant strains had already adhered to and invaded M cells: no difference could be detected between parent and mutant strains in their interaction with these bacteria. Bacterial association with M cells was accompanied by a redistribution of Ulex europaeus 1 staining of M cells and by the formation, as detected by scanning electron microscopy of M cell surface protrusions indistinguishable from the "membrane ruffles" previously described in association with other wild type Salmonella. These observations demonstrate that Salmonella invasion of murine M cells may proceed via mechanisms independent of the inv locus which is essential for invasion of cultured cells. The multifactorial nature of Salmonella invasion may account for the ability of many Salmonella to infect a range of hosts and to invade a variety of cell types.

1190 Organ Involvement in Hepatointestinal Schistosomiasis
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The endoscopic, radiological and histological findings in several of our patients with schistosoma mansoni infection are described. Seventy two patients had hepatosplenic schistosomiasis. Endoscopic sclerotheraphy was effective in 45 patients with bleeding varices. Ultrasound of the liver was suggestive of peri-portal fibrosis in 48 of these 72 patients and in 30 of whom liver biopsy demonstrated schistosoma granuloma or perportal fibrosis. Fibrosis showed congestion erosions or ulcerations in the stomach in 40 of these patients and in 23 patients in the duodenum. Schistosoma ova with inflammatory changes were seen in endoscopic biopsies from the stomach in 3 out of twelve and five out of eighteen patients with these biopsies. The colonoscopic findings were suggestive of schistosomiasis. Eight patients had schistosomatis polyps and one had colonic calcifications. Schisto- soma ova were seen in surgical specimens from patients presenting with acute abdominal pain. Schistosoma was absent in a series of malignant and mesenteric vein thrombosis in three, in which mesenteric angiogram showed a blocked inferior mesenteric vein by ova.

1191 Intestinal Immune Cells in S. Stercoralis Infection
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Introduction: Strongyloides stercoralis may cause a wide spectrum of disease in humans, ranging from a chronic asymptomatic infection to a hyperinfective, often fatal syndrome. In rodents, spontaneous expulsion of related parasites after experimental infection is common. Mast cells, goblet cells and eosinophils have been identified as possible effectors of this expulsion. The aim of the present study was to assess the intestinal immune response in chronic mild strongyloidiatis.
Methods: We performed a jejunal biopsy in 19 immunocompetent patients with at least one positive stool examination for S. stercoralis and few or no symptoms. Seven healthy controls. Specimens were processed for both histopathological and analysis by the three-stage immunoperoxidase technique, using the following monoclonal antibodies: CD2, CD3, CD4, CD8, TgR-7/7 (TgR, 7/7, Ki67+), Ki67 (proliferating cells), HLA-DR and collagen IV. In addition, CD25+ cells, mast cells, CD3 expressing cells, calprotectin-containing cells (Mac 387+) and neutrophil elastase+ cells were stained by the alkaline phosphatase method. Positive cells were counted using a Image Analyser.
Results: Jejunal morphology and the numbers of different T-cell subsets, mast cells, eosinophils and goblet cells were unaffected by S. stercoralis infection. Conversely, the number of mature macrophages and of dividing enterocytes in the crypts was reduced. Crypt enterocytes did not express HLA-DR in both groups. The expression of HLA-DR by villus enterocytes was similar in patients and controls. There were no activated (CD25+) cells in the mucosa of either patients or controls.

Conclusions: Architectural damage to the mucosa and the resulting immunemediated diarrhoea apparently do not develop due to the absence of an immune response against the parasite. On the other hand, the infection is allowed to persist for several years.

1192 Does Serum Angiotensin Converting Enzyme Level Raise in Familial Mediterranean Fever?
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The diagnosis of familial Mediterranean fever (FMF), which is a periodical disease of unknown origin, has usually been based on a knowledge of ethnic status, a positive family history, the exclusion of other disease entities, and in addition to clinical findings of polyserositis and elevation of acute-phase reactants during periodic attacks. However, diagnosis of FMF is difficult for clinicians in some cases and there is no specific biological test for FMF. Angiotensin converting enzyme (ACE) is a carboxypeptidase that hydrolyses an Angiotensin II to Angiotensin I and widely found in human tissues. ACE is also produced by sarcoid granuloma cells and elevated serum ACE level is a useful test in the diagnoses of sarcoidosis and monitoring the activity. Persistent raise of serum ACE level in FMF was claimed in a recent case report and FMF has been suggested another cause of raised serum ACE level. However, this claim has not been proved by another study up to now. In this study we aimed to investigate the serum ACE level in our FMF group and to clarify the idea whether ACE level may be a marker of disease or this relation was a fortuitous. Seventeen patients (6 male and 9 female, with a median age of 27) followed at our center with a diagnoses of FMF were enrolled to the study. The serum sample was obtained in asymptomatic phase of disease in 13 patients and during an acute attack in 2 patients. Serum ACE level was measured by EIA and results are expressed as U/L. The range normal of serum ACE level was 5–10 U/L and the minimum detection limit was 1 U/L in this method. The serum ACE level was found in a minimal level in all patients and no elevation was detected.

Conclusion: This study clearly showed that serum ACE level has not been raised in FMF patients. It is well known that ACE production is increased in only sarcoidosis and certain other granulomatous diseases. Therefore, it seems that, there is no reason for the elevation of this enzyme level in FMF patients.

1193 Study of Antigenic Sites on the Asialoerythropoietin Receptor Recognized by Autoantibodies
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Background & Aims: Antibodies against the asialoerythropoietin receptor are frequently found in sera of patients with autoimmune hepatitis. The study was designed to identify the antigenic sites on the receptor recognized by specific antiasialoerythropoietin receptor antibodies.
Methods: Isolated asialoerythropoietin receptor from normal human liver was used as an antigen in an ELISA test to detect specific antibodies in the sera of patients with autoimmune hepatitis. Positive sera were further tested against the same antigen by Slot blot, Western blot and immunoprecipitation. The mature, unglycosylated and partially glycosylated forms of the asialo-erythropoietin receptor synthesized by HepG2 cells were tested against positive patients' sera. The mature receptor in HepG2 differs from the receptor in human normal liver by the H2 subunit sequence and the carbohydrate chains. The recognition by the same sera of the n-terminal translated unglycosylated form of the H1 subunit of the receptor was also screened.

Results: Sera from patients with autoimmune hepatitis recognized the native form of the human mature receptor. No reactivity was found when these sera were tested against the denatured human protein. In addition, neither the unglycosylated H1 subunit nor any of HepG2 synthesized asialoerythropoietin receptor forms bound to the antibodies.

Conclusions: Anti-asialoerythropoietin receptor antibodies in the sera of patients with autoimmune hepatitis are directed against conformational structures of the mature hetero-oligomeric form of the protein. The carbohydrate chains are probably part of the conformational antigenic sites.

1194 Interferon Induced Autoimmunity
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Purpose: To study the role of alpha interferon (IFN) in antibody production during chronic hepatitis C (CHC) treatment.
Methods: We studied 54 CHC patients measuring thyroid stimulating antibody (TSAb), antilistst cell (ICA), antithyroglobulin (AT) and antiliver and kidney autoantibodies (AKA) before and during IFN treatment.
Results: When ANA was investigated, 4 patients were found to develop it during treatment. None of the 6 patients showing ANA before treatment, did increase ANA titles with IFN. In one of these 6 patients, the antibody disappeared.

No patient developed SMA during treatment. Seven patients were SMA- before IFN treatment: titles increased in one of them while they became negative in 6 patients.

Other studied antibodies (AMA, Ad, ICA, AI, Ap, and TSAb) were not observed in any case.

Six patients presented with AM and 3 with AT previously to IFN treatment showed a title increase during treatment. All of them also showed thyrotropin (TSH) changes.

Six different cases develop AM and nine cases AT during IFN treatment. A coincidence was observed in two patients developing AM, AT and ANA.

Conclusions: 1- IFN is capable of inducing ANA frequently associated with AM and AT 2. IFN may drop previously positive ANA and SMA. 3. IFN increase or develops AM and AT titles. 4. AMA, Ad, ICA, AI, Ap or TSAb are not observed during IFN treatment.
1195 Glutamine Enriched Enteral Feeding Reduces Rat Plasma Nitrogen Levels
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Nitric oxide (NO) is a potent vasodilating and immune modulating agent that is produced in many cell types including endothelial cells and macrophages. It is a product of the enzymatic conversion of L-arginine (ARG) to L-citrulline (CIT) by NO synthase. Nitric oxide is the stable endproduct of the NO-pathway. It has been shown that the in vitro production of NO in endothelial cells can be inhibited by L-glutamine (GLN). We hypothesized that GLN enriched feeding also inhibits NO production in vivo.

To investigate this, nitric oxide measurements were performed in rats fed GLN enriched diets (6.25%, 12.5% and 25%) and compared to rats fed balanced control diets. The respective diets were fed for one or two weeks. Nitrate was measured in the diet, in plasma samples (day 7 and 14) and in samples of 24 hours urine collections. Plasma amino acids were determined weekly.

Results: In a dose dependent manner GLN supplementation significantly increased plasma levels of GLN (from 630 to 1200 μM, 91%, p < 0.0001), ARG (from 120 to 139 μM, 17%, p < 0.001) and CIT (from 50 to 75 μM, 54%, p < 0.0001). Nitrate levels in the diets did not differ (≤ 1.70 μM/L). Food Intake (≤ 18.0 g) and nitrate intake (≤ 31 μM/Day) showed no differences between the groups. Glutamine supplementation resulted in significantly lower plasma nitrate levels (≤ 50%) in all GLN fed groups (≤ 15 μM/L) compared to control groups (≤ 2.5 μM/L, p < 0.0001). No further reduction was observed after two weeks of feeding. Between 1 and 4 μmol more nitrate was excreted compared to intake in all groups without any significant differences.

Conclusions: The increase in plasma nitrate levels by GLN enriched feedings indicates for the first time an inhibitory effect of GLN on NO production in vivo. This effect was not related to the amount of GLN supplementation. Lower nitrate levels were not due to a diminished availability of ARG as substrate for NO synthases, since plasma ARG levels were significantly increased by GLN feeding.

1196 Prophylaxis Against Pneumococcal Infection after Splenectomy
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Splenectomy predisposes to serious infections from Streptococcus pneumoniae. The aims of the present study were to evaluate prophylaxis against pneumococcal infection after splenectomy.

561 patients splenectomised from 1984–1993 were identified and the hospital records were available for 555 patients. The hospital records and the discharge letters were searched for information on splenectomy and information about pneumococcal vaccination. General practitioners of living, apparently unvaccinated patients were asked for evidence of vaccination. To study differences in relation to the operative indications for splenectomy, the patients were classified into 5 major groups: haematological, trauma, incidental, malignant, or unknown.

The total vaccination rate was 62%, but vaccination rates from 47% to 91% in five different groups of indications were observed. Patients undergoing splenectomy during gastrointestinal cancer surgery or because of inadvertent intraperitoneal trauma had the lowest vaccination rates (≤ 41%). The vaccination rate depended on the risk of mortality. 64% of the patients were vaccinated at an inappropriate time in relation to the splenectomy. Recording of splenectomy was missing in 10%, and vaccination status was missed in 25% of the discharge letters.

The pneumococcal vaccination rates in patients after splenectomy were not satisfactory. The majority of patients were vaccinated at an inappropriate time in relation to the splenectomy. The discharge letters often lacked information concerning the patients’ vaccination status. More effort is needed to reach an acceptable level with respect to prophylaxis against pneumococcal infection after splenectomy.

1207 Helicobacter Pylori: Is It a Risk Factor for Hepatic Encephalopathy in Cirrhotic Patients?
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Objective: To determine whether Helicobacter pylori (Hp) infection is a risk factor for hepatic encephalopathy in patients (pts) with liver cirrhosis. Method: 108 cirrhotic pts undergoing upper GI endoscopy for detection of oesophageal varices were included in this study: 34 pts Child-Pugh grade A, 60 pts grade B and 14 pts grade C. The diagnosis of liver cirrhosis was either posthepatic cirrhosis, alcoholic cirrhosis or mixed; Bilirubinostis fibrosis and posthepatic cirrhosis. Diagnosis of Hp infection was done by histopathology using antral and fundal biopsies, hp fast test and serologically by estimating Hp IgA antibody titers by ELISA (more than 20 U/ml). Estimation of serum NH3 using an enzymatic assay for all pts was done and the results were compared with that of 24 normal subjects as a control group.

Results: Serum NH3 is significantly higher in cirrhotics than in normal controls (P < 0.001) 86 cirrhotic pts with Hp +ve were similar to 22 Hp –ve with regard to age, sex, aetiology of cirrhosis and Child score. Hp +ve had significantly high NH3 in comparison with Hp –ve pts (P < 0.1). Also significant high NH3 in pts grade C compared with grade A (P < 0.01) and grade B (P < 0.01). Detection of Hp IgA antibodies by ELISA is a sensitive test as it was positive (more than 20 U/ml) in 70 pts with positive hp fast test and positive histopathology for Hp. There was a significant positive correlation between serum NH3 levels and Hp IgA antibody titers in cirrhotic pts (r = 0.9, P < 0.001).

Conclusion: Hp infection as ammonia producer can be considered as a risk factor for hepatic encephalopathy in cirrhotic patients and may warrants eradication.

1211 Effects of Canrenoate Potassium on Portal Hemodynamics in Patients with Compensated Liver Cirrhosis
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Aim: Long-term administration of spironolactone is reported to reduce portal pressure in patients. We examined the effects of acute administration of canrenoate potassium, an aldosterone antagonist, on portal hemodynamics in compensated cirrhotic patients using noninvasive duplex Doppler ultrasonography.

Methods: Baseline values were obtained in the fasting state, and then 200 mg of canrenoate potassium in 10 ml of saline solution was intravenously administered to 22 patients, whereas 10 ml of saline solution was administered as a control in 8 patients.

Results: The portal cross-sectional area, portal blood velocity and portal blood flow decreased by 5.3 ± 9.2, 10.4 ± 8.7% and 13.0 ± 12.4%, respectively at the nadir 60 min after administration and these decreases persisted until 120 min. Placebo did not affect these parameters of portal hemodynamics. Eleven responders who had a more than 10% fall in portal blood flow 50 min after administration had significantly higher levels of plasma aldosterone than non responders who had less than 10% fall. The reduction rate of portal blood flow was closely correlated with portal aldosterone level.

Conclusion: These findings suggest that aldosterone antagonist directly causes a reduction in portal blood flow probably through inhibition of aldosterone-induced vasoconstrictive action.

1212 Cytoprotective and Cytoinjurious Factors in Chronic Liver Diseases with Bleding Gastro-Oesophageal Varices
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Portal hypertension and subsequent bleeding gastro-oesophageal varices are frequent complications of chronic liver diseases. The pathogenesis of bleeding is still unclear, many factors are known to be involved. The aim of this study was to evaluate the possible role of some factors in the pathogenesis of bleeding varices, in attempt to study the integrity of GfT mucosa which depend on cytoprotective and cytoinjurious factors. We measured epidermal growth factor (EGF), prostaglandinE2 (PGE2), thromboxane (TXB2), 6-ketoPGF1, leukotrienes LT4C, LT4D and cyclic-AMP (c-AMP) in specimens from oesophageal, gastric and duodenal mucosa. This study included 10 healthy subjects (group I), 10 patients with portal hypertension without history of bleeding varices (group II) and 19 patients with portal hypertension and history of bleeding gastro-oesophageal varices (group III). Patients were classified according to Child-Pugh’s system into Child A (7), Child B (11), Child C (11). Homogenization, extraction and purification of the mucosal specimens were done to allow measurement of PGE2, TXB2, 6-ketoPGF1 and LT4C, LTD4 using ELISA technique, EGF and c-AMP were assessed by RIA method. The data revealed that tissue levels (ng/mg protein) of PGE2, EGF in group I were significantly higher than those of group II (p < 0.05) and III (p < 0.01). On the other hand significant increase in TXB2, LTD4 & LTD4 in group II and III compared to group I (p < 0.05, 0.01) was detected in all different biopsies. However c-AMP (mmol/mg protein) and 6-ketoPGF1 showed significant reduction in group II and III when compared to group I (p < 0.05, 0.01) in oesophageal specimens only, this could explain the predominance of bleeding from oesophageal varices than gastric varices. It was concluded that there is an imbalance between prostaglandins and leukotrienes in patients with chronic liver diseases, this may be related to alteration of arachidonic acid metabolism causing mucosal damage and ulceration initiating varical bleeding. The results may be of help in the effective intervention to control bleeding process, prevention of rebleeding and to choose the best line of treatment.
Dilatuzam in Low Flow Portal Arterialization for Liver Protection

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Ischemia during hepatectomy and liver preservation of transplantation causes liver damages. We performed portal arterialization (PA) to prevent injuries caused by ischemia, and have reported energy metabolism was maintained in PA, the rate of which was 25% in total hepatic blood flow (THBF). The advantage of decreasing the flow of PA is to facilitate operative procedures and control of bleeding, but it may reduce protective effects. We studied effects of dilatuzam in low flow PA for liver protection in mongrel dogs (12.2 ± 2.8 kg). Portal venous flow (PVF) and hepatic arterial flow (HAF) were measured by transit-time flowmeter. THBF was calculated at sum of PVF and HAF. Low flow PA was at the rate of 15% in THBF. The portal vein was clamped and the hepatic arteries were ligated under portacaval shunt. Then PA was performed with a roller pump from the right femoral artery to the portal vein through a 6Fr. tube for 120 minutes. Dogs were divided into two groups. The dilatuzam group (Group D, n = 4) was received with continuous administration at a dose of 10-5 mg/kg/min of dilatuzam intraportally from 30 minutes before PA, and control group (Group C, n = 7) with none. Aortic pressure (AoP), portal venous pressure (PVP) and hepatic venous pressure (HVP) were measured, and portal venous resistance (PVR) was calculated with them. Oxygen extraction of the liver was calculated with oxygen saturation and hemoglobin of arterial, portal venous and hepatic venous blood. Arterial ketone body ratio (AKBR), ATP and energy charge were indexed in energy metabolism. Histological findings after PA were examined in hematoxylin and eosin (HE), and thrombomodulin (TM) stain. After PA, AoP decreased, but PVF, PVP, and ATP extraction increased. Therefore, the results were observed in them between two groups. AKBR was 0.52 ± 0.24 in Group D at 120 minutes of PA, which was significantly (p < 0.05) higher than Group C (0.20 ± 0.10). ATP and energy charge showed a tendency to be high in Group D. In histological findings, cytosplasm was maintained in Group D on HE stain, and sinusoid function also was preserved in Group D on TM stain. In conclusion, our results suggest that administration of dilatuzam reduce liver damage due to ischemia in low flow PA.

Somatostatin Effectiveness in Serious Upper Gastrointestinal Hemorrhage

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The aim of this study was to estimate the effectiveness of intravenous infusion of somatostatin in patients with serious upper gastrointestinal hemorrhage (GH).

Methods: The study included 40 patients, 24 men and 16 women with mean age 55.4 ± 8.6 years, who were admitted to the hospital because of GH. Twelve of them suffered from gastric ulcer, 27 from duodenal ulcer and 1 had had erosive hemorrhagic gastritis. All the diagnoses had been proved endoscopically. Patients were divided randomly in two groups A and B. The group A received somatostatin 250 μg as bolus infusion initially, followed by 250 μg per hour for 5 days. The group B received cimetidine 200 mg intravenously every 6 hours for 7 days. Groups A and B were compared for the number of patients in whom the GH stopped with medical treatment a) the duration of hemorrhage b) the number of blood units transfused. Student t-test and x2 methods were used.

Results: GH stopped by medical treatment in 19 (95%) patients of group A and 14 (70%) patients of group B (p < 0.05). One patient from group A (5%) and 6 (30%) from group B needed surgical treatment. The GH stopped in 4.3 ± 0.98 hours in group A and 9.8 ± 1.31 hours in group B (p < 0.05). The patients of group A needed 2.65 ± 0.73 blood units and those of group B 4.86 ± 0.96 (p < 0.05).

Conclusion: Somatostatin administration reduced statistical significantly the need of surgical treatment, the duration of hemorrhage and the number of blood units compared with those of cimetidine.

Medical Treatment of Portal Hypertension Using Verapamil, Ketanserin and Propranolol Alone and in Combinations

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Bleeding from oesophagogastric varices and portal hypertensive gastropathy is a major cause of morbidity and mortality. No patients with portal hypertension disease. The aim of this study was to evaluate the potential synergistic effect of portal hypertensive agents with different modes of action, using combinations of ketanserin, verapamil or ketanserin and propranolol and to optimize the doses used for each drug to avoid the deleterious effects of these agents.

Fifty patients with portal hypertension due to cirrhosis and/or hepatic schistosomiasis were randomly allocated into four groups. Group I (12 patients) treated with verapamil 80 mg t.d.s. Group II (10 patients) treated with ketanserin 20 mg b.i.d. Group III (15 patients) treated with combination of verapamil 80 mg b.i.d. and ketanserin 20 mg b.i.d. Group IV (13 patients) treated with propranolol 40 mg t.d.s. and ketanserin 20 mg b.i.d. Clinical and laboratory assessment, upper gastrointestinal endoscopy, liver biopsy and splenic pulp pressure (SPP) measurement were done before and after one month of treatment. It was found that verapamil has produced significant increase in SPP. While, ketanserin with or without propranolol has produced significant reduction of SPP. However, addition of propranolol to ketanserin allowed the use of smaller and fixed doses of both agents avoiding the production of serious side effects. It was concluded that verapamil has no benefit in the treatment of portal hypertension. Ketanserin, in smaller doses, produced nearly the same effect of reduction of portal pressure without producing major side effect. Combination of ketanserin and propranolol proved to be better than each agent alone, particularly in comparison with propranolol. This allowed the use of smaller and fixed dose of each agent which minimized the side effects.

Effect of Verapamil on Portal and Splanchnic Hemodynamics in Patients with Advanced Posthepatic Cirrhosis Using Duplex Doppler Ultrasound

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Purpose: To assess the effect of verapamil (80 mg) oral administration on portal and splanchnic haemodynamics in patients with advanced posthepatic liver cirrhosis. Verapamil should be further investigated in the treatment of patients with advanced liver cirrhosis with prospective studies measuring portal and wedge hepatic pressure.

Acute Portal Venous System Thrombosis. Systemic Treatment with Heparin and Recombinant Tissue Plasminogen Activator (r-tPA) or Heparin alone In 10 Patients


Some authors have reported successful anticoagulation or thrombolytic therapy in some patients with acute mesenteric thrombosis. We report the efficacy of systemic r-tPA with heparin or heparin alone in the treatment of acute portal venous system thrombosis in 10 patients. Methods: 10 consecutive patients [9 men, 1 woman, mean age 51 years (27–71 years)] with acute extrahepatic portal vein thrombosis (5), left portal vein thrombosis (3) and superior mesenteric vein thrombosis (2) were studied. In all patients the ultrasonic diagnosis was based on the presence of an echogenic thrombus in the venous lumen. The cause of vein thrombosis was hepatic cirrhosis (4), pancreatitis (2), biliary tract infection (2), myeloproliferative disorders (1), protein C deficiency (2). Treatment with systemic infusion of r-tPA (100 mg over 2 h) with intravenous heparin were performed in 5 patients. The remaining 5 patients (asymptomatic or contraindication of r-tPA) were treated with continuous hepatic systemic infusion only (2) or subcutaneous low molecular weight heparin twice daily (3).

Results: In 3 of the 5 patients treated with r-tPA ultrasonography showed total resolution of the thrombus 7 days (1) and 15 days (2). The remaining 2 had partial resolution of the thrombus. In 4 of the 5 patients treated with heparin alone (3 in 3 with subcutaneous heparin) ultrasonography showed total resolution of the thrombus 7 days (1) and 30 days (3) later, and partial in 1. No bleeding occurred, one patient had hepatic cirrhosis. Whereas total resolution of the thrombus was achieved, 3 patients with hepatic cirrhosis had bleeding from oesophageal varices 1 month, 6 months and 26 months later.

Conclusions: The treatment with heparin can produce a complete recanalisation of acute portal vein system thrombosis. These data suggest that systemic r-tPA seems not increase the efficacy of heparin. A prospective study should be useful in order to confirm these results.
1221  
**Stapler Transsection of Oesophagus for Bleeding Varices**
S. Malinier, M. Drews, T. Kosliski, J. Smieja. Dept. of General Surgery University School of Medicine, Poznani, Poland

This study was performed to assess the efficacy of stapler transsections of the oesophageal haemorrhage from esophageal varices. Patients and methods. Between 1988 and 1995-25 patients (aged from 32 to 70 years) have been operated on. Hepatic cirrhosis was the main cause of variceal appearing. Child's hepatic failure evaluation showed stage A in 11 patients and stage B in 14 patients. According to the endoscopic variceal evaluation scale-stage I was observed in 2 patients stage II in 10 and stage III in 13 patients. Emergency indications for the surgical treatment were present in 3 patients, selective indications -- in 22 patients.

The operation technique. Consisted of introducing of a stapler device (ILS) by a gastrotomy to the subdiaphragmatic part of the oesophageus. Then a bend was tied around the oesophageal wall upon opened stapler working head. Finiring of the device formed a double layer end to end anastomosis transsecting and ligating the submucosal varices. When the vagal trunks couldn't be saved a pyloromyotomy was performed.

Results. There were 4 important rebleedings and 2 anastomotic leaks postoperatively. Five patients died, 3 of them were operated on in emergency during a massive haemorrhage. After one year 11 variceal relapses were observed.

Conclusions. 1. Stapler transsection of the oesophagus should be performed after the control of massive haemorrhage.
2. One half of the patients treated by this method have variceal reappearing during the first year.

1222  
**Portal Hemodynamics and Portal Hypertensive Gastropathy in Liver Cirrhosis**
M. Nakajma, I. Itabashi, T. Nakajma. Department of Internal Medicine, Saitama Medical School, Saitama, Japan; The Third Department of Internal Medicine, Saitama Medical School, Moroyama, Japan

We evaluated the association between portal hypertensive gastropathy and portal hemodynamics.

The subjects were 49 patients with liver cirrhosis complicated by esophageal varices in whom the clinical course were observed for 5 years. They were classified into the group who developed a splenorenal shunt during the course (11 patients) and that who did not (38). They were no complicating with hepatocellular carcinoma and no treatment of esophageal varices. Furthermore, they had no collateral circulation of the portal system except esophageal varices and spleno-renal shunt. Endoscopic findings of portal hypertensive gastropathy were divided into two criterias (mild and severe).

Incidence of portal hypertensive gastropathy during the course, the splenorenal shunt group (5-4) was lower than non-shunt group (18-27). Grade of portal hypertensive gastro-pathy (mild/severe) at the ending of observation were portal hypertensive gastropathy were the splenorenal shunt group (3:1) and non-shunt group (14:15). Since no difference were observed in the size of spleen, the diameter of the main trunk of the portal vein, or blood biochemical findings between the two groups during the observation period.

The development of the splenorenal shunt, i.e., the state of the development of the collateral circulation seems to be involved in the development of portal hypertensive gastropathy.

1223  
**Clinical Outcome Two Years after Implantation of a Tips for Recurrent Variceal Bleeding**
G. Schwantrier, A. Gebauer, J. Vavrik, M. Rohrmoser, C. Schnutka-Klibl, E. Brownstone, D. Tscholakoff, W. Weiss. Department of Internal Medicine and Department of Radiology, KA Rudolfstiftung, Vienna, Austria

Objective: At present there is only sparse data on midterm outcome after TIPS implantation. The role of TIPS in the management of portal hypertension thus remains controversial. The aim of this study was to assess clinical course 2 years after TIPS procedure.

Methods: The study was designed as a prospective, uncontrolled cohort study. 46 patients who underwent successful TIPS implantation were followed prospectively by clinical examinations, duplex sonography and portal venography. Mean follow-up in surviving patients was 24.1 + 9.0 months. The Kaplan-Meier method was used to calculate cumulative rates of survival, variceal rebleeding, shunt stenosis or occlusion as well as rates of primary and secondary rebleeding and 24-month mortality. Patients were stratified according to their CHILD-PUGH class. The Generalized Wilcoxon Test (Breslow) was performed to detect differences between strata.

Results: The cumulative rate of survival was 80.4% at 1 year and 70.2% at 2 years. The cumulative rebleeding rate was 12.4% at 1 year and 21.3% at 2 years. The mortality rate of episodes of variceal rebleeding was 22.2%. Variceal rebleeding was associated with shunt normalisation in all cases, and successful shunt revision resulted in control of the bleeding. The cumulative incidence of shunt stenosis or occlusion was 41.2% at 1 year and 54.9% at 2 years. 23.3% of patients without shunt abnormalities after 1 year developed shunt stenosis or occlusion during the second year after TIPS procedure.

Shunt revision was successful in 96.6% of cases. Secondary patency rate was 88.1% after 2 years. The risk of variceal rebleeding and shunt stenosis did not differ significantly between CHILD-PUGH classes.

Conclusions: Successful TIPS implantation results in a low rate of morbidity and mortality from variceal rebleeding over 2 years. TIPS creation in combination with careful follow-up examinations represents a safe and effective long-term treatment of recurrent variceal bleeding. Even in patients in whom no shunt abnormality was detected during the first year routine duplex follow-up examinations should be continued at 3-month intervals.

1224  
**Artificial Neural Network Analysis of Prognostic Variables for Prediction of Early Mortality after TIPS: Development and Validation**
F. Jalan, I. M. Ala-Korpela, Y. Hitton, D. N. Redhead, A. J. Stanley, A. Elton, J. D. Bell, P. C. Hayes. MMR Unit, Hammersmith Hospital, London; 2. Raahe Institute of Computer Engineering, Finland; 3. Department of Radiology, Royal Infirmary Edinburgh, UK; 4. Department of Medicine, Royal Infirmary Edinburgh, UK; 5. Department of Statistics Unit, Royal Infirmary Edinburgh, UK

Background and Aims: TIPS is followed by deterioration in liver function tests and early mortality in about 20-30% of patients. The purpose of this study was to develop and validate a model based upon artificial neural network (ANN) analysis of prognostic variables and compare this with a model based upon logistic regression (MLR).

Methods: 82 consecutive patients undergoing TIPS for variceal haemorrhage were studied. They were divided into two groups. Group I (56 patients) comprised the patients that were used to train the ANN and establish the model based upon the results MLR. Group II (16 patients) comprised the patients that were used in a blinded manner to assess the trained neural network and also the MLR.

ANN: A feed-forward fully-connected ANN with 10 hidden neurons (DynaMind) was trained with the 25 clinical variables related to clinical or biological data obtained from patients in Group I (input) to predict early mortality. MLR: Significant independent predictors (sodium; p < 0.001 and Pugh score p < 0.001) were combined using the formula: p = e^(-1 + e^0). The predicted probability of survival and x = 13.42 - 0.1429 X (sodium) + 0.445 X (Pugh score).

This network and the MLR model were then applied to predict early mortality of patients in Group II.

Results: Sensitivity and specificity for predicting early mortality were 100% and 87.5% for the ANN and 25% and 93.8% for the MLR.

Conclusions: This study illustrates that ANN analysis can be useful in the prediction of early mortality before TIPS is inserted, using routine clinical and biochemical parameters. Moving from the assessment of outcome by current methods towards ANN analysis will require similar comparisons, prospective evaluation and an open mind.

1225  
**Long Term Patency of Transjugular Intrahepatic Portosystemic Shunt (TIPS): A Surgical Prospective Experience**
D. Azoulay, D. Castaing, H. Bismuth, Hepato-Biliary and Liver Transplantation Center, Paul Brousse Hospital, Villejuif, France

Stent obstruction is the main argument against the use of transjugular intrahepatic portosystemic shunt (TIPS) for the long term management of portal hypertension. This prospective study analyses the impact of a stringent follow-up on the long term patency rate of TIPS performed by a surgical team. From November 1991 to December 1995, 122 attempts of TIPS placement were performed and successful in 115 cases (94%). Follow-up included Doppler ultrasonography at 15 days, 1 month, every 3 months and when patients (pts) developed recurrent complication. Transjugular venography was systematically performed at 1 and every 6 months, when Doppler ultrasonography was doubtful and when the pts developed recurrent complication. End points for follow-up were death, liver transplantation (LT) or survival with TIPS in place. Fifty nine pts (51%) had a follow-up below 6 months (27 deaths, 16 LT, 11 recent survivors with a TIPS). Five pts (49%) have a complete follow-up of at least 6 months with a TIPS in place (mean 20 ± 2 months, range 6 to 55 months) and are analysed here. The primary patency rate was 36/65 (64%) with a mean follow-up of 18.4 ± 5 months. Twenty four episodes of TIPS obstruction occurred in 22 pts: 12 within 2 months, 4 between 2 and 6 months, 8 after 6 months. Obstruction was treated successfully by TIPS dilatation in 2 cases and coaxial TIPS deployment in 20 cases, "two in one" stenting in 2 cases and by portacaval shunt. Actuarial primary patency rate of TIPS was 77%, 70%, 60%, 56% at 6, 12, 24 and 36 months respectively. Actuarial survival rate of TIPS was 96% at 6 months and 2 years. Actuarial survival was 90% and 83% at 1 and 2 years. Pts were followed prospectively and followed carefully, assisted patency rate comparable to portacaval shunt may be achieved. TIPS may be considered as a long term treatment of portal hypertension.
ERCP for Diagnosing Helicobacter and Helomuscos Pancreaticus

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This retrospective study presents the findings made in 8 patients (P) with helomuscos and 4 P with hemomuscos panreatitis (HP), which were treated at our hospital from 1988 to 496.

Results: Helomuscos: Causes for H were hemorrhangiosoma of the liver in 1 P; pseudo-anerysm of the hepatic artery in 1 P; cholecytitis in 3 P; liver biopsy in 3 P. All P showed colics, 6 P iriters, 1 P hematemesis and 3 P melena. Emergency endoscopy established hemorrhage from the papilla in 2 P with the front-view endoscope and in another 2 P with the lateral-view endoscope. Blood clots in the bile duct were observed in 1 P with ERCP. After EPT these were excrated from the bile duct with a Dormia-basked. Angiography produced evidence of hemomuscos in 2 P. As for therapy, embolisation failed in 1 P with arroion bleeding from the right hepatic artery. Embolisation was successful in 1 P with pseudo-anerysm of an intrahepatic liver artery. 3 P were operated on. H stopped spontaneously in 4 P (hemorrhangiosoma 1 P, state after liver biopsy 3 P). Hemomuscos panreaticus: 2 P showed chronic pancreatitis and 2 P a pancrea-ca. 4 P displayed melena, 2 P iriters and 1 P epigastric pain. Hemorrhage from the papilla was observed in 1 P with the front-view endoscope and in 4 P with the lateral-end view endoscope. ERCP demonstrated blood clots in the pancreatic duct and bile duct in 1 P, blood clots in the pancreatic duct in 1 P and blood clots in the bile duct in 1 P. Angiography produced evidence of HP in 2 P. As for therapy embolisation was successful in 1 P with chronic pancreatitis, fibrin-adhesive was successfully applied via endoscopy in the pancreatic duct of 1 P with pancreas-ca., and 1 P with chronic pancreatitis was operated on. Hemorrhage stopped spontaneously in 1 P with pancrea-ca.

Summary: 1. As for our patient group, the ERCP method for diagnosing helomuscos and hemomuscos panreatitis ranked higher than angiography. 2. No patient died as a result of helomuscos or hemomuscos panreatitis.

Management of Bile Duct Injuries of Laparoscopic Cholecystectomy with Endoscopic Sphincterotomy or Stenting: A Comparison

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Laparoscopic cholecystectomy (LC) has several advantages over open cholecystectomy, the rate of bile duct injury is higher in the former. Several endoscopic retrograde techniques were advocated in management. We compared the efficacy of sphincterotomy with temporary stenting. The 31 patients, referred after LC with the clinical diagnosis of bile leak between Jan 94, and March 95 were studied. At endoscopic retrograde cholangiography (ERC), the patients without leak (2), with retained stones (5), with bilomas requiring percutaneous drainage (1), and with transsection (2) were excluded. The remaining 21 (12 female, 9 male with median age of 51 and range 28-74) were randomized for two treatment arms: sphincterotomy or stenting. In 12/21, leak was from cystic duct remnant. Tannenbaum stents of 8.5 FR size (Wilson Cook Company, Winston-Salem, NC, USA) were used. A prior sphincterotomy was not perormed. All the patients were followed up until the resolution of the symptoms and signs in the hospital. Stented patients were called for a second endoscopy, two weeks after the first one. For the first four stented patients, ERC was performed before stent removal, to confirm the healing. For the remaining 17 patients, removal was without fluoroscopic guidance. Leaks eventually resolved in all. Symptoms resolved more rapidly in the stent group in comparison to sphincterotomy group: 1.9 ± 8-13 days (mean ± SD, range) vs. 2.9 ± 1.0, 2-5 days; p < 0.05. Mean hospital stay was also shorter in the stent group: 2.7 ± 0.1-4 days vs. 3.9 ± 1.1, 2-4 days, p < 0.05. No procedure-related complication occurred. Our study suggests that for the patients with isolated common bile duct injury or cystic duct leak, temporary moderate size stent (8.5 FR) insertion, across the site of the leak without ES is as effective as sphincterotomy and it offers faster improvement. Advantages of this new type of stent without side holes and, possibly, shorter stented periods require more studies.

Increasing Prevalence of Right-Sided Colon Polyps

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Introduction: Colorectal cancer is the second leading cause of cancer mortality in Europe. Actually, sigmoidoscopy is the most frequently used screening method. The aims of this study were 1. to determine in a large population the percentage of polyps which would be not detected by sigmoidoscopy; 2. to determine if there is an increasing prevalence of lesions isolatedly located in the right colon.

Material and methods: All the protocols of total colonoscopy (13,500) performed at Erasme Hospital from 1983 to 1994 were retrospectively reviewed. For patients with polyps, the following parameters were recorded: age, sex, location of the polyps, size of the polyps. Patients were divided in two periods: a) from 1983 to 1989; b) from 1990 to 1994.

Results: Polyps were detected in 1441 patients (period 1983-89) and in 1544 patients (period 1990-94). For the global population, the sex ratio male/female was 2/1 and the mean age was 61.9 y for males and 65.2 y for females, respectively. In the global series, 50.6% of patients had polyps located into the rectosigmoid (50 cm from the anal verge). The percentage of patients having polyps located only into the right colon or above the splenic flexure statistically increased between the 2 periods.

Sizes of the polyps were similar in the different segments of the colon.

Conclusions: The sensitivity of sigmoidoscopy to detect polyps is about 50%. Our data suggest a continuing trends in the prevalence of right-sided colon polyps. That must be taken into account in evaluation of cost-effectiveness of screening endoscopic method.

Colorectal Adenomas and Flow Cytometric Analysis

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Colorectal adenomas have a definite but unpredictable potential to become malignant. The currently accepted criteria are not sufficient to predict the transfor-mation through the adenoma-carcinoma sequence. During this sequence the genetic instability of the epithelial cells increases resulting in structural and numerical chromosome aberrations (aneuploidy). Flow cytometry permits a measurement of DNA-ploidy and S-phase fraction; it has been suggested to use data from flow cytometry to further define biologic behaviour of colorectal adenomas. Aim of the present study was to evaluate prevalence of aneuploidy among polyps endoscopically removed and to relate DNA-index and S-phase fraction to size, histological type, dysplasia and site of polyps. Flow cytometric analysis was performed on 44 polyps of patients who underwent endoscopic polypectomy (32 M, 12 F; mean age 65, range 35-89). In our series, prevalence of DNA aneuploidy was 18.2%; in detail results are summarized in the following table.

<table>
<thead>
<tr>
<th>Size</th>
<th>Histological type</th>
<th>Dysplasia</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 cm</td>
<td>tubul tubvill</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>1-2 cm</td>
<td>tubul tubvill</td>
<td>low</td>
<td>high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diploid (%)</th>
<th>94 (75)</th>
<th>86 (77)</th>
<th>82 (83)</th>
<th>58 (59)</th>
<th>100 (100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneuoploid (%)</td>
<td>100 (100)</td>
<td>100 (100)</td>
<td>100 (100)</td>
<td>100 (100)</td>
<td></td>
</tr>
<tr>
<td>S-phase</td>
<td>7.7</td>
<td>6.7</td>
<td>7.6</td>
<td>7.0</td>
<td>4.0</td>
</tr>
<tr>
<td>m ± SD</td>
<td>4.8 ± 2.2</td>
<td>3.0 ± 3.7</td>
<td>5.3 ± 3.2</td>
<td>2.7</td>
<td>5.0 ± 2.9</td>
</tr>
</tbody>
</table>

*p<0.05 (chi²-test)

Conclusions: Our preliminary data show that the prevalence of aneuploidy is significantly higher in distal polyps. Size, histological type and grade of dysplasia of adenoma were not related to data from flow cytometry.
in parts per million (ppm). Individuals presenting CH4 concentration > 50% than CH4 concentration in the surrounding air were considered CH4 producers.

Fifteen out 48 patients (31%) and 36/65 controls (54%) were found to be CH4 producers (p = 0.02). The amounts of CH4 detected in breath of patients and controls are shown in the figure below. A close correlation was found between the two breath tests (laser diode and chromatography) (r = 0.72) except if the latter failed to detect 4/15 (27%) of the CH4 producers revealed by the laser diode.

Data emerging from this study failed to demonstrate a higher frequency of CH4 producers in the colonic polyas patients as compared to normal controls.


1268 | Colonic Glutathione Content and Glutathione S-Transferase Activity in Patients with X-Linked A-Gammaglobulinaemia and Patients with Adenomas M.J.A.L. Grubben 1, C.C.M. vd Braak 1, W.H.M. Peters 1, J.W.M. vd Meer 2, F.M. Nagengast 1, 1 Dept. of Gastroenterology, University Hospital Nijmegen, The Netherlands; 2 Dept. of Internal Medicine, University Hospital Nijmegen, The Netherlands

X-linked agammaglobulinaemia (XLA) is a primary immunodeficiency disorder. Patients with XLA have a 30-fold greater incidence of rectal cancer compared to the normal population. Glutathione (GSH) and GSH-related enzymes are involved in the metabolism and detoxification of cytotoxic and carcinogenic compounds. The glutathione S-transferase (GST) activity in the mucosa along the gastrointestinal tract is reciprocal to tumour incidence in humans.

Aim and methods: we investigated GSH content and GST activity in normal colonic mucosa at three levels (ascending colon, sigmoid and rectum) of XLA-patients (n = 8, mean age 34 ± 2 years) and patients with colonic adenomas (n = 25, age 60 ± 12 years) and in normal healthy controls (n = 10, age 24 ± 3 yrs).

Statistical analyses were assessed by Mann-Whitney U test. 

Results: values are given as means ± SEM.

<table>
<thead>
<tr>
<th>GST (mM/mg/min/mg protein)</th>
<th>Asc. colon</th>
<th>Sigmoid</th>
<th>Rectum</th>
</tr>
</thead>
<tbody>
<tr>
<td>XLA</td>
<td>237 ± 17*</td>
<td>222 ± 19*</td>
<td>143 ± 17*</td>
</tr>
<tr>
<td>Adenoma</td>
<td>333 ± 23</td>
<td>316 ± 27</td>
<td>285 ± 19</td>
</tr>
<tr>
<td>Control</td>
<td>ND</td>
<td>321 ± 29*</td>
<td></td>
</tr>
</tbody>
</table>

* p < 0.03 XLA versus adenoma, *p < 0.02 versus XLA-rectum, *p < 0.01 control versus XLA, ND: not determined.

Conclusion: XLA-patients have a lower GST-activity at all levels in the colon compared to patients with adenomas. The rectal GST activity in XLA-patients also differs from healthy controls. In XLA-patients rectal GST activity is lower than the proximal GST activity. The increased risk of colorectal cancer in XLA-patients might partly be explained by a lower detoxification capacity in the mucosa.

1279 | p53 and Proliferating Cell Nuclear Antigen as Prognostic Factors in Colorectal Cancer S. Knezevic-Janis 1, S. Cerovic 1, Lj. Rabrenovic 1, Z. Bogdanovic 1, V. Cuk 1, V. Todoric 1, A. Skaro-Milic 1, J. Dimitrijevic 1, V. Tatic 1, 1 Institute of Pathology, Military Medical Academy, Belgrade, Yugoslavia; 2 Institute of Medical Research, Belgrade, Yugoslavia

In light of the role of p53 in cell proliferation, we were interested in markers of the cell cycle whose expression might be correlated with p53 protein overexpression. Formalin-fixed paraffin embedded surgical specimens of 29 CC of different Duces's stages were analysed. Nuclear p53 protein overexpression in tumours and proliferative activity of tumour by identifying proliferative cell nuclear antigen (PCNA) were detected by immunohistochemistry. p53 protein overexpression was identified in 48.2% CC and found to correlate with stage of disease (22.5, 40.0 and 80.0% in Duces A, B and C stages respectively), site of tumor (52.38% p53 positive tumor in left colon versus 37.5% positive CC in right colon) and nonmucinous histological type (61.9% of p53 positive tumor in nonmucinous e.g. 25.0% in mucinous tumor). Nuclear immunoreactivity for P53 to a very weak degree was expressed in 93% of CC. High PCNA distri- tion score (3 > 50% PCNA positive nucleus) was more frequently found in p53 positive CC (71.42%) and in Duces' C stage of disease (all 10 cases) and the difference was statistically significant. Our results suggested that overexpression of p53 protein and higher PCNA score in later stages of CC indicate higher proliferative rate of tumor and therefore may have prognostic implications. Our results also indicate that mucinous defer from nonmucinous CC as well as proximal defer from distal CC in their genetic lesions.

1280 | Colorectal Cancer: Prognostic Factors and Chemotherapy de Waziers 1, L. Gervot 1, A. Pohli-Leszczowska 2, V. Carrière 3, P.H. Cugnenc 2, A. Berger 4, F. Carrot 5, P. Beaume 6, 1 INSERM U75, CHU-Necker, 75732 Paris Cedex 15, France; 2 ENSAT, 31076 Toulouse, France; 3 INSERM U178, 94807 Villejuif Cedex, France; 6 Hôpital Larnarc, 75007 Paris, France

Colorectal cancer is one of the most frequent causes of death by cancer in developed countries. Until now, few prognostic factors for colorectal cancer have been recognized and chemotherapeutic agents do not demonstrate much significant progress in the treatment of this disease. Epidemiological studies suggest that colorectal cancer can be attributed, at least in part, to carcinogens and mutagens present in diet and environment. The relevant binding of the xenobiotics or their reactive metabolites to DNA is believed to initiate chemical carcinogenesis. Using a HPLC-post labelling method, we investigated DNA adduct levels in control colons from patients without colorectal adenocarcinoma and in nonmucosal and tumoral tissues from patients with colorectal adenocarcinoma. The DNA adduct level is significantly higher (p < 0.001) in nontumoral than in control or tumoral colon samples. For the first time, we demonstrated in humans that the presence of numerous adducts in colonic mucosa is associated with colorectal cancer, and that the frequency of these adducts might be a finding of great interest.

Since human colorectal tumors are insensitive to most chemotherapeutic agents there is a need for the discovery of new drugs that would show activity against this disease. We compared the drug-metabolizing enzyme expression in human tumors and in several differentiated populations isolated from the human colon carcinoma cell lines HT-29 and Caco-2. We showed that these cells could be used as models for candidate anticancer screening. Moreover, to increase the sensitivity of these cells to anticancer agents for which the metabolism is known we began to transfect these cells with the cDNA of the P450 implicated in the formation of the antineoplastic metabolites. This strategy, if it appears effective, could lead to possible gene therapy.

1281 | Prognosis of Mucinous Colorectal Cancer D. Lomanto, G. Dalsasso, A. De Luca, F. Giacozzetti, M. E. Zarba, A. Salvio, L. De Angelis, G. Memmii, C. Tattarelli, V. Speranza. 1 Clinica Chirurgica-University of Rome “La Sapienza”, Italy

Purpose of the Study was to compare recurrence and survival rate of patients with adenocarcinoma (ADK) and mucinous carcinoma (MC) of colon rectum.

Methods: We studied retrospectively 380 pts. operated for colorectal cancer. We classified the pts. in two groups: in the first 36 pts. (9.5%) with mucinous carcinoma (MC), defined as a neoplastic lesion of the mucosa with elevated present of mucin (60% of the volume), and in the second group 344 pts. (90.5%) with adenocarcinoma (ADK). We analyzed in these pts. the following parameters: age, sex, localization, stage, resectability, recurrence disease, therapies, and long term survival. Mean age was 54 yrs. in MC group and 63 yrs. in ADK group.

Results: We observed more frequency rectal localization vs. other colonic sites in both groups (50% in MC group vs. 90.5% in ADK group). As for staging disease according to Duke's classification, in the MC group, the incidence of stage A was 8% and of stage B-12% in Mc group vs. 27.8% for ADK group (p < 0.05). Among the pts. with recurrent disease (correcting the data for the perioperative mortality and excluding the pts. in stage D), we found that local recurrence rate was 72.7% in MC group and 46.5% in ADK group. The metastasis in MC group was 9% and 45.7% in ADK group, while the presence of both (metastasis + local recurrence) was 18.2% in MC group and 20% in ADK group. Overall survival rate at 5 yrs. was 45% for the MC group and 56% for the ADK group.

Conclusion. Our study show a different biological behaviour between MC and ADK especially for the local recurrence. This behaviour, for us and other Authors, is related to the presence of elevated quantity of mucin.

1282 | Multivariate Analysis of Prognostic Factors in Resected Colorectal Cancer: A New Prognostic Index A. Guerra, F. Bordi 1, F.J. Jiménez 2, J.M. Martínez-Péfluela 1, B. Larrinaga 1, D. Gastroenterology, H.V.C. y H.N., Pamplona, Spain; 1 Dept. Pathology, H.V.C. y H.N., Pamplona, Spain

Aims: The aims of the present study is to analyse different clinico-pathological variables of colorectal cancer to assess their prognostic value in order to elaborate a prognostic index helpful to select patients for adjuvant therapy.

Material and Methods: 108 surgically treated patients of colorectal cancer with controlled 5-year survival were studied. Eighteen clinico-pathological variables y new biological parameters for image analysis (DNA or tumoral ploidy, proliferating cellular nuclear antigen PCNA and nuclear organizing regions adEA) were analysed. Statistical analysis: Cox regression method.
Prognostic index has been calculated as beta regression coefficients of independent variables.

Results: A final multivariate analysis model (RR = relative risk) included: elevated CEA (RR 8.1), No CEA (RR 3.7), C1-C2 stages (RR 2.4) D stage (RR 6.9) histological grade III (RR 3.9) lymphatic invasion (RR 4.7) and pancytopenia (RR 3.7).

Prognostic index (PI) scoring: CEA postoperative: Normal = 0/No CEA = 2/CEA Elevated = 3 Staging: A-B1-B2 = 0/C1-C2 = 1/0 = 3/0 Plodixoid tumors = 0/Neoploid tumors = 2 Histological grade: I = 0/I = 0/II = 2 Lymphatic invasion: Absent = 0/Presen = 2

Risk groups: Low (PI 0-5), Moderate (PI 6-9) and High (PI > 10). After stratifying tumoral stages and grades according to PI different risk subgroups in B2 and C1-C2 stages and in the three differentiation grades could be established with significant differences concerning 5-year survival.

Conclusions: 1. The new prognostic index improves the prognostic information provided by conventional staging in B2 and C1-C2 stages due to the possibility of establishing subgroups of different risk and 5-year survival. 2. Different risk subgroups are also determined in each histological grade according to PI with significantly different 5-year survival. Therefore this new index improves the prognostic significance of histological grade as an independent variable. 3. This PI can be helpful to improve prognostic information and allows a better selection of patients for adjuvant therapy.

1283
Prognostic Value of Lymphocytic Infiltration and Tumoral Growing Margin in Surgically Treated Colorectal Cancer
A. Guerra, F.J. Jiménez, F. Borda, B. Larrinaga, J.M. Martinez-Peñauela, C. Jiménez. Hospital de Navarra, Pamplona, Spain

Peritumoral lymphocytic infiltration and the type of tumoral growing margin have been considered of prognostic value by some authors in colorectal cancer, but results still remain controversial. The aim of the present study is to evaluate lymphocytic infiltration and tumoral growing margins in a series of colorectal adenocarcinomas, analysing possible influence upon 5 years survival.

Material and Methods: 108 surgically treated colorectal adenocarcinomas were included in the study. Kaplan-Meier and Logrank tests were used for statistical analysis.

Results: 5 Years survival

<table>
<thead>
<tr>
<th>Lymph infiltration</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>No lymph infiltration</td>
<td>58.6 ± 5.2%</td>
</tr>
<tr>
<td>Moderate</td>
<td>67.4 ± 7.2%</td>
</tr>
<tr>
<td>Severe</td>
<td>64.7 ± 7.8%</td>
</tr>
<tr>
<td>Expanding margin</td>
<td>58.6 ± 5.2%</td>
</tr>
</tbody>
</table>

Conclusions: 1. Colorectal carcinoma 5 years survival rates are higher when lymphocytic infiltration is moderate or severe, but statistical significance is not reached. 2. Survival rate decreases with the presence of an infiltrating tumoral growing margin with statistical significance. 3. Evaluation of lymphocytic infiltration and tumoral growing margin supplies prognostic information in surgically treated colorectal carcinoma.

1284
Peritoneal Carcinomatosis (PC) in Colorectal Cancer (CRC) Patients: Factors Influencing Survival
V. Durand1, E.D. Dorval1, P. Boullier2, G. Regimbeau2, Z. Bencherif1, J. Viguier1, P. Garraud, E.H. Metman1, G. Calais3. Services de Gastroentérologie, CHU, F 37044 Tours; Services de Chirurgie Viscérale et de, CHU, F 37044 Tours; Services de Radiothérapie, CHU, F 37044 Tours

In our institution for PC with CRC.

Patients and methods: 23 patients (15 men, 8 women) aged 64 years (extr: 24–83) were followed from November 1993 to January 1996. In all cases PC was diagnosed either macroscopically (clinical or CT scan assessment) or by biopsies during surgery. PC and CRC diagnosis were synchronous in 7 patients and metachronous in 16 with a mean delay between diagnosis of 14.9 months (extr: 0–137 months). CRC was located in the sigmoid colon in 13 patients, descending colon 2 patients, transverse colon 2 patients and right colon 2 patients. One patient had two synchronous CRC: Eight occlusions were diagnosed in 7 patients and required a surgical treatment in 3 cases. Survival, calculated since PC diagnosis, was analysed according to age, gender, OMS, CEA, histological grade, staging, resection, liver metastasis, ascites presence or occurrence and PC treatment (chemotherapy N 8, palliative surgery N 9, corticosteroids N 11, symptomatic treatment N 4).

Results: In these cases 28% and 78% at 1 and 2 years respectively and median survival was 5 months. Gender, age, presence of liver metastasis, CRC resection and resection and occlusion had no influence on survival. In contrast, a better survival was observed in patients without ascites or good performance status and patients treated by chemotherapy or palliative surgery.

1285
Overexpression of p53 Protein in Colorectal Carcinoids
Cheng Jhy-Young, Lin Jih-Chang. Division of Colorectal Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, R.O.C.

Purpose: The overexpression of p53 protein is considered to be a potential marker for the transition to advanced stages of tumor progression in many human cancers. The frequency and prognostic significance of such events in colorectal carcinoid tumors remain unknown.

Methods: Thirty-one paraffin-embedded specimens of colorectal carcinoid tumor were studied by immunohistochemical staining. The association of p53 with tumor size, tumor size, invasion level, tumor stage, DNA pattern and patient survival were analysed.

Results: p53 protein was detected in 5 (16%) of 31 colorectal carcinoid tumors. There was a correlation between p53 expression and tumor size, tumor size, stage and DNA ploidy (p = 0.05). In addition, p53 overexpression indicated a poor prognosis in survival (p < 0.001).

Conclusions: Although the overexpression of p53 protein is uncommon in colorectal carcinoid, the expression has an association with clinicopathological criteria and may be used as an associated parameter to predict patient survival.

1286
Prognostic Value of P-53 Protein in Surgically Treated Colorectal Carcinoma
A. Guerra, F.J. Jiménez-Pérez, F. Borda, B. Larrinaga, J.M. Martinez-Peñauela, C. Jiménez. Hospital de Navarra, Pamplona, Spain

P53 gene alteration with abnormal expression of P53 protein has been reported in several malignant tumors. In some studies this abnormal expression has shown an independent prognostic value. The aim of the present study is to determine P53 protein expression in a series of surgically treated colorectal carcinoma, analyzing its relation with overall 5 years survival and survival according to tumor stage and differentiation grading.

Material and Methods: 75 surgically treated colorectal adenocarcinomas were included in the study. Anti-P53 antibody (Dako) was used for evaluation of P53 protein expression. Kaplan Meier and Logrank tests were used for statistical analysis.

Results: Overall 5 years survival was 63.12 ± 4.8% for the whole series. Depending on P53 protein expression, results were as follows:

<table>
<thead>
<tr>
<th>P53+ (n=31/41%)</th>
<th>P53- (n=44/59%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>48 ± 4.9%</td>
</tr>
<tr>
<td>Dukes A/B1/B2</td>
<td>62.8 ± 12.7%</td>
</tr>
<tr>
<td>Dukes C/D1/D2</td>
<td>33.6 ± 15.8%</td>
</tr>
<tr>
<td>Grade I-II</td>
<td>63.4 ± 10.2%</td>
</tr>
<tr>
<td>Grade III</td>
<td>0%</td>
</tr>
</tbody>
</table>

Conclusions: 1. Colorectal adenocarcinomas with P53 protein expression have poorer prognosis and lower 5 years survival than tumors without this protein, although statistical significance is not achieved. 2. In poorly differentiated tumors, 5 years survival is significantly lower when P53 protein is present. 3. P53 protein determination might be useful in colorectal cancer in order to improve prognostic information.

1287
Does Tumor Heterogeneity Influence the Staining for P53 in Colonic Adenocarcinomas and Their Lymph Node Metastases?
Ataoðlu Öµür, Çekil Betül, Kayhan Buðak, Gönül Ahmet, GÜTF, Ankara, Türkiye

A high percentage of colonic carcinomas show positive staining for p53 immunohistochemically. Using a polyclonal antibody for p53 (CM1-Novacastlab.) which is specific for wild and mutant forms, we investigated whether or not the tumor heterogeneity significantly affects the staining of the colonic adenocarcinomas and their lymph node metastasis with p53 antibody. In 40 colon carcinoma specimens containing 61 colorectal adenocarcinoma with lymph node metastases, positive staining was found in 37 carcinomas. Three cases (2 well-differentiated mucinous adenocarcinomas and 1 signet-ring cell carcinoma) showed no positive staining for P53. In these cases, a large number of lymph nodes also did not stain. One poorly differentiated adenocarcinoma showed positive staining for the tumor but the lymph node metastasis of the case was not positive for P53. The results show that the tumor heterogeneity does not significantly influence the staining of colon adenocarcinomas and their
positive lymph nodes, and p53 expression of the colonic adenocarcinomas is retained in their lymph node metastases.

**1288 DNA Ploidy Pattern and P53 Expression in Some Colonic Lesions in Egypt**
Department of Clinical Tropical Medicine, Surgery, Molecular Biology, Oncology and Pathology, Ain Shams and Cairo Universities, Cairo, Egypt.

**Background Aim:** The assessment of premalignancy and increased cancer risk is rather difficult. Ulcerative colitis and colonic adenomas represent important premalignant conditions in the colon. The increasing incidence of colonic cancer in these patients made the search for detection of premalignancy of great value. This study was designed to determine DNA ploidy pattern and P53, the tumor suppressor gene, expression in some colonic lesions as ulcerative colitis and colonic adenomas in Egypt.

**Patients & Methods:** DNA ploidy and S phase fractions were assessed by flow cytometry together with detection of P53 by RT-PCR-SSCP method in colonic and rectal biopsies from 18 patients with ulcerative colitis, 8 patients with colorectal adenomas and 10 patients with colorectal carcinoma in addition to 20 patients with infective and nonspecific colitis as control group.

**Results:** Diploid histograms were found in 12 ulcerative colitis cases, all colonic adenoma cases and all control subjects. All colorectal cancer cases and 6 patients with ulcerative colitis exhibited DNA aneuploidy. Out of these 6 ulcerative colitis cases, four showed low grade dysplasia and two cases were indefinite for dysplasia. S phase fractions were highest in colorectal cancer (18.4 ± 6.4%) followed by ulcerative colitis (17.4 ± 5.0%) compared to colorectal adenoma (14.3 ± 3.9%) and control subjects (13.8 ± 2.1%) and a correlation was found between S phase fraction values and disease duration but not with disease activity in ulcerative colitis. P53 expression was detected in 6 (60%) of colorectal cancer and one case of ulcerative colitis all of which showed aneuploidy. Follow up of the 6 cases with ulcerative colitis showing aneuploidy without or with P53 expression (1993–1996) revealed early neoplastic transformation in one case. Conclusion: (1) DNA aneuploidy and P53 could be useful biomarkers of colorectal cancer risk and have a prognostic potential. (2) DNA aneuploidy and P53 can be valuable complement to endoscopy and histological examination in colonic cancer surveillance especially in high risk individuals.

**1289 Long-Term Outcome Following Surgery for Malignant Large Bowel Obstruction**
First Dept. of Surg., Nippon Medical School, Tokyo, Japan.

This study determined the factors causing poor prognosis of patients with obstructing colorectal cancer. Seventy-six patients with bowel obstruction who had undergone curative surgery were studied in comparison with 1,039 patients of no bowel obstruction. Postoperative complications (control cases) in the period from 1976 to 1994. Poor prognosis in survival was obtained after surgery for obstructing colorectal cancers (p = 0.025, log rank test). Tumour differentiations were not so poor in obstructing colorectal cancers (p = 0.181), and outcome of poor-prognostic obstructing colorectal cancers was not related to tumour location, poor differentiation and vascular invasion. Tumour stage in Dukes’ classification of obstructing colorectal cancer was more advanced than control cases (p = 0.004). In the respect of tumour stage, there were no significant difference in survival between obstructing and control cases of stage A and B in Dukes’ classification (p = 0.620 and 0.904, respectively). On the other hand the 5-year survival rate in stage C obstructing cancers was 37 per cent against 57 per cent of survival rate in stage C control cases (p = 0.065). Thus it was suggested from these results that lymph nodes metastasis was most influential factor for poor prognosis in obstructing colorectal cancer. To dissect lymph nodes adequately, we attempt to remove intraoperatively locates in obstructing bowel by suction or lavage through colon with saline. These intraoperative procedure led to improve in survival compared with control (p = 0.886, log rank test).

**1291 CT Evaluation of the Resectability of Locally Advanced Rectal Cancer after Radiation and Chemotherapy**
N. Momot, J. Solovoyova, V. Bereznyk, Ukraine.

**Purpose:** To determine accuracy of CT in evaluating the resectability of locally advanced rectal cancer in patients who underwent radiation and chemotherapy (5FU).

**Materials and Methods:** 128 patients with locally advanced rectal cancer were studied. CT both before and after postoperative treatment. Optional distention and better visualization of rectal wall were achieved by wall dilation distention of rectum with air insufflation. CT findings were compared with surgical and histopathological specimen.

**Results:** Postoperative histological confirmed complete tumor disappearance in 26 patients, considerable reduction of tumor mass (more than 50% of initial size) – in 88 patients. 106 patients of the both group underwent sphincter-saving resection and 8 – abdomino-perineal resection. Remaining 14 patients had minimal or no effect and were identified as inoperable. CT results were correct in 105 cases (82%), equivocal – in 15 cases (12%) and incorrect – in 8 patients (6%).

**Conclusion:** CT has a high diagnostic value in determining the efficacy of preoperative radiation and chemotherapy and evaluating subsequent resectability in patients with locally advanced rectal cancer.

**1292 Safety of DVT-Prophylaxis with Enoxaparin vs. Dextran-70 and Heparin in Digestive Surgery-Play-The Winner Designed Studies**
Harstad County Hospital, Norway.

The aim was to compare the safety of DVT-prophylaxis with enoxaparin vs. dextran-70 and unfractionated heparin in digestive surgery.

**Materials:** In the first study comparing enoxaparin and dextran-70, 327 patients undergoing digestive surgery in two Norwegian hospitals were included. In the second study, comparing enoxaparin and heparin, 183 patients from two other hospitals were enrolled.

**Methods:** In a Play-the-Winner (PTW) designed study the treatment of any next patient will depend on the outcome of the previous. If successful, the next patient receives the same treatment, if not, the comparative regimen will be given. Excessive bleeding according to specified criteria, severe adverse reaction, clinically detected DVT or pulmonary embolism (PE) were criteria for classification as "loser." The PTW-design will allocate most patient to the superior treatment. The main variable in PTW studies is the number of consecutive patients receiving the same treatment.

**Results:** In the first study 200 patients were allocated to enoxaparin and 127 to dextran-70 (60% < 0.05). The rate of success was identical in the enoxaparin group and 74.8% in the heparin group. The survival analysis confirmed superiority of enoxaparin (p < 0.01). In the second study enoxaparin had a success rate of 80% and unfractionated heparin 81%. The survival analysis showed no significant difference between ulcerocolitis patients treated with enoxaparin vs. heparin.

**Conclusion:** From a safety point of view DVT-prophylaxis with enoxaparin was found to be superior to dextran-70 and clinical equal to unfractionated heparin in digestive surgery.

**1293 Intraluminal Prosthesis (SBS-Tube) Enhances Healing in One Layer Colon Anastomoses**
Dept. of Surgery A, Odense University Hospital, Denmark; Biomedical Laboratory, Odense University, Denmark; Dept. of Anatomy C, Aarhus University, Denmark; Copenhagen Wound Healing Center, Bispebjerg Hospital, Denmark.

In one layer colonic anastomoses the risk of anastomotic insufficiency is approximately 6.2% (Sarin S, Lighthood RG. Br J Surg 1989; 76: 495–5). Several factors impair healing in anastomoses. Among these are local ischemia, infection, insufficient adaptation of the cut ends and insufficient surgical technique. Purpose: To compare healing in one layer colonic anastomoses performed with or without a new intraluminal prosthesis (SBS-tube). Method: In 16 pigs the sigmoid colon was transected and an anastomosis was performed ends with extramucosal continuous suturing. In the SBS-tube group (n = 8) the colon was slipped over the SBS-tube and the ends were approximated before suturing. The integrity and position of the SBS-tubes were examined post operatively by x-ray every second hour. After 96 hours the anastomoses were tested for leakage and breaking strength, and histology was performed. Measurements of tissue oxygen tension in the colonic wall at the anastomotic line, ± 1 cm, and ± 5 cm were performed after suturing and after 96 hours. Results: 75% of the tubes dissolved in less than 2 hours. Histology (see Figure): The SBS-tube group had a significantly better structure of layers (L) and mucosal epithelial covering (E). Similarly a tendency in favor of the SBS-tube group was found in tissue gap (A) and inflammation (I) but not in breaking strength (B) and amount of granulation tissue (G). Oxygen tension in the Anastomotic line was also in favor of the SBS-tube group.

**Conclusion:** The SBS-tube facilitates the sewing of the anastomosis and seems to enhance healing parameters and restoring normal histology. This might be due to a better apposition of the cut ends and to a reduced suture tension.

**1294 Analysis of Low Density Lipoprotein Receptor (LDLR) mRNA Expression by Polymerase Chain Reaction Assay in Colorectal Cancer**
M. Notomioli, M.G. Canuso, A. Cavallini, M. Bianco, A. Di Leo.
Lab. Biochemistry IPRSS "S. De Bellis" Castellana Grotte (Bari) Italy.

Proliferating tumour cells express increased numbers of LDLR molecules on...
their surface which enable them to bind and take up cholesterol-delivering LDL particles for growth and replication. Recently, the LDL and its mRNA have been detected in 19 samples of human colon carcinoma [1]. On the contrary, in the previous studies we have demonstrated the absence of LDLR only in 17% of S3 specimens of human colon adenocarcinoma (CRA) [2].

Aim of this preliminary study was to verify whether the absence of LDLR in most neoplastic samples was due to the loss of its transcript.

Materials and Methods: Twenty CRA neoplastic samples without LDLR protein, previously evaluated by ELISA method, were studied. LDLR mRNA expression was investigated by the reverse transcriptase polymerase chain reaction method (RT/PCR), and the relative PCR products by HPLC. Results: Both LDLR and LDLR mRNA samples, while LDLR mRNA (1.34 pg/μg total RNA), but not LDLR, was found in the remaining 7 CRA samples.

Conclusions: The LDLR absence was due to the loss of its mRNA in 65% of the cases (13/20). In the remaining 35% of cases (7/20), the absence of LDLR with high levels of LDLR mRNA may be due to a block of the translation process, with a subsequent store of mRNA within cells. Further studies will be required to determine the molecular events regulating the LDLR metabolism in neoplastic colorectal mucosa.


1295 Polyamine Levels and Polyamine Oxidase Activity in Human Colorectal Cancer
M. Linsalata, B. D’Atoma, A. Di Leo. Lab. Biochemistry, IRCCS “S. de Bellis” Spec. in Gastroenterologia Castellana G. (BA) Italy

Polyamines (putrescine, spermidine and spermine) are low molecular weight amines required for normal cellular growth. Polyamine biosynthesis is known to increase with mitogenesis, and elevated polyamine concentrations are found in tumour tissues including gastrointestinal mucosa [1,2]. As regards the mechanisms maintaining cellular polyamine levels, the regulation of biosynthesis has been already clarified, but little is known about the regulation of their degradation pathway. During catabolism, N₂-acetylated polyamines are converted back to spermidine and putrescine by polyamine oxidase (PAO). Therefore, this enzyme seems to play an important role in modulating polyamine levels in the actively proliferating tissues such as neoplastic ones. In order to obtain more information about the metabolism of polyamines in human colorectal cancer, our aim was to evaluate polyamine levels and PAO activity in colorectal adenocarcinoma (CRA) and in surrounding mucosa. Materials and Methods: Twenty-five patients (18 males and 7 females; mean age 69 yrs, range 33-87) with CRA entered the study. Polyamine levels and PAO activity in neoplastic colorectal tissue and in surrounding uninvolved mucosa were analysed by HPLC [3,4]. Data were assessed by Student’s-t test for paired data. Results: (polyamines are expressed as nmoi/g weight tissue, PAO activity is expressed as nmoi of putrescine formed for 30 minutes for mg of tissue protein). M ± p < 0.01

<table>
<thead>
<tr>
<th>Put</th>
<th>Spd</th>
<th>Spm</th>
<th>Total</th>
<th>PAO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplastic tumor</td>
<td>32 ± 2.1*</td>
<td>297 ± 170*</td>
<td>531 ± 353*</td>
<td>859 ± 533*</td>
</tr>
<tr>
<td>Normal mucosa</td>
<td>13 ± 5.4*</td>
<td>188 ± 124</td>
<td>483 ± 343</td>
<td>664 ± 468</td>
</tr>
</tbody>
</table>

Conclusions: Higher polyamine levels and a lower PAO activity were found in CRA samples than in normal mucosa. This suggests that PAO in neoplastic tissue is no more able to modulate polyamine levels and induces an abnormal polyamines accumulation.


1296 Immunohistochemical Studies on the Histogenesis of Colorectal Carcinoma Induced by DMH
T. Horio, M. Onda, Y. Otsawa, T. Okuda, Y. Suniyama. The Third Department of Surgery, School of Medicine, Toho University, Tokyo, Japan

To elucidate the mechanism of the development in human colorectal carcinoma, we studied the kinetics of neuroendocrine cells in the tissue of experimentally-induced colorectal carcinoma in rats by DMH administration.

Materials and Methods: Thirty-six-week-old male rats (Donryu strain) were injected subcutaneously in the hip with DMH, at a dose of 20 mg/kg, once a week for 20 weeks continuously.

Results: We sequentially observed the evolution of colorectal carcinoma by endoscopic examinations. The process of the evolution was classified into 4 types; small elevation type, flat elevation type, dome type, and elevation type with adjacent normal mucosa.

Neuroendocrine cells such as endogenous peptides and biogenic monoamine as well as in normal colorectal mucosa were found in response to the tumor progression in each type. No physiological roles of these cells has been evidenced so far.

Conclusion: It is highly suggested that trophic action of gastrointestinal hormones, which is known in normal gastrointestinal mucosa, possibly effects to the progression of the colonic carcinoma induced by DMH.

1297 Immunohistochemical Study of Peptide and Amine Cells in Human Colorectal Cancer
Y. Ozawa, M. Onda, T. Horio, T. Okuda, Y. Suniyama. Third Department of Surgery, School of Medicine, Toho University, Tokyo, Japan

Aim: In order to clarify the histological occurrence, differentiation and development of colorectal cancer, the incidence and degree of peptide and amine cells in colorectal cancer tissue were studied relationship with its growth and progress.

Materials and Methods: The subjects consisted of 220 cases colorectal cancer surgically removed in our department. Immunohistochemical activities were stained by streptavidin-biotin (SAB) technique using formalin-fixed, paraffin-embedded tissue sections Haematolysin-eosin-stained specimens were used for histological classification.

Results: In normal colorectal tissue, many peptideY-, moderate numbered glucagon-immunoreactive cells and many glucagon-immunoreactive cells were found. The other hand well- and moderately-differentiated adenocarcinoma tissue contained moderately numbered peptideY- and many glucagon-immunoreactive cells. Tissue of poorly differentiated regions contained small numbered peptideY- and many glucagon-immunoreactive cells. Peptide and amine cells were recognized significantly in the following cases: high blood vessel invasion, lymphatic invasion cases, high lymph node metastasis, positive cases of peritoneal dissemination and liver metastasis. Peptide cells appeared highly in a considerably deep focus infiltrating through the invasion.

Conclusions: Although the precise meaning of peptide cells in the focus of colorectal cancer has remained obscure, it is suggested that peptide and amine cells may be secreted from colorectal cancer tissue, and then has strong influence on the differentiation and development of colorectal cancer.

1298 Diagnostic and Prognostic Evaluation of Adenosine Deaminase Activity in Human Colorectal Tumors

Colorectal cancer is one of the most frequently occurring cancer in humans and there is an attempt to devise more sensitive tumor markers. High activity of adenosine deaminase (ADA) have been found during rapid growth state and/or after stimulation by growth factors. The study included patients with: colorectal cancer (10), polyps (8), resected colon carcinoma (4), patients without pathological manifestation during colonoscopy (6). The ADA activity (U/g prot.) was determined in endobioscopic samples obtained from carcinoma or polyp adjacent tissue, anastomoses after carcinoma resection and healthy tissue farther from lesion. The ADA activity was especially high in carcinoma adjacent tissue, i.e. endoscopically looking healthy (65.49 ± 24.33 vs healthier 10.15 ± 0.18; p < 0.001). It means that ADA is important as early marker of abnormal proliferation, to discriminate normal and malignant colon epithelium and point to radical surgical resection. Estimating ADA activity from polyp adjacent tissue, the same trend was shown but significantly lower than in carcinoma (26.92 ± 8.92 vs 14.28 ± 5.87; p < 0.05). The enzyme activity from anastomosis varied from (13.38 to 40.65) with mean value 31.37 ± 12.69. Obtained results could be useful in assessing prognosis and clinical outcome of the disease. The ADA activity of polyps varied from anastomosis (13.38 to 14.28) with mean value 13.87 ± 4.65. Immunohistochemical study of polyps showed that 60% of polyps was not ADA active. Immunohistochemical study of polyps and carcinoma showed that 50% of polyps was not ADA active. Immunohistochemical study of polyps and carcinoma showed that 50% of polyps was not ADA active.

1299 Effects of Pro-Oxidant Systems on the Lipid Peroxidation and Antioxidative Capacity in Human Colon Carcinoma and Polyps
D. Pavlović, S. Nagomi, G. Kocić, T. Cvetković, I. Stamenković, V. Djordjević. Institute of Biochemistry & Clinic for Gastroenterology, University of Niš, Yugoslavia

There is convincing evidence that cell procrooxidant state can promote to neo- plastic growth, and that antioxidants are antipromoters and anticarcinogens. The study included 8 patients with 10 colon carcinomas and 6 with 8 polyps. Biop- tates were from tissue surrounding malignant lesion and polyp as well as from normal tissue farther from alternative spot. The level of lipid peroxidation products was examined in homogenates after exposure to suspensions of prooxidant system (ascorbate + iron) measuring MDA (nmol/mg prot). Ob- tained results show that used prooxidant system was capable to produce much greater effects in control healthy tissue (MDA concentration 4.14 ± 0.9 and 3.37 ± 0.88) than in corresponding tissue surrounding carcinoma (2.19 ± 0.46; < 0.005) or polyps (1.89 ± 0.59; p < 0.01). The antioxidative capacity of biopate was tested using model of Fe⁺⁺ induced generation of MDA in phospholipid tissue suspension and expressed as percent of the inhibition of MDA formation. The antioxidative capacity of tissue surrounding carcinoma (72.2 ± 11.5%) vs control healthy farther tissue (50.7 ± 13.47%; p < 0.05). However, there was not significant change in antioxidative capacity of polyps biopate compared with normal mucosa. Decreased, small numbered somatostatin-, immunoreactive cells were found in colorectal carcinoma tissue sections. This is consistent with fact that transformation of normal into malignant tissue makes cells less peroxidisable. The increase of antioxidative capacity together with the decrease of lipid peroxidation in tissue surrounding carcinoma indicates...
that this change apparently occurs in early stage of complex sequences of malignant transformation.

**1300** Dissimilatory Activation Pattern of the Carcinogen Dimethylhydrazine (DMH) on Intracellular Polyamine Metabolism in Various Organs

Chr. Lüser, F. Starp, U.R. Fölsch. I. Medical Department, Christian-Albrechts-University of Kiel, Germany

Polyamines, and especially the key enzyme of polyamine de novo synthesis (ODC) are well known to play an important role in cell growth as well as tumour carcinogenesis. Weekly administration of the potent carcinogen dimethylhydrazine (DMH) is known to highly induce predominantly carcinoma of the colon after 6 months' treatment in rats. Simultaneously treatment of ODC inhibition with the ODC activator L6-serine significantly reduces DMH-induced carcinoma formation (Cancer Res 43: 1983; Anti Cancer Res 7: 1987). Furthermore, it is known that carcinogens have different activation patterns on polyamine metabolism in various organs (Lüser et al., Pancreas 10: 1995).

**Methods:** Male Wistar rats (180 g) were s.c. injected with a single dose of DMH (20 mg/kg b.w.t.) and 5–7 animals were killed 4, 8, 12, 24, 72, 120, 168, and 240 hours after DMH or saline injection, respectively. Polyamines, ODC, S-adenosylmethionine, DNA polymerase activity and DNA were analysed in distal colon, proximal colon, small intestine, liver, and pancreas. Additionally, 7 animals were simultaneously treated with DFMO (2% in drinking water plus 3 x 300 mg/kg b.w.t. i.p. during daytime) and sacrificed 7 days after a single injection of DMH.

**Results:** DMH treatment resulted in a significant increase in ODC activity and putrescine concentration in the proximal and distal colon after 7 days and DNA-polymerase activity after 10 days, while the other parameters were unchanged in the colon during the whole experiment. In small intestine ODC, SAM-D, putrescine, and spermidine were in part significantly and prolonged increased between 8 and 168 hours. While in the liver SAT was significantly increased after 78 and 240 hours, no changes were found in the pancreas. DFMO treatment completely prevents DMH-induced activation of polyamine de novo synthesis in the gut.

**Conclusions:** A single dosage of the potent colon carcinogen DMH resulted in dissimilar activation patterns in different organs: in the colon polyamine de novo synthesis is significantly induced after 7 days, in small intestine putrescine and spermidine de novo synthesis is increased between 8 and 168 hours, interconversion pathway is induced in liver, while no changes were found in the pancreas. Interestingly, ODC activation of polyamine de novo synthesis appears late, which is different from findings in other carcinogens. These findings further contribute to a better understanding of carcinogen-induced complex intracellular biochemical mechanisms (DFG Li 4592/1-1, AIR 589-92).

**1301** Telomerase Expression in Colorectal Cancer

S. Odowu, A.G. Morris, I.A. Fraser. Walsgrave Hospital, Coventry and Warwick University, Coventry, England

Telomeres are DNA sequences found at the ends of all chromosomes. They have no synthetic function, but protect chromosomal ends during cell division. The telomeric sequence shortens with each cell division and when it reaches a critical length the cell dies (senescence).

Telomerase is an enzyme not expressed by somatic tissues, but found in some tumour cells in some organisms, preventing cell senescence and thus rendering the cell immortal. This immortalization may be an important step in the process of tumorigenesis.

There has been little work on telomerase in colorectal cancer to date. We have studied the expression of telomerase in colorectal tumours and used the enzyme as a marker of progression of colorectal cancers. Using telomerase, it is possible to detect telomerase in cancer cells in situ, and hence to assess the risk of tumour progression.

**Results:** We have found that telomerase activity is detected in a high percentage of colorectal tumours and is an early feature of tumour progression. This sensitive test for detecting telomerase activity could be a useful tool for early diagnosis and follow-up of malignant disease in the future.

**Conclusions:** The presence of telomerase activity occurs in a high percentage of colorectal tumours and is an early feature of tumour progression. This sensitive test for detecting telomerase activity could be a useful tool for early diagnosis and follow-up of malignant disease in the future.

**1302** The Value of Flow Cytometry in Colorectal Carcinoma

H. Abdulkarim, D. Dingbo, Q. Aydinli, S. Akpoge, F. Igni, H. Karonoglu, A. Demirkazik, F. Gay, Dept. of Medical Oncology, Dept. of Immunology, Ankara University School of Medicine, Ankara, Turkey

There has been a considerable number of conflicting reports on the role of DNA ploidy and S-phase fraction (SPF) as prognostic factors in colorectal carcinoma (CRC).

Paraffin-embedded tumor specimens from 55 patients with operable CRC were studied by flow cytometry in order to determine the prognostic value of DNA ploidy and SPF.

**Results:** Two hundred patients (40%) had aneuploid tumors and 33 (60%) had diploid ones. Mean SPF was calculated as 10.1% (range: 1.2%–34.8%) in all patients. There were no significant correlations between DNA ploidy and the other clinical and histological parameters used in the study. Twenty-two patients (40%) had aneuploid tumors and 33 (60%) had diploid ones. Mean SPF was calculated as 10.0% (range: 1.2%–34.8%) in all patients. There were no significant correlations between DNA ploidy and the other parameters used in this study. SPF was found to be significantly higher in aneuploid tumors and rectal tumors (p = 0.035, respectively) and higher in adenocarcinomas (p = 0.025, respectively) and age and SPF were found to be significant factors for OAS in univariate analysis (p = 0.0225, p = 0.0283 and p = 0.0256, respectively). Adjuvant chemotherapy and age (≤ 60 years) yielded better DFS rates in univariate analysis (p = 0.0095 and p = 0.0074, respectively). While age and histologic grade of the tumor were the independent significant factors for OAS (p = 0.033 and p = 0.011, respectively), DNA ploidy and histologic grade of the tumor were found as independent prognostic factors for DFS (p = 0.0046 and p = 0.0029, respectively).

In conclusion, we can say that DNA ploidy status may be a weak prognostic factor for patients with CRC, whereas SPF seems to be a more important factor than DNA ploidy in the assessment of the prognosis.

**1303** Dual Nature of Colorectal Cancer Mucin and Its Significance

J.R. Jass, Y. Ajioka. University of Auckland, Auckland, New Zealand

Mucin secretions within colorectal cancers appear to be of a dual nature. MUC2 codes for the protein component of secretory mucin produced by goblet cells. MUC1 codes for the protein component of glycolycocalyx material produced normally by columnar cells and upregulated in cancers. The expression of MUC1 and MUC2 apomucins was studied in a series of colorectal cancers with the aim of distinguishing subtypes with differing histogenesis and prognosis. A series of 51 colorectal cancers was stained immunohistochemically with monoclonal antibodies to the mucin protein core structures MUC1 and MUC2. Four phenotypes were recognised: MUC2+/MUC1−, MUC2+/MUC1+, MUC2−/MUC1+ and MUC2−/MUC1−. The distribution of pathological and prognostic features within the four groups was studied.

The phenotype MUC2+/MUC1− was closest to normal large bowel mucosa. Cancers with this phenotype showed a negative correlation with lymph node metastases (p < 0.05). MUC2+/MUC1− cancers were associated with contiguous adenoma (villous and tubulovillous) and exhibited abundant mucin secretion (p < 0.05). MUC2+/MUC1+ cancers were frequently accompanied by a marked peritumoural lymphocyte reaction (p < 0.05). Those with no lymphocyte reaction were associated with lymph node spread. MUC2+/MUC1− cancers were the most aggressive of the four phenotypes.

The preceding data support the earlier suggestion that MUC2−/MUC1− cancers may arise de novo and provide an approach to classification that cuts across traditional methods and may be highly relevant to etiology, pathogenesis and prognosis.

**1304** Cathepsin B Like Activity in Colorectal Adenomas

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Cathepsin B is one of the proteases that may play a key role in invasion and metastasis of colorectal cancer cells. It has been demonstrated that neoplastic cells possess cathepsin B at the plasma membrane whereas the enzyme is present only intracellularly in lysosomes of normal cells. Increased cathepsin B activity has also been reported in serum of patients with colorectal adenomas. The aim of this study is to evaluate cathepsin B activity in serum of patients with colorectal adenomas.

**Results:** We have studied endoscopic resection of colorectal adenomas and had no other disease were included in the study. Patients were divided into three groups: I (n = 20) Tubular adenomas; II (n = 20) Villous adenomas; III (n = 17) High grade dysplasia adenomas. A control group of healthy donors (n = 20) was also evaluated. Cathepsin B activity was measured in serum using L-BAPA as substrate, adding EDTA and DTT, at a reaction pH 6. Results: Control: 0.163 ± 0.03 U/l; 0.168 ± 0.05 U/l; 0.178 ± 0.07 U/l. Statistical significance was found between the four groups (p < 0.01) and when comparing group III with the rest of groups (p < 0.05).

**Conclusions:** 1. The increase in expression of cathepsin B activity may be a sensitive marker for progression from the premalignant to the malignant stage in the development of colorectal cancer. 2. It might be questionable to consider a high grade dysplasia adenoma as a local lesion, when systemic biological modifications are found.
Effect of Radiotherapy on the Potential Doubling Time (Tpot) of Rectal Cancer

P. Michel, J. Hemet, M. Paresy, A. François, B. Paillot, Centre des Tumeurs Digestives, Hôpital Charles Nicolle, F-76031 Rouen Cedex, France; Laboratoire d’AnatomoPathologie, Hôpital Charles Nicolle, F-76031 Rouen Cedex, France

Aim: The benefit of radiotherapy in adjuvant treatment of rectal cancer is demonstrated. However many questions remain about the modalities of this treatment which could be improved by a better understanding of the biological effects. We have evaluated the influence of radiation (34.5 Gy in 15 fractions and 3 weeks) on Tpot of rectal cancer.

Methods: Four hours after infusion of 250 mg of bromodeoxyuridine (BrdU) endoscopic biopsies of the tumor were taken and we have studied the following kinetic parameters: labelling index (LI) of BrdU, duration of the S phase (Ts) and Tpot, with Begg’s method. 36 measures have been done: 19 in patients with colonic cancers without prior chemotherapy or radiotherapy (group 1), 10 in patients with rectal cancers after radiotherapy (group 2) and 7 out of these 10 have also been investigated before radiotherapy (group 3). The means values of LI, Ts and Tpot were compared with Mann-Whitney’s U test.

Results: The LI, Ts and Tpot values (mean ± SD) were:

<table>
<thead>
<tr>
<th>Group</th>
<th>LI (%)</th>
<th>Ts in hours</th>
<th>Tpot in days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>11.7 ± 6.0</td>
<td>14.3 ± 4.4</td>
<td>5.1 ± 2.7</td>
</tr>
<tr>
<td>Group 2</td>
<td>8.7 ± 8.8</td>
<td>15.0 ± 4.1</td>
<td>12.6 ± 8.7</td>
</tr>
<tr>
<td>Group 3</td>
<td>10.3 ± 5.2</td>
<td>13.1 ± 4.1</td>
<td>5.5 ± 3.3</td>
</tr>
</tbody>
</table>

The comparison between these groups suggests a decrease of Tpot value in the radiotherapy group (1 vs 2 p = 0.048) however no difference was shown neither between group 2 and 3 (p = 0.097) nor between colon and rectum (tumors p = 0.81). No difference were reported for LI and Ts. In the subgroup of diploid tumors a significant difference has been found for Tpot (1 vs 2 = 0.001; 2 vs 3 p = 0.008) and LI (1 vs 2 p = 0.008).

Conclusion: These results suggest a decreased of kinetic activity of rectal cancer after radiotherapy, mainly in diploid tumors.

Potential Doubling Time (Tpot) and Node Involvement of Colorectal Cancer

P. Michel, J. Hemet, M. Paresy, A. François, B. Paillot, Centre des Tumeurs Digestives, Laboratoire d’AnatomoPathologie, Hôpital Charles Nicolle, F-76031 Rouen Cedex, France

Aim: In colorectal cancer (CRC) the node involvement determined by pathologic examination of surgical specimen is the main prognosis factor. Among new prognosis factors, the Tpot of CRC remains in evaluation. In this study we have studied relation between Tpot and node status of CRC.

Methods: Four hours after infusion of 250 mg of bromodeoxyuridine (BrdU) endoscopic biopsies of the tumor were taken. We have studied the kinetic parameters: ploidy, labelling index (LI) of BrdU, duration of the S phase (Ts) and Tpot (Tpot = LI/Ts) with Begg’s method. After surgical resection of the tumor, pathologic exam determined the node involvement (N+ vs N−). Values of LI, Ts and Tpot were compared with Mann-Whitney’s U test.

Results: 19 ACR were studied. No difference were shown for kinetics parameters (ploidy, LI, Ts and Tpot) between N+ and N− groups.

<table>
<thead>
<tr>
<th>n</th>
<th>LI (%)</th>
<th>Ts (hour)</th>
<th>Tpot (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m ± D</td>
<td>m ± D</td>
<td>m ± D</td>
</tr>
<tr>
<td>Diploid</td>
<td>8</td>
<td>5.8 ± 3.0</td>
<td>9.7 ± 2.6</td>
</tr>
<tr>
<td>Aneuploid</td>
<td>11</td>
<td>13.1 ± 3.0</td>
<td>10.7 ± 3.0</td>
</tr>
<tr>
<td>N+</td>
<td>12</td>
<td>10.0 ± 1.3</td>
<td>10.5 ± 0.8</td>
</tr>
<tr>
<td>N−</td>
<td>5</td>
<td>12.6 ± 2.0</td>
<td>9.6 ± 1.3</td>
</tr>
</tbody>
</table>

LI was significantly lower in diploid tumors (p < 0.05) and Tpot was shorter in aneuploid tumors (p < 0.05). Ts values were not different between diploid and aneuploid tumors.

Conclusion: The present results suggest that kinetic parameters of CRC are not linked to the node involvement.

Gut: first published as 10.1136/gut.39.Suppl_3.A181 on 1 January 1996. Downloaded from http://gut.bmj.com/ on September 17, 2023 by guest. Protected by copyright.
attenuated by a cyclooxygenase inhibitor. We used the colonic epithelial cell line HCA-7, colony 29 to study the modulatory effect of TFGa on bradykinin induced chloride secretion and to show the possible interaction between local PG synthesis.

Methods: HCA-7 cells were grown in DMEM (10% FCS), seeded on Snapwell filters and formed confluent monolayers within 10-12 days. Cells were either treated for 24 h in the presence or absence of NS398 (10-5 M), a specific cyclooxygenase-2 (COX-2) inhibitor, added two hours before removing cells from the wells. The filters were placed into an Ussing chamber bathed in oxygenated Krebs-Henseleit solution and voltage clamped by continuous application of a short circuit current (SCC). Basal SCC (μA/cm²) and resistance (Ωcm²) were measured and after an equilibration period bradykinin (BK) (10-6 M) was added. All drugs were added to the basolateral side of the monolayer. Data are expressed as mean ± SEM.

Results: The modestly increased baseline resistance (control 138 ± 9.9 vs TGFa 162 ± 16.2Ωcm², n = 20, p = 0.03). The COX-2 inhibitor NS398 did not affect basal resistance of controls but enhanced resistance of TFGa pretreated monolayers (TGFa 162 ± 16.2 vs TGFa+NS398 178 ± 17.2Ωcm², n = 13, p = 0.6). Δ SCC due to BK was attenuated by TGFa (control 13.3 ± 2.7 vs 9.2 ± 1.8 Ωcm², n = 11, p = 0.03). Δ SCC to BK was further reduced by NS398 in basal and TFGa pretreated cells (control vs control + NS398: 13.3 ± 2.7 vs 6.6 ± 1.4 Ωcm², n = 6, p = 0.049); TGFa vs TGFa+NS398: 12.6 ± 2.1 vs 0.1 ± 1.3 Ωcm², n = 6, p = 0.03).

Conclusion: These data provide evidence of the regulatory role of growth factors and BK stimulated ion transport in intestinal epithelial cells with a central role of PG synthesis which may have important implications in pathological conditions such as inflammatory bowel disease.

Acknowledgment: J Betingler is supported by a grant from the Swiss National Foundation.

Nonsteroidal Anti-Inflammatory Drugs Inhibited Human Colonic Cancer Cell Migration in Culture

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Recently, it was reported that nonsteroidal anti-inflammatory drugs (NSAIDs) inhibited carcinogenesis in the colon, possibly inhibiting cyclooxygenase (COX). Intake of NSAIDs is believed to reduce the relative risk of colorectal cancer in humans. The mechanism of reduction is not clear, but as NSAIDs are potent inhibitor of tumor promotion in rodent models of colon cancer, inhibition of COX may be involved in the mechanism for its antitumor activity. Recently, we established a new, simple and convenient model to analyze the cancer cell migration using a human colonic cancer cell line. Using this model, we assessed the migration capacity of colonic cancer cell line (Human rectal adenocarcinoma: SW837) and assessed the effects of aspirin (ASA) and indomethacin (IND) treatment. Methods: SW837 cells (3.5 × 105 cells) were inoculated into the 1.8 cm2 monolayer area (diameter, 15 mm) by silicone fence in a plastic culture dish and cultured in L-15 medium with 10% FBS. Inoculated cells formed round shaped cell sheet in 3 h and subsequently silicon fence was removed and then the cancer cell migration was monitored. The number of migrated cells and the area of free space in a unit cell in 24 h or 48 h were counted. The effects of ASA (0.1 × 10-2, 0.2 × 10-2, 0.3 × 10-2 mm) and IND treatment (0.01, 0.03, 0.1 mm) were assessed. Cell growth of the controls, ASA and IND treatment groups were detected using monoclonal anti-5- bromodeoxyuridine antibody (BrDU) and BrDU labeling index (BrDU positive cell number/total cell number × 100) were calculated randomly selected unit area. Results: After the removal of the fence, cancer cells started to migrate and spread to all directions from the edge of the cell sheet. The number of cancer cells migrated from the cell sheet 48 h after the start of migration was presented in a table. Data: mean ± SD, *p < 0.05, **p < 0.01, n = 4, mm: distance from the edge of cell sheet.

D3 action is mediated by a high affinity nuclear receptor (VDR) that regulates target gene transcription by binding to specific sequences of DNA known as D3 response elements (VDREs). VDR may bind to VDREs as a homodimer or as a heterodimer with a retinoid X receptor (RXR). The ligand for RXR is 9-cis retinoic acid (9-cisRA) which has the potential to modify D3 action. 9-cisRA has been proposed as a chemotherapeutic agent in its own right. We have previously demonstrated that 9-cisRA inhibits both normal and malignant human colorectum and the presence of functional VDR in primary cultures. In addition, 9-cisRA differentially modifies D3 action in two human colon cancer cell lines. The aim of the present studies was to determine the mechanisms by which 9-cisRA modifies D3 action in HT-29 and Caco-2 cells.

HT-29 and Caco-2 cells were treated with D3 and 9-cisRA (10-6 M) and RXRα protein was assessed by Western analysis. Nuclear extracts from human tissue also were assessed. Using these cell lines, we have previously demonstrated that TGFα expression in human normal mucosa and malignant tissue from 15 human specimens. In studies of 9-cisRA may have a direct effect on the transcription of D3 responsive genes but further investigations are necessary to elucidate these pathways. It is important to determine the action of 9-cisRA on D3 signaling before it can be considered as an antiproliferative agent.

Establishment and Characterization of a New Human Rectal Neuroendocrine Carcinoma Cell Line


Human colorectal neuroendocrine carcinomas (NEC) are rare, and there are a few reports of NEC cell lines available for study. We have reported rectal NEC xenograft in nude mice at 4th UEGW (1995). This tumor derived from a metastatic inquinal lymph node of a 58 year-old Japanese female. We succeeded in establishing of a human NEC cell line from this tumor. This cell line has been maintained in culture for more than 1 year. The cells grew in a monolayer, thereafter tended to pile up and formed a cluster. The doubling time was approximately 44 hours at the 10th generation. Immunohistochemical studies of these cells showed positive reactivity for somatostatin, chromogranin A, NSE, S-100, gastrin, glucagon, pancreatic peptide, CEA, p53, and PCNA, although negative reactivity for serotonin and VIP. These results were similar to formalin-fixed, paraffin-embedded tissue samples of the original tumor and xenograft tumor.

This cell line provides an excellent model to study the biological behavior of NEC, enabling future studies on the treatment of the disease.

Gastrointestinal Hormone mRNA Expression in Human Colonic Adenocarcinomas, Hepatic Metastases and Cell Lines

Ph. Biesele1, D. Parrau2, J. F. Cantaloube1, Ph. De Micco1, G. Monges2.
1 Regional Center for Blood Transfusion, Marseille, France; 2 Paol Calmettes Institute, Marseille, France

Purpose To investigate the expression of four main hormones of the digestive tract by performing reverse transcription polymerase chain reaction (RT-PCR) on a series of samples including both tumoral and healthy colonic tissues, hepatic metastases and colonic cell lines, as well as to study the patterns of labelling obtained with serological and morphological markers.

Methods – After extraction and reverse transcription, gastrin, somatostatin, cholecystokinin (CCK) and transforming growth factor alpha (TGFα) mRNA were detected by performing RT-PCR and using specific primers for immunohistochemical assays against the corresponding proteins were also performed.

Summary – The cell lines expressed all four mRNAs. Gastrin mRNA was present in most of the tumoral and metastatic samples, while the somatostatin transcript was detected in all the samples and was frequently over-expressed in the normal colon. TGFα mRNA was systematically expressed in tumours of the present and transverse colon, but not in those located in the rectum; the expression of CCK mRNA was systematically absent in the left colon.

Conclusions – The data presented here shed some light on the transcriptional events involved in the production of the various hormones present in the gastrointestinal tract, in both healthy and tumourous tissue. The various mRNAs
by present and normal

11317

Purpose:

In individual analysis, a reduced dose of cell stress-catabolic hormone directly for Ki-ras genotype and DNA sequencing tumour in status sample microdissected are identified. 18 A214 increase Background: P.A. Institute of Medicine, Centre for Cancer Therapeutics, The Royal Marsden Hospital & Institute of Cancer Research, Sutton, Surrey, UK; 3 Dept of Haematopathology, The Royal Marsden Hospital & Institute of Cancer Research, Sutton, Surrey, UK Background: We have previously shown that detection of mutations in codons 12 or 13 of Ki-ras in whole tissue samples from early colorectal adenocarcinomas do not predict relapse. However, tumours may not be homogeneous for Ki-ras genotype and a few mutated cells can be responsible for subsequent relapse. Therefore, would microdissection of specific areas of colorectal tumours increase the rate of detection of mutations and are there differences between regions within the tumour? Methods: Blocks were retrieved from patients who had undergone apparently curative resection for early colorectal adenocarcinoma but subsequently developed tumour recurrence. Blocks from patients with no relapse after more than 5 years follow up were also used. PCR amplification and direct sequencing to detect Ki-ras status was used firstly, in whole tissue samples. Secondly, in microdissected samples prepared from the 1 mm leading edge of tumour and thirdly, in microdissected samples from the central tumour core at least 2 mm away from the leading edge.

Results: Eight patients with relapse and 5 long term survivors were identified. A stoller-Collier modification of Dukes staging was stage A in 2, B1 in 18 and B2 in 3 patients. A sequence was obtained in all 23 whole tissue samples, in 22 of the leading tumour edges and 20 of the tumour centres. The same genotype was always found in both the microdissected samples from the same tumour in 4 tumours these were mutated. No mutation was found in a microdissected sample which was not detected in the whole tissue sample. In 1 patient, a mutation was detected in the whole tissue sample, but not in the microdissected sample. It is likely that this mutation arose from the epithelium surrounding the tumour rather than from the tumour itself.

Conclusions: These findings suggest that colorectal tumours are homogeneous for Ki-ras genotype and that using PCR amplification followed by direct sequencing of whole tissue samples is accurate, so microdissection of tumours is not necessary. These results also support the hypothesis that the Ki-ras status of a colorectal adenocarcinoma is determined early in its development. (Dr. H.J.N. Andreewy is supported by the British Digestive Foundation)

1317 Colon Cancer and Glut Hormones

J. Payer Jr., M. Huorka, I. Duriš, P. Ondrejka, M. Ilková, P. Holčíčky, Ist. Dept. Int. Med., Faculty Hospital Michal'kovicza 13, 813 69 Bratislava, Slovakia

The etiopathogenesis of colon cancer (CC) seems to be multifactorial. Hormonal imbalance may be involved Somatostatin (S) has an antiproliferative influence on mucosal cells. The main antiangiogenesis of S is the inhibition of cell proliferation via inhibition of hepatostatin (HS). Cortisol (C) as a stress-catabolic hormone may be involved in development of some malignant diseases. Patients suffering from CC, S, G and C circadian rhythm was studied. Seven blood samples were withdrawn during 24 hours for RIA analysis. Fisher's periodogram and Hallberg's cosinor analysis was applied for each individual set of measurement. A 24-hour endogenous circadian rhythm of S, G and C was confirmed. The results were compared to the circadian rhythm of the hormones observed in healthy subjects (N) (n-12), patients with ulcerative colitis (UC) (n-10), and colon polyps (P) (n-9). Higher 24 hours amplitude of S compared to N (p < 0.05), higher mesor (p < 0.05) of G compared to all other groups and lower 24 hours amplitude, (p < 0.01) of C compared to all other groups were found. These findings may reflect the role of G in the etiopathogenesis of CC and results of C secretion could indicate a reduced responsiveness in patients with malignant diseases. S blood levels probably do not reflect its antiprotective effect at cellular and subcellular levels.

1318 Edible Mushroom (Agaricus Bisporus) Lectin, a Cell Growth Inhibitor, Stops Growth of HT29 Colon Cancer Cells in G, and Decreases the Expression of C-myc

L.G. Yu, S. Ward, R.C. Evans, R.V. Gilles, J.M. Rhodes. Department of Medicine, University of Liverpool, Liverpool, UK; 2 Department of Biochemistry, University of Liverpool, Liverpool, UK Purpose: The Thomsen-Friedenreich (TF) antigen (Gal(1-3GalNAc)α-) is a common onco-fetal carbohydrate antigen in intestinal epithelia. Our previous work has shown that the non-cytotoxic TF-binding lectin from the edible mushroom Agaricus Bisporus (ABL) inhibits proliferation in a range of malignant and normal epithelial cells (Cancer Res. 1995; 55: 4627) and has to be internalized to produce its inhibitory effect (Gastro. 1995; 106 (4): A568). The present study was designed to assess the relationship of this inhibitory effect by ABL to cell cycle and the expression of protooncogenes c-myc and p53.

Methods: 1) HT29 colon cancer cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) with 5% fetal calf serum (FCS). The cells were partially-synchronized by culturing in 0.5% FCS for 2 days. ABL (80 µg/ml) or PBS (control) was added for 8 hours at 37°C. 4% FCS was added to stimulate cell growth. Cells were fixed at various times after treatment with propidium iodide. Total DNA content per cell was assessed using a flow cytometer. 2) Subconfluent HT29 cells were prefuced in serum-free DMEM for 1 day before addition of ABL (30 µg/ml). RNA was extracted at different time by the guanidinium thiocyanate-pheno1-chloroform method. Northern Blots were probed with cDNA for c-myc or p53.

Results: After 21 hours addition of FCS, the proportion of ABL treated cells in G0/G1 had increased from 81.1% to 90.6% compared to a decrease to 70.8% (n = 3) in control. The expression of c-myc mRNA was decreased by 48 ± 7% (n = 3) in the presence of ABL and this effect on c-myc of ABL was abolished by co-incubation with asialo fetuin which expresses GalNAcA. No significant effect on p53 mRNA expression was found.

Conclusion: Mushroom lectin inhibits proliferation by holding cells in G,. The decrease of c-myc mRNA expression may provide a partial explanation for the anti-inhibitory effect.

1319 Expression of the Transforming Growth Factor Alpha, Epidermal Growth Factor and Epidermal Growth Factor Receptor, in Colorectal Cancer and Its Liver Metastasis

T. Saga, N. Tanaka, T. Monda, Y. Kanazawa, K. Kurokawa, H. Takasaki, K. Yoshimura, H. Kan, H. Maruyama, H. Sasabe, T. Yamada, Z. Naitoh, G. Asano, T. Takizawa, Y. Ide. Surg. of Shitya Hn., Nippon Medical School, Tokyo, Japan; 1st Dept of Surg., Nippon Medical School, Tokyo, Japan; 2nd Dept of Pathology, Tokyo, Japan; 3 Dept of Histopathology, CRC Section (Dr. Maruyama); 1st Dept of Surg., Nippon Medical School, Tokyo, Japan; 2nd Dept of Pathology, Tokyo, Japan. Transforming growth factor α (TGFα) which is structurally homologous to epidermal growth factor (EGF) binds to epidermal growth factor receptor (EGFR) and is implicated in the growth and proliferation of colorectal cancer. To evaluate the role of TGFα, EGF and EGFR in colorectal cancer progression, we investigated their expression in colorectal cancer and its liver metastasis.

Materials and method: Immunohistochemical staining was performed on paraflin-embedded specimens of 32 colorectal cancer and 40 liver metastasis. EGFR, EGF and TGF expression were evaluated semiquantitatively.

Results: Overall expression of TGFα, EGF and EGFR in primary lesion were 40.6%, 75.2% and 78.3%, respectively. In metastatic liver lesion, a significantly higher rate of TGFα and EGFR expression was found (77.5% and 87.5%), but there was no difference in the expression of EGF (87.5%). Synchronous expression of TGFα and EGFR occurred in 52.5% in liver metastasis compared with 34.1% in primary lesion. And overexpression of TGFα and EGFR in the hepatocytes surrounding metastatic cancer cells were observed. Conclusions: These results suggests that autocrine/paracrine interaction of TGFα and EGFR play an important role in liver metastasis of colorectal cancer and hepatocytes are also involved in these interaction.
**Gastrointestinal Emptying of Solid Food in Relation to Body Mass Index: A Scintigraphic Evaluation**

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It's known that different physiologic conditions including body size can modify gastric emptying. Few studies in the literature have compared gastric emptying to the Body Max Index (BMI). We have evaluated gastric emptying rate of solid meal in volunteers of varying sizes to determine whether BMI and gastric emptying rate are correlated. 

Twelve healthy volunteers (males, mean age 42 ± 12 (SD) yrs, age range 23-54 years) with different BMI (mean 26.6 ± 4.2 (SD) kg/m², range 18.5-31.8 kg/m²) were studied. All the subjects, after an overnight fast, ate a standard 700 kcal meal consisting of chicken liver labelled in vitro with 150 μCi 99mTc-sulphur colloid. Immediately after the meal, the subject was asked to lie supine for radioaccounting with two scintillators placed opposite one another and connected to a computerized rate meter to evaluate gastric radioactivity decay. Results were expressed as emptying index at 120 min (EI) calculated by means of the following formula: EI = [(100-RR)/RAI] x 100; where RR = % residual radioactivity at time t; RA = area under the emptying curve at time t (≥ 120 min). 

**Results:** Are shown in fig. They demonstrate an inverse linear relationship between gastric emptying rate and BMI. 

**Conclusion:** The variable of BMI must be taken in account when gastric emptying is evaluated.

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**Gastric Emptying Time and CLO-Test in Patients with NUD: Effect of Cisapride**

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This study was designed to compare the gastric half emptying time (GET 1/2) in patients with non-ulcer dyspepsia (NUD) and healthy controls, and to study the effect of cisapride on GET 1/2 in NUD patients. All NUD patients had normal ultrasound and normal upper endoscopy. Gastric biopsy was taken from the antrum for CLO-test.

All underwent a solid gastric emptying test using a Technetium-99 labeled egg meal. NUD patients received oral cisapride 10 mg tid ac for 2 weeks and had a repeated gastric emptying test after treatment. Symptoms were scored before and after cisapride treatment. In total 35 patients with NUD and 22 healthy controls were studied.

The pre-treatment GET 1/2 in NUD patients was 90.92 ± 28.47 min. This value was significantly different from that of healthy controls who had a mean GET-1/2 of 77.64 ± 14.23 min (p = 0.0023). CLO test was positive in 20/35 patients (57.1%). After 2 weeks of cisapride treatment, the GET-1/2 decreased.
significantly (80.92 ± 28.47 min VS 73.59 ± 21.63 min, P < 0.0001) in the NUD group. Significant symptom improvement was obtained similarly in the CLO positive and CLO negative NUD patients. The GET-1/2 after cisapride treatment was reduced to the same extent in both CLO positive and CLO negative patients.

This study suggested that cisapride can improve dyspeptic symptoms and shorten GET-1/2 in NUD patients regardless of their CLO status. Delayed gastric emptying may be one of the permissive factors in the pathogenesis of NUD and may account for the symptomatology in this group of patients.

1326 The Effect of Phenytoin on Gastric Dysrhythmia in Diabetic Patients

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Patients with diabetes frequently complain about gastrointestinal symptoms. Almost half of these patients have delayed gastric emptying. In EGG, the frequency of gastric dysrhythmia observed more frequently than normal population. It has been thought that at least in some diabetic patients gastric dysrhythmia might still be the probable causes of delayed gastric emptying.

In this study, we examined 42 diabetic patients and 20 healthy controls. The diabetic patients consist of 33 female and 9 male, whereas the control group was 13 female and 7 male. The mean age was 52 ± 12 for the diabetic patients and 34 ± 12 for the controls. The average duration of diabetes was 7 ± 5 years. The average duration of EGG observations was one after an overnight fasting period with cutaneous electrodes. The electrogastragrams were recorded for 30 minutes fasting period and 30 minutes postprandial period. Patients with abnormal EGG records were given 300 mg, 200 mg phenytoin P.O. at 7 p.m. and 12 p.m., respectively. In the following morning EGG records were repeated.

52 percent of diabetic patients had peripheral neuropathy, 26 percent had autonomic neuropathy, and 59 percent had upper gastrointestinal symptoms. While 15 diabetic patients had abnormal EGG records, in controls only 2 were abnormal (p < 0.05).

Table 1: The effect of phenytoin on gastric dysrhythmia

<table>
<thead>
<tr>
<th>Before phenytoin</th>
<th>After phenytoin</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of normal slow waves</td>
<td>49 ± 13</td>
<td>70 ± 11</td>
</tr>
<tr>
<td>Tachygastric percent</td>
<td>33 ± 13</td>
<td>19 ± 6</td>
</tr>
<tr>
<td>Percentage of hypertonicity</td>
<td>17 ± 11</td>
<td>10 ± 7</td>
</tr>
<tr>
<td>Power ratio (postprandial/fasting)</td>
<td>1.38 ± 1.02</td>
<td>1.97 ± 0.78</td>
</tr>
</tbody>
</table>

In this study, it has been found that diabetics have more EGG abnormalities compared to normal subjects. Phenytoin reduces the gastric dysrhythmia in most of the patients. It is concluded that the therapeutic benefit of phenytoin is due to its effects on the activity of ectopic pacemaker foci in the antrum.

1327 Solid Meal Gastric Emptying in Hypothyreosis – A Prospective Clinical Study

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Objective. The study aimed at the evaluation of the gastric emptying (GE) kinetics of a solid meal in hypothyroxic patients before and after a substitutive treatment with L-thyroxin. Methods. Twelve female hypothyroxic patients (aged 45.3 ± 8.7 years (25–62 SD) and a control group of 12 healthy women (aged 34.5 ± 8.1 years) were examined. The GE of a 99mTc-labeled solid meal was measured with the use of a gamma camera in every patient before the treatment, and in 10 of them a repeat GE examination was performed after the restoration of euthyroidism; the median duration of the treatment was 5.5 mo (range 2.5 to 12 mo). Results. The mean gastric transit time (MTTGE) and the fraction of the test meal retained in the stomach after 90 min (F90) were statistically significantly greater in untreated hypothyroxic than in healthy controls (MTTGE: 42.01 ± 1.96 min patients vs 40.06 ± 1.01 min controls, p = 0.0043; F90: 64.3 ± 15.4% patients vs 50.8 ± 8.2% controls, p = 0.0173). In ten patients in whom a second GE measurement was taken after the achievement of euthyroidism, a slight increase of the GE was observed (MTTGE: 41.46 ± 1.49 min before vs 41.04 ± 1.81 min after the treatment). The results were not statistically significantly different from that of the healthy controls. No relationship was found between the GE and the severity of clinical symptoms of hypothyroidism. GE remained, however, slowed in some patients despite the restoration of euthyroidism. Conclusion. We conclude that: (i) long-lasting hypothyroidism is accompanied by a slightly slowed GE of solids, and (ii) restoration of euthyroidism does not imply a parallel improvement of the hypothyroidism-associated delay in GE.

1328 Patterns of Solid Meal Gastric Emptying in Hypothyreotic Patients-Efect of Pharmacological Management

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Objective. The study aimed at the evaluation of the kinetics of gastric emptying (GE) of a solid meal in hypothyreotic patients during a pharmacological treatment with thiamazole until the moment of euthyroidism restoration. Methods. Fourteen female patients (33.4 ± 2.6 yrs; mean ± SEM) with recently diagnosed hypothyreosis took part in the study. Twelve age-matched healthy women (34.5 ± 2.3 yrs) constituted a control group (C). Every patient underwent the GE examination before treatment (I). In 12 patients the GE was re-examined on the 3rd treatment week (II). After the achievement of euthyroidism, which happened after 4.5 ± 1.3 months; interquartile range 2.0 to 7.3 mo), a third GE measurement was taken in patients (III). The GE of a 99mTc-labeled solid meal was measured with the use of a gamma camera. Time-activity curves form the gastric region of interest were used, after subjection to appropriate corrective procedures, to calculate the mean gastric emptying time (MTTGE) and the fraction of the test meal retained in the stomach after 90 min (F90). Results. Before the treatment and on the third week of management the GE of hypothyreotic was not statistically significantly different from that of healthy controls (MTTGE: 39.28 ± 0.3 min [I]; 39.21 ± 0.64 min [II] and 40.06 ± 0.29 [III]; F90: 46.9% ± 1.9% [I]; 47.9 ± 3.7% [II] and 50.8 ± 2.4% [III]). The restoration of euthyroidism was accompanied by a slight but statistically significantly increase in the GE – p < 0.05 in the case of F90 vs the pre-treatment situation. Also the patients’ GE was found to be slightly but statistically significantly faster than in healthy controls (MTTGE: 38.72 ± 0.39 min [III], and F90: 42.2 ± 2.3% [III] – p < 0.05 vs C for both parameters). Conclusion. We conclude that in hypothyreotic women the GE of solids does not differ significantly from age-matched healthy female controls and remains unchanged during a pharmacological treatment. After achievement of euthyroidism a slightly but statistically significantly faster GE is observed in the patients compared to healthy controls.

1329 Gastric Emptying of Fat Determines the Pattern of Postprandial Gastric Emptying in Humans

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The purpose of this study was to determine factor(s) accounting for the functional relationship between the gallbladder (GBE) and gastric (GE) emptying. Methods. Two nearly iso-caloric but differing with regard to their fat content semiliquid meals were used. A low-fat meal (LFM; 0.94 kcal/ml, 500 ml) of fat (20.2 g fat) was consumed by 19 healthy subjects (8 M and 11 F, aged 27.8 ± 1.7 years) on 19 occasions. A high-fat (HFM, 1.18 kcal/ml, 250 ml, 21.3 g fat) was eaten by 12 healthy subjects (8 M and 4 F, aged 33.8 ± 3.0 years) on 22 occasions. Gastric emptying volume and antral cross-sectional area was measured ultrasonographically before and at 10-min intervals for one hour after meal ingestion. Data are means ± SE. Results. The two meals evoked different patterns of GE and GBE (Fig. 1). At 60 min postprandially 154.7 ± 17.0 kcal contained in 165 ± 19 ml of antral volume (IV) and at the same time the HFM the corresponding values were 205.0 ± 11.4 kcal in 190 ± 11 ml. At that time, however, 3.5 ± 0.4 g fat was evacuated from the stomach with LFM, as opposed to 16.2 ± 0.8 g fat with HFM. Considering the fractional GBE as a dependent variable, whereas volume, energy, and fat emptied from the stomach as possible predictive factors, a forwardly performed stepwise multiple linear regression revealed that only the GE of fat was a significant predictor of the postprandial GBE; multiple R = 0.8817, p = 0.00015. Conclusion. The gastric evacuation of fat appears to be a crucial factor determining the time-course of the GBE evolved by a semiliquid caloric meal.
**1331** The Effect of Cisapride on Gastric Emptying in the Critically Ill Patient

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**Background:** Early administration of enteral nutrition to critically ill patients is associated with improved clinical outcome including reduced sepsis, improved wound healing, maintenance of intestinal mucosal integrity, and decreased mortality. In critically ill patients, gastric emptying is often markedly delayed and precludes enteral nutrition. The efficacy of prokinetic therapy in improving gastric emptying is not well demonstrated in critically ill patients, especially those with severe sepsis.

**Purpose:** To evaluate the effects of cisapride, a gastrointestinal motility agent, on gastric emptying in critically ill patients. Methods: In a randomized, double-blind, placebo-controlled study, we recruited mechanically ventilated patients expected to be critically ill for at least 48 hours. The antrum was imaged with a chain scanner, the proximal stomach with a 5-3 MHz phased-array transducer. After calibration, in vitro calibration was evaluated by scanning a porcine stomach. Thereafter, four male volunteers, median age 45 years, were included and examined in the morning after ingestion of a 500 ml soup meal (20 kcal). One subject was scanned on 6 consecutive days. Scanning was performed fasting, and up to 35 min postprandially by conventional 2D scanning of the antrum and 3D ultrasound of the total stomach. Volume estimation of the stomach was in 3 dimensions were performed after manual tracing on a Unix workstation. Results: This 3D system yielded a strong correlation (r = 0.997) between true and estimated volumes in vitro. The limits of agreement were -9.1 ± 70.1 ml in the volume range 1200-1900 ml. Compared to manual tracing, the mean difference was 7.7 ± 1.9 ml in the volume range 30-100 ml. The volume of the total gastric volumes ranged from 12.5% to 46.0%, less than for antral area variability. The average half emptying time in healthy subjects was 22.1 ± 3.6 min. Intragastric distribution of the meal, expressed as Proximal/Distal volume, varied on average from 3.6 ± 2.1 (min) to 2.7 ± 1.9 (min) SD. Conclusions: This 3D ultrasound system using magnetic scanhead tracking demonstrated high in vitro accuracy, calculated gastric emptying rates more precisely than 2D ultrasound, and enabled estimation of intragastic distribution of a soup meal in healthy subjects.

**1333** Accommodation of the Proximal Stomach is Fat Dependent in Functional Dyspepsia

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**Aims:** Patients with functional dyspepsia seem to have impaired accommodation of the proximal stomach to a meal. The objective of this study was to examine whether the amount of fat in the soup influenced gastric accommodation in functional dyspepsia.

**Methods:** 11 patients, 9 females and 2 males, median age 40 years (range 21-52 years), were scanned fasting in a sitting position after ingestion of 500 ml meat soup (Toro). On two separate days, the patients randomly ingested either 2 or 13 g of bovine fat in the meal (20 vs. 170 kcal). An ultrasound scanner, CFM 750 Virgmond Sound, with a 3.25 MHz transducer was used to acquire images 10 min after a 4 min background and subsequently, sections of a sagittal area and an oblique frontal diameter were applied on the proximal stomach. 3D ultrasound with a tilting device for acquisition was used to scan the distal stomach. Volumes of the gastric antrum were estimated on a Unix workstation after scanconversion and manual contouring using software from Advanced Visual Systems®. All subjects were asked to score total symptoms (1-9) provoked by the meal. Statistical differences were analyzed using Wilcoxon signed ranks test.

**Results:** The size (±SD) of the proximal stomach was larger after high fat compared with low fat content, both in the sagittal (22.1 ± 3.4 cm² vs. 15.5 ± 4.4 cm²; p = 0.01) and the frontal section (6.8 ± 0.8 cm vs 6.0 ± 0.8 cm; p = 0.01). Volume of the proximal stomach increased more than 2.5-fold in the patients, male (61%), age 54.0 ± 19.1%; 47% were post-operative, 83% were receiving narcotics and the mean SAP score was 9.5 (±2.9). As acetaminophen is only absorbed in the small bowel, acetaminophen absorption rate can be used as an index of gastric emptying. 1.6 g of acetaminophen suspension was administered via a nasogastric tube into the stomach (day 1). Blood samples were drawn at t = 0, 30, 60, 90, 120, and 180 minutes for measurement of plasma acetaminophen levels determined by the enzymatic degradation method. We measured the maximum plasma concentration (Cmax) time to reach Cmax (min) and area under the plasma concentration-time curve t = 180 (AUC180) umol/min/mL. The following morning (day 2), patients were randomized to take a meal with or without cisapride, with or without gastric emptying was measured. Results: The difference (day 2 - day 1) in Cmax was 49.1 umol/L in the cisapride group compared to 12.3 umol/L in the placebo group (p = 0.005). The time reach to Cmax was also significantly shorter in day 2 than in day 1 (40.8 minutes vs. 4.2 minutes; p = 0.02). The difference in the area under the time-acetaminophen concentration curve was also greater in the cisapride group (5534 vs 2832; p = 0.09). Conclusions: Cisapride enhances gastric emptying in critically ill patients. Since intolerance to enteral feedings is associated with increased morbidity, improved gastric emptying with cisapride may improve mortality and morbidity in this patient population. Studies to specifically examine the effects of Cisapride on tolerance of enteral nutrition and infectious morbidity are needed. Supported by the Janssen Research Foundation.

**1334** Effects of Medium-Chain and Long-Chain Triglycerides on Antral Motility

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The use of medium-chain triglycerides (MCT) as additional caloric source in diets is limited by the frequent occurrence of abdominal symptoms. Recently, we have shown that MCT accelerates intestinal transit but little is known on the effect of MCT on gastrointestinal motility. Therefore, we have investigated the effects of both equimolar and equicaloric amounts of MCT and long-chain triglycerides (LCT) on antral motility and duodenal transit time (DCTT; ileocoe H2 breath test) and CCK release (RIA).

Eight healthy subjects (age 19-28 y) were studied on 4 separate occasions, after spontaneous occurrence of duodenal phase III, in random order during continuous intraduodenal administration of: (a) saline (control), (b) MCT 15 mmol/h, 67 kcal/h (MCT-1), (c) MCT 30 mmol/h, 135 kcal/h (MCT-2) or (d) LCT 15 mmol/h, 135 kcal/h, each for 360 min. Results: Both doses of MCT resulted in a sign. faster reoccurrence of phase III (MCT-1, 7 ± 5 min, p < 0.05; MCT-2, 56 ± 13 min, p < 0.05) compared to saline (151 ± 18 min). LCT, on the other hand, sign. (p < 0.05) delayed reoccurrence of phase III compared to saline (290 ± 30 vs 151 ± 18 min), and induced a fed motor pattern. MCT at both doses did not interrupt interdigestive motility. Migrating motor complex (MMC) cycle length was sign. (p < 0.05) shorter during MCT (MCT-1, 65 ± 7 min; MCT-2, 53 ± 6 min) compared to saline (127 ± 14 min) resulting from a sign. (p < 0.05) shorter duration of phase II. Phase III amplitude and velocity were sign. (p < 0.05) reduced during MCT. Inflation of LCT did not affect DCTT (105 ± 13 min) compared to saline (101 ± 9 min), whereas DCTT was sign. (p < 0.05) accelerated during MCT (MCT-1 56 ± 6 min; MCT-2 69 ± 9 min). DCTT was positively correlated with MMC length (r = 0.46, p = 0.05). LCT but not MCT sign. (p = 0.05) increased plasma CCK levels. Conclusions: LCT induces a fed motor pattern, whereas MCT maintains interdigestive antral motility with shorter MMC cycle length resulting from a shorter duration of phase III. MCT accelerates intestinal transit. The effect of MCT is independent of CCK.

**1336** Intraduodenal Antrodistal Motility and Gastric Acid Secretion. Effect of Acid Inhibition


In man intradigestive acid secretion and antral motility are closely related with cyclic variations in acid secretion synchronous with the various phases of the migrating motor complex (MMC). Duodenal acidification inhibits antral motility but little is known on the effect of acute acid inhibition on antral motility. We have simultaneously studied antral motility (proximal and distal antral motility) and acid secretion from 10 min portions using phenol red as marker recovery) in 9 healthy subjects (age 20-31 yr). Each subject was studied twice in random order during 1) saline i.v. (control) for 1-2 complete MMC cycles and 2) during acute acid inhibition with lansoprazole i.v. (bolus 20 mg, continuous infusion 4 mg/hr) for 1-2 complete.
MMC cycles. Plasma gastrin and pancreatic polypeptide (PP) levels were determined (RIA).

Results: In the control study acid output in phase III (2.1 ± 0.3 mmol/l/min) and in phase IV (6.7 ± 0.2 mmol/l/min) was significantly (p < 0.05) increased over early phase II and phase I (1.2 ± 0.2 and 1.2 ± 0.2 mmol/l/min resp.). Famotidine increased gastric pH to > 6 within 30 min. After acid inhibition duration of MMC cycle during famotidine (106 ± 8 min) was reduced but not significantly different from the control experiment (133 ± 14 min). Phase distribution of the MMC cycle was not significantly different between famotidine (I, II and III: 12 ± 3%, 83 ± 2% and 5 ± 1% resp.) and control (I, II and III: 12 ± 3%, 82 ± 3% and 4 ± 1% resp.). Plasma PP levels significantly (p < 0.05) decreased during famotidine. A218 cm² (I), in nonpropulsive transpyloric antral contractions, was prevented by famotidine i.v. does not significantly interfere antroduodenal motility and PP secretion.

1337 Gyceryl Trinitrate Improves Intragastric Meal Distribution and Prevents Meal-Induced Discomfort in Patients with Type I Diabetes Mellitus

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Purpose: Impaired accommodation reflux of the proximal stomach is often seen in patients with diabetes. Nitrogen monoxide (NO) serves as a neurotransmitter in this reflex, and we hypothesised that glyceryl trinitrate (GTN), an exogenous donor of NO, could improve accommodation and intragastric meal distribution in patients with diabetes.

Methods: A double blind, placebo-controlled, cross-over study was designed in twenty patients with type 1 diabetes (DM) and twenty healthy controls (HC). All received GTN or PLC in random order five minutes prior to a 500 ml soup meal. Two proximal sections, a sagittal area (SA) and a frontal diameter (FD), and an antral area (AA) was outlined by ultrasound. Symptom score was assessed by visual analogue scales.

Results: GTN had no significant effect on the sagittal area (SA) or on the frontal diameter (FD). An estimated volume (eV) based on these measures (eV = SA × FD) was neither significantly different with GTN compared to PLC. GTN decreased significantly (p < 0.05) antral area (AA) 5 min after soup in patients with diabetes (16.1 cm² ± 4.3 with PLC vs. 19.5 cm² ± 4.5 with GTN). This effect was consistent throughout the investigation period in DM. In HC, there was a similar tendency (p = 0.14) 5 min after soup (16.4 cm² ± 6.6 vs. 13.2 cm² ± 5.6). GTN had a significant (p = 0.04) effect on the intragastric meal distribution in DM, increasing eV/AA ratio from 9.1 ± 4.0 to 11.9 ± 6.4. GTN also prevented meal-induced symptoms in patients with diabetes.

Conclusion: GTN improves intragastric meal distribution and prevents postprandial symptoms in patients with type 1 diabetes mellitus.

1338 Relationship between Early Postprandial Symptoms and Transpyloric Flow

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Background: Patients with functional dyspepsia (FD) exhibit increased sensitivity to gastric distension (mechanoreceptors) and to meals rich in fat (duodenal chemoreceptors).

Aim: to relate early transpyloric antral and emotility to early postprandial symptoms in FD using duplex sonography.

Methods: Twelve patients with FD were investigated during 3 min of fasting, during 3 min of ingesting 500 ml of a meat soup and during the first 10 min postprandially.

Results: Transpyloric forward flow commenced on average 52 sec and postpropulsive transpyloric flow (generated by propulsive antral contractions) 115 sec after start of drinking the soup. Initial nonpropulsive transpyloric flow (i.e., pendulating flow not generated by antral contractions) lasted 58 sec. Postprandial symptoms occurred in all patients and commenced on average 142 sec after start of ingestion. In all subjects symptoms appeared after commencement of transpyloric emptying. A negative correlation was found between intensity of fullness and duration between start of emptying and start of symptoms. No correlation was found between antral distension and symptoms.

Conclusion: The inverse relationship between symptom intensity and duration of the emptying period before symptoms suggests that meal related symptoms in FD patients are mainly due to gastric mechanoreceptors.

1339 Duodeno-Jejunal Postprandial Motility in Severe Chronic Idiopathic Dyspepsia: Comparison with Motor Patterns of Healthy Volunteers and Relationship with Results of Radionuclide Gastric Emptying

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Our goal was to describe the duodeno-jejunal postprandial motility in dyspeptic patients having an objective delay at radiouclide gastric emptying.

Methods: Ten patients, 5 men and 5 women, (median age: 52 years; range 34–76), with daily symptoms were studied. Gastric emptying of solids was delayed in all patients: lag phase > 60 min (N = 40) (n = 6), decreased emptying rate to < 50% of normal (N = 25) (n = 8). Duodenal emptying was also delayed in all patients (N = 6 cases with an half emptying time > 113 min. A four port recording device registered duodenoejugal motility during three hours after a 750 kcal-meal (carbohydrates: 50%, lipids: 30%, proteins: 20%). The duodenal and jejunal areas under curves (AUC) were calculated by a validated software on the whole 3 hours and on each of the 6 half-hours of the postprandial period. Manometric results in dyspepsics were compared to those of 20 healthy volunteers, 10 men and 10 women, median age 30 years (range 21–46) studied in the same conditions.

Results: a) in volunteers, postprandial motility was characterised, at each level of recording, by a maximal motor activity during the first half hour, followed by a significant decrease with a slow emptying pattern of the liquid meal. b) In all postprandial periods, the postprandial motor activity was always higher than the duodenal one (p < 0.01). b) The global overall AUC and the AUC on each of the successive half hours were not different between dyspeptic and volunteers. c) in all dyspeptic patients, duodenal and jejunal AUCs were significantly (p < 0.01) greater than the jejunal one in 6 cases. d) Lag phase duration was correlated with the duodenal AUC in the first hour (p = 0.05; r = 0.01). No other correlation was found between duodenal or jejunal motor parameters and results of radionuclide gastric emptying for solids or liquids.

Conclusion: In severe dyspepsia with a gastric emptying objectively delayed, the kinetics of the duodenjejunal postprandial motility was always different from that observed in volunteers. The correlation between lag phase and duodenal motor index suggests that duodenum could act as a brake in some dyspeptic patients.

1340 Gastric and Gallbladder Emptying after a Mixed Meal are not Coordinated in Liver Cirrhosis: An Ultrasound Monitoring

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An impaired contractility has been suggested as a contributing factor to the increased incidence of gallstones in liver cirrhosis, but the few studies on gallbladder emptying in cirrhics offered contradictory results. Ingestion of a meal triggers the physiological pathway of gallbladder emptying, therefore it seems very important to assess simultaneously the rates of gastric and gallbladder emptying.

Gastric and gallbladder emptying were measured using ultrasound techniques after a solid-liquid meal (14 kg fat, 465 kcal) in 24 patients with liver cirrhosis and in 12 controls. None of the subjects had gallbladder disease. Sequential changes in cross-sectional area of the gastric antrum and in gallbladder volume were represented as a monoexponential process after the test meal. Cirrhotic patients were analyzed according to the severity of disease (Child classes). The presence of portal hypertension was assessed by endoscopy. Differences between groups were analyzed using the two-tailed Student’s t test for unpaired observations and the correlations by linear regression (Pearson’s coefficient).

We found all parameters of gastric emptying following the solid-liquid meal similar in patients and controls. On the contrary, gallbladder emptying was significantly diminished in cirrhotic patients: the area under curve was reduced in Child A (p = 0.01), Child B (p = 0.04) and Child C (p = 0.014) cirrhotics. No correlation was found between the parameters of gallbladder and gastric emptying. Gallbladder refluxing began earlier in cirrhotics than in controls, before completion of gastric emptying. Our results indicate the lack of a quantitative coordination between gastric and gallbladder emptying in liver cirrhosis. They also show the hypothesis that diminished gallbladder contractility could contribute to the increased gallstone formation in liver cirrhosis.

1341 Effect of Intraduodenal Application of Acid and Lipids on Gastric Tone in Healthy Subjects

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Gastric emptying of fat leads to inhibition of antral motility and relaxation of the proximal stomach, which are likely mediated by neural duodenogastric reflexes. An acid intraduodenal pH also induces an inhibition of the antral motility, but the effect on the tone of the proximal stomach is unknown. Aim of this study was to compare the relaxation of the proximal stomach after intraduodenal perfusion of different doses of a citric acid solution (pH = 2.2) and a nutrient solution (intraaliment 23% of total parenteral nutrition) at constant gastric emptying. Gastric and jejunal emptying were studied. After an overnight fast a duodenal tube was placed through the nose with a side hole in duodenal bulb. A second tube with a 1200 ml balloon at the tip was placed in the proximal stomach and connected to a barostat. After a 30 min accommodation period, the balloon was inflated at a pressure of 1 mmHg above the minimal distending pressure of the stomach and volume was continuously recorded. A citric acid solution was infused at a rate of 1 ml/min into the duodenal bulb at rates of 1, 5 and 10 ml/min, each for one minute. After each infusion the maximal volume of the proximal stomach and the slope (velocity of relaxation, ml/sec) from onset to maximal relaxation were recorded. Each following infusion was given after gastric volume had returned to basal value. The same procedure and the same infusion rates were
repeated with Intralipid. Results are expressed as median. Results. The basal volume of the proximal stomach was 48 ml. A similar relaxation was obtained with both 20% fat and lipids from the lowest infusion rate (gastric volume 139 ml after 1 ml citric acid and 182 ml after 1 ml intralipid, n.a.), and no further volume increase was achieved with higher doses (max. gastric volume 167 ml after 10 ml citric acid and 187 ml after 10 ml intralipid; n.a. compared to values after 1 ml). Results of gastric relaxation (slope) were similar with both citric acid (2.9 ml/sec) and lipids (3.6 ml/sec). Conclusions. Intraduodenal acid and fat infusions exert a similar dose-independent relaxation of the proximal stomach. This relaxation occurs at a similar velocity, which support a common reflex mechanism for acid and fat.

Comparison of Radiologic and Isotopic Measurement of Gastric Emptying

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Scintigraphic measurement of isotopes labelled nutrients is currently the gold standard technique for the evaluation of gastric emptying function. However, its availability is often limited. Radiologic gastric emptying of radiopaque markers could constitute a cost effective and easily available procedure but it remains unknown to many practitioners. We conducted a 5 yr retrospective study with 46 patients suspected of gastroparesis and submitted to both radiologic and isotopic gastric emptying tests, to verify if the radiologic emptying correlated with the isotopic one, and if the former could be an alternative to evaluate gastric emptying in the clinical setting.

Methods: the gastric emptying of a meal containing Tc-99m beef liver was measured in the nuclear medicine laboratory, and was considered as our reference standard. The radiologic test required patients to ingest 10 radiopaque markers (consisting of 5 mm pieces of a 12 Fr radiopaque feeding tube) swallowed with 240 ml of 7-UP and a bun. Abdominal X-Rays (PA) were obtained 2, 4, and 6 hrs later, and the number of residual markers in the stomach was counted at each time point.

Results: a) significant relationship (r = 0.66; p < 0.00001) was found between the emptying time of isotopes and pellets. b) isotopic emptying was considered abnormal in 24/46 patients. In these patients with identified gastroparesis, the number of pellets or pellets in the stomach after 6 hrs was significantly higher than in those with normal isotopic emptying (5.1 ± 1.2 vs 2.2 ± 0.6; p < 0.01), c) both tests correlated perfectly in 85% subjects: both tests were normal in 21/46 and abnormal in 15/46 patients. d) three patients showed normal pellets emptying but had a small delay in isotopic transit (T25: < 160, 160, 190 min; n < 150 min). Seven patients with normal isotopic transit showed a delayed pellet emptying; 6 of these 7 patients were diabetics clinically classified with gastroparesis.

Conclusion: X-Ray determination of residual markers in the stomach 6 hrs after their ingestion seems to correlate with isotopic evaluation of the gastric emptying rate. In some circumstances, the radiologic test appeared even superior than the isotopic one to identify gastroparesis. The marker test is easy to realize in any clinical set up and appears to be a cost effective tool for the clinician.

Treatment of Diabetic Gastroparesis with Cisapride

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Studies in gastroparesis mostly focus on gastric emptying in a limited patient (pt) sample. We evaluated the effects of cisapride (CIS) on symptoms and glucose control in pts with diabetic autonomic neuropathy.

Methods. Patients (pts) with a history of insulin-dependent diabetes mellitus ≥ 5 yrs, under medical control ≥ 3 months and with chronic abdominal symptoms, suggestive of delayed gastric emptying due to autonomic neuropathy, were eligible. They received CIS 10 mg qid. Patients were evaluated at start and after each month during a 3 month period. Several dyspeptic symptoms and hypoglycemia were scored as absent, mild, moderate, severe, very severe. HbA1c was also measured. Dose changes, daily insulin-intake and glucose control (unsatisfactory, satisfactory, good and very good) were documented. Results. 544 pts (55 ± 13 yrs, 331 females, 174 with diabetic nephropathy, 294 with retinopathy and 316 with sensory neuropathy) participated. After 8 and 12 wks of treatment, 86% and 90% of pts had no or only mild symptoms. Before study, 65.2% of pts had no symptoms of hypoglycemia, 83% at end of the study. Only 4% still had main hyperglycemic symptoms of hypoglycemia. Glucose control was evaluated as good or very good in 31% of pts prior to study, 54% and 62% after 8 and 12 wks of treatment. After 12 weeks, the HbA1c decreased in 38% (71%) of pts. CIS was well tolerated. Dose increase was not required, while a decrease occurred in a few pts only. Conclusions. These data support that CIS relieves dyspeptic symptoms and may have a beneficial effect on glucose control in diabetic neuropathy, indicating that the difficult diabetic control in these pts may be related to disordered gastric emptying. There was no evidence for tachyphylaxis over this 3-month study period.

Overlapping Irritable Bowel Syndrome and Delayed Gastric Emptying Identify Different Subgroups among Patients with Functional Dyspepsia

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Classifications based on non-quantitative symptom questionnaires failed to recognize, among patients with chronic functional dyspepsia (FD), distinct subpopulations characterized by different pathophysiological patterns. We evaluated if dyspepsia subgroups identified by a questionnaire quantitating (0–3) the influence of dispeptic symptoms (epigastric pain, postprandial fullness, nausea, vomiting) on usual activities present different clinical and gastric motor patterns. A large group of strictly selected consecutive FD pts (total score ≥3 with at least one symptom ≥2) in the absence of organic, systemic, metabolic diseases were included in the study. The presence of at least 3 of Manning's criteria was required to diagnose irritable bowel syndrome (IBS). Prevalent pain (epigastric pain ≥2 with any other symptoms ≤1) was present in 84 pts (17%); prevalent discomfort (postprandial fullness and/or nausea and/or vomiting ≤2 with pain ≤1) was present in 222 pts (46%); the remaining 177 cases (37%) resulted unclassifiable. Results of scintigraphic GE of solids (638 kcal; 90% of chicken liver) were expressed as GE rates (%emptied/h). Fifty healthy volunteers served as controls (HC; GE rates: 40 ± 11%/h).

1344

Prevalent pain Prevalent discomfort Unclassifiable

Males/females (%) 61/39% 40/60%* 40/60%* Age (yrs) 41 ± 13 39 ± 12 39 ± 13 Overlapping IBS 12% 30%/* 30%/ Overlapping N 39 ± 13 28 ± 13%/** 30 ± 14%/** Delayed GE (%) 11% 42%/** 30%/* m ± SD; *p < 0.001 vs HC, **p < 0.005 vs prevalent pain, p* < 0.05 vs unclassifiable; X², ANCOVA adjusted for sex and age.

Conclusions: Patients with prevalent pain and patients with prevalent discomfort represent two distinct FD subgroups, respectively characterized by: 1) prevalent male gender, lower frequency of associated IBS, normal gastric emptying; 2) prevalent female gender, higher frequency of associated IBS, delayed gastric emptying.

Identification of Gastric Contraction by Surface Electrogastrography


Purpose: The aim of this study is to identify gastric contraction by surface electrogastrography (EGG).

Method: Simultaneous recording of antropyloroduodenal manometry and EGG was made in 10 functional dyspeptic patients during an hour fasting period. For EGG signal acquisition, high cutoff frequency was set 10 Hz and signal sampling frequency was 16 Hz.

Result: During motor quiescence period, the EGG showed normal smooth sine wave form. On time domain frequency analysis, there was only single dominant frequency of three cycles per minute, namely first harmonic. During antral contraction, the slow wave showed configurational change resulting in a late peak on its wave form. On time domain analysis, there was marked increase in second harmonic during contraction. When the power of second harmonic was compared to the manometric peaks, the increase in second harmonic was well matched with each group of gastric contractions.

Changes of Motility in the Stomach Transplant Implanted to the Small Intestine

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The objective was to study the morphofunctional restructuring of the stomach tissue implanted to the small intestine.
A tubular transplant on vascular pedicle was formed on the greater curvature of the stomach in 6 dogs. It was implanted into the initial portion of the small intestine. We used the electrophysiological parameters, the microbiology of the stomach stump, the transplant, the adjuvant and adjuvanting portions of the small intestine. We used the computer-assisted method of processing electric myogram data taken from implanted electrodes, impedancemetry, histologic and histochemical methods. Observation period was 1.5–3 years.

The obtained results indicate that from the first hours of transplantation in the transplant, besides the basic spectrum maximum located in the frequency range typical for basal stomach motility rate (0.05–0.10 Hz), there were noted additional maxima in the range of jejunum frequencies (0.27–0.29 Hz) and ileum frequencies (0.20–0.23 Hz). It is necessary to mention that the power of the basic maximum in the transplant was 6 fold higher than in the stomach stump. Within the further observation we found the restoration of the adhesion of the transplant. The impedancemetry findings confirmed the transplant contractions with the frequency of the stomach basal electric rate and the intestine basal electric rate.

The dystrophic abnormalities found in the smooth muscular tissue were presumably related with the adaptation of transplant muscular fibers to bowel peristalsis.

**1347 Simultaneous Validation of the Ultrasonographic Method and the Sulfasalazine Salivary Test for Gastric Emptying, Oro-Cecal and Duodeno-Cecal Transit Time Assessment — Comparison with the Isotopic Technique**

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**Aims:** To validate echographic gastric emptying after ingestion of a dyspeptic test meal and sulfasalazine (SAZ) salivary test in order to determine orocecal (OCTT) and duodeno-cecal transit time (DCTT) in comparison with the isotopic technique. **Methods:** Twelve healthy male volunteers were enrolled. In phase 1, after fasting for twelve hours, each volunteer consumed a dyspeptic test meal (1020 kcal) labelled with Indium 111-DTPA (11.1 MBq) and SAZ (2 gm). Gastric emptying time was assessed simultaneously by ultrasound and scintiscans. Salivary samples were collected from the 4th to the 14th hour and the first detection of sulfapyridine (SP) in saliva allowed the determination of OCTT. In phase 2, measurements of saliva appearance time were realized after administration of SAZ (2 gm) and Indium 111-DTPA (11.1 MBq) into the duodenum through a nasogastic tube. DCTT was assessed using the same method as OCTT. In both periods, scintiscans were taken until the visualization of the cecum. **Results:** The correlation between the two methods in the assessment of GE time was strong (110 ± 22 min and 72 ± 25 min; r = 0.70; p = 0.02). OCTT assessed by both methods was respectively 506 ± 83 min and 276 ± 56 min (r = 0.63; p = 0.07). The correlation between the two methods in the evaluation of DCTT was highly significant (232 ± 74 min and 178 ± 38 min; r = 0.083, p = 0.0002). Conclusion: This study validates echographic gastric emptying measurement in dyspeptic conditions. SAZ salivary test is a simple, non invasive, rapid and validated method for the evaluation of intestinal transit time useful in clinical pharmacology studies. It’s possible to study simultaneously gastric emptying time by ultrasound and OCTT by SAZ test. DCTT can be measured by the SAZ test but it requires further studies.

**1348 Polymerase Chain Reaction: A New Golden Standard for Diagnosis of Helicobacter Pylori Infection?**

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**Polymers chain reaction (PCR) has been recently proposed as a more reliable diagnostic tool for the identification of HP [1]. Aim of the present study was to compare diagnostic accuracy of this test in respect to rapid urease test (RT), histology (hiH) and culture (CO).**

**Patients & Methods:** 43 pts (22 males and 21 females), with a mean age (± SD) of 50 yrs (± 14), undergoing upper GI endoscopy for ulcer-like dyspepsia were enrolled. During endoscopy five antral biopsies were collected to evaluate HP infection which was assessed by RT (1 biopsy), hiH (2 biopsies, Giemsa), CO (1 biopsy) and PCR for urea gene. hiH and CO forces were disinfected with glutaraldehyde 2%, and specimens for each test were collected with different forces. Moreover, a ‘wash-out’ test (search of HP DNA in PCR in 10 ml of sterile saline solution collected after lavage of biopsy channel) was performed.

**Results:** HP infection was detected in 35/43 pts (81%) by PCR, in 26/43 pts (60%) by RT, in 24/43 pts (56%) by hiH and in 18/40 pts (45%) by CO. In three pts culture and PCR were unreliable for contamination of grown plates. No wash-out test was positive.

**Conclusions:** PCR seems to be the most accurate method to detect HP infection in the present series. Higher accuracy of PCR seems to be particularly useful to assess the presence of HP in cocoid form, such as after antibiotic or antisecretory therapies, or in pts with low bacterial charge, such as dyspeptic pts [1].

**1349 Is Helicobacter Pylori Serology on Plasma Accurate?**

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**Introduction:** Serology is an important epidemiological research tool for investigating H pylori. Serology is conventionally performed on serum but in a retrospective survey that we wished to perform the only sample available was plasma. We aimed to verify a commercial H pylori serology kit (Shield Diagnostica, antigen and antibody, plasma) against a gastric biopsy sample from same patient. **Methods:** Patients attending the endoscopy unit were enrolled into the study and H pylori status was determined by histology, rapid urease test, culture and 13C-urea breath test. Patients were defined as H pylori positive if any one of these three tests were positive. H pylori serology status was defined if only one test gave a positive result. 10 ml of serum and plasma was obtained from each patient and anti-H pylori IgG was measured by ELISA with a value of > 10 I/U defined as positive. **Results:** 96 patients were subjected to histology, rapid urease test, culture and serology for H pylori. In 30/36 (83%) the histology and rapid urease test were concordant. Rapid serology was positive (seropositive) in 6/36 pts (17%) and the rapid urease test was positive in 7/36 pts (19%). Serology was positive in 14 out of 16 (88%) patients and this was not associated with any other factor. Conclusions: This study demonstrates that the rapid urease test and serology is a fast, reliable and sensitive test for the detection of H pylori that can be performed in plasma.

**1350 B-Cell Clonality in Gastric Mucosa: The Significance of H. pylori Infection**

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**Data from our group (Gut, 1996 in press) indicate that gastric B-cell clonality is much more frequent than MALT (Mucosa Associated Lymphoid Tissue) lymphoma of which it is considered a precursor lesion. Therefore, despite the present study was to evaluate the behavior of clonality in patients with and without H pylori infection after eradication. Methods: We followed for up to twenty-six months fourteen H pylori positive and one H pylori negative patients initially subjected to upper endoscopy and tested for B-cell clonality. H pylori infection was treated according to standard regimen including omeprazole bid or tid plus amoxicillin bid or tid. In case of lack of eradiation amoxicillin was substituted by clarithromycin. B-cell clonality was tested by VDJ-PCR using two protocols (Fr1 and Fr2) and reverse transcriptase-PCR (RT-PCR) and validated method and criteria. Conclusions: The obtained results indicate that from the first hours of transplantation in the transplant, besides the basic spectrum maximum located in the frequency range typical for basal stomach motility rate (0.05–0.10 Hz), there were noted additional maxima in the range of jejunum frequencies (0.27–0.29 Hz) and ileum frequencies (0.20–0.23 Hz). It is necessary to mention that the power of the basic maximum in the transplant was 6 fold higher than in the stomach stump. Within the further observation we found the restoration of the adhesion of the transplant. The impedancemetry findings confirmed the transplant contractions with the frequency of the stomach basal electric rate and the intestine basal electric rate. The dystrophic abnormalities found in the smooth muscular tissue were presumably related with the adaptation of transplant muscular fibers to bowel peristalsis.

**Polymerase chain reaction:**

**1351 Sensitivity and Specificity of 14C Urea Breath Test for Helicobacter Pylori Infection Diagnosis in Patients with Gastric Duodenal Ulcers**

M. Di Silvio 1, J. Larish 2, B. Vega 1, M. Dehena 2, M. Bibilodos 3, F. Amigo 2, L. Rodriguez 2, I. Almaguer 1, J. Torres 2, 1 Clinical Research Byk Gulden Mexico; 2 TRI-MED Specialties, USA; 3 Centro Medico Nacional Siglo XXI IMSS, Mexico

**Objective:** The aim of this preliminary report is to compare the sensitivity and specificity, in an ongoing clinical trial, of 14C urea breath test (UBT) versus rapid urease test (CLOtest), microbiology and histology, in order to evaluate H pylori infection diagnosis in patients with florid duodenal ulcer.

**Methods:** 36 patients (23 male) mean age 51 with no prior proton pump inhibitors or antibiotics intake 30 days before the study or history of gastric
surgery were included. Fasted patients swallowed 1 gelatin capsule with 200 mg of sugar beads containing one microcart of 14C-labelled urea; after 15 minutes a breath sample was collected in a balloon, the isotope linked to scintillation fluid was quantified by beta-counter. At endoscopy several samples were taken from antrum and corpus and used for CLOtest, histology and microscopy; a gastric biopsy was taken for molecular analysis.

Results: 34/46 (94%) patients with endoscopically demonstrated florid duodenal ulcer had positive CLOtest, positive in histology (GiemsA, H&E) and positive cultures for H. pylori. In this test 14C-UTB readings showed an average of 1766±416 counts/min, cut-off value 0.15/184. 2 patients with negative CLOtest, histology and culture showed also very low 14C-UTB readings (6 and 4 DPM respectively). In this study 14C-UTB, as a tool for H. pylori detection, had sensitivity and specificity of 98% and 100% respectively.

Conclusions: Non-invasive 14C-UTB is an excellent method for H. pylori infection diagnosis, easy to perform and timeless, with accuracy and reproducibility comparable to gold standard methods.

**1352 Detection of Helicobacter Pylori in Post-Treatment Gastric Biopsy: Comparison between Current Histology, CLO Test and H.P.-DNA PCR**


**Background/Aims:** A sensitive and specific methodology is necessary for detection of H. pylori in gastric biopsy to evaluate post-treatment microendoscopic presence. This would allow to differentiate recrudescence from reinfections.

The aim of this study was to compare the sensitivity of gastric biopsy, CLO test and H.P.-DNA PCR for the detection of H. P. in a group of recently treated patients with peptic ulcer disease.

**Patients and Methods:** H.P.-DNA PCR was performed gastric biopsies from 50 treated patients (33 males and 17 females) (age: 48 ± 12 years), in whom successful treatment was defined only by histological means and CLO test. Therapeutic schemes were as follows: Treatment 1 (11 patients) Amoxicillin 500 mg b.i.d. during plus Metronidazol 500 mg b.i.d. plus Diridolor Bismuth Tripotassic 120 mg q.i.d. during 14 days. Treatment 2 (19 patients) Omeprazole 20 mg b.i.d. plus Nitrofurantoin 250 mg b.i.d. during 3 days. Treatment 3 (20 patients) Amoxicillin 1 gr b.i.d. plus Lanzoprazol 20 mg/day. H. pylori eradication was defined on histological grounds (gastric histology: 10% buffered formal fixation; paraffin inclusion; GiemsA and HE staining). CLO test (Delta West Pty, Ltd. Bentley, Australia) and the absence of H.P.-DNA by PCR (amplification of a 296 bp of the species-specific antigen of H. P. and visualization of the amplified product in agarose gel with Ethidium Bromide and U.V. light), all of them performed within 6 to 8 weeks after the end of treatment.

**Results:**

<table>
<thead>
<tr>
<th>Histology &amp; CLO test</th>
<th>PCR</th>
</tr>
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<tbody>
<tr>
<td>Positive Negative</td>
<td>Positive Negative</td>
</tr>
<tr>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
</tr>
</tbody>
</table>

1 out of 6 (16.7%) reinfeeted patients received treatment 1, 3 of them (50%) treatment 2 and the other 2 (33.3%) treatment 3.

Conclusions: H.P.-DNA PCR is more sensitive than conventional accepted methods for assessing H. P. presence in the immediate post-treatment period, and is clearly superior to histology and CLO test. This would allow discriminate between residual replication and true reinfection of H. P. on a long term follow up basis of these patients.

**1353 The Occurrence of IgG Antibodies to High Molecular Weight Proteins of H. Pylori Antigen Among Duodenal Ulcer Patients and Practically Healthy Persons in Lithuania**

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**Purpose**—To assess in duodenal ulcer (DU) patients and practically healthy persons the presence of high molecular weight (85 and 120 kDa) IgG antibodies to H. pylori (HP). **Material and Methods:** The sera of 22 consecutive patients with DU and 18 practically healthy medical students were analysed for IgG antibodies in ELISA and immunoblot using eight different HP preparations of HP (NCTC 11637) as antigen. ELISA results were expressed as relative antibody activity (positive > 35). Presence of high molecular weight IgG antibodies to HP by western blotting method were assessed semiquantitatively. Results: The highest ELISA signal was seen in patients with DU and in DU patients with positive CLO test and controls. In the sera of DU ulcer patients, antibodies to 120 kDa protein were expressed in 21/22 cases and to 85 kDa in 18/22 cases. In control group sera reacting to 120 kDa protein was found in 13/18 cases and to 85 kDa antigens in 12/20 samples. The frequency and expression of 120 kDa antigens in DU patients were significantly higher (P < 0.001 according to the x2 test) in comparison with the control group. No statistically significant differences in frequency of 85 kDa antigen were revealed between the groups. Conclusion: Our pilot study showed high frequency of 120 kDa antigen among Lithuanian DU patients (95.6%) as well as the control group of practically healthy persons (73.2%). The prevalence of virulence factors of HP infection (especially CagA—cytoskeleton-associated protein related to 120 kDa protein) could likely explain high peptic ulcer morbidity and complication rate as well as high gastric cancer rate in Lithuania.

**1355 Plasma Nitrate/Nitrite Level is Higher in Patients with Peptic Ulcer Disease and Chronic Gastritis – The Increase is Independent of Helicobacter Pylori Status or Eradication**

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Plasma nitrate/nitrite levels reflect the endogenous nitric oxide production in fasting human. Both elevated and unaltered nitric oxide synthase activity in the gastric mucosa, and in contrast, decreased levels and in the plasma have been reported in patients with peptic ulcer disease. Helicobacter pylori (H. pylori) infection has been shown to induce nitric oxide synthesis in the gastric mucosa in vitro, but no data is available about the in vivo conditions.

To answer the questions whether 1) nitric oxide synthesis is enhanced, 2) the increase is disease specific, and 3) whether it has any correlation with H. pylori infection; we measured plasma nitrate/nitrite levels in 50 patients (mean age 50 ± 15 y.o.) with upper gastrointestinal symptoms. We also studied the effect of H. pylori infection and the follow-up gastritis in these patients. Blood was obtained from patients with upper gastrointestinal symptoms immediately after gastroscopy, and was repeated at 4 weeks after successful H. pylori eradication. Plasma nitrate/nitrite was measured by HPLC at 50 μM using a cadmium column for nitrate measurement.

Plasma nitrate/nitrite level was significantly higher both in patients with peptic ulcer disease (87 ± 48 μM, n = 12) and chronic gastritis (47 ± 18 μM, n = 23), when compared with that in patients with reflux oesophagitis (33 ± 5 μM, n = 6) or dyspepsia symptoms (29 ± 10 μM, n = 31). No correlation with histology grading, plasma nitrate/nitrite level increased significantly as the severity of chronic gastritis progressed (grade I = 44 ± 14 μM, grade II = 49 ± 21 μM, grade III = 113 ± 56 μM). There was no difference in plasma nitrate/nitrite levels between H. pylori positive (n = 32) and negative (n = 18) patients (61 ± 39 μM vs. 42 ± 18 μM). Successful eradication of H. pylori did not alter the elevated plasma nitrate/nitrite levels (data not shown).

Based on the elevated plasma nitrate/nitrite levels observed, nitric oxide synthase activity of gastric mucosa is enhanced in patients with peptic ulcer disease. This increase, however, is specific neither for peptic ulcer disease nor for H. pylori infection, since it can also be observed in patients with chronic gastritis and after the successful eradication of H. pylori.

**1356 Screening for IgG Antibodies Against Helicobacter Pylori**

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Screening for IgG antibodies against HP can be used for omitting endoscopy in selected cases. The present study was done in order to assess the best screening strategy. The population consisted of non selected consecutive patients referred for endoscopy closely related to peptic ulcer disease.

We also studied the effect of H. pylori infection and the follow-up gastritis in these patients. Blood was obtained from patients with upper gastrointestinal symptoms immediately after gastroscopy, and was repeated at 4 weeks after successful H. pylori eradication. Plasma nitrate/nitrite was measured by HPLC at 50 μM using a cadmium column for nitrate measurement.

Plasma nitrate/nitrite level was significantly higher both in patients with peptic ulcer disease (87 ± 48 μM, n = 12) and chronic gastritis (47 ± 18 μM, n = 23), when compared with that in patients with reflux oesophagitis (33 ± 5 μM, n = 6) or dyspepsia symptoms (29 ± 10 μM, n = 31). No correlation with histology grading, plasma nitrate/nitrite level increased significantly as the severity of chronic gastritis progressed (grade I = 44 ± 14 μM, grade II = 49 ± 21 μM, grade III = 113 ± 56 μM). There was no difference in plasma nitrate/nitrite levels between H. pylori positive (n = 32) and negative (n = 18) patients (61 ± 39 μM vs. 42 ± 18 μM). Successful eradication of H. pylori did not alter the elevated plasma nitrate/nitrite levels (data not shown).

Based on the elevated plasma nitrate/nitrite levels observed, nitric oxide synthase activity of gastric mucosa is enhanced in patients with peptic ulcer disease. This increase, however, is specific neither for peptic ulcer disease nor for H. pylori infection, since it can also be observed in patients with chronic gastritis and after the successful eradication of H. pylori.
Detection of Helicobacter Pylori in Faece by PCR Assay

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Helicobacter pylori (Hp) is the major cause of chronic gastritis and has been associated with gastric cancer [1]. There are some evidences for a faecal-oral transmission, even if few data are available about Hp detection in faeces. Recently, Hp genome has been detected by PCR in faeces from patients with gastritis [2]. Notwithstanding, faecal samples can easily give false-negative results because different chemicals present in faeces, such as polysaccharides, inhibit PCR [3]. Aims of our study were: 1) to remove the possible inhibitors present in faeces and 2) to detect by PCR the presence of Hp in faecal samples of symptomatic patients undergoing endoscopy in our Institute. Patients and Methods: Fifty consecutive patients (28 males, mean age 51.8 ± 10.4, and 22 females, mean age 48 ± 12.8) entered the study. Faecal samples were suspended in phosphate buffered saline pH 7.4. The mixture was filtered by polypropylene filter (mesh opening 149 μm) in order to remove PCR inhibitors. DNA was extracted from faeces by Tri-Reagent (Mol. Res. Center Inc, Cincinnati, OH, USA), and subsequently amplified by the primers taken from urease gene A. PCR products were separated and identified by electrophoresis on 2% agarose gel. Results:

<table>
<thead>
<tr>
<th>Warthin Stary</th>
<th>PCR</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hp positive</td>
<td>34</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Hp negative</td>
<td>16</td>
<td>0</td>
<td>16</td>
</tr>
</tbody>
</table>

Hp specific DNA was detected in 86% of faecal samples with a specificity of 100%. Conclusions: The present findings suggest a faecal oral route of Hp transmission. Nevertheless, an unequivocal pattern of Hp spread cannot be established. The presence of Hp DNA in our samples may be due to DNA from non viable or viable cells present in faeces. Finally, since Hp detection in faeces by PCR is a non-invasive method, it may represent a useful tool for the follow-up after eradication therapy.

Reference:

Determination of the Antibodies Raised against H. Pylori (Hp) by a Western Blot Method in 136 Patients with Gastroduodenal Ulcer, Gastric Malt Lymphoma

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Different gastrointestinal diseases could be related to a particular antigenic profile of Hp strains. The aim of this study was to compare, by using Hp serological test by Western Blot (Helico Blot 2.0, Genelabs), the different antibodies present in patients with gastric (GU) or duodenal ulcer (DU), gastric MALT lymphoma or non ulcer dyspepsia. Fifty-one patients with DU, 21 with GU, 17 with gastric MALT lymphoma and 35 with dyspepsia and normal gastro-duodenal endoscopy were selected by a positive Hp Elisa serological test (Enzygnost, Berhing). By using Western Blot serology, the presence of antibodies against different molecular weight antigens (19.5, 26.5, 30 or 35 kD) or against VacA (89 kD) and CagA (116 kD) was compared in the different groups. Results are shown in the table (percentages of patients with antigen):

<table>
<thead>
<tr>
<th>Antigen</th>
<th>19.5 kD</th>
<th>26.5 kD</th>
<th>30 kD</th>
<th>35 kD</th>
<th>89 kD</th>
<th>116 kD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DU</td>
<td>51</td>
<td>88</td>
<td>73</td>
<td>75</td>
<td>45</td>
<td>86*</td>
</tr>
<tr>
<td>GU</td>
<td>52</td>
<td>86</td>
<td>62</td>
<td>62</td>
<td>62</td>
<td>76</td>
</tr>
<tr>
<td>MAL</td>
<td>35</td>
<td>94</td>
<td>53</td>
<td>53</td>
<td>35</td>
<td>76</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>40</td>
<td>83</td>
<td>43</td>
<td>46</td>
<td>37</td>
<td>43</td>
</tr>
</tbody>
</table>

* p < 0.01 as compared with the group with dyspepsia.

The serology by Western Blot confirms the strong prevalence of CagA in patients with DU but is not able to distinguish a particular pattern in patients with GU or gastric MALT lymphoma.

Sensitivity and Specificity of a Rapid Whole Blood Test for "In Office" Diagnosis of Helicobacter Pylori

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Purpose: to evaluate sensitivity and specificity of a new commercially available whole blood test for "in office" evaluation of Helicobacter pylori (Hp) status (Medcard, Medimar, Milano Italy).

Methods: Dysequilibrated patients with no previous intake of drugs acting on Hp pylori underwent upper GI endoscopy with biopsies for culture, urease test and histology (Haematoxylin & Eosin, Giemsa). Before endoscopy, each patient was evaluated for IgG to Hp pylori by an "in house" ELISA assay (previously validated: sensitivity and specificity 94%) and by Medcard. Patients were considered H pylori+ if both biopsy tests (Giemsa and/or culture/urease) and/or ELISA serology tested +ve.

Results: 94 patients (MF: 55/39, age: range 20-81, mean 43.1 yrs) have been evaluated; 55/94 (58.5%) tested positive Hp+. Tab. 1: Giemsa/urease/culture/ELISA and Medcard H pylori positivity according to endo-

<table>
<thead>
<tr>
<th>G/D/P/U</th>
<th>GC</th>
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<tbody>
<tr>
<td>Giemsa/urease/culture/ELISA+</td>
<td>42%</td>
<td>63%</td>
</tr>
<tr>
<td>Medcard+</td>
<td>37%</td>
<td>59%</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>59</td>
</tr>
</tbody>
</table>
1362 How Do Two Diagnostic Tests for H. pylori at 1 Month Compare to Two ¹³C-Urea Breath Tests (UBT) in Assessment of Eradication?


Introduction: To evaluate the eradication of H. pylori it has been suggested that either 2 diagnostic techniques might be used 1 month (m) post-treatment, or that UBT alone might be performed at both 1 and 3 m post-treatment. Data from 7 multinational studies conducted to the standards of Good Clinical and Laboratory Practice are presented for a series of time points.

Methods: Patients who had an active DU and positive CLoTest™ pre-treatment, were evaluated post-treatment. H. pylori was assessed by UBT (excess 3.5 ¹³CO₂ per m = positive) and at least 1 other test, [CLoTest, histology (Hx), or culture (Cx)]. Before and 1, 3, 6, or 12 m post-treatment, dependent on study, UBT, Hx, and Cx (antral and corpus biopsies) were processed by central laboratories. H. pylori status assigned from the pooled result of UBT at 1 and either 3, 6, or 12 m was compared with the pooled result of the two subset of diagnostic tests at 1 m, and also the UBT alone at 1 m, in the same subset of patients.

Results: 1BGT (1 m = 3) (1 m + 6 m) (1 m + 12 m) % H2 -ve (n = 277) % H2 -ve (n = 477) % H2 -ve (n = 69)
Pooled UBT 59.9 50.3 49.3
Two tests 61.2 54.7 50.7
UBT alone 64.3 56.0 50.7

Conclusions: 2 diagnostic tests at 1 m post-treatment or the pooled result from controls at 1 m correlated significantly with a definitive assessment of H. pylori eradication. UBT alone at 1 m gives a slightly raised estimate of eradication, but on balance compares favourably for clinical practice by not requiring endoscopy whilst giving a rapid answer.

1363 Current Use of Helicobacter Serology for Pre-Endoscopy Screening in the UK

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Considerable savings have been reported using Helicobacter pylori (HP) serology as a pre-endoscopy screening test for young dyspeptics although the extent of these savings and the efficacy of various clinical strategies have been disrupted. We conducted a survey amongst UK hospital gastroenterologists and general practitioners with an interest in gastroenterology to establish current practice in the management of dyspepsia under the age of 45 years. Postal questionnaires were sent to 536 members of the British Society of Gastroenterology and 164 members of the Primary Care Gastro Society in Gastroenterology. The response rate was 66%.

HP serology is currently used by 25% of general practitioners and 17% of gastroenterologists. Following screening, most general practitioners would eradicate infection prior to endoscopy (82.4%) whilst most gastroenterologists (74.5%) would endoscopy patients before treatment. 70% of gastroenterologists would endoscopy sero-positives but 30% would endoscopy sero-negatives. Of those not currently using serology, 78% would use it as a pre-endoscopy test if it was available. 106 different drug regimens were used by respondents as first line HP treatment. 83.4% used triple therapy and the most popular combination was that of omeprazole, amoxicillin and metronidazole (38.2%). Following treatment 57% of respondents re-tested selected patients, 29% re-tested all patients and 14% never re-tested.

Our survey shows that in the UK, HP serology is being used as a pre-endoscopy screening test for young dyspepsia by only a fifth of gastroenterologists. There are wide variations in strategies preferred by hospital gastroenterologists and by general practitioners. Trials comparing symptomatic outcome and economic consequences of different HP serology based clinical strategies are needed.

1364 Helisal Rapid Whole Blood Test for the Diagnosis of Helicobacter Pylori

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Diagnosis of Helicobacter pylori by histopathology, culture, urea breath tests or serology using enzyme linked immunosorbent assay (ELISA) are relatively time consuming. A test kit for diagnosing H. pylori using diluted whole blood has become commercially available (Helisal™- Cortecs Ltd). This test is easy to perform, requires no laboratory equipment. Our aim was to independently assess its diagnostic accuracy.

Dyspeptic patients referred for investigation at our hospital were invited to participate. Patients who had received proton pump inhibitors over the previous month or had previously received antibiotic eradication therapy were excluded. ¹³C urea breath test was used as the gold standard for H. pylori status. All urea breath tests and rapid whole blood tests were performed by a single investigator.

39 patients were recruited in this study (median age 52.5, range 10 – 72 years, 51 males. All rapid whole blood tests were completed within ten minutes. Of the 59 patients H. pylori positive by urea breath test, 4 were false negative by rapid whole blood test. Of the 33 patients H. pylori negative by urea breath test, 11 were false positive by rapid whole blood test. Sensitivity and specificity of the kits for H. pylori were 93% of 67% respectively.

The Helisal rapid whole blood test was quick and easy to perform. In our hands, its sensitivity was good but its specificity was less impressive.

1365 Intragastric Urea Activity in Helicobacter pylori (Hp) Infection after Urea Application

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The purpose of the study was to evaluate whether intragastric ammonia production with exogenous urea as substrate by bacterial urease could be a criterion of severity H.p. infection and efficacy of therapy.

Methods: In 31 patients (pts), F, 19-68 yrs, and E, 18-61 yrs with peptic ulcer (6 pts) or gastritis (25 pts) and H.p. infection (in 14 severe), the ammonia output (mg/h) in basal (BAO) and pentagastrin (6 μg/kg s.c.) stimulated gastric juice (MAO) was estimated. In 15 pts MAO after repeated stimulation during i.g. infusion of urea solution (7.5 g/50 ml H₂O + 4%) was collected. This test was repeated after treatment with triple or bismuth salt therapy when indicated.

Results. The ammonia output (A.O.) in MAO before treatment was almost twice higher than in MAO (20.9 ± 12.5 vs 10.9 ± 4.8, p < 0.01). After effective therapy (8/15) it decreased by 40% in BAO, 57% in MAO, and 42% in MAO (p < 0.05). Ineffective therapy (3/15) did not affect the ammonia output significantly. The ratio of A.O. in MAO was markedly higher than in BAO/MAO and MAO/MAO before treatment (3.86 ± 2.92 vs 2.16 ± 1.41; p < 0.01) and vs 1.93 ± 0.93; p < 0.01). After effective therapy MAO/BAO decreased by 37% and MAO/MAO by 30% (p < 0.05), what was not the case after ineffective therapy. MAO/BAO ratio of A.O. after single stimulation was also reduced (1.45 ± 0.36 vs 2.98 ± 2.47) after effective treatment (p < 0.05).

Conclusion. The ammonia output in the pentagastrin stimulated gastric juice secretion could be simple and nonexpensive test of total gastric Helicobacter pylori infection and efficacy of therapy, especially when performed after application of exogenous substrate: urea for bacterial urease.

1366 Does a Second Biopsy Specimen Increase CLO-test Accuracy for Helicobacter Pylori (HP) Detection after Eradication Treatment in Duodenal Ulcer (DU) Patients


Rapid urease test is considered as a reliable and inexpensive method for HP detection. Histology (HIS) is the reference method although misdiagnosis is possible when HP density is low. It is suggested that the positivity of CLO-test is related to the HP burden. Translocation of HP to the fundus after anti-secretory treatment has been reported. The aim of our study was to evaluate the diagnostic accuracy of CLO-test(©)–Delta west Pty Ltd) in DU patients after HP eradication treatment. We compared CLO results with HP density and assess possible benefits by adding a fundic (F) or antral (A) biopsy. Patients and methods: 123 patients (81 men), with DU had 2A + 2B biopsies for HIS [modified Giemsa, Warthin Starn] and immunohistochemoinal (IHC) [Rabbit anti HP antibodies DAKO B 471] analysis 4–6 weeks after end of eradication therapy. All patients had a CLO test with one A biopsy (CLO1). 63 patients had a second one (CLO2) with one A and one F biopsy together while 60 patients had also a second one with two A biopsies together (CLO2a). Start t-test, X² test, Bartchloweez. Results: there were differences between CLO1 and CLO2 or CLO2a concerning the qualitative results. The time for the test to become positive was significantly shortened only when a second A biopsy was added (1.98 ± 0.28 vs 1.99 ± 0.75 h) p < 0.001. CLO-test compared to HIS had 56% Se, 98% Sp, 100% ppv and 66% npv while compared to IHC has 77% Se, 100% Sp, 100% ppv and 86% npv. CLO positivity was strongly correlated to HP density (p < 0.01). Conclusions: 1) the specificity of CLO-test is excellent for detection of HP after eradication treatment in DU patients, while its sensitivity is mediocre compared to IHC (77%) and poor compared to histology (58%) 2) The addition of a second biopsy specimen either A or F in the CLO-test does not improve its diagnostic value and 3) The disagreement between HIS and IHC (15/123 patients) needs further evaluation in order to avoid HP overdiagnosis.
1367 13C-Urea Breath Test and the Density of Helicobacter Pylori in Gastric Mucosa – Study of the Patients with Functional Dyspepsia

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The studies of Influence of Helicobacter pylori gastritis on symptoms of functional dyspepsia has produced inconclusive results. The 13C-urea breath test is a noninvasive method to detect the presence of H. pylori infection. The relationship between the results of 13C-UBT and the density of H. pylori in histologic samples is not established. The aim of our study was: 1. to analyse the relationship between the results of 13C-urea breath test and the density of H. pylori in histology and 2. to analyse the association between the symptoms of functional dyspepsia and the density of H. pylori in gastric mucosa.

Material and methods: 29 patients with functional dyspepsia were evaluated by gastroscopy and ultrasonography of upper abdomen. Every patient had a nonerosive H. pylori positive chronic gastritis without any other macroscopic abnormality. Biopsies from duodenum, antrum and corpus were taken for histological examination. The scores of the density of H. pylori were graded on a scale ranging from 0 to 6 (antrum 0–3, corpus 0–3). The dyspepsia symptom scores (range 0 to 12) were recorded by a standardized questionnaire. All patients received the 13C-UBT and the 13C-enrichment was analyzed by isotope ratio mass spectrometry. Statistical analysis was made by using simple linear regression analysis.

Results: The mean density of 13C-UBT was 43.0 ± 21.1, 000, the mean dyspepsia score was 4.2 ± 2.4 and the mean value of the density of H. pylori was 3.6 ± 1.4. There was a statistically significant association between the density of H. pylori in histological examination and the delta-value of 13C-UBT (p = 0.01, Pearson r = 0.48). There was no association between the symptoms of functional dyspepsia and the delta-value of 13C-UBT (p = 0.55, Pearson r = –0.12).

Conclusions: These data suggest that the delta-value of 13C-UBT is associated with the density of H. pylori gastritis. The severity of symptoms caused by functional dyspepsia are not associated with the density of H. pylori in gastric mucosa.

1368 Diagnostic Value of a Commercial IgG Enzyme-Linked Immunosorbent Assay (ELISA) Kit for Helicobacter Pylori Infection Diagnosis

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Enzyme-linked immunosorbent assays (ELISAs) are considered good non-invasive methods to diagnose H. pylori infection. The aim of this study was to evaluate the clinical usefulness of a commercial H. pylori antibody test kit.

Methods: A total of 400 patients attended the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. H. pylori was diagnosed if culture was positive or histology was positive in at least one of the biopsy samples shown to be positive. Ten milliliters of blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for H. pylori by a quantitative commercial IgG ELISA, based on an acid glycine extract: Helico G, Porton, Cambridge, UK. All the test was performed in duplicate according to the manufacturer’s instructions and by the same person. Results were evaluated on the basis of different cut-off values.

Results: In the study population, 86.8% of the patients were H. pylori positive (by culture). The serology results were as follows:

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 U/mL</td>
<td>96.3</td>
<td>53.7</td>
<td>94.9</td>
<td>78.6</td>
<td>2.1</td>
</tr>
<tr>
<td>10 U/mL</td>
<td>97.2</td>
<td>75.4</td>
<td>98.5</td>
<td>81.8</td>
<td>6.6</td>
</tr>
<tr>
<td>11 U/mL</td>
<td>94.7</td>
<td>85.4</td>
<td>99.3</td>
<td>70.8</td>
<td>6.4</td>
</tr>
</tbody>
</table>

PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio.

The area under the receiver operator characteristic (ROC) curve was 0.96.

Conclusions: This study confirms the diagnostic efficiency of this IgG commercial ELISA in detecting H. pylori infection. According to the manufacturer, 10 U/mL is the most appropriate cut-off value. The competitive cost of this technique and the fact that it is non-invasive render this method an optimum tool to study H. pylori infection in large population groups.

1369 Measurement of Helicobacter Pylori Antibodies in Saliva: A Non Invasive in Comparison with 13C-Urea Breath Test and Serology


Background & Aim: Numerous serological Kits are available to provide cheaper, non invasive and more rapid diagnosis of the Helicobacter Pylori (Hp) infection. This study evaluated the accuracy of the determination of IgG antibodies in saliva for detection of Hp status using 13C-Urea Breath Test (UBT) as golden standard.

Patients & Methods: 24 patients (mean age 50, sex: 10 F, 14 M) presenting bleeding peptic ulcer endoscopically documented with two antral biopsies and rapid urease test (RTU) and 24 controls (mean age 23, sex: 4 F, 20 M) without peptic disease were studied. We realized to all the patients venous puncture for serology tests (Helico-G), collection of saliva using OMNI-Sal collection device (SDS), and 13C-UBT. We exclude those patients in treatment with omeprazole, antibiotics or eradication therapy in the previous four weeks. The cut-off of salivary antibody was established between 0.8–1 U/ml and for serum Ig G titers in 10.

Results: In cases: 6 patients were UBT negative, being positive both serologies. In the biopsies and RTU all except one, were negative for Hp infection. We review the results and we found that all these patients had taken antibiotics for urinary infection during the hospitalization. We repeat the UBT 3–4 weeks later and 4 were positive and 2 continue negative. The control group had false positives due to low sensibility, spontaneous eradication or urea-producers pathogens.

Conclusions: The determination of specific Hp antibodies could be a valid method for determine Hp infection in patients with peptic disease but isn’t good for screening test.

1370 14C-Urea Breath Test in Detection of Helicobacter Pylori-Associated Gastric Diseases


Purpose: High urease activity of Helicobacter pylori (Hp) is used to detect this bacterium by non-invasive urea breath test (UBT). We employed the microtitre version of the test in which 1.5 mL of 13C-urea is given orally in capsule. The objectives of the study were: 1. to evaluate a microdose (37 kBq) 13C-urea enclosed in a quick dissolve capsule; 2. to assess whether the fasting period is required before the procedure of 14C-UBT; 3. to determine whether breath test results are changed when they are mailed to a remote site for analysis; 4. to define the diagnostic ranges of 14C-UBT for Hp-positive and Hp-negative patients.

Methods: In the study we breathe tested 239 consenting patients (18–75 year old) without previous antibiotic or antulcer therapy or gastric surgery. The breath samples were collected and analyzed before (at basal state) and at 10 min intervals after the ingestion of 37 kBq 13C-urea by patients prior to their endoscopy. With the cut-off value > 100 DPM as positive, UBT results correlated highly significant with combined results of invasive gold standards i.e. CLO-test and histology score.

Results: The breath test performed locally were almost identical with those read at remote laboratory. The data found for fasting and fed states of subjects agreed in 87%. When 14C-urea was dissolved in water and confined for 5 min in the mouth (without swallowing), both 30 Hp positive and 30 Hp negative patients with gastric UBT showed the presence of urease activity in the breath.

Conclusions: 1. 14C-urea in quick dissolved capsule is a convenient, non-invasive test for detection of gastric Hp with accuracy and reproducibility equal to those of gold standards; 2. feeding does not affect the accuracy of the test; 3. the results can be analyzed within 10–15 min locally or at a remote site; 4. orally applied liquid 14C-urea may lead to false positive results due to oral urease activity.

1371 Antibody Response to Helicobacter Pylori Antigens: Sensitivity and Specificity of IgG-ELISA and an H. Pylori Specific Immuno-Blot System


Background: H. pylori infection is either detected by invasive means using the urease test (HUT), histology, culture or noninvasively by 14C-urea breath test or serology. Antibody response may be determined either by ELISA or by immunoblott technique. Aim of our study was to investigate the sensitivity and specificity of a new immunoblot system in comparison to other methods.

Methods: 66 patients with chronic gastritis (CG), 29 with gastric (GU) and 25 patients with duodenal (DU) ulcer were tested for presence of H. pylori infection by HUT, histology, IgG-ELISA (Biored, Germany) and a new commercially available immunoblot (BAK, Germany) based upon H. pylori specific antigens. For evaluation of IgG-ELISA and immunoblot 66 patients with positive and 43 patients with negative HUT and histology served as reference for sensitivity and specificity respectively, as well as for positive (PPV) and negative (NPV) predicted value.

Results: Both methods showed highest sensitivity in DU sera, while specificity was best in CG patients. In most of the calculated parameters immunoblot results exceed all those of IgG-ELISA.
ELISA  Sensitivity  Specificity  PPV  NPV
CG  77%  67%  70%  56%
GU  76%  38%  76%  37.5%
DU  94%  14%  74%  50%

Conclusion: Tested immunoblot-system represents a suitable alternative for IgG-ELISA with even higher sensitivity and specificity and implies the possibility of screening for specific antigens of H. pylori strains in patients.

1372 Fibrinogen and H. pylori in Asymptomatic Post MI Patients and Healthy Controls
J. Rajput-Williams, N.R. Williams, P.G. Johnson, R.J. Dickinson.
1 Papworth Hospital, Cambridge, UK; 2 BSA, Brentford, UK;
3 Hinchinbrooke Hospital, Huntingdon, UK

A link between H. pylori seropositivity and coronary heart disease via plasma fibrinogen has been suggested, although this has been disputed. Fibrinogen (and Factor VII) were measured in non-smoking men who recently had a myocardial infarction (MI; n = 33) and healthy controls (n = 27) with known H. pylori status (assessed by 13C-urea breath test, BSA, UK). Results are presented below.

Table. Plasma fibrinogen. Results are mean (95% confidence interval). Statistical significance was assessed by t-test. Paired tests of comparisons are marked a, b and c.

<table>
<thead>
<tr>
<th>H. pylori</th>
<th>Fibrinogen (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control positive</td>
<td>2.68 (2.48–3.81)</td>
</tr>
<tr>
<td>Control negative</td>
<td>2.07 (1.85–3.06)</td>
</tr>
<tr>
<td>Post-MI negative</td>
<td>3.04 (2.82–3.26)</td>
</tr>
<tr>
<td>Post-MI positive</td>
<td>3.26 (2.84–3.89)</td>
</tr>
</tbody>
</table>

Methods: One-hundred and sixty-one patients with duodenal ulcer were prospectively studied. An endoscopy with biopsy samples (H&E stain) taken from antrum and body was performed, and a 13C-urea breath test (according to the European standard protocol, measuring 13CO₂ difference; 13CO₂ was also performed at initial moment. Both procedures were repeated one month after completing therapy: “classic” triple therapy, omeprazole or lansoprazole plus one antibiotic, or omeprazole plus two antibiotics (amoxicillin, clarithromycin, metronidazole). Eradication was defined as the absence of H. pylori both by histologic and breath test methods.

Results: At initial moment: 95.6% of patients (n = 153) were H. pylori positive by histologic methods, and 97.5% (n = 156) were positive by breath test (propotion of positive agreement = 0.96). Kappa for H. pylori diagnosis after therapy was 0.88 (EE: 0.08). A correlation between 13CO₂ and histologic lesions at initial moment was observed, both at the antrum (r = 0.23; p < 0.01) and body (r = 0.27; p < 0.01). Similarly, a correlation agreed in both gastric antrum (p < 0.01) and body (0.3; p < 0.001) was demonstrated. A significant difference was observed when comparing mean 13CO₂ in patients with different degrees of histologic gastritis, both at initial moment (antrum: W Kruskal-Wallis = 8; p = 0.05; body: W = 12; p < 0.05) and after therapy (antrum: W = 60; p = 0.001; body: W = 23, p < 0.001).

Conclusion: A high concordance was observe between 13C-urea breath test and histology in the diagnosis of H. pylori infection. A correlation exists between breath test values and histologic lesions of gastric mucosa.

1373 Is There Any Correlation between 13C-UREA Breath Test Values and Response to H. pylori Eradication Therapy?
J.P. Gisbert, D. Boixeda, Martin C. de Anglia, F. Bermejo, T. Pérez, I. Jiménez, J.M. Pajares, J.M. Ramón y Cajal Hospitals, Madrid, Spain; 1 la Princesa Hospitals, Madrid, Spain

Purpose: To study whether there is a correlation between urea breath test values prior to treatment and the response to H. pylori eradication therapy in patients with duodenal ulcer.

Methods: Two hundred and one patients with duodenal ulcer were retrospectively studied (mean age: 47 ± 12 years; 69% males). Initially, an endoscopy with biopsy samples (H&E stain) taken from antrum and body and a 13C-urea breath test (according to the European standard protocol, measuring 13CO₂ difference; 13CO₂ was performed. Both procedures were repeated one month after completing therapy: “classic” triple therapy (n = 29), omeprazole or lansoprazole plus amoxicillin (n = 56), and omeprazole plus two of the following antibiotics: amoxicillin, clarithromycin, metronidazole (n = 114).

Results: Overall, eradication was achieved in 66% (n = 132). The corresponding rates for the therapy groups were: “classic” triple therapy: 64%; omeprazole or lansoprazole plus amoxicillin: 33%; omeprazole plus two antibiotics: 83%. Mean 13CO₂ levels was −31.5 ± 23. There were no differences when comparing values of patients with therapy success (33 ± 24) and failure (30 ± 20). No differences were observed when considering therapies separately and comparing eradication rates depending upon breath test levels prior to therapy. Breath test values did not influence the eradication in the logistic regression model. Mean 13CO₂ values after therapy in patients with eradication failure ran in parallel with initial values. Conclusion: No correlation was observed between urea breath test values before treatment and the response to H. pylori eradication therapy in patients with duodenal ulcer. Thus, we conclude that quantification of this diagnostic method is not useful to predict the success or failure of eradication therapy.

1374 Breath Test for the Diagnosis of H. pylori Infection: Concordance with Histologic Methods and Correlation with Histologic Lesions of Gastric Mucosa

Purpose: To study the concordance between 13C-urea breath test and histology in the diagnosis of H. pylori infection, and to evaluate whether there is a correlation between breath test values and histologic lesions of gastric mucosa.

1375 Usefulness of the Combined Use of IgG and IgA ELISA Methods for Diagnosing Helicobacter Pylori Infection
C. Martín de Anglia, D. Boixeda, R. Cantón, N. Mir, S. Valdezarza, F. Bermejo, J.P. Gisbert, A.L. San Roman. Gastroenterology and Microbiology Departments, "Ramón y Cajal" Hospital, Madrid, Spain

 Aim: To determine the diagnostic value of the combined use of IgG and IgA ELISA methods to diagnose H. pylori infection.

Methods: A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. An endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. H. pylori was diagnosed if culture was positive in at least one of the biopsy samples obtained. Ten milliliters of venous blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for H. pylori by a commercial IgELISA (G.A.P. Test IgA, Bio-Rad, Italy) and a commercial IgELISA (Helicog, Porton, Cambridge, UK). The tests were performed in duplicate according to the manufacturer's instructions and by the same person. Two interpretations were possible: 1) Assumption 1: a serological result was considered positive for H. pylori when both methods (IgG and IgA) were positive, and negative when at least one of them was negative. 2) Assumption 2: a serological result was considered positive when at least one of the methods was positive, and negative when both methods were negative. Titres higher than 10 U/ml were considered positive (following manufacturer's recommendations) for both tests.

Results: In the study population, 89.8% of the patients were H. pylori positive (by culture). The serology results were as follows:

<table>
<thead>
<tr>
<th>Cut-off IgG/IgA</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/10 U/ml*</td>
<td>94.1</td>
<td>85.3</td>
<td>98.2</td>
<td>62.5</td>
<td>6.26</td>
</tr>
<tr>
<td>10/10 U/ml**</td>
<td>99</td>
<td>80</td>
<td>97</td>
<td>94</td>
<td>4.95</td>
</tr>
</tbody>
</table>

PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio; Assumption 1: **Assumption 2:

Conclusions: 1) The combined use of both serological methods provided more useful information compared with single IgG or IgA determinations. 2) The high specificity and PPV for assumption 1 render both determinations very useful when the clinician wishes to accurately know the "true" infection H. pylori status. 3) The extremely high sensitivity obtained with the assumption 2 renders this method very useful for screening large population groups.

1376 Diagnostic Value of a Commercial IgA Enzyme-Linked Immunosorbent Assay (ELISA) Kit forHelicobacter Pylori Infection Diagnosis
C. Martín de Anglia, D. Boixeda, N. Mir, S. Valdezarza, J.P. Gisbert, L. de Rafael, R. Cantón. Gastroenterology and Microbiology Departments, "Ramón y Cajal" Hospital, Madrid, Spain

Enzyme-linked IgA immunosorbent assays (ELISAs) are good non-invasive methods to diagnose H. pylori infection, but scarce information are available on IgA ELISAs. The aim of this study was to evaluate the clinical usefulness of a commercial IgA H. pylori enzyme test kit.

Methods: A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from gastric antrum and gastric body were obtained for histology and culture. H. pylori was diagnosed if culture was positive in at least one of the biopsy samples obtained. Ten milliliters of venous blood were collected at the time of endoscopy for serological assessment. Serum samples were analyzed for H. pylori by a semiquantitative commercial IgA ELISA, based on purified specific antigens: G.A.P. Test IgA. Bio-Rad, Italy. The test was performed in duplicate according to the manufacturer's instructions and by the same person. Results were evaluated on the basis of different cut-off values.
Results: In the study population, 89.8% of the patients were H. pylori positive (by culture). The serology results were as follows:

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<tr>
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<th>PPV (%)</th>
<th>NPV (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 U/ml</td>
<td>98.3</td>
<td>34.1</td>
<td>92.9</td>
<td>70.5</td>
<td>1.0</td>
</tr>
<tr>
<td>10 U/ml</td>
<td>96.4</td>
<td>80.5</td>
<td>97.7</td>
<td>71.7</td>
<td>4.9</td>
</tr>
<tr>
<td>11 U/ml</td>
<td>94.2</td>
<td>80.5</td>
<td>97.7</td>
<td>81.1</td>
<td>4.8</td>
</tr>
</tbody>
</table>

PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio.

The area under the receiver operator characteristic (ROC) curve was 0.9.

Conclusions: This study confirms the usefulness of this IgA commercial ELISA in detecting H. pylori infection. According to the manufacturer, 10 U/ml is the most appropriate cut-off value. The high sensitivity and positive predictive values render this method very useful for screening large populations groups.

1377 Blind Gastric Biopsy in the Diagnosis of Helicobacter Pylori Infection
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Gastric mucosal tissue is usually required for the diagnosis of helicobacter pylori (HP) infection. Serology, though a reliable method in initial diagnosis, is useless in assessing the response to the treatment. Breath test, on the other hand, is not widely available. We performed gastric mucosal biopsies through open-ended 18 FR naso-gastric tube (NGTs) with Olympus FB-25 KF naso-gastric forceps (Olympus, Japan) in 33 patients (19 female, 14 male, median age 38 yrs; range 11-72) with dyspeptic symptoms. The average distance between the end of NGT and nasal insertion site was 50-55 cm. Four specimens were obtained from each patient. Blind gastric biopsy (BGB) was repeated in 15 HP+ve patients one month after completion of treatment with 500 mg cidoxyfuramicin, 14 days, and omeprazole 20 mg bid, 28 days. Upper GI endoscopy was performed using a Fujinon FG-7/C2 panendoscope (Fujinon, Japan), immediately after BGB. The sites of biopsies were noted and four other specimens, two from corpus, and two from antrum, were obtained with the same type of forceps. Serological testing was performed from sera of 28/33 patients. All of the biopsies were evaluated by the same pathologist with hematoxylin-eosin staining in blinded fashion. 31/33 of initial biopsies obtained by endoscopic biopsy (EB) were +ve for HP. BGB was +ve in 30/31 of EB+ve. After treatment 13/35 (37%) were +ve for HP in both EB and BGB specimens and 2/13 (15%) were still +ve. All but one of the BGB specimens were negative. In 47/68 (68%), BGB were in accordance with EB. The only BGB sample with discordant result with EB was from distal esophagus, one of the first experiences. Serology was in accordance with biopsy results in all but one who was +ve by histology and -ve by serology. BGB was performed without anesthesia and tolerated well.

We concluded that the BGB is an easy, safe, reliable and cheap method in obtaining gastric mucosal tissue for HP evaluation. Its clinical value awaits further studies.

1378 IgA Values and Gastrointestinal Diagnosis of Helicobacter Pylori Infection
C. Martin de Anglés, D. Boixeda, L. de Rafael, R. Canton, N. Mir, J.P. Gisbert, A. García Plaza. Gastroenterology and Microbiology Departments. "Ramón y Cajal" Hospital, Madrid, Spain

Aim: Given the close association between H. pylori infection and different gastrointestinal conditions we undertook a study to assess whether IgA antibody mean values to H. pylori can discern the gastrointestinal condition among patients.

Methods: A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from duodenal bulb, gastric antrum, gastric body, and gastric fundus were obtained for histology and H. pylori culture. In patients who had undergone Billroth-II surgery biopsies were obtained from efferent loop, surgical stoma and gastric fundus. H. pylori infection was diagnosed if culture was positive in at least one of the biopsy samples obtained. In all patients IgA specific antibodies against H. pylori infection were determined. A semiquantitative commercial IgA ELISA based on purified specific antigens (G.A.P. Test IgA, Bio-Rad, Italy) was used.

Results: Table shows mean values of IgA specific antibodies and patients with positive culture for H. pylori.

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 U/ml</td>
<td>98.3</td>
<td>34.1</td>
<td>92.9</td>
<td>70.5</td>
<td>1.0</td>
</tr>
<tr>
<td>10 U/ml</td>
<td>96.4</td>
<td>80.5</td>
<td>97.7</td>
<td>71.7</td>
<td>4.9</td>
</tr>
<tr>
<td>11 U/ml</td>
<td>94.2</td>
<td>80.5</td>
<td>97.7</td>
<td>81.1</td>
<td>4.8</td>
</tr>
</tbody>
</table>

PPV = Positive predictive value; NPV = Negative predictive value; LR = Likelihood ratio.

The area under the receiver operator characteristic (ROC) curve was 0.9.

Conclusions: This study confirms the usefulness of this IgA commercial ELISA in detecting H. pylori infection. According to the manufacturer, 10 U/ml is the most appropriate cut-off value. The high sensitivity and positive predictive values render this method very useful for screening large populations groups.

1379 IgG Values and Gastrointestinal Diagnosis of Helicobacter Pylori Infection
C. Martin de Anglés, D. Boixeda, R. Cantón, S. Valdeza, C. de la Serna, J.P. Gisbert, L. de Rafael, Gastroenterology and Microbiology Departments, "Ramón y Cajal" Hospital, Madrid, Spain

Aim: Given the close association between H. pylori infection and different gastrointestinal conditions we undertook a study to assess whether IgG antibody mean values to H. pylori can discern the gastrointestinal condition among patients.

Methods: A total of 400 patients attended at the Endoscopy Unit because of symptoms attributable to the upper gastrointestinal tract were studied. At endoscopy, multiple biopsies from duodenal bulb, gastric antrum, gastric body, and gastric fundus were obtained for histology and IgG antibody specific antibodies against H. pylori infection were determined. A quantitative commercial IgG ELISA based on an acid glycin extract (Helico G, Pontor, Cambridge, UK) was used.

Results: Mean values of IgG specific antibodies and patients with positive culture for H. pylori:

<table>
<thead>
<tr>
<th>Endoscopic diagnosis</th>
<th>IgG (U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>77.7 ± 49.3</td>
</tr>
<tr>
<td>Gastric</td>
<td>83.5 ± 38.4</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td>104.2 ± 38.4</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>90.2 ± 33.1</td>
</tr>
<tr>
<td>Pyloric channel ulcer</td>
<td>110 ± 0</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>94.2 ± 28.1</td>
</tr>
</tbody>
</table>

Different symbols p < 0.05. In the remaining comparisons between different groups: p > 0.05.

Conclusions: The highest values of IgG specific antibodies to H. pylori corresponded to gastric ulcer, gastric cancer, Billroth-II gastric surgery and bulb duodenitis with erosions, but the small statistically significant differences between these diagnostics limit the usefulness of these findings.

1380 Prescribing Patterns for Dyspepsia in Primary Care
B. Nodjie, M.J. Daly, R.V. Heatley. Division of Medicine, St. James’s University Hospital, Leeds, England; Department of Pharmacy, St. James’s University Hospital, Leeds, England

Background Expenditure on drugs for dyspepsia in primary care remains high, yet there are few published studies on the indications currently used by general practitioners (GPs) for prescribing different classes of drugs. We report a prospective observational study of prescribing patterns in our area. Methods GPs were recruited from 5 local multi-partner surgeries, representing a cross-section of doctors respecting to size, funding holding status and prescribing expenditure. Each GP prospectively recorded details of all consultations for dyspepsia over a 4 month period. Results 257 consecutive consultations were recorded. Percentages of patients in specified dyspepsia sub-groups receiving each class of drug are summarised in the table: [Nil = No prescription, Ant = antacid, Mot = motility agent, HZA = H2- antagonist, PPI = proton pump inhibitor, HpE = H. pylori eradication]

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>Nil</th>
<th>Ant</th>
<th>Mot</th>
<th>H2A</th>
<th>PPI</th>
<th>HpE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>144</td>
<td>99</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>new</td>
<td>59</td>
<td>9</td>
<td>44</td>
<td>5</td>
<td>31</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>consulted</td>
<td>85</td>
<td>9</td>
<td>24</td>
<td>11</td>
<td>35</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>ulcer-like</td>
<td>22</td>
<td>18</td>
<td>9</td>
<td>0</td>
<td>68</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>reflux-like</td>
<td>50</td>
<td>8</td>
<td>40</td>
<td>2</td>
<td>16</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>non-specific</td>
<td>72</td>
<td>7</td>
<td>35</td>
<td>15</td>
<td>33</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Previously</td>
<td>113</td>
<td>5</td>
<td>9</td>
<td>5</td>
<td>35</td>
<td>31</td>
<td>14</td>
</tr>
<tr>
<td>investigations</td>
<td>27</td>
<td>11</td>
<td>19</td>
<td>7</td>
<td>37</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>minor disease only</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>33</td>
<td>31</td>
<td>14</td>
</tr>
<tr>
<td>peptic ulcer disease only</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>33</td>
<td>31</td>
<td>14</td>
</tr>
<tr>
<td>reflux oesophagitis</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>18</td>
<td>70</td>
</tr>
</tbody>
</table>

Different symbols p < 0.05. In the remaining comparisons between different groups: p > 0.05.

Conclusions: The highest values of IgG specific antibodies to H. pylori corresponded to bulb duodenitis, pyloric channel ulcers, gastrangitis and gastric cancer, but the small statistically significant differences between these diagnostics limit the usefulness of these findings.
1381 Evaluation of Duodenogastric Reflux and Antral Motility by Color Doppler Sonography in Patients Undergoing Cholecystectomy

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Purpose: To evaluate duodenogastric reflux, along with antral motility and gastric emptying of a liquid meal in patients underwent open and laparoscopic cholecystectomy.

Material and methods: 53 patients (15 male and 38 female), aged 35–56 years, underwent a treatment open or laparoscopic cholecystectomy. Color Doppler sonography (CDS). Duodenogastric reflux, antral motility, and gastric emptying of 400 ml liquid meal were evaluated. As a control group served 23 asymptomatic healthy volunteers.

Results: This approach was feasible in 51 (96.2%) of the 53 subjects studied. Duodenogastric reflux was demonstrated in 16 (59.3%) of the 27 patients underwent open cholecystectomy and in 22 (84.6%) of the 26 patients after laparoscopic cholecystectomy. The frequency of the duodenogastric reflux and the reflux index were significantly increased in patients after laparoscopic cholecystectomy as compared with open cholecystectomy and asymptomatic volunteers. Gastric emptying and antral motility index of antral contractions were significantly decreased in these patients.

Conclusions: Color Doppler sonography is useful for evaluating of gastroduodenal, especially in patients underwent laparoscopic cholecystectomy. These simple, noninvasive method can be used to understand the pathogenesis of such disorders.

1382 Prognosis of Dyspepsia among Patients in General Practice. Dyspepsia Subgroups and Patient Characteristics

V. Meinecke-Schmidt, T. Jorgensen. Dept. of General Practice, The Panum Institute and Surgical Dept. K, Bispebjerg Hospital, University of Copenhagen, Denmark

Aim: To assess the courses of different subgroups in dyspepsia.

Methods: In 1991 to 1993 all patients consulting 93 general practitioners (GPs) because of dyspepsia (N = 7270) had a structured interview, covering 18 dyspepsia symptoms. The patients were classified in dysmotility-like (dys), reflux-like (refl) ulcer-like (ulc) or uncharacteristic (unch) dyspepsia. Patients with two or more presentations to the GP were classified as relapsing (relap) dyspepsia. A random sample of 300 patients with dys, refl and ulc and all patients with unch (n = 114) and reflux-like (n = 57) were interviewed after an average period of 17–53 months through the GP. Both GPs and patients were asked to fill in a questionnaire. Information on consultation habits, upper endoscopy, dyspepsia symptoms and medication within the last year were also recorded.

Results: Among eligible patients, 98% of the doctors and 85% of the patients returned the questionnaires. Frequencies of various end-points according to the dyspepsia subgroups are shown in the table.

<table>
<thead>
<tr>
<th>End-point</th>
<th>Ulc %</th>
<th>Relf %</th>
<th>Dys %</th>
<th>Unch %</th>
<th>Relap %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms disappeared</td>
<td>8</td>
<td>10</td>
<td>19</td>
<td>28</td>
<td>1</td>
</tr>
<tr>
<td>Dyspepsia subgroup unchanged</td>
<td>46</td>
<td>32</td>
<td>35</td>
<td>27</td>
<td>--</td>
</tr>
<tr>
<td>Further consultations</td>
<td>66</td>
<td>51</td>
<td>59</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>Dyspepsia medication</td>
<td>65</td>
<td>53</td>
<td>33</td>
<td>23</td>
<td>63</td>
</tr>
<tr>
<td>Upper endoscopy</td>
<td>10</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

Patients with ulcer dyspepsia had the highest frequencies of consultation, endoscopies, medication and unchanged symptoms, whereas patients with uncharacteristic dyspepsia had the lowest frequencies. Relapsing dyspepsia seldom disappeared. Among the 67 deaths 24% were due to gastrointestinal disorders.

Conclusions: A classification of dyspepsia patients in general practice reveals differences in course, consultations, investigations performed, and medication given. The classification could be useful tool in decision making.

1383 Demographic, Socio-Economic and Stress Factors in Patients with Upper Gastrointestinal Symptoms (Dyspepsia) Who Seek Medical Help: Impact on the Therapeutic Response to Cisapride

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Stress factors and personality traits seem to influence the appearance and symptomatology of non ulcer dyspepsia and other related conditions. In order to assess the prevalence of economic, socio-demographic and stress factors in dyspeptic patients, as well as to determine whether an influence exists on the initial symptom score and the response to treatment with cisapride, an open multicenter study was carried out in a Portuguese population of dyspeptic patients.

96 ambulatory patients with dyspeptic symptoms since at least four weeks were studied. Patients with history, symptoms or signs of organic underlying disease were excluded. At selection upper gastrointestinal symptoms were assessed and patients were asked to complete a stress questionnaire giving details of socio-economic situation, health, living habits and stress factors according to the Holmes and Rahe scale. Patients were treated with cisapride 5 mg t.i.d. for 4 weeks and their symptoms were reassessed at the end of treatment. It was possible to establish a relationship between some stress factors and the severity of initial symptoms and their response to treatment. Independence at work, regularity of meals, number of medical visits and non gastrointestinal symptoms were all correlated to the severity of the initial symptoms.

The response to the treatment was good in the vast majority of patients (p < 0.0001) and also influenced by the independence at work, the regularity of meals and their smoking habits. The other 17 stress factors evaluated were not significantly correlated with the patient symptomatology either before or after treatment.

In conclusion in this patient population only 4 out of 20 stress factors were correlated with dyspeptic symptoms and its treatment. This lack of correlation for the majority of stress factors is perhaps due to the number of patients and the big variability in this population and their response.

1384 Symptom Profile of Dyspepsia in Latin America: A Multicentric Study

I.M. Bustos Fernandez 1 and the General Trial Coordinator, and Dyspepsia Study Group. 1 Instituto de Gastroenterología Dr. Bustos Fernandez, 1428 Buenos Aires, Argentina

Dyspepsia is a broad symptom complex, overlapping with the irritable bowel syndrome (IBS). Studies often focus on epigastric pain. We studied the symptom profile in dyspeptic patients (pts) in Latin American populations and the response to cisapride (CIS).

Method: Phase I: 7.13 GP's in cooperation with local gastroenterologists, from Argentina, Bolivia, Paraguay, Uruguay and Venezuela enrolled 4020 pts with dyspepsia (> 4 weeks). Pts were evaluated for demographic and disease characteristics, as well as symptoms, and classified into dysmotility-like (D), ulcer-like (UL), reflux-like (RL) or non-specific (NS) dyspepsia. Phase 2: Pts were treated with CIS 10 mg t.i.d. for 4–8 weeks; pts with alarm symptoms, UL symptoms or history of ulcer/GORD, or receiving medication for GI symptoms or regular NSAIDs were excluded.

Results: 3744 cases (47.8 ± 1.5); 19–92 yrs; 87,781/3 M/F were eligible for analysis: 47.3% had DL dyspepsia, 12.1% UL, 13.1% RL and 3.2% NS. Mixed types of dyspepsia were: 3.6% DL + UL, 12.2% DL + RL, 2.2% UL + RL, and 65% DL + UL + RL. Concomitant disease was present in 50% of pts, history of previous ulcer and oesophagitis in 7.2% and 16% resp. Excessive use of alcohol, coffee or smoking was found in 20%, 53% and 28% resp. The most common symptoms were: postprandial fullness (in 83%), epigastric bloating (63%), belching (72%), postprandial nausea (66%), diffuse epigastric pain (84%), early satiety (62%) at intolerance (58%) and heartburn (53%). Localized epigastric pain was present in 49%, nocturnal pain in 19%, periodic discomfort or pain in 46% and relief by meals or antacids in 32%. 55% had concomitant symptoms of IBS (37% UL + RL, 74% in the mixed DL + UL + RL). Of the 2965 pts treated with CIS, 67% and 21.6% had excellent and good responses resp.; 6.7% experienced adverse events (leading to discontinuation of treatment in 23 pts only).

Conclusions: DL symptoms prevail among the Latin American dyspeptic population. Overlap with IBS is very common. Pts (after exclusion of significant UL or alarm symptoms) respond well to CIS.
upper GI symptoms. Although the high number of patients seen per week by doctors in Japan must increase detection rates of upper GI disease, the data does suggest a higher incidence of these disorders when compared to other countries in the survey. Sweden had the lowest incidence with 80% of GP's seeing 10 or less patients per week with upper GI symptoms. Clear differences were seen in the habits of doctors from different countries to H. pylori (Hp) eradication programs. In those patients testing positive for Hp, eradication was considered logical by over 50% of doctors in 4 countries and by under 50% of doctors in the remaining 7 countries. The percentage of doctors agreeing that patients with duodenal ulcer need further investigation prior to Hp treatment, varied from 42% to 72%.

In summary, this IGGCP international survey demonstrates the different approaches taken by the participating countries in the management of upper GI disorders and highlights the fact that any conclusions drawn from limited data (from one or a few countries) may not apply on a worldwide basis.

The Clinical Presentation of Peptic Ulcer Disease

RJF Loffeld, BFM Werdmuller, A.B.M.M. van der Putten. Department of Internal Medicine, Ziekenhuis De Heel Zaandam, The Netherlands

According to the literature the discriminative value of the classical ulcer symptoms is rather poor. A prospective study was done in order to assess the presentation of peptic ulcer. Consecutive patients undergoing upper GI endoscopy received a questionnaire consisting of 62 different questions. 23 questions were related to the upper abdomen. Eleven questions were scored on a linear scale, a symptom score was calculated (minimum score 2, maximum score 55). In addition the reason for doing the endoscopy, the duration of complaints, the medical history, smoking habits, alcohol use, and use of anti-ulcer drugs were noted. Patients with a gastric (GU) or duodenal (DU) ulcer were included. Patients with concomitant abnormalities like gastric carcinoma or reflux esophagitis were excluded. As a control group patients, in whom endoscopy did not reveal abnormalities were included. This group, for the sake of the study, was divided into two groups, as functional dyspepsia (FD), was subdivided pending on whether his history was positive (FD+) or negative (FD--) for peptic ulcer.

GU was diagnosed in 43 patients (c24, 24, mean age 67), DU in 60 (c20, c27, mean age 52), FD in 94 (c49, 49, mean age 55), and FD-- in 382 (c148, c134, mean age 47). Patients with GU were significantly older (p < 0.0001) than the other groups; while FD-- patients were the youngest. DU was more often diagnosed in men, while FD-- was present more often in women. Patients with DU and FD were significantly more often treated with anti-ulcer drugs prior to endoscopy (p < 0.001). The symptom score was 14 in GU, 16.6 in DU, 19.5 in FD+, and 16.7 on FD--. Patients with FD+ had significantly higher symptom score than the other groups. The mean ± SD of number of complaints present was 8.1 in GU, 9.2 in DU, 9.6 in FD+, and 9.2 in FD--.

No statistical differences were present. If all ulcer patients (amalgamation of GU, DU and FD+) were compared with FD-- a prior history of complaints or peptic ulcer (sens 64%, spec 56%, ppv 44%, npv 74%); pain after a meal (sees 35%, spec 70%,ppv 51%, npv 70%); and smoking (sens 38%, spec 74%, ppv 44%, npv 69%) were the only features linked to peptic ulcer.

Meal (sees 35%, spec 70%, ppv 51%, npv 70%); and smoking (sens 38%, spec 60%, ppv 44%, npv 69%) were the only features linked to peptic ulcer.

The aim of the present study was to evaluate the prevalence of peptic ulcer in rural residents with abdominal complaints.

We interviewed 2304 subjects above 15 years of age, which was 74.6% of the population of a rural district of Estonia. The interview was based on a questionnaire compiled to screen out persons with abdominal complaints. All 854 subjects with abdominal complaints were offered upper endoscopy, 575 (67.3%, 374 female, 194 male) agreed to be investigated. Peptic ulcer disease was defined as an active peptic ulcer, a scar or a deformed duodenal bulb.

Peptic ulcer was diagnosed in 71 cases (50 male, 21 female), the overall prevalence was 12.3%. The prevalence increased with age, reaching the peak in the 4th life decade in males and in the 5th life decade in females. Duodenal ulcer occurred 2.2 times more frequently than gastric ulcer. In 23 cases (32%) the diagnosis of the peptic ulcer was made for the first time. The prevalence of peptic ulcer in rural residents with abdominal complaints was 12.3%, the proportion of newly diagnosed cases being extremely high.

The Monthly Variations of Symptomatic Duodenal Ulcer Activity in Taiwan: A Comparison Between Subjects with and without Hemorrhage

Chung-Jyi Tsai. Chi Mei Foundation Hospital, Yung Kang City, Tainan, Taiwan

The occurrence of peptic ulcer has geographic, temporal, socioeconomic and ethnic variations. Controversy exists regarding duodenal ulcer (DU) seasonality. We have observed that patients with DU may be divided into those whose ulcers recurrently bleed as distinct from those whose ulcers repeatedly cause pain. It is still not known which or when DU patients would bleed. The purposes of the prospective studies (1) to investigate the seasonal incidence of DU activity in a developed subtropical country, (2) to compare the seasonal incidence of DU patients with pain and that of those with hemorrhage, and (3) to clarify the roles of sex and age factors play.

Methods: All of the reports of endoscopic examination of the upper gastrointestinal tract performed from April 1, 1989 to March 31, 1995, were reviewed
to identify patients with DU disease. Active bleeding due to DU was confirmed when a definite bleeding site or visible vessel or a blood clot within an open crater in the mucosa of the duodenum was identified. Excluded were all patients who had any extrinsic factors that might influence the exacerbation of DU disease during the study period, hemorrhage, and 623 patients with adenocarcinoma were used as the control diagnoses. The 12 months of the year were divided according to the climate in Taiwan into four seasonal periods, viz., winter (Jan.-Feb.), spring (Mar.-Jun.), summer (Jul.-Aug.), and autumn (Sep.-Dec.). Statistical analysis was done with linear test, correlation regression with Pearson correlation, and ANOVA with post hoc comparisons were used as appropriate.

Results: During the years of the study, 10351 DU were diagnosed. Among these, 10886 patients presented with hemorrhage, and 623 patients with adenocarcinoma. The monthly distribution of total DU patients revealed a trend toward more occurrence from Nov. to Mar. (p < 0.001). In the patients with DU hemorrhage, the peak incidence was in the months from Nov. to Mar. (p < 0.001). There was no significant variation in the peak was in the winter months through Feb. (p > 0.001). In the DU patients with pain, the peak months were from Dec. to Feb. (p < 0.001). Significant seasonal variation, peaked in winter, was also observed (p = 0.04). In both groups, the monthly and seasonal variations were unaffected by age or sex. There were no significant monthly variations of control diagnosis for hepatoma (p = 0.94) or colorectal adenocarcinoma (p = 0.79).

Conclusions: Both groups of DU patients presenting with hemorrhage and those with pain demonstrated similar monthly and seasonal fluctuations, the incidence being significantly greater during the cold season. These data suggest that climatic changes may influence pain and hemorrhage in the DU patients, which brings important epidemiological and therapeutic implications.

1391 Helicobacter Pylori Infection and Chronic Antral Gastritis in Patients with Non-Ulcer Dyspepsia
S. Grzyw, M. Stefanikov, J. Dmitrjevic, P. Stamenkovic. Internal department, Health centre, Leskovac, Yugoslavia
We made a prospective study on 66 patients, averaged 46.6%, with the symptoms of non-ulcer dyspepsia and histological findings of chronic superficial (21% or 31.8%) and atrophic (45% or 68.2%) antral gastritis. Helicobacter pylori (Hp) has been proved in biopic sample of antral mucosa by urease test and histological check-up of preparations coloured with hematoxylin-eosin. Endoscopically, diffuse erythema was found in 31.2% of Hp positive patients and polycolority of antrum with bizzare reddish-pale zones in 38.9%, but without statistically significant difference with regard to Hp negative patients (p > 0.05). Chronic mucous erosions were present in 87.5% Hp positive and 10% Hp negative patients, which is statistically significant difference (p < 0.05). Hp infection existed in 47.6% chronic superficial gastritis and 46.7% chronic atrophic antral gastritis. In the group of active superficial gastritis there were 90.9% with Hp infection. The group with active atrophic gastritis contained 87% of Hp positive and 13% Hp negative patients which is statistically significant difference (p < 0.01). At low degree of chronic gastritis atrophy Hp was positive in 46.7% of patients, at medium degree in 35% and in high degree of atrophic gastritis in 22.9%, but differences are not statistically significant with regard to Hp negative patients (p > 0.05). Intestinal metaplasia was found in 18 (40%) patients with atrophic gastritis, but without statistically significant difference between Hp positive and Hp negative patients (p > 0.05). Our research shows that endoscopically seen chronic anter gastritis of the stomach represents an important factor of chronic gastric antral activity and hence important factor of the development of gastrointestinal metaplasia and dyspepsia as precancerous lesions.

1392 Colonization of Human Achloridric Stomach by Bifidobacteria
G. Brandi, S. Sarchielli, P. Mordenti, S. Tambelli, C. Calabrese, P. Mattarello, B. Biavati, G. Bisacco, Dipartimento di Medicina Interna e Gastroenterologia, Bologna University, Italy; Istituto di Microbiologia Agraria e Tecnica, Spia University, Italy
Aim of the study was to ascertain whether and which populations of bifidobacteria are able to colonize the stomach of subjects with achloridria induced either by autoimmune atrophic gastritis (CAG), or by meperazine (Ome) treatment (20 mg/day for 1 month) for reflux esophagitis. The isolation of bifidobacteria was made on samples of gastric biopsies (4 for the antrum and 4 for the corpus) of 14 subjects (6 CAG: mean age 39 yrs; 8 Ome: mean age 48 yrs) by using BLA and TPF added with propionic acid. The mean pH value of the juice 7.3 in CAG subjects and 6.8 in Ome. For design we used the isolates, the genus Bifidobacterium, we took into consideration morphology, Gram stain, fermentation products and the presence of the fructose-6-phosphate phosphoketolase enzyme. Fifty-two strains were isolated on samples of gastric biopsies of 14 examined have been grouped by cell protein electrophoresis. They were characterized through the following determinations: G-C% of DNA, fermentations of 47 complex carbohydrates, DNA-DNA hybridization. Fifty-two strains could be subdivided into 9 groups and 4 enterobacteriae isolated on 10 subjects. The fact that the bifidobacteria are not located to the same oral cavity: B. dentiunculus, B. infantum (two new species recently isolated from human dental caries) and B. dentium. The remaining 3 strains (all from the same subject), which were recognized as a single group, do not hybridize with any species of the genus Bifidobacterium or with Gardnerella vaginalis.

The efficacy of fedotozine (F) administered for 6 weeks had already been demonstrated in functional gastrointestinal disorders, both in functional dyspepsia (1) (FD) and irritable bowel syndrome (2) (IBS). However, the chronic administration of these drugs can justify long-term treatment. Methods. During an open, prospective, uncontrolled, multicenter study in France, we evaluated the safety of prolonged administration of F (30 mg tid for one year) in dyspeptic outpatients seeking medical advice (diagnostic criteria of FD left to the investigator, concomitant treatments allowed). The course of symptoms and their impact on the quality of life (QoL) were secondary criteria. Safety was evaluated every 3 months by monitoring adverse events (AE), standard blood tests, EEG and EGG (2 subgroups). The overall therapeutic result was evaluated every 3 months and QoL every 6 months (QQLP questionnaire (3)). Statistical analysis was purely descriptive. Results. 165 patients (28% gastroenterologists, 72% general practitioners) treated 624 patients with FD, most often associated with IBS (64%) or gastroesophageal reflux (13%). The follow-up period was 1 year. The study was completed by 66% of patients. The mean duration of exposure to treatment was 296 days (range 1 to 483), corresponding to 506 patient years. AE were recorded in 246 patients and were potentially treatment-related in 179 (the most frequent were dyspepsia, diarrhea, and flushing). The incidence of AEs was 2.5%. There were 30 serious AE, of which 6 were potentially treatment-related and which mainly concerned the GI tract. Laboratory tests showed the absence of any abnormal trend or specific abnormality. ECG and EEG further demonstrated the safety of F. Improvement or resolution of symptoms according to the patient and the investigator was reported in 84 and 87% cases respectively. Efficacy was maintained over time. Patients noted an improvement in QoL for health-related items (digestion, pain, state of health, general form, diet). Conclusion. This study carried out in a large number of patients (equivalent to 506 patients followed-up for 1 year) demonstrated the very good clinical, ECG/EEG, biochemical and haematological safety of F (30 mg tid) administered for a long period. Good efficacy results, stable over time, and improvement in QoL were obtained.

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1394 Efficacy of Fedotozine in Functional Dyspepsia: A Meta-Analyses of Individual Data from Randomized, Placebo-Controlled Studies
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A meta-analysis of the therapeutic efficacy of fedotozine (FZ) in functional dyspepsia was carried out on all the individual data from the phase III randomized, double-blind studies comparing a placebo group (PL) with a group receiving FZ 30 mg t.i.d. Methods. Since the study design was identical (a one to two week run-in period followed by six weeks treatment in parallel groups), meta-analysis of 3 multicentre studies carried out in France and the UK was justified. Inclusion and evaluation criteria were similar for the 3 studies. Therapeutic efficacy was evaluated on the mean overall score of the intensity of the 5 dyspepsia symptoms assessed daily by the patient. The mean treatment effect (T) for the 6 weeks, the study effect, and the TxS interaction were tested by intent to treat ANCOVA with adjustment for the means at run-in. The difference between FZ and PL at each of the 6 treatment weeks was assessed by ANOVA. Results. 658 patients (FZ: 331, PL: 327; M: 39%; F: 61%) with a mean age (± SD) of 44 ± 15 years were randomized in these 3 studies. The percentage of withdrawals was higher in the PL group (PL: 22.6%; FZ: 15.7%; p < 0.05). The effect of FZ on the overall dyspepsia intensity score was greater than that of PL (p = 0.002) with no significant difference in the magnitude of treatment effect between the studies (interaction TxS not significant, which justifies generalization of results. The PL overall score improved from 12% (week 1) to 29% (week 6) compared to run-in. The FZ overall score improved from 18% (week 1, p = 0.036 vs PL) to 36% (week 6, p = 0.001 vs PL). Moreover, the effect of FZ was significantly greater than that of PL 4 dyspepsia symptoms out of 5 (bloating/epigastric pain < 0.001, epigastric pain (p < 0.007), slow digestion (p < 0.057), and nausea/vomiting (p < 0.05), early satiety was NS. When meta-analysis was carried out on the 2 phase III studies alone, FZ was again more effective.
than PL and to a similar extent. There was no evidence of any effect due to patient characteristics (age, body mass index, sex) or to pre-inclusion gastroenterological or psychotropic treatments on the therapeutic effect of T2. A post-hoc meta-analysis allowed a comprehensive assessment of all available efficacy data from phase IIb and III studies. Fedotozine proved significantly more effective than placebo on both the overall dyspepsia intensity score and on 4 of the 5 dyspeptic symptoms.

### 1395 Evaluation of the Quality of Life in Functional Gastrointestinal Disorders. Results of a 6-Month Study of Fedotozine Versus Usual Treatments

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The objective of this general practice study was to evaluate the effects of functional gastrointestinal disorders on the quality of life (QoL) as well as changes in patients with their treatment. The study was open, prospective, and 3-ized, six-month pharmacoeconomic study with 252 patients (irritable bowel syndrome: 74%; dyspepsia: 26%) compared fedotozine 30 mg per os tid. (n = 141, group F) with treatments usually prescribed by the investigator (n = 111, group T). The Functional Status Questionnaire was used to evaluate the 3 main dimensions of QoL: (i) physical, (ii) psychological, and (iii) social, as well as several sub-dimensions including overall satisfaction with general well being. The questionnaire was filled in by the patients at D0, D45, and D180. QoL scores are expressed as a percentage of the baseline (QoL) to 100 (best QoL). Results: The reliability of the questionnaire was satisfactory with Cronbach α coefficients ranging from 0.69 to 0.88. At D0, scores were comparable between the two groups. The psychological dimension was improved in both groups, followed by the social dimension (74.6% and 73.6% T), and the physical dimension (89.8% T; 90.0% T). Overall assessment of general well being was very perturbed at D0 (41.9% T and 49.4% T). Intragroup analysis showed a significant improvement at D45 and D180 for the two groups for the physical (p ≤ 0.05) and psychological (p ≤ 0.05) dimensions. The sub-dimensions relations and general well being improved significantly at D45 and D180 only for group F (p ≤ 0.05 and p ≤ 0.01). Intergroup analysis showed that the improvement in the overall general well being score was significantly greater for group F at D45 (10.3% versus 3.3%; p = 0.02) as well as at D180 (24.4% versus 5.8%; p = 0.03). These results correspond to improvements compared to inclusion scores for F and T of 11% and 6% at D45, and 46% and 20% at D180, respectively. Conclusion: Functional gastrointestinal disorders affected the psychological and social dimensions of the QoL as well as the overall satisfaction of patients with their general well being. From D45 to D180 both fedotozine and the usual treatments had a beneficial effect on QoL. Only the fedotozine group showed significant improvement in general well being of the patient and from D45 to D180 the improvement was significantly greater in group F than in group T.

### 1397 Bilitec 2000 Study in Evaluation of Duodenogastric Biliary Reflux Following Conventional and Laparoscopic Cholecystectomy

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Several clinical studies showed that episodes of the duodenogastric biliary reflux (DGR) increased following cholecystectomy.

The aim of present study was to evaluate the incidence of gastric biliary reflux following conventional (CC) and laparoscopic cholecystectomy (LC). Twenty-five patients were randomized following the surgery and all biliuric secretion concentration results were within the normal values.

In the 1st group (following CC) the presence of biliary reflux was noted during gastroscopy in 50% of patients versus 36% of patients following LCG. Significant increase of incidence of bilirubin in six episodes was obtained in 8 patients (40%) of 1st group and only 5 patients (50%) of 2nd group, during 24-hour Bilitec studies. Conclusion: The incidence of DGR and total exposure of gastric mucosa to biliary contents increased both following classical and laparoscopic cholecystectomy, but significantly higher after CC.

### 1398 Reflux Gastritis in Children with Glardiasis

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The purpose of the study: Considering that glardiasis, a frequent parasitic disease in children can generate pyloric incompetence with jejunudo-duodenogastric reflux (JDGR) and that epigastrica is a common symptom in school age children infected with lamblia, the authors have studied the role of JDGR as a possible factor generating gastritis in these children. Patients and methods: Two groups of patients were studied: group I (20 children) aged 7–17 years with glardiasis and group II – controls (10 healthy children). The methods used included: a) tests for the support of the diagnosis of glardiasis (barium meal and/or gastroscopy with radiological biopsy) in group I and b) detection of JDGR by the determination in the gastric aspirate of: total bile acids (spectrophotometry); sodium (flame photometry) and pH in both groups. Results: a) statistically significant increased levels of the bile acids in the gastric aspirate in children with glardiasis as compared with controls: W = 1.84 ± 0.71 μmol/L; W = 0.42 ± 0.4 μmol/L, P < 0.001; b) a 90% incidence of the cases with high levels of bile acids in children with glardiasis; c) the presence in these children of endoscopic and histopathologic changes of the gastric mucosa, interpreted as reflux gastritis and d) the absence of statistical significance between the values of sodium and pH in the gastric aspirate in the two groups. Association of drugs regulating digestive motility with the etiologic treatment clearly improved the course of these cases. Conclusion. The study indicates the presence of reflux gastritis in 90% of the investigated children with glardiasis and recommends the determination of the bile acids in the gastric aspirate as a sensitive test for the detection of JDGR.

### 1399 The Houston Classification (HC) of Gastritis Applied in the “Real World”

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Purpose: To assess the usability of the HC in the day by day practice.

Methods: During a 3 months period, 113 patients with upper gastrointestinal symptoms (MF: 55/58; range 19–67; mean 49.7 yrs), underwent endoscopy. According to HC classification (40.7% in the group with one area of damage, 59.3% in the group with two affected areas), the authors have studied the observed prevalence of chronic lingual (LCh); corpus (C); and angularis (A) and in addition 2 antral biopsies were taken for Helicobacter pylori (HP) culture and urease testing. The specimens were histologically assessed and scored according to the HC guidelines. Serum IgG to HP were assessed by enzyme linked immunosorbent assay (ELISA) (sensitivity and specificity of 94%). 3/4 techniques testing positive gave H pylori status (gold standard).

Results: A total of 66/113 (60%) patients were HP+ve (histology/urease test/culture/serology). The endoscopic findings were: macroscopically normal (n = 26; HP+ 50%), atrophic gastritis (n = 59; HP+ 54%), atrophic gastritis + antrum (n = 12; HP+ 67%), gastric ulcer (n = 5; HP+ 80%) and duodenal ulcer (n = 11; HP+ 100%). Sensitivity and specificity of samples taken compared to the gold standard were (%):

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>C</th>
<th>AN</th>
<th>A + C</th>
<th>AN + C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>91</td>
<td>89</td>
<td>89</td>
<td>98</td>
<td>97</td>
</tr>
<tr>
<td>Specificity</td>
<td>87</td>
<td>84</td>
<td>94</td>
<td>98</td>
<td>95</td>
</tr>
</tbody>
</table>

The biopsies from the angulus revealed 15 cases of atrophy (moderate 1 and mild 14) that would otherwise not have been detected.

Conclusions: 1. The combination of antral and angular biopsies showed the highest rate of HP detection, 2. The additional biopsy specimen from the angulus added little to the diagnosis. However, in geographic areas with high prevalence of gastric carcinoma it may help detect early pre-neoplastic lesion.

### 1400 Nuclear Volume of Type I Gastric Intestinal Metaplasia

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The three-dimensional nuclear size may be viewed as a dynamic reflection of the metabolic state of the nucleus and as a physical correlate of its total content of biochemical constituents. Among these were histone and nonhistone proteins, inorganic materials, water, RNA and DNA.

Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type. It has been postulated that intestinal metaplasia of gastric mucosa, characterized by incomplete differentiation and by sulphomucin secretion (type III intestinal metaplasia), is closely related to intestinal type gastric carcinoma, whereas other non-sulphomucin-secreting types (types I and II) are not associated with the former cancer sites where the risk of cancer is relatively low (gastric cancer and chronic gastritis).

The aim of this study was to estimate the mean volume-weighted nuclear volume of epithelial cells in type I intestinal metaplasia in various pathological states of gastric mucosa.

Material and Methods. Endoscopic mucosal biopsies from gastric cancer (n = 25), gastric ulcer (n = 32), and chronic gastritis (n = 40) patients were analyzed. After standard fixation, embedding, sectioning, routine HE and AB-PAS staining, the point sampling nuclear clear intercept was estimated by the original test system and objective x100, at total magnification of x1200. To obtain the mean nuclear volume, the cubed nuclear intercept was multiplied by 0.3. In each case, two objective fields were analyzed. For the statistical analysis Student’s two-tailed t-test was used.

Results. In type I intestinal metaplasia found in gastric carcinoma patients there is significantly greater nuclear volume (118.34 ± 13.2 μm³) than in type I intestinal metaplasia in other pathological states of gastric mucosa (77.72 ± 8.5 μm³).

Discussion. The sampling of intercepts by points is a mathematical necessity to ensure an unbiased estimation. Our results suggest that nuclear volume may be used in early detection of precancerous states of gastric mucosa.
A Flow Cytometric Study of Gastric Nuclear DNA Ploidy in Gastritis
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Purpose: This study aimed to assess the gastric nuclear DNA ploidy pattern and correlate it with the clinicopathologic findings in gastritis.

Patients & Methods: Forty patients (32 males and 8 females; mean age 42 ± 5.8 yr) with endoscopic evidence of gastritis were enrolled in the study in addition to 20 patients not showing endoscopic evidence of gastritis as control group. Endoscopic assessment was done to every patient and at least two biopsies were taken from the site of lesion, close to each other, one for histopathological examination and Giasma staining for Helicobacter pylori and the other for determination of DNA content (ploidy) and S phase fractions by Flowcytometry.

Results: Whereas only diploid DNA histograms were found in control subjects, patients with gastritis showed diploid histograms in 34 (85%) cases while 6 (15%) specimens exhibited DNA aneuploidy. S phase fractions were higher in gastritis than control cases and showed significant direct correlation with age and duration of complaints but not with activity of gastritis. All the six lesions showing DNA aneuploidy were antral lesions and were positive for Helicobacter pylori. Their histopathological examination revealed atrophic gastritis in the 6 cases with intestinal metaplasia in 4 (66.7%) of these cases and low grade dysplasia in 2 (33.3%).

Conclusions: This study suggests that determination of gastric nuclear DNA content (ploidy) may help to identify individuals with increased cancer risk as aneuploid histograms were found in non dysplastic mucosa. (2) Thus combination of endoscopy, histology and flowcytometry can be integrated surveillance procedures for follow up of patients with gastritis for early detection of malignant transformation.

Neural Networks in the Investigation of Gastric Lesions
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Objective: To compare the accuracy of two different artificial neural networks (ANN), for the discrimination of benign and malignant gastric lesions using morphometric and textural data of the nucleus.

Study Design: This study was carried out on 39 cancer cases, 34 cases of gastritis and 83 cases of ulcer. In each case 100 cells were measured from gastric smears stained by the Papancioclu technique using a custom image analysis system. The mean of 300 of the cells were used and the remaining cells were used as a test set using two different neural network architectures: Back propagation (BP) and learning vector quantizer (LVQ).

Results: The application of BP and LVQ established correct classification of more than 81% of the benign cells and more than 95% of the malignant cells, obtaining an overall accuracy of 97% at cellular level and 99.1% at patient level in both neural networks.

Conclusion: This study indicates that the use of ANNs and image morphometry may offer useful information on the potential of malignancy of gastric cells and may improve the accuracy of cytopathological diagnosis.

Do Dyspeptic Patients under the Age of 45 Need to be Investigated?
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Age under 45 years and negative non-invasive tests for detection of Helicobacter pylori (HP) infection are the most often recommended criteria to avoid unnecessary endoscopy in dyspeptic patients without obvious clinical signs of organic diseases.

Aim: To evaluate the diagnostic field of open access upper gastrointestinal endoscopy in relation to the age and Hp status of the patient.

Methods: 135 consecutive dyspeptic patients aged 18 years and over referred for upper endoscopy by their GPs were included. Patients’ Hp status was established by histology (2 antral, 2 corpus, 2 duodenal biopsies). Gastritis was scored according to the Sydney classification.

Results:

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>No (%)</th>
<th>Sex</th>
<th>Age</th>
<th>M/F</th>
<th>&lt; 45 ≤ 45 yrs</th>
<th>Hp posit</th>
<th>Hp negat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal ulcer</td>
<td>44 (33%)</td>
<td>30/14</td>
<td>34/10</td>
<td>41/3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>10 (7%)</td>
<td>4/6</td>
<td>1/1</td>
<td>9/1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Gastric carcinoma</td>
<td>1 (1%)</td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric erosions</td>
<td>21 (15%)</td>
<td>12/9</td>
<td>14/7</td>
<td>17/4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic gastritis</td>
<td>4 (3%)</td>
<td>4/2</td>
<td>3/2</td>
<td>6/1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other diseases</td>
<td>7 (5%)</td>
<td>3/4</td>
<td>3/4</td>
<td>6/1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal findings</td>
<td>12 (9%)</td>
<td>7/5</td>
<td>12/0</td>
<td>0/12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>135</td>
<td>63/72</td>
<td>88/47</td>
<td>112/23</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There is an overlap between duodenal ulcer and gastric erosions in 4 cases and between chronic gastritis and gastric erosions in 20 cases. The only case of gastric cancer was 36 years old female. Only 9% of all patients have normal endoscopic and histological findings.

Conclusions: Among populations with high prevalence of Hp infection more than half of dyspeptic patients have clinically relevant disease at the age under 45 years. Presence of Hp infection is important predictor for organic disease.

Gastric Duplications: Diagnosis and Management
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Purpose: Intestinal duplications are a rare congenital disease. They appear in the whole gastrointestinal tract, especially in the ileum. In the literature 112 cases of gastric duplications are described, 80 of them in children. Here we describe two cases, of gastric duplication cysts in adults. Diagnostic findings and surgical therapy are discussed.

Patients: a) A 23 year old patient had pain in the right upper abdomen, nausea, vomiting and attacks of fever. No pathological findings were described in endoscopy. CT-show a fluid filled structure with obstruction of the duodenum. A duodenal duplication or choledochoyst was discussed. b) A 59 year old patient with pain in the left upper abdomen since one year was admitted to our department. CT showed no sign of malignancy, but showed a mass. CT scan and sonography presented a big cyst (14 × 13.5 × 9 cm) in the left upper abdomen close to the pancreas body, probably a pancreas pseudocyst. In ERCP no pathological findings. Sonography was normal.

Methods: Both patients had a diagnostic laparotomy. At the first patient a subtotal gastrectomy (Billroth I) was accomplished. For the second patient a tangential resection with a small wall of gastric mucosa was performed. Results: There were no perioperative problems. At the first patient an early dumping syndrome was successfully treated conservatively. The second patient had a good recovery without complications.

Conclusion: Gastric duplications in adults are extremely rare. Diagnosis is often missed. Symptoms are unspecified pain in the upper abdomen, vomiting and fever. Some patients have weight loss. Complications are rare. Chronic infections and ruptures are described. For diagnosis, CT-show with oral contrast should be preferred. Endoscopy is negative in most cases. Therapy is surgical. Local excisions with a small wall of gastric mucosa in most cases is sufficient. Sometimes, a subtotal gastrectomy is necessary.

Pharmaceutical Versus Non-Pharmacological Acute Upper Gastrointestinal Bleeding
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This is a prospective study comparing the outcome between pharmaceutical and non pharmaceutical upper gastrointestinal bleeding (GI) due to benign peptic ulcer.

Methods: A total of 907 patients were studied prospectively. They were suffering from acute upper GI bleeding due to endoscopically and histologically identified benign peptic ulcer. The patients were divided in two groups. Group A included 506 patients who had received ulcerogenic drugs (either aspirin or NSAID’s) and Group B, 401 patients with no history of drug consumption. The two groups were comparable in all clinical and endoscopic parameters which are known to influence prognosis: age, sex, history of previous GI bleeding, associated diseases, shock on admission, endoscopic stigmata and location of ulcer, need for haemostasis, rebleeding, need for transfusion and duration of hospital stay.

Results: Emergency surgical intervention for persistent or recurrent bleeding was required in 38 patients (7.5%) in Group A and in 42 (10.5%) in Group B (p = 0.148). The overall mortality was 2.95% for Group A and 1.2% for Group B. Endoscopic stigmata, median transfusion requirements, median duration of hospital stay, endoscopic haemorrhage did not differ significantly. There were differences in sex distribution (more women than men), age, history of previous GI bleeding, associated disease, shock on admission (p = 0.073) and gastric ulcer (p = 0.002). Interestingly in Group A patients rebleeding rate was significantly less.

Conclusions: Despite clinical presentation pharmaceutical haemorrhage do not seem to differ in mortality, morbidity and hospital stay than non pharmaceutical.

Helicobacter pylori Infection Increases the Risk of Peptic Ulcer Bleeding – A Case-Control Study
K. Hült, F. Leverkus, J. Labenz. Elisabeth Hospital Essen, Germany
Purpose: The study was designed to evaluate the role of H. pylori infection in the pathogenesis of peptic ulcer bleeding.

Methods: 128 patients presenting with upper GI bleeding and 128 matched controls (age and gender) were studied prospectively. In all patients and controls a standardized questionnaire was performed. Patients were investigated endoscopically with assessment of H. pylori infection by a rapid urease test,
culture and histology. In controls, the current H. pylori status was determined using a 13C-urea breath test. Statistics included the Cochran-Mantel-Haenszel test and a conditional multiple logistic regression analysis (CMLR).

Results: 72 patients had peptic ulcer bleeding (gastric ulcer (GU): n = 39; duodenal ulcer (DU): n = 33) and 56 patients bled from other sources. H. pylori infection was more frequently detected in ulcer patients than in controls (GU: OR 4.59, 95%-CI 1.22–16.3, p = 0.033). CMLR suggested that H. pylori infection is an independent risk factor for peptic ulcer bleeding (OR 3.3 95%-CI 1.5–7.0, p = 0.002). No interactions could be detected between the infection and NSAID use.

Conclusions: H. pylori infection increases independently the risk of peptic ulcer bleeding. Thus, the cure of the infection will lead to a decreased incidence of ulcer bleeding. However, it cannot be expected that curing H. pylori infection in NSAID users will substantially diminish the risk of ulcer complications.

1410 Clinical Investigation of Bleeding Peptic Ulcer in the Elderly
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Introduction: The rapid increase in the elderly population of Japan has led to an increased number of elderly patients with bleeding peptic ulcer.

Objectives: We compared the clinical characteristics of bleeding peptic ulcer in patients over 70 years of age or older in whom hemostasis was performed by heater probe treatment (elderly group) with those less than 70 in whom similar treatment was performed (younger group).

Methods: Over a period of 9 years, 274 patients were enrolled, 48 in the elderly group and 226 in the younger group.

Results: The incidence of concomitant disease was significantly higher in the elderly group (83.3%) than in the younger group (33.3%) (p < 0.01). The incidence of emergency surgery (younger group 5.8% vs. elderly group 6.3%) and the rate of mortality due to hemorrhage (2.2% vs. 2.1%, respectively) were similar in the two groups.

Conclusion: Bleeding peptic ulcer in elderly patients was thus characterized by a high incidence of concurrent disease. Despite this, the results of the present study indicate that the rates of mortality and emergency surgery in elderly patients with bleeding peptic ulcer who undergo heater probe treatment are comparable to those in younger patients, provided that their general condition is monitored carefully and that endoscopic hematostatic procedures.

1411 Fifty Years of Upper Gastrointestinal Haemorrhage in NE Scotland
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The mortality associated with acute Upper Gastrointestinal Haemorrhage (UGIH) has not generally reflected the major improvements in patient care introduced over the past 50 years and this has been confirmed by the recent Royal College Assessment (RCA) which estimated that influence of outcome of UGH have been the subject of many studies, but no study has addressed the impact of changes in medical practice and demographic characteristics in a single community. There have been three whole-community studies over 5 decades which provide data on the management and outcome of upper gastrointestinal bleeding in NE Scotland and these studies provide an exceptional record of the changing patterns of UGH in a single community.

There has been an increase in age (in 1950 1.5% and 1990’s 18.5% of patients admitted were over 80 years of age), the use of ulcerogenic drugs and co-morbid disease in patients presenting with UGH. However, the incidence of UGH has remained static (117,000 admissions per adult population per year) over the last 25 years and at present is similar to other recent large studies. Endoscopy has replaced barium meal as the investigation of choice and with the introduction of powerful anti-ulcer drugs semi-elective surgery for ulcer hemorrhage has disappeared. The proportion of gastric ulcer, oesophagitis and mallory-weiss tear have increased, whereas the proportion of duodenal ulcer and undiagnosed patients has declined. These changes in the diagnostic mix may reflect more accurate diagnosis or a true change in the incidence of certain diagnoses. An independent risk factor for peptic ulcer bleeding is increased co-morbidity which in turn is associated with mortality from 13.7% to 3.8%.

The factors determining outcome in UGH are constantly changing and this review demonstrates this within a single community. Despite an increasing aged population with it’s associated co-morbid disease we have shown that by optimising patient care the mortality rate for UGH can be reduced.

1412 High Prevalence of Upper GI Tract Asymptomatic Diseases as Causes of Micro and Macrocytic Anemia in Adults
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Oxymic mucosa trough acid and intrinsic factor secretion determines the availability for absorption of alimentary iron and vitamin B12 that are crucial in the haemagobiosynthesis. Furthermore duodenal mucosa is the main site for the absorption of reduced iron. The functional and structural integrity of gastric and duodenal mucosa is crucial since some diseases in which this integrity is lost, could result in anemia e.g. peptic ulcer disease (PUD), corporeal atrophic gastritis (CAG), celiac disease. Since we investigated in a consecu- tive anemic outpatients population referring to our Hematology Dept., the role played by gastric and duodenal mucosa integrity as possible cause of anemia.

During a three-month period, 266 anemic consecutive outpatients (213 microcytic, 53 macrocytic) were observed, active gastrointestinal haemorrhage, faecal occult blood positivity, and all haematological and M-glycemia constituted exclusion criteria for this study. 80 anemic patients (age 20–76, M 24, F 56) 36 macrocytic, 44 microcytic, without GI complaints, resulted eligible and were investigated with a screening procedure consisting in the siderometric determinations of gastric, IgG anti H pylori, antiendomysial IgA antibodies (EMA). Positivity of at least one of these determinations was further investigated with upper GI endoscopy with multiple antral (n = 2), fundic (n = 4) and duodenal (n = 2) biopies. Patients negative to the screening also underwent gastroscopy. Results Gastrin was found increased in 35 pts, IgG Hp in 37 pts and EMA 16 pts. patients further control.

Endoscopy/histology Microcytic Macrocycotic
Normal 22 (22.7%) 14 8
PUD Hp+ 6 (8.1%) 4 2
CAG 21 (28.4%) 8 3 (anemic persons)
Adult CD 12 (16.2%) 10 2
H+ antl giros 13 (17.3%) 7 6

Conclusion: This study in a consecutive asymptomatic anemic population established us to identify 39 out of 74 pts (52.7%) in whom upper GI diseases were the cause of anemia. The occurrence of both types of anemia is strictly distributed in PUD and CAG. Only 29.7% of anemic screened patients had no alteration of gastric and duodenal mucosa. Evaluation of unexplained anemia in adults should include a thorough investigation of upper GI tract.

1413 Incidence for Gastric-Inestinal Haemorrhagic Complications during Anticoagulant Therapy in a Danish Population-Based Cohort
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Background – Recent clinical trials has established new indications for oral anticoagulation with warfarin; the efficacy was achieved with a low incidence of bleeding complications which may not be reproduced in clinical practice. Gastrico-intestinal bleeding is the most frequent type of major bleeding and the objective of this study was to estimate the incidence of major gastrointestinal bleeding requiring hospitalization among unslected outpatients treated with oral anticoagulants.

Design – Through The Drug Prescription Register we identified a cohort of the 120,564 people commencing oral Anticoagulant therapy in 1992 in the County of North Jutland. All discharge diagnoses for hospitalizations in this cohort from 1992 to October 1994 were reviewed for potentially bleeding complications followed by patient record review; death certificates were studied for deaths during follow-up.

Results – The 684 patients represented 754 years at risk. There were 20 major gastro-intestinal bleeding events (2.7 per 100 treatment-years) in 19 patients of which none were fatal. Nearly all events were severe; requiring transfusion of two units of blood or more. Ten patients required four units of blood or more.

Conclusion – The rates of major gastro-intestinal haemorrhages in this inception cohort was two to four times as high as in recent prospective trials and illustrates the continuous difficulties in translating the efficacy of oral anticoagulation in trials into effectiveness in clinical practice.

1416 Upper Gastrointestinal Bleeding Today. A Prospective Analysis of 1350 Cases
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Upper gastrointestinal bleeding continues to be a serious and common clinical problem. In the last decades considerable improvement has been achieved concerning diagnostic and therapeutic approach to these patients. We present our data accumulated prospectively on 1350 patients admitted in our hospital over a 4 year period with upper gastrointestinal bleeding.

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During the last 4 years 1350 patients (14–96 years) admitted in our hospital with upper gastrointestinal bleeding (UGIB) or presented UGIB while were inpatient for any other reason. No exclusion have been made for age or comorbid disease. Emergency endoscopy was performed during the first 24 hours after admission or immediately after resuscitation in patients with massive bleeding. All patients have been managed by a team of gastroenterologists and surgeons in close cooperation. In all peptic ulcers, patients with active spurring or oozing bleeding, or a non bleeding visible vessel, endoscopic injection hemostasis with adrenaline diluted 1:10.000 in saline 0.9% (A/S) was performed during emergency endoscopy. Variceal bleeding was managed with endoscopic, sclerotherapy and emergency surgical therapy.

Peptic ulcer remains the main cause of UGIB (68.3%) following by gastrointestinal erosions (12.6%). We observed an increase in the incidence of peptic ulcer with a simultaneous decrease in the incidence of gastroduodenitis as a cause of UGIB in comparison to the previous decade. In patients with peptic ulcer the operation rate was 8.7%. Overall mortality was 2.5% and in patients with peptic ulcer as a cause of bleeding 2.2%. All patients who died had serious comorbid disease and 73.5% were over 65 years old.

In conclusion peptic ulcer remains the main cause of upper gastrointestinal bleeding. Close cooperation between surgeons and gastroenterologists and endoscopic therapy has improved clinical outcome in patients with UGIB and reduced mortality.

### 1417 NSAID Utilization and Frequency of NSAID Induced Gastroduodenal Bleeding

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Estimation of frequency of adverse drug reactions (ADR) is usually based on drug utilization in the number of packages, number of prescriptions, single drug units. But, differences in drugs formulations (tablets, capsules, suppositories, solutions), weight of the active substance in drug packages and weight of every single unit in the package are neglected. Because of that, estimation of drug utilization is not precise enough, comparisons of different studies can not be made, and therefore neither can estimations of ADR.

An internationally accepted statistical unit for drug utilization which takes into account all the parameters mentioned above is a defined daily dose (DDD). It is by agreement established drug quantity most often used for most frequent indications.

In this study utilization of NSAIDs prescribed to outpatients of the Niš region (1.6 million inhabitants) in 1995 expressed in DDDs and the number of DDDs leading to one hospitalized hematemia and/or melena (HM) induced by NSAIDs are analyzed. The number of HM (endoscopically found gastric or/and bulbar lesions) is already known.

The utilization of acetylsalicylic acid (ASA) was 40917.2 DDDs. One HM appeared on every 7886.7 DDDs or more (as there is no evidence of sold unsupervised drugs, they could not be taken into account). The DDD for orally (O) or rectally (R) applied ASA is 3000 mg, so appearance of one HM can not be expected below 25393.1 g of ASA taken.

One HM can not be expected below 46679.9 DDDs of ibuprofen (O the DDD is 1200 mg), 189450.2 DDDs for diclofenac (O, parenterally-P. The DDD is 100 mg) and for piroxicam (O, P, P. The DDD is 20 mg) 160174 DDDs.

Because of advantages, introduction of DDDs in ADR research can lead to easier and more precise estimation of ADR frequency. The DDDs are also a good tool for further investigations in the ADR field, including ADR in the digestive system, too.

### 1418 The Influence of Daily Dose on the Outcome of Aspirin-Induced Acute Upper Gastrointestinal Bleeding

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Aim: To examine the effect of prior use of aspirin on the clinical course of acute upper gastrointestinal bleeding (UGIB) regarding the daily dose.

Methods: We studied 345 patients admitted over a one-year period with UGIB and significant endoscopic findings. History of aspirin intake during the week preceding the onset of bleeding was positive in 59 cases (mean age 63, SD 16.6; 45 males, 14 females). These patients were included into two groups regarding daily dose aspirin: Group 1 with low-dose (< 325 mg) for prevention of arterial occlusive events, and Group 2 with high doses of aspirin (antiaggregatory/antiplateletic doses).

In each patient hospitalization was collected on prior history of ulcer, gastrointestinal protective agent use, comorbid conditions, mode of presentation, endoscopic findings and clinical course. Statistical analysis was performed using Student's t and Chi-square tests.

Results: 9 cases were excluded.

Conclusions: 1) A substantial proportion of UGIB is associated to aspirin intake in the week before the onset of bleeding; low-doses were responsible of over a third of bleeding episodes related to this drug. 2) The "low-dose aspirin" group was older, with longer intake and more comorbid conditions than the "high-dose aspirin" group.

### 1419 Nonsteroid Anti-Inflammatory Drug-Associated Acute Nonvariceal Gastrointestinal Bleeding in the Elderly: Incident Cases and Morbimortality

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Aim: To determine the incidence of nonsteroid anti-inflammatory drugs (NSAIDs)-associated acute upper gastrointestinal bleeding (UGIB) and the impact of these drugs on the clinical course in elderly patients.

Methods: We conducted a prospective study on 142 consecutive patients aged 65 years or older (mean age 76, SD 7; 97 males, 45 females) admitted with UGIB diagnosed endoscopically over a one-year period. These patients were divided into two groups: Group A with use of NSAIDs in the week before admission and Group B without NSAIDs.

Data collected: Age and sex, prior ulcer disease and therapy, symptomatology prior to bleeding, mode of presentation, endoscopic findings, transfusion requirements, need for urgent endoscopic and/or surgical treatment, duration of hospital stay and mortality. Incidence rates of UGIB were estimated on a general adult population of 142,776 (elderly population 14%). Statistical analysis was performed using Student’s t and Chi-square tests.

Results:

- Variables
  - Group A
    - Age (mean ± SD): 75.4 ± 7.3
    - Males: 62%
    - Prior ulcer: 27.6%
    - Protective agents: 15.5%
    - Anticoagulation: 10.3%
    - Mortality: 3.4%
    - Gastric ulcers: 4.1%
  - Group B
    - Age (mean ± SD): 77.2 ± 7.9
    - Males: 72%
    - Prior ulcer: 43%
    - Protective agents: 31.3%
    - Anticoagulation: 5.3%
    - Mortality: 3.6%
    - Gastric ulcers: 4.1%

- p Differences
  - Age: 0.028
  - Males: 0.000
  - Prior ulcer: 0.000
  - Protective agents: 0.000
  - Anticoagulation: 0.777
  - Mortality: 0.000
  - Gastric ulcers: 0.390

UGIB incidence for adult younger population: 72 per 100,000 UGIB incidence for elderly population: 560 per 100,000 Rate Ratio = 3.28; CI 95% (2.6–4.1)

Conclusions: 1) In our community the incidence of UGIB for elderly is high, and a relevant number of cases (40.8%) is associated with NSAIDs exposure in the week before admission. 2) Elderly patients with NSAID/UGIB differ in the source of bleeding and prior history of peptic ulcer disease. 3) NSAID treatment is not an adverse prognostic factor in acute UGIB in the elderly.

### 1423 Schönen–Henoch Purpura in Adults (Gastrointestinal Manifestation and Endoscopy)

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During a 10 years period 62 adult patients were admitted with diagnosis of Schönen-Henoch purpura in our hospital. 25 female and 37 male patients ranging from 30 to 87 years (mean: 59.5 years) and presenting with cutaneous, joint, renal and particularly abdominal involvement were investigated retrospectively. During the course of the disease, all patients developed purpuric rash (100%). 14 (22.9%) patients had joint symptoms and renal involvement occurred in 15 (19.3%) patients. In this study, we discuss 15 (24%) patients with gastrointestinal symptoms appearing in Henoch’s purpura. Analysis of the gastrointestinal clinical features revealed: abdominal pain 13 (86%), massive colonic bleeding in 3 (20%), colonic blood loss 10 (66%) vomiting 6 (40%) and diarrheas in 3 (20%) patients. Surgical consultation was obtained for 4 of the 15 patients and laparotomy was performed in 2 patients. All the patients underwent lower and upper endoscopic examination, in 3 patients the authors saw purpuric mucosal lesions in duodenum and in 8 patients were also found colonic-like elevated lesions in colon, additionally, biopsy from colonic lesions showed leukocytoclastic vasculitis. It is concluded that endoscopy can be helpful in the diagnosis and treatment of Schönen-Henoch purpura, especially is in those without typical skin rash.
Clinical Uniformity of Inflammatory Bowel Disease at Presentation in the North and South of Europe

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Background: A prospective epidemiological survey conducted by The European Collaborating Centre Group on IBD (EC-IBD) has assessed the incidence of non-specific inflammatory bowel disease (IBD) in the North and South of Europe. The protocol was also designed to study whether the clinical features of IBD are different in these two areas, because of genetic or environmental factors. Two European centres participated in the study, 8 were from the North and 12 from the South.

Methods: All centres used uniform criteria of disease definition in ulcerative colitis (UC) and Crohn’s disease (CD) and a common protocol for recording clinical and epidemiological data.

Findings: Altogether 2201 patients with IBD aged 15 years or more were identified. Of the 1379 with UC 869 were from the North and 510 from the South. Of the 706 with CD, 477 were from the North and 229 form the South. An analysis of the diagnostic measures used in making the initial diagnosis of UC or CD in the North and South showed that every patient with colitis had an endoscopy and that a biopsy or operation specimen was available for pathological examination in most cases. For CD over 80% of cases had an X-ray and tissue was available for pathological examination in 87–92% of cases. There was no difference in the proportion of cases investigated by each method in the North and South of Europe, except that radiology was used a little more often in the South. The analysis of duration and nature of presentation of UC and disease site and extent and evidence that the initial clinical features of disease vary from Iceland in the North to Mediterranean countries in the South. Conclusion: This study provides evidence that further improvement of investigation of IBD are available both in the North and South of Europe, definitions of disease are uniform, clinical presentation of IBD is similar, and therapeutic management during the first year of disease follows a common pattern in most centres.

Is Intestinal Permeability Really Increased in Patients with Inflammatory Bowel Disease?


Introduction: During the last years there is much interest in the intestinal permeability of patients with Inflammatory Bowel Disease (IBD) as this may play a role in the pathogenesis of IBD. However, methods used to measure the urinary sugar concentrations show lack of reproducibility and results are often conflicting. The aim of this study was to evaluate intestinal permeability in patients with IBD (Crohn’s disease (CD) and ulcerative colitis (UC)) versus controls, using a validated, newly developed analysis method.

Methods: After an overnight fast, 27 patients with IBD (8 CD, 19 UC) at time of diagnosis (IBD-new), 23 patients with long-standing CD > 10 years, but during an inactive period (CD-long) and 39 controls, ingested a solution consisting of 10 gram lactulose (L) and 1 gram mannose (R) in 65 ml of water. Urine was collected for 5 hours and urine L and R excretion was measured using a validated, newly developed fluorescent detection HPLC [1]. Results are expressed as mean ± SEM. Statistical analysis was performed by one-way ANOVA.

Results. The LR ratio for IBD patients (IBD-new: 0.01 ± 0.002; CD-long: 0.02 ± 0.002) was not significantly different compared to controls (0.01 ± 0.002). However, the % recovery of R was significantly decreased for CD-long patients, compared to controls (p < 0.001). No significant correlations were observed between either disease activity indices (albumin, ESR, CRP or CDAI) and LR ratio or disease activity indices and % recovery of the sugars. Conclusions. The LR ratio was not increased in patients with IBD. The excretion of the monosaccharide mannose was decreased for patients with long-standing CD. Whether this observation is related to malabsorption and reduced adaptive capacity of the small intestine of patients with long-standing CD remains to be established.


Decreased Trace Element Status in Patients with Inflammatory Bowel Disease

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Introduction. Trace element deficiency is described in patients with Inflammatory Bowel Disease (IBD), mainly in active Crohn’s disease (CD). Those trace elements, which are antioxidants, may play an important role in the pathophysiology of IBD as scavengers of free radicals. The aim of this study was to evaluate trace element status in various groups of IBD patients (CD and ulcerative colitis (UC)).

Methods: In 27 IBD patients at time of diagnosis (IBD-new: 8 CD, 19 UC) and in 31 patients with long-standing, but recently inactive CD (> 10 years with one or several bowel ressections; CD-long) and in 15 controls, trace element status was assessed by serum values of selenium (Se), zinc (Zn), magnesium (Mg), copper (Cu) and whole blood glutathione peroxidase (GPx). Statistical analysis was performed by ANOVA.

Sequences of Loeplis Cationic Protein (ECP), “Neurotoxin” (EPX) and Myeloperoxidase (MPO) as Markers of Clinical Activity in Inflammatory Bowel Disease (IBD)


Eosinophils may be the predominant cell type in the inflamed intestinal mucosa of IBD patients and disease activity may have been postulated to be involved in the pathogenesis of IBD. Aim: to evaluate if serum levels of protein released by eosinophils (ECP and EPX) and neutrophils (MPO) are related to clinical activity and autoantibodies in IBD pts. Methods: 104 consecutive outpatient patients affected by ulcerative colitis (UC: n = 62; mean age 63 years, range 17–74 yrs) or Crohn’s disease (CD: n. 44; mean age 41 yrs; range 15–76 yrs) were included in the study. Pts on steroids or other immunosuppressive agents, were not included. Pts were submitted to prick-by-prick tests for food allergens (milk, apple, pear, celery, onion, garlic, tomato, capsicum, peanut, banana, flour) and prick test for common inhalants (Dermapthaphagoides D.F. D.PT, Gramineaceae, Candida Albicans, Compositae, Betulaceae, Parietaria). Serum, ECP, EPX and MPO levels were tested by commercial kits (Pharmacia, Uppsala, Sweden). Results: 34% of pts have positive prick test irrespective of the type of disease. 55–70% of positive tests were found in pts in remission, but no statistically difference was found with disease clinical activity. Pts with positive prick test have ECP, EPX and MPO serum levels similar to those with negative prick tests (p: n.s.). MPO serum levels are related to clinical activity in IBD pts especially in UC pts (P < 0.02 ≤ 0.228). A significant correlation was found between serum levels of ECP with MPO (r = 0.537; p < 0.0001) and EPX with MPO (r = 0.517; p < 0.001). Conclusions: MPO serum levels are related to clinical activity in IBD pts with a positive correlation with serum ECP and EPX levels. 34% of our pts had a positive reaction to food and/or inhalant allergens. These data indicate that MMN neutrophils might trigger eosinophils which contribute to tissue damage by releasing their active proteins.

Humoral Immune Response to Human Stress (Heat Shock) Shock Proteins in Inflammatory Bowel Disease

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Purpose: Human Stress Proteins (HSP) is a large group of intracellular proteins expressed when cells are exposed to different kinds of stress. They appear to have a cytoprotective function which diminish cellular damage. HSP’s are believed to be involved in the pathogenesis of IBD, supported by the finding of enhanced mucosal expression of the stress proteins HSP 60 and HSP 70 in IBD. The level of antibodies to HSP’s seems to be elevated in other autoimmune diseases. In this study the presence of circulating antibodies to HSP 60 and 70 was compared to the expression of mRNA for the proteins in colon mucosal biopsies from a series of IBD patients.

Methods: Sera from IBD patients and controls were tested for antibodies by an ELISA based on HSP 60 and 70 from recombinant sources as the primary antigens. There were no correlations layers. Endocochelial colorectal biopsies were tested by PCR for the expression of HSP 60 and HSP 70 mRNA.

Results: Antibodies against HSP 60 were found in all patients with IBD, and no difference was found in titre level between patients with IBD and healthy controls. Antibodies to HSP 70 were not found. Using PCR to detect expression of HSP 60 and 70 it was found that both were expressed in both healthy subjects and patients with IBD. The sequence specificity excluded bacterial expression as a false positive signal.

Conclusion: It has been found previously that patients with Ulcerative Colitis have elevated levels of antibodies to HSP 70. This could not be reproduced although it was found that antibodies present in sera of patients with IBD expressed HSP 70. This and the finding of circulating antibodies to HSP 60 suggest that the circulating antibody response to these two proteins is without importance in IBD. HSPs could still be involved in the pathogenesis of IBD acting as a local immunological mediator induced by inflammation.
1440 Acute Pancreatitis in Patients with Chronic Inflammatory Bowel Disease

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Several case reports on co-existence of pancreatic dysfunction and chronic inflammatory bowel disease, especially Crohn's disease, have been published during the past few years. However, only few studies have estimated the risk of acute pancreatitis in patients with chronic inflammatory bowel disease.

Aim: To estimate the risk of acute pancreatitis in patients with chronic inflammatory bowel disease in the Danish population.

Methods: The study included all patients discharged from Danish hospitals with a diagnosis of chronic inflammatory bowel disease and acute pancreatitis, registered in the Danish National Registry of Patients (1977 to 1992). Age- and sex-specific incidence discharge rates for acute pancreatitis in patients with chronic inflammatory bowel disease and the background population were calculated. The expected numbers of acute pancreatitis were calculated and divided into groups according to sex, age and calendar-time in three age-groups.

Results: Overall, 15572 patients were discharged and followed for 93774 person-years yielding an average follow-up of 7.7 years for Crohn's disease and 8.9 years for ulcerative colitis. The incidence discharge rate (IRR) for acute pancreatitis was increased in both patients with Crohn's disease (IRR = 3.0, 95% CI: 2.0-4.3) and in patients with ulcerative colitis (IRR = 1.5, 95% CI: 1.1-2.0), especially in the age-group from 15-64 years. No patients < 15 years had acute pancreatitis.

Conclusion: Patients with chronic inflammatory bowel disease are at an increased risk for acute pancreatitis.

1441 HLA Class II DRB1*0301 or DRB3*0301 Gene Involvement in Genetic Susceptibility to Inflammatory Bowel Disease (IBD)?

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Recent European studies of HLA class II genes involvement in IBD genetic susceptibility have shown a negative association of HLA DRB1*0301 with IBD as well as with Crohn's disease (CD) compared with ulcerative colitis (UC). HLA DRB1*0301 and DRB1*11, 12, 13 and 14 alleles are associated with an allele HLA DRB3 polymorphic locus (at least 4 alleles described). Recently a non-European study have shown an increased risk of CD in individuals who inherit HLA DRB3*0301 allele. The aim of the present study was to analyze the relationship between HLA DRB1 and DRB3 locus in the susceptibility to IBD.

Methods and patients: One hundred thirty one UC and 157 CD patients were included in this study and compared with 200 ethnically matched controls. HLA DRB1 and DRB3 class II alleles were determined by PCR-SSO and if necessary by Reverse Dot Blot (Innolipa, kits from Innogenetics®).

Results: DRB1*0301 and DRB3*0301, 02, 03 allele distribution was analysed in patients groups and controls. A decrease frequency of DRB1*0301 allele was observed in patients (respectively 4% and 7% in UC and CD) versus 15% in controls (p < 0.001). Considering the DRB3 locus, a non significant increase frequency of DRB3*03 allele characterize CD patients (8.6% versus 4% in UC and 4.9% in controls). Finally, the analysis of DRB3 alleles subtypes (165, 113 and 86 DRB3 alleles in controls, CD and UC respectively) shows that the DRB3*03 allele is more represented in CD patients (23.8% vs 10.9% in controls and 12.6% in UC).

Conclusion: The DRB3 locus is not involved in the protective effect conferred by the MHC class II DRB1*0301 allele. We cannot confirm the strongly association of HLA DRB3*0301 allele with CD in an European population of CD patients.
or radionuclides as energy-sources which impede exposure to radiation. Thus repeated measurements within a short period of time may be harmful. US measurements on the other hand are easy to perform and do not have such side effects. This study was planned to compare the new methodology of US of the os calcis with the conventional DXA of the lumbar spine. Methods: Bone mineral density (BMD) was measured in 36 IBD patients considered at risk for osteoporosis due to persistent disease activity and/or prolonged steroid intake (24 with Crohn’s disease and 12 with ulcerative colitis) aged 24 to 65 years. We performed DXA at the lumbar spine and US of the left os calcis, both examinations within the same day. DXA measurements were expressed as g/cm², US measurements as speed of sound (SOS; m/s), considered to represent density and elasticity, and attenuation of US (BUA: dBM²Hz) indicating bone density and trabecular structure. Results: in our hands short term precision of DXA was 0.8%, that of US 1.1% for BUA and 1.8% for SOS. DXA and SOS values are closely correlated (r² = 0.699, p < 0.00001), whereas BUA showed a weaker but still significant correlation with DXA-values (r² = 0.414, p < 0.01). Comments: 1) Both indices, SOS and BUA, correlate with measurements obtained by conventional DXA of the lumbar spine; 2) US densitometric measurements have an acceptable reproducibility; 3) in IBD patients US may contribute to detect short-term variations due to disease activity, bed rest, or treatment influences (steroids or cyclosporin) and, thus, give new insights in pathophysiology of IBD-associated bone disease.

Familial Prevalence of Inflammatory Bowel Disease in Relatives of Finnish Patients with Crohn’s Disease or Colitis
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In order to evaluate the extent of the genetic component underlying inflammatory bowel disease (IBD) 880 Finnish subjects suffering from ulcerative colitis (UC) or Crohn’s disease (CD) were studied. We complete a questionnaire addressing to the occurrence of IBD in their first-degree relatives. The questionnaire was completed by 570 patients (65%), of whom 554 individuals (276 men and 278 women) were unrelated.

UC was prevalent in 930 (52%) and CD in 226 (41%) subjects; in 38 subjects (7%) the exact nature of the disease was indeterminate. 13 (5.7%) CD patients and 21 (7.2%) of those with UC had at least one sibling with IBD. Five subjects with CD and 12 (4.1%) with UC had a parent suffering from UC. Five (2.2%) CD patients and 7 (2.4%) UC patients had at least one affected child. There was a tendency towards genetic anticipation (earlier onset of IBD in successive generations) in both UC and CD. Thus in four families with CD the mean difference between ages at diagnosis in the first and second generation was 20 years and in five UC families 17 years. In conclusion, at least one affected first-degree relative was detected in 13.1% of UC patients and in 10.2% of CD patients.

Thrombophilia in Inflammatory Bowel Disease
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Thrombo-embolic complications are important in inflammatory bowel disease (IBD). Thrombophilia may contribute to this thrombotic tendency. It is unclear whether patients with IBD and a previous history of thrombo-embolic complications form a specific subgroup. The aim of our study was to determine the frequency of a range of thrombophilic abnormalities in patients with IBD and in the subgroup of patients who have also suffered from thrombo-embolic problems.

Serum levels of antithrombin III, protein C, protein S and lupus anticoagulant and the presence or absence of activated protein C resistance was assessed as a thrombophilia screen. All tests were performed in the absence of anticoagulant therapy.

18 patients were studied. 11 had IBD alone (age range 27–78, 5 male and 7 had BD and previous thrombo-embolic complications (age range 22–76, 3 male). Thrombo-embolic problems included 5 deep vein thromboses, 2 axillary emboli and 1 axillary vein thrombosis. The ratio of ulcerative colitis to Crohn’s disease and active to inactive patients in the two groups were similar. Of those with IBD alone, thrombophilic abnormalities were detected in 6/11 patients, one patient had both antithrombin III and protein S deficiency, one had both antithrombin III deficiency and lupus anticoagulant and one had activated protein C resistance. Borderline abnormalities in protein S deficiency and lupus anticoagulant were detected in three other patients. Of those with previous thrombo-embolic problems, one had activated protein C resistance, one had antithrombin III deficiency, one had protein C deficiency and one was borderline positive for lupus anticoagulant.

In summary the prevalence of the recognizable thrombophilic abnormalities is high (approx 60%) in IBD. Patients who have suffered from thrombo-embolic complications are not more likely to have thrombophilia. IBD patients requiring bariatric surgery may need reduced heparin prophylaxis. Those with documented thrombophilia may need longer term anticoagulation.

Adhesive E Coli in Inflammatory Bowel Disease

Escherichia coli (E. coli) have been implicated in the aetiology of inflammatory bowel disease (IBD) as patients with active ulcerative colitis (UC) are more likely to carry strains adhesive to buccal epithelial cells. No previous study has investigated the coliform flora in patients with IBD and healthy controls over a prolonged period.

Four face samples were collected over a 12 months period from 13 patients with UC, 8 with CD and 12 healthy volunteers. 10 E. coli colonies were isolated from each sample and typed by REP-PCR. The adhesiveness of each E. coli subclone was assessed by a buccal epithelial adhesive assay. Our adhesiveness standard E. coli strain (E851) had a mean buccal epithelial adhesion index (BECAI) of 15% and the non-adhesive standard (SC13), a mean of 0. The Mann-Whitney, Fisher’s exact and Kruskal-Wallis tests were used to analyse the results.

Patients with IBD carried significantly more adhesive E. colis than healthy controls (UC median BECAI 6, P = 0.007, CD median 8, P = 0.03, Controls median 0). This association did not change over time as more healthy controls carried non-adhesive E. colis (BECAI < 5) at most of the four collection time points with UC patients (9/12 and 2/12 respectively, P = 0.06). There was an association between adhesiveness and site of disease as patients with proctitis and extensive colitis were more likely to carry adhesive strains than patients with left colonic or small bowel disease (P = 0.02). Eight percent of E. coli strains followed for one year changed adhesiveness without changing REP-PCR pattern suggesting that the gene for adhesiveness is situated on a plasmid.

In conclusion, we can confirm that not only patients with UC but also those with CD are more likely to harbour adhesive E. colis than healthy volunteers. The carriage of adhesive E. coli may be more related to site of infection than type of IBD.

Immunquantitation of a Novel Endothelial Cell-Specific Surface Antigen in Inflammatory Bowel Disease
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The aim of the present study was to investigate in detail the immunohistochemical properties of the two endothelial specific markers 1F10 (continuous endothelia) and MS-1 (discontinuous endothelia) in bowel tissues of patients suffering from chronic inflammatory bowel disease (IBD).

Immunohistochemical techniques were employed to study the morphology and phenotypic expression of these two proteins in routinely processed bowel tissues from 27 patients with Crohn’s disease (CD), 18 patients with ulcerative colitis (UC), and from 20 normal controls.

All patients with IBD and controls showed a low to moderate 1F10 immunohistochemical staining restricted to the lamina propria and submucosa. In contrast to UC patients and healthy controls, 1F10 immunoreactivity was strongly de novo expressed in the anastomotic bowel in CD patients regardless of the histological severity of the inflammatory process. Neither in Crohn’s disease nor in ulcerative colitis we observed immunoreactivity for MS-1 on endothelia surfaces.

From this we can conclude that endothelia in patients with IBD do not undergo metaplasia. The high immunoreactivity of 1F10 antigen in the muscularis propria in CD indicates a state of topical immunological activation and may be important in the maintenance of chronic inflammation by facilitating leukocyte migration into sites of Crohn’s disease involvement. Further studies of the factors controlling endothelial cell differentiation in the bowel of CD patients may help to explain the features observed in this study.

Prothrombotic State in Inflammatory Bowel Disease (IBD)

Patients with Crohn’s disease (CD) and Ulcerative Colitis (UC) show an increased risk of thromboembolic events. Aims were to investigate parameters of prothrombotic function and the prothrombotic activity in IBD patients. Patients and methods: 22 consecutive patients affected by UC (13 M, 9 F; mean age 43.50) and 12 affected by CD (5 M, 7 F; mean age 49.59) were studied and compared with 20 healthy control subjects. In CD patients the disease activity was evaluated by Rachmilewitz index and in CD patients by Crohn’s disease activity index (CDAI). In all patients platelet count (PLT), PT, aPTT, Fibrogen (FBG), antithrombin (AT), protein C, Protein S, factor XIII (FXIII), plasminogen (PLG), spontaneous platelet aggregation in platelet-rich plasma (PRP-SPA) and a whole blood (WS-SPA) and aPL were evaluated. The parameters of hemostatic function were analyzed by variance and analysis of the frequency of aPL by Fisher exact test. Results: In both UC and CD patients PLT, FBG were significantly

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increased (p < 0.05), FXIII was significantly decreased (p < 0.05) compared with controls. CU patients showed a higher aPL positivity (p < 0.05) than CD patients and the control group. The increase of PLT and FgB was related to the activity of disease; on the other hand the decrease of FXIII and the positivity of aPL was not related to the disease activity or to the site of lesions. In IBD patients, PAI, PRP-SPA, WS-SPA, PC, PS and AT didn’t show a significant difference vs. the control group. For what concerns hemostatic parameters were not statistically significant differences in UC and CD.

Conclusion: Our data suggest that 1) in both UC and CD patients, the only alteration of hemostatic function was a decrease of FXIII levels. 2) In all presenting data, there was no significant relationship between hemostatic parameters and disease activity. 3) aPL were significantly increased in UC in comparison with CD.

1448 | ANCA in Ulcerative Colitis (UC): Comparison between ANCA + and ANCA – Patients and Longitudinal Follow Up

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Positivity for ANCA has been described in about 65% patients with UC. The significance of this positivity is still unknown. The aim of our study was first to compare ANCA + and ANCA – UC patients on the basis of clinical data to follow longitudinally the patients that showed the reproducibility of the results over time. Patients and methods: Forty seven consecutive UC patients, with ANCA determination, were included in the study. ANCA positivity was determined using an immunohistochemical method. Results: There were 24 ANCA + and 23 ANCA + patients. There was no significant difference between these 2 groups in duration of the disease or in smoking. The comparison between these 2 groups showed no significant difference in location and evolution (assessed by need for surgery and immuno-suppressive treatment) of the disease. The frequency of extraintestinal manifestations was however significantly higher in the ANCA + group (35% - including 8.5% of sclerosing cholangitis- vs 8%; p < 0.05). Twenty out of the 47 patients had several successive tests for ANCA. Five of them showed a change in their ANCA status. These changes were not consistently associated with a modification in location, systemic manifestation, activity or treatment of the disease. In conclusion, 1) The ANCA status may determine subgroups of the disease with different risk of systematic manifestations 2) some patients (25%) had a change in ANCA status over time, but this was not associated with any clinical feature.

1449 | IgM Specific Anti-Mesologies Antibodies in Patients with Inflammatory Bowel Disease (IBD)

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IgM specific anti-mesologies antibodies were found significantly increased in patients with IBD, especially in Crohn's disease (CD). A persistent mesologies infection has been implicated in the pathogenesis of Crohn's disease, via a chronic granulomatous vasculitis process, but data from other studies are not consistent with this hypothesis. In this prospective study we were to assess a possible causal relationship between mesologies infection and IBD, by titrating serum IgM specific anti-mesologies antibodies in patients with exacerbated IBD.

Materials-Methods: Sixty nine (69) patients (40 males and 29 females, mean age 48.7 years) with exacerbated IBD were included in this study. Forty four (44) patients suffered from ulcerative colitis (UC) and 25 from Crohn's disease. The diagnosis of the exacerbated IBD had been established by endoscopy, X-ray, histology and determination of UCAI (> 20) and CDAI (> 150). The control group comprised of 60 healthy blood donors. Sera of all patients and controls were examined for the presence of IgM and IgG specific anti-mesologies antibodies. The indirect immunfluorescent method was used for antibody detection. Titters of IgM antibodies in excess of 1:80 were considered indicative of persistent mesologies infection.

Results: High IgM antibody titters (> 1:80) were detected in none of our patients whereas specific mesologies antibodies in IBD were detectable in 81.8% (36/44) of UC, 88.0% (22/25) of CD patients and 85.0% (51/60) of controls (p < 0.10; NS). Conclusion: High titers of IgM specific anti-mesologies antibodies were not detected in patients with exacerbated LC or CD. A causal relationship between persistent mesologies infection and IBD is not likely.

1450 | Faecal Calprotectin Concentration as a Marker of Disease Activity in Inflammatory Bowel Disease

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A non-invasive test to quantify bowel inflammation is greatly needed in the management of Inflammatory Bowel Disease (IBD). Calprotectin is an abundant neutrophil protein, which is very stable in faeces and is significantly increased in adults with IBD. The aim of this study was to investigate whether faecal calprotectin is raised in children with IBD and to determine its usefulness as a marker of disease activity.

Faecal calprotectin was estimated in 45 spot samples of faeces, collected from 29 children receiving treatment for IBD, (5.0 to 15.2 years) and was compared to a group of 25 children and 31 adult controls. The level of disease activity was scored by the abdominal pain blinding to faecal calprotectin results. Faecal calprotectin concentration was determined by an ELISA. The data was expressed as mean ± SD, the disease groups were compared using an unpaired T test.

In children with Ulcerative Colitis (8992 ± 5591 ug/l, p = 0.001) and Crohn's disease (10499 ± 6746 ug/l, p < 0.001) the stool calprotectin concentration was significantly increased over control range (3056 ± 2303 ug/l). The mean faecal calprotectin level rose significantly with increasing severity of disease (p < 0.001). In children felt clinically to be in remission 40% had UC and 58% with Crohn's disease had stool calprotectin concentrations > 95th centile of the control range.

Additionally, one newly presented child with UC had eight spot stool samples collected longitudinally. His faecal calprotectin concentration decreased from 500,000 ug/l before treatment to 6846 ug/l when clinically in remission two months later (within control range).

The elevated faecal calprotectin in patients with IBD is likely to reflect the severity of disease activity and indicates that many children have active disease even when free of symptoms. Although further investigation is required, these preliminary studies illustrate the potential of this test for the screening and monitoring of IBD.


1451 | Antineutrophil Cytoplasmic Antibodies in Estonian Patients with Inflammatory Bowel Disease

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Antineutrophil cytoplasmic antibodies (ANCA), originally found to be associated with vasculitides, have been reported to be present in inflammatory bowel disease (IBD). The ANCA staining pattern in IBD is most often perinuclear (p-ANCA). The presence of ANCA might prove the evidence of possible involvement of autoimmune mechanisms. However, the antigen to which these antibodies are reactive is not yet known.

The aim of the study was to determine the prevalence and pattern of ANCA in patients with inflammatory bowel disease in Estonia. Enzyme-linked immunosorbent assay (ELISA), using myeloperoxidase, proteinase-3 and lactoferrin as antigens, was performed to characterize the antigen specificity. 64 sera of the patients with ulcerative colitis (UC), 16 with Crohn's disease (CD), 30 with irritable bowel syndrome and 87 healthy persons have been studied. Sera were analyzed for the presence of ANCA by the indirect immunofluorescence on ethanol-fixed neutrophils using fluorescin labelled anti-IgG. ELISA for specific ANCA was performed using antigens mentioned. ANCA were detected in 31/84 (48%) patients with UC, 3/16 (19%) patients with CD and 4/110 (4%) in controls. The immunofluorescence staining were mostly perinuclear (p-ANCA), but at the same time, ANCA with cytoplasmatic pattern (c-ANCA) were also revealed. There was no correlation between ANCA and the duration or extent of the ulcerative colitis and Crohn's disease. In ELISA with purified proteinase-3, lactoferrin and myeloperoxidase only a few sera elicited binding above the normal range.

Although, the prevalence of UC and CD in Estonia is much lower than in Scandinavia and Northern Europe, there seem to be no differences in immunological features. ANCA occur significantly more often in ulcerative colitis than in Crohn's disease. The ANCA pattern is predominantly perinuclear. The antigenic target for ANCA needs to be determined in further studies.

1452 | Epidemiology of Inflammatory Bowel Disease (IBD) in the Province of Liège: Study of Subjects Older than 60 Years

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IBD unusually may occur in subjects older than 60 years. The aim of this work was first to determine the incidence of Crohn's disease (CD) and ulcerative colitis (UC) in a population older than 60 years (group 1), and second, to compare their clinical features to those observed in one population younger than 60 years (group 2), with IBD occurring during the same period. Patients and methods: Prospective study of the new IBD cases occurring in the province of Liège between 1/693 and 31/594. Incidence in groups 1 and 2 were calculated from the whole population for 2 consecutive years. Chi 2 and Fischer test: 104 new cases of IBD were recorded during the study. In group 1, there were 25 new cases (24%), including 10 CD (40%), 11 UC (44%) and 4 undetermined colitis (16%). In group 2, the comparison between hemostatic parameters was not significant, included cases, 46 CD (58%), 25 UC (32%), and 8 undetermined colitis (10%). In group 1, mean age at onset was 67 years for CD and 67.5 for UC. The incidences were 4.5 and 5 over 10 2 for CD and UC respectively. This data is different from group 2, where the incidence was significantly higher than the one of UC: 5.8 and 3.2 over 10 2 respectively (p < 0.02). Sex ratio (M/F) was 1.7 and 1.5 for CD, and 0.6 and 1.2 for UC, in group 1 and 2 respectively. There was no significant difference in the clinical features (symptoms, location, systemic manifestations) at onset for both diseases. In
conclusion. In the province of Liége, 1) the incidence of IBD is as high after 60 years of age as in younger subjects; 2) these 2 groups do not have different clinical features at onset.

1453  Value of Pathological Examination of the Cecal Specimen to Predict the Outcome of Patients with IBD Limited to the Colon

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In patients (pts) with IBD limited to the colon who need colectomy, distinction between Crohn's disease (CD) and ulcerative colitis (UC) may be of great importance before deciding the restoration procedure, especially lasso-anal anastomosis. Our aim was to study whether gross and microscopic findings on the cecal specimen may predict the final outcome of the disease.

Methods. From 1978 to 1993, 147 pts with IBD had total colectomy in our hospital with extracolonic involvement. Before surgery, 42 pts (28.7%) had UC without a definite colitis (IC). Final diagnosis CD was based on the occurrence of extracolic involvement (small bowel or anus) during the post-operative follow-up.

Results. 22 out of the 101 pts were definitively classified as CD because of the occurrence of typical small bowel involvement (n = 8), anal lesions (n = 8), or both (n = 6). Extracolic CD involvement occurred more frequently in pts with granuloma (71/10) compared with the other pts (18/91; P < 0.001); in contrast, the risk of extracolic involvement was not significantly different between CD classified as probable CD (6/43), probable UC (3/33) and IC (3/15). Among the 12 histological criteria, only 2 were found, using a multivariate analysis (Cod model), to be significantly associated with a higher risk of extracolic CD involvement: granuloma (RR = 4) and local inflammation with intervals of normal mucosa (RR = 1.8).

Conclusion. In pts without granuloma, the occurrence of extracolic CD involvement after surgery is poorly predicted by the pathological examination of the cecal specimen.

1454  Phosphoprotein Patterns of Intestinal Mucosa in Chronic Inflammatory Bowel Diseases

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Protein phosphorylations/dephosphorylations play a fundamental and almost universal role in the regulation of cellular functions. Consequently, defective protein phosphorylation/dephosphorylation can give rise to a variety of disease states. This aspect has not yet been investigated in chronic inflammatory bowel diseases (IBD). Here we demonstrate and compare phosphoprotein patterns in normal and chronically inflamed intestinal mucosa of patients with ulcerative colitis (UC) or Crohn's disease (CD). Methods. Samples of colonic mucosa were obtained by endoscopic forceps biopsy from patients with normal mucosa (n = 11), UC (n = 9) or CD (n = 9). Homogenized tissue was incubated with [-32P]ATP under conditions allowing for endogenous Mg-dependent protein phosphorylation. Endogenous phosphatases were inhibited with microcin-LR. Following second dimensional electrophoresis (SDE, isoelectric focusing followed by SDS-PAGE) phosphoprotein patterns were analysed with a PDI-Scanner or with PDQuest image master software. Following autoradiography, 210 phosphoprotein spots were detected in normal mucosa as compared to 42 ± 5 in UC and 36 ± 3 in CD. UC and CD mucosa differed in 35 and 28 phosphoproteins, respectively, from normal, importantly. UC and UC mucosa differed in 35 phosphoproteins. Major differences were detected in phosphorylatable proteins in the range of 120 to 70 kDa and 32.5 to 25 kDa at isoelectric points between pH 5.4 to 7.9. The nature and function of the various phosphoproteins and related protein kinases is unclear at present. Conclusions: The incubation of normal, UC or CD mucosa with [-32P]ATP resulted in phosphorylation of numerous proteins that could be detected in characteristic and reproducible patterns by second dimensional electrophoresis. The phosphoprotein patterns of normal, UC and CD mucosa exhibited extensive and characteristic differences, potentially providing a new diagnostic tool in the distinction of IBD. The potential role of impaired protein phosphorylation/dephosphorylation in the etiopathogenesis of IBD merits further investigations.

1455  Incidence of Inflammatory Bowel Disease (IBD) in the Puy-De-Dome Department of France in 1993–94

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Background. The aim of this prospective epidemiological study was to investigate the incidence of Crohn’s disease (CD) and ulcerative colitis (UC) in this county, using the same methodology as the Nord-Pas de Calais region and to determine whether a North-South gradient of IBD in France is real.

Methods. From 01/01/93 to 31/12/94, each Gastroenterologist collected patient data fulfilling the first criteria for clinical symptoms compatible with IBD. Data were reported on a questionnaire by an interviewer practitioner. The final diagnosis of CD, UC was made in a blind manner by two expert Gastroenterologists and recorded as definite, probable, or possible diagnosis.

Results. 1145 patients were interviewed, among which 117 new cases were identified with 100 (74.1%) CD, 31 (23.0%) UC, 4 (2.9%) unclassifiable chronic colitis and 51 (25.9%) acute colitis; 11 (5.6%) cases were unclassified. The annual incidence rate per 100,000 8.95 for CD (9.6 for men and 7.1 for women) and 2.5 for UC (2.4 and 2.7). These figures are higher than those of age-specific incidence rates for CD between 40-49 years (15.3) and for UC between 80-89 years (6.8). The sex-ratio F/M was 0.8 for CD and 1.2 for UC. The mean age at the time of diagnosis was 42.3 years for CD and 54.4 years for UC. The incidences for CD and UC, definite and probable, are respectively 4.8 and 2.5 in the North and 6.6 and 2.3 in this county.

Conclusions. 1) These preliminary findings revealed a high incidence of IBD in this county, and close to the highest incidences in the North. The incidence rate in France for UC is lower than CD, contrary to the other countries of Northern Europe. 3) This study doesn’t show any North-South gradient for CD.

1456  Prevalence of Helicobacter Pylori (H.p.) Infection In Inflammatory Bowel Disease (I.B.D.) – A Controlled Study

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Objectives To evaluate H.p. prevalence in patients with IBD submitted to several therapeutic regimens. Material and Methods 60 patients were studied prospectively, 30 with CD (mean age ± SD 39.45 ± 14.63) and 30 with UC (mean age ± SD 43.13 ± 13.19). Results were obtained in 60 healthy volunteers (control group – CG). These groups were matched by age, gender and weight. Analysis of some parameters were carried out by x² and Kruskal-Wallis tests. Results Prevalence of H.p. was as follows: IBD group (n = 22) and non-operated patients, a significant decrease in the prevalence of H.p. was verified in operated patients (31.8%) p = 0.003. Conclusions 1) Prevalence of H.p. infection was similar in IBD sub-groups and also between these and CG. 2) A significant decrease was shown in patients with previous surgery. These patients were submitted to intensive drug treatment (several antimicrobial agents) and had medical intractability. 3) In the IBD group no other factors were detected that may influence H.p. status.

1457  General and Cancer Specific Mortality in the Follow-Up of a Cohort of IBD Patients in Florence


A population-based study identified all the patients with a diagnosis of ulcerative colitis (UC) or Crohn’s disease (CD) resident in the Florence area in the period 1978–1992. Overall, 920 patients were included in the follow-up since the date of diagnosis, January 1st 1978 (for cases diagnosed before the start of the study) or the date of migration into the area until death or end of study period (January 1st 1992). An annual mortality file was available for observation, with a median follow-up of 9.7 years. A linkage with local town offices and the Regional Mortality Registry allowed the identification of 64 deaths and the retrieval of individual death certificates. Expected deaths were estimated on the basis of 5-year age group, gender and calendar year specific mortality rates of the general population in order to calculate Standardized Mortality Ratios (SMR) for overall mortality and selected groups of causes. Specific cancer sites were considered separately. Observed (O) vs. Expected deaths (E) were calculated assuming a Poisson distribution. General mortality was significantly lower than expected in UC (SMR 0.7; 95% CI: 0.5–0.9), due to a reduced number of cardiovascular deaths. Smoke-related causes of death were also reduced in UC, in particular cancers of the respiratory tract (which tended to be increased among CD patients). Overall, there was only a limited evidence of an increased mortality for colorectal cancer (significant for rectal cancer in UC patients: SMR 5.0, 95% CI 1.0–14.6). A non significant excess of endometriophagic myeloid malignancies was observed in UC patients. Mortality from gastrointestinal causes were increased among CD patients (SMR 3.9; 95% CI 1.1–10.0), but not in UC. These preliminary results suggest a specific mortality pattern for Italian IBD patients.
The Polymorphism of Motilin Gene Differentiates Genetic Subgroups of Patients with IBD

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Several lines of evidence suggest the importance of genetic factors, such as the HLA class II genes, in the susceptibility of ulcerative colitis (UC) and Crohn's disease (CD). We have recently defined the subchromosomal localization of the motilin gene very close to the HLA-DR locus (Hum Genet 1994: 94: 671). Aim of the study was to investigate DNA polymorphisms of the motilin gene in a population of inflammatory bowel disease patients. Methods: 88 patients with firm diagnosis of UC (49) and CD (39) were studied. Control values were obtained by 60 unrelated blood donors. Anti-neutrophil cytoplasmic antibodies (ANCA) were identified by indirect immunofluorescence (perinuclear pattern). PCR of the second exon of motilin gene was performed to study the different alleles (1 and 2) of motilin gene. Results: are summarized in the table. Patients with CD had a significant increase of the allele 2 frequency (p < 0.03 - 3\). After stratifying patients according to their ANCA reactivity, ANCA-negative CD patients did not differ from healthy subjects, while ANCA-positive subjects had a striking increase of allele 2 frequency (p < 0.02).

Conclusions: These results provide further evidence for genetic heterogeneity in patients with CD. It is also intriguing to hypothesize that the polymorphism of the motilin peptide produced by the nucleotide change might explain some of the intestinal mot abnormalities we found in CD patients (Gastroenterology 1995; 104: A470).

Prevalence of Antineutrophil Cytoplasmatic Antibody In Unaffected Relatives of IBD Patients

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Presence of ANCA has been suggested as a genetic marker of disease susceptibility in ulcerative colitis (UC). However, a wide difference of their prevalence (3-30%) in unaffected first degree relatives has been reported. Aim: To determine the prevalence of ANCA in unaffected first degree relatives in families in which more than one member was affected with UC or Crohn's disease (CD). Method: 22 families which included 47 affected members (28 UC and 19 CD patients) and 94 unaffected first degree relatives were studied. ANCA reactivity was investigated by indirect immunofluorescence also in 169 consecutive blood donors and 275 patients without familial history (195 UC and 80 CD). Results: are given in the table (values of p obtained with Fisher test). No significant difference of ANCA reactivity was found between patients with or without family history.

<table>
<thead>
<tr>
<th>Controls</th>
<th>UC familial</th>
<th>UC sporadic</th>
<th>CD familial</th>
<th>CD sporadic</th>
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<tbody>
<tr>
<td>ANCA+ve (p vs Controls)</td>
<td>3.5%</td>
<td>31%</td>
<td>5%</td>
<td>1%</td>
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There was no evidence of clustering of antibodies in particular families. In four out of seven families in which both UC and CD coexisted, all the affected members were ANCA negative.

Conclusions: ANCAcs are associated with ulcerative colitis. Their presence is neither increased in patients with family history nor in their unaffected first degree relatives.

The Presence of ANCA Identifies Only a Weak Clinical Heterogeneity in Patients with IBD

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Antineutrophil cytoplasmatic antibodies (ANCA) have been suggested as a potential marker of genetic heterogeneity in IBD. However, their relation to different clinical features (UC and CD) and Crohn's disease (CD) is unclear. Aim: To investigate a possible relation between ANCA reactivity and clinical characteristics of the patients. Methods: 237 UC (mean age 42 yrs, 147 male and 90 CD patients (mean age 36 yrs, 53 male) were studied. The determination of ANCA reactivity was performed by indirect immunofluorescence also in 169 consecutive unrelated blood donors. Patients were characterized by clinical features: gender, age at onset, disease location and severity (Trichrome and CDAI scores) need for surgery, pouchitis, extra-intestinal manifestations, clinical course (remission or frequent relapses [> 2/year]), therapy (need of steroids, need for immunosuppression). Results: ANCA positivity was infrequent in our patients being found only in 68 (28%) UC and 8 (9.5%) CD respectively. ANCA were found also in 2 (1.2%) blood donors. After stratifying patients according to their ANCA reactivity, the majority of clinical features were equally distributed between the two groups. ANCA reactivity was significantly more frequent only in UC patients using steroids (34% vs 19%; p = 0.019) and in CD patients with colonic localization (26% vs 15%; p = 0.009). Moreover, a slight decrease of incidence was present in UC patients in remission (21% vs 46%; p = 0.047). However, ANCA positivity had only 32% accuracy in differentiating UC from CD, and a 54% accuracy in predicting UC patients with steroids need. Conclusions: ANCA may well represent a marker of genetic heterogeneity. However, on clinical ground, the correlation with clinical features is rather weak with a poor accuracy and a low negative predictive value.

Antioxidant Enzymatic Systems in Inflammatory Bowel Disease

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Introduction: The transmembrane redox enzymatic system has three main functions: growth control, reducing transferrin iron III and antioxidant actions through the reduction of ascorbic acid, vitamins E and ubiquinone, and lipid hydroperoxide (HPR) inactivation. Oxygen free radicals have probably a role in either producing or amplifying the inflammatory response in Inflammatory Bowel Disease (IBD). Aim of Study: Activities of several enzymatic parameters of oxidative stress were evaluated in IBD patients, ulcerative colitis (UC) and Crohn's Disease (CD), between male and female patients and state of disease. Material and Methods: 37 patients with IBD were studied, 16 male and 21 female, 18 with UC and 19 with CD. Age range between 17 and 72 years. A control group of 36 for RTM, 174 for RMeHb and 55 for ACP1 and 25 for EQ, age and sex matched was used as comparison. Diagnosis of UC and CD was based on clinical, radiological, endoscopic and histological grounds. The activity of the RTM was assayed by the technique of Orringer and Roer modified by us: it is expressed in mmol/hour of ferricyanide reduced by intact erythrocyte. Other enzymatic systems were measured by standard spectrophotometric methods. The statistical analysis was done by parametric methods. Results: Patients with IBD showed RTM activity 4.625 ± 0.079 while the controls showed 6.013 ± 3.622 (difference statistically significant: p < 0.05). No difference was found in men, while in female the mean values of 4.417 ± 2.183 was statistically significant compared with female controls (7.145 ± 4.510 ± 0.05). A non statistically significant difference was found neither between UC and CD patients, nor between the active or quiescent phases of the disease. Both RMeHb and ACP1 were statistically significant when compared with controls (17.62 ± 4.87 in IBD patients vs 13.87 ± 7.165 in controls p < 0.05), 99.94 ± 4.183 in IBD patients vs 154.7 in controls p < 0.001), respectively. No statistically significant difference was found in EQ. Conclusions: The results suggest an increased production of oxygen free radicals which can induce tissue injury.

Antioxidant Cell Antibodies in IBD: A Marker of Vascular Injury?

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Mesenteric vasculitis has been reported as a possible pathogenic mechanism in Crohn's disease (CD) [1]. Moreover it is well known that vascular endothelium plays an active role in inflammatory and immune processes through expression of endothelial adhesion molecules and of class I and II HLA molecules, cytokine production and expression of procoagulant activity. Antienoidal cells antibodies (AECA) have been detected in various autoimmune vasculitides and there is some evidence that these antibodies can mediate endothelial injury and correlate with disease activity [2]. Recently AECA have been detected in inflammatory bowel disease (IBD) [3] but their clinical significance is still unknown. Aim of the present study was to assess the prevalence of AECA in IBD as compared to normal controls.

Sera of 70 patients with IBD (47 UC; 23 CD) and 40 normal controls were tested for AECA by ELISA on unfixed human umbilical vein endothelial cells. Sera positive for AECA were found in 20/70 (28.5%) IBD patients and in 3/40 (7.5%) controls (p < 0.01). No statistical difference have been observed in the prevalence of AECA in UC (13/47; 27.3%) as compared to CD (7/23; 30.4%).

The prevalence of AECA showed no correlation with age, sex disease duration, disease extent and disease activity. However a higher prevalence of AECA...
Assessment of disease activity is very important in the management and treatment of IBD. The most accurate method is found out that leukergy was the most accurate technique used in the assessment of the IBD activity. It is obviously superior to other acute phase reactants, and it is even more accurate than endoscopy score defined by Baron and histology scores defined by Truelove.

Leukergy in Inflammatory Bowel Disease; A Test in the Assessment of Disease Activity

Results: While OQL and UCAI were similar in CD and UC, the difference was still beneficial in greater CD patients. This difference cannot be attributed to the demographic or clinical characteristics which were similar in CD and UC. Greater recognition of these impairments will alter the clinical approach to these patients.

1464 Inflammatory Bowel Disease in People of Afro-Caribbean Descent
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Inflammatory bowel disease had been considered uncommon in immigrant populations in the UK, until studies in Leicester found a high incidence of ulcerative colitis in people of Indian origin. Early studies in Afro-Caribbean immigrants described Crohn's disease only. A postal questionnaire to all doctors registered with the London IBF Forum asked for details of patients of Afro-Caribbean origin having inflammatory bowel disease.

Twenty one patients were identified, 13 being female. Eleven patients were born between 1960 and 1989, and 4 were born in the United Kingdom. Thirteen patients were aged under 30 at the time of diagnosis. Twelve patients had ulcerative colitis (6 total) with only 6 having Crohn's disease. 2 cases were classified as indeterminate colitis.

This survey has established that in people of Afro-Caribbean origin: ulcerative colitis is more common than Crohn's disease. The majority of patients were born in the UK and the disease started at an early age. Immigrants from the Indian subcontinent also have ulcerative colitis more frequently than Crohn's disease. However inflammatory bowel disease is mostly seen in the immigrant generation with a mean interval of 11 years after arrival in the UK.

This survey has demonstrated differences in the occurrence of inflammatory bowel disease that may encourage research into environmental factors in their aetiology.

Quality of Life and Physical Functioning are Different in Crohn's Disease and Ulcerative Colitis
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Crohn's Disease (CD) and Ulcerative Colitis (UC) are chronic, debilitating diseases; they surround their impact on patients functioning. The aim of this study was to assess and compare the Quality of Life (QOL) and the Physical Functioning of patients with CD and UC.

Methods: Patients with CD and UC attending the Gastroenterology Out-Patient Clinic were evaluated using the Flanagan-Burckhardt 16-item QOL questionnaire (a 7-point scale, where 1 = highly dissatisfied and 7 = highly satisfied) and the Burchardt 10-item Fibromyalgia Impact Questionnaire (FQ, a 4-point scale, where 0 = best and 3 = worst functioning). Data were calculated as mean ± SD.

Results: The response rate was 98%. There were 41 CD and 72 UC patients; their ages (43.8 ± 14.5, 41.6 ± 16.0 yr.), M/F ratio (0.64, 0.89), educational status, percentage receiving formal education (46%, 47%), mean disease duration (6.8 ± 5.3, 8.8 ± 8.5 yr.), disease activity indices, and drug treatments were comparable. The QOL of CD patients (5.9 ± 1.0) was significantly worse than UC patients (6.3 ± 0.6, p < 0.01). Specifically, CD patients were less satisfied with relationships with partners with spouse (p < 0.01), active recreation (p < 0.025) and independence (p < 0.001). The QOL of 20 CD patients who had undergone surgery (6.0 ± 0.9) was different from 21 UC patients who had not had surgery (5.7 ± 1.1). Physical Functioning was worse in CD (0.6 ± 0.8) than UC patients (0.6 ± 0.5, p < 0.005). In particular, the items on physical functioning (p < 0.005), ability to do the job (p < 0.01) and fatigue (p < 0.002) were worse in CD.

Conclusion: While OQL and UCAI were similar in both CD and UC, the deficit is appreciably greater in CD patients. This deficit cannot be attributed to the demographic or clinical characteristics which were similar in CD and UC. Greater recognition of these impairments will alter the clinical approach to these patients.

Computerized Clinical Guidelines in Inflammatory Bowel Disease (IBD)

Purpose: HOLMES is an hybrid artificial intelligence system that integrates three software tools: a) an Expert System b) an Hypertext c) a Computer based training. The aims of this Windows 95 based environment are: 1) Interactive teaching and training for students or practicing physicians 2) Patient specific clinical guidelines for medical decision support in the diagnosis and treatment of suspected IBD 3) Assisted compilation of accurate Computerized Clinical Patient Record 4) Computer guided collection of relevant data in a specific data base.

Software: The medical knowledge of the system is based on the practical experience of gastroenterologyst collected by the Delphi's method in a national survey, epidemiological data and a systematic review of the medical literature (1980–1996). The knowledge base consists of production rules compiled in an expert system language developed in C and based on the Rete algorithm.

The hypertext is highly integrated with the expert system and can explain the reason for each question and the line of reasoning followed in suggesting or confirming a diagnosis or treatment hypothesis. Patient data activate specific modulatory agents of the knowledge base and the conclusion of the rules fired suggest the best clinical decision or diagnostic hypothesis. In the first stage, data from medical interview, physical examination and simple laboratory tests are used to decide if the criteria for the hypothesis of IBD are satisfied and the differential diagnosis among ulcerative colitis, Crohn's disease and indeterminate colitis is calculated by the OMGE score. Parallel processing of the same differential data is used for indirect evaluation of the relative importance of all the important validated severity scores. Treatment guidelines for Crohn's disease are based on the clinical pattern, global evaluation of the patient and severity scores. Treatment of ulcerative colitis is based on severity scores and extension of the disease. In 50 patients affected by IBD the diagnostic accuracy of the program compared with the independent diagnosis made by expert clinicians and confirmed by 2 year follow up was 94% in 3 cases the correct diagnosis was suspected and in 3 patients the CD was probable. This promising preliminary results are being verified in a prospective multicentre study with different case-mix and differential diagnosis contexts.

Which Factors Determine Bone Mineral Density in Inflammatory Bowel Disease?
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Background: Though low bone mineral density (BMD) is well recognised in inflammatory bowel disease (IBD), the relative roles of corticosteroids and systemic effect of inflammation are not well understood. Patients and methods: Three groups of IBD patients were studied. 1) Newly diagnosed patients – who had not received any treatment (15 Crohn's disease (CD), 12 ulcerative colitis (UC)) 2) Patients with intermediate duration 1-4 years of IBD (for CD: 14 CD patients (median 3.2 gm corticosteroids) and 10 UC patients (median 2.8 gm corticosteroids); 3) Patients with longstanding disease (median 8 years for CD and 7 years for UC) (9.5 gm corticosteroids) and 26 UC patients (median 8.6 gm corticosteroids). Lumbar BMD was measured by dual energy X-ray absorptiometry. Records were kept of their smoking status, alcohol intake, bone fracture history, menstrual history, and experience of use of oral contraceptive pill and hormone replacement therapy. Body mass index was measured, Crohn's disease activity index and Powell-Tuck index (for UC) calculated, and their physical activities graded.

Results: Both newly diagnosed and intermediate-duration patients with CD had a significantly lower lumbar and forearm BMD scores compared with