1362 Neuroendocrine Differentiation in Colon Carcinomas

U. Sveversen, T. Halvorsen, R. Mørvik, H. L. Waldum. Institute of Cancer Research, University of Trondheim, N-7005 Trondheim, Norway; Department of Pathology, University Hospital of Trondheim, N-7006 Trondheim, Norway

Neuroendocrine (NE) differentiation was evaluated in 91 patients with colon carcinomas by immunostaining with antibodies against human chromogranin A (CgA) and neuron specific enolase (NSE). NE differentiation was documented in 25% of the colon carcinomas. In patients who died during the study, NE expression in tumor was found in 42%, while the corresponding percentage in survivors was 15% (p = 0.006). CgA and pancreastatin-like immunoreactivity (PST-LI) were determined by radiomunnoassay methods in sera from 56 patients of these patients. Elevated serum levels of CgA and PST-LI were found in 36% and 43%, respectively, and when combined, in 61% of the patients. Of the patients with serum elevation of CgA/PST-LI, 28% had positive immunohistochemistry for either NSE or CgA, versus 5% in those with normal serum levels of CgA/PST-LI (p < 0.04). In patients with colon tumors of midgut origin, CgA concentrations were increased in 50% (8/16), versus 30% (12/40) in those with hindgut derived tumors (p = 0.1). For PST-LI we found the inverse relationship, respectively 25% (4/16) and 55% (22/40) (p = 0.07).

In patients who died during the study, 53% had raised serum values of CgA, versus 29% in those who survived (p = 0.13). The corresponding figures for PST-LI elevation were 59% and 37%, respectively (p = 0.15). In conclusion, we have demonstrated NE differentiation in 25% of the colon carcinomas. Furthermore, we have for the first time found elevated serum levels of CgA and PST-LI in patients with colon carcinomas. In accordance with previous studies, our data confirm that NE differentiation is an indicator of poor prognosis.

1363 Exploring the Immunogenic Susceptibility of Crohn’s Diseases at the HLA-DPB Locus

B. A. Volk, J. Mella, R. Rathmer, E. Roschmann. Department of Medicine, University of Freiburg, Germany

Introduction: Although the etiology of Crohn’s disease (CD) is not known there is an increasing body of evidence for a genetic predisposition. Considering the data for immunogenic events in the pathogenesis of the disease, likely candidate genes are those involved in the immunological process. It has been claimed, that genetic markers for CD might be located on chromosome 6 in the human lymphocytes antigen class II region genes. Therefore, we determined the allele frequencies of the HLA-DPB1 gene in CD and normal controls. Methods: 37 unrelated patients with the diagnosis of CD based on standard clinical, histological and immunological criteria and 47 unrelated normal control patients among a German population were included in this study. The alleles of the HLA-DPB1 gene were determined according to a modified protocol of the recommended PCR oligotyping procedure of the 11th International Histocompatibility Workshop. The polymorphic second exon of the DPB1 gene was amplified by PCR and hybridized with 25 sequence specific oligonucleotide probes to assign the HLA-DPB1 alleles on the basis of known sequence variations. Results: Out of the 36 different HLA-DPB1 alleles so far known, the HLA-DPB1*0101 allele was found to be positive in 19% (7/37) of patients with CD and 9% (4/47) in the control population, resulting in a relative risk estimate of 2.51 (95% confidence limits: 0.674–9.334). A slightly higher frequency of the allele HLA-DPB1*0301 was observed in patients with CD (11/37) compared to normal control patients (6/47) with a relative risk estimate of 2.89 (CI: 0.953–8.765). No major differences were observed comparing frequencies of other DPB1 alleles in our study group. Conclusions: These data demonstrate a minor role for the HLA-DPB1 alleles contributing to the genetic susceptibility of Crohn’s disease.

1364 Expression of Vascular Adhesion Molecules and Early Mucosal Changes in Crohn’s Disease

T. Yamaguchi, K. Morise, K. Kusugami, K. Kanzayama, H. Yamamoto, T. Konagaya, Y. Sato, A. Imada, A. Ishihara. First Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, Japan; Department of Gastroenterology, Daido Hospital, Nagoya, Japan

To identify early mucosal changes in Crohn’s disease, distribution and localization of mononuclear vascular adhesion molecules were examined by immunohistochemistry. Monolayer specimens were obtained from 20 patients with ulcerative colitis and 14 patients with colonic cancer or polyposis, respectively. The specimens were fixed in PLS solution, frozen in dry ice, and sectioned on microtome. An indirect immunoperoxidase method was used applying a series of monoclonal antibodies to human vascular endothelial cells (ELAM-1), vascular cell adhesion molecule-1 (VCAM-1), lymphocyte function associated antigen-1, sialyl Lewis X, and very late antigen-4. To determine the phenotypic characteristics of vascular endothelial cells and mononuclear cells, an immunoperoxidase double staining method was applied.

In the mucosa of normal controls, ICAM-1 was expressed on vascular endothelial cells within the lamina propria, while ELAM-1 staining was weakly positive on vascular endothelial cells and VCAM-1 on follicular dendritic cells in the lamina propria. In the macroscopically normal areas of Crohn’s disease, ICAM-1 and ELAM-1 were expressed on vascular endothelial cells. In contrast to normal control mucosa, expression of ICAM-1 and ELAM-1 was strongly found on vascular endothelial cells in areas without aggregation of inflammatory mononuclear cells in several cases of Crohn’s disease. Double staining method revealed that most of ICAM-1 positive vascular endothelial cells and ELAM-1 positive vascular endothelial cells were CD4+ positive. In ulcerated lesions of Crohn’s disease, ICAM-1 and ELAM-1 were expressed on vascular endothelial cells, and ICAM-1 positive mononuclear cells were markedly increased in the lamina propria, which was similar to the findings of ulcerative colitis.

In conclusion, these findings suggest that the expression of cellular adhesion molecules on vascular endothelial cells may play an important role in facilitating leukocyte migration into sites of early inflamed mucosa and maintaining chronic inflammation in Crohn’s disease.

1365 The cAMP and Therapy Results Correlation in Ulcerative Colitis

A. Zlatkina, E. Belousova, E. Vinnitsky, N. Vorobiova. Moscow Regional Research Clinical Institute: National Center of Surgery, Moscow, Russia; Academy of Medical Science, Moscow, Russia

The cyclic nucleotide concentration (cAMP and cGMP) were determined in rectal mucosal biopsates (RMB) in 67 patients with Ulcerative colitis (UC) to research the correlation between effectiveness of treatment and intercellular regulation state. The cAMP and cGMP concentration were measured by radioimmunoeassay. The healthy persons were used as a control. Accordingly to cAMP level two groups of patients were examined: 31 patients with cAMP rectal concentration not more than in controls (1500 pmol/g) and 36 patients with high cAMP concentration (more than 2000 pmol/g). In group with high cAMP level the treatment was unsatisfactory in 13 persons (41.9%), but in group with normal cAMP level only 3 (8.3%) cases without therapeutic effect have been noticed. Thus, the correlation between the initial cAMP concentration in RMB and effect of treatment have been observed. Perhaps, patients with high cAMP content are more resistant to the treatment than persons with its normal level. We believe that intercellular regulation may influence on the results of therapy in UC and had to be taken into consideration in the drug therapy choice.

1366 Liver Histopathology and Liver Function Tests in Ulcerative Colitis

K. Aksoz, B. Unsal, S. Kogay, Y. Songur. Gastroenterology Clinic, Atatürk State Hospital, Izmir, Turkey

Hepatobiliary disorders are well known complications in patients with Ulcerative Colitis. In this study we reevaluated the liver biopsies from 31 patients (12 female and 19 male patients) with Ulcerative Colitis who admitted to our clinic during 1991–1993. None of the patients showed clinical or biochemical signs of hepatobiliary disease. 15 patients (48.4%) had completely normal biopsy findings. 7 patients (22.6%) showed fatty infiltration of the liver, 4 patients had focal necrosis (12.9%) and in 1 patient cholangitis (3.2%) was detected. In the remaining group minimal lesions were seen. The histopathological findings were unrelated to either activity and age of colitis. As a result, in the absence of clinical and biochemical parameters, changes in liver histology...
can be seen in patients with Ulcerative Colitis regardless of the duration and activity of the disease and age.

**1367** Experimental Colitis in Rat. Increased Permeability of 51Cr-EDTA and the X-Ray Contrast Medium Iodixanol
R. Andersen, J. Hosaka, L. Aabakken, A. Stordahl, F. Laerum. Experimental Radiology, Institute for Surgical Research, The National Hospital, University of Oslo, Norway

Increased urinary excretion of enterally administered water soluble radiographic contrast media have previously been shown in states of broken intestinal mucosal integrity, however not compared with current probes. In this study we compared the permeability properties of the enterosorptive dimeric contrast agent, iodixanol, and the well established permeability probe 51Cr-EDTA, from the non-perforated colon after experimental induction of colonic inflammation and ulceration.

Triiodobenzene sulfonic acid, 15 mg and 30 mg, dissolved in 40% ethanol, was instilled by enema procedure in the colon of 36 and 34 rats respectively. Thirty-six rats (controls) received saline. Fourteen days later, the rats had 3 ml iodixanol 320 mg/ml and 0.1 ml 51Cr-EDTA, 100 μCi/ml, applied as an enema. Urine was collected for the next six hours and subjected for HPLC and gamma activity counting.

Urinary recovery of 51Cr-EDTA and iodixanol, as a measure of colonic permeability, increased gradually with severity of colonic inflammation and ulceration. The correlation between iodixanol and 51Cr-EDTA excretion was strong, r = 0.93.

The contrast medium molecule iodixanol (cross-sectional diameter = 15 Å), shows equally good or better properties than 51Cr-EDTA (10.5 Å) when used as intestinal permeability probe in inflamed rat colon. The radioaque properties of iodixanol allows intestinal exposure control. The possibility for simple, accurate and rapid quantification by x-ray fluorescence technique, further increase the prospects for this contrast medium and similar substances as future intestinal permeability probes.

**1368** Enterosorbents’ Therapy of Patients with Chronic Colitis and Diarrhoea
S. Andreychin, V. Kopcha. Ternopil Medical Institute, Ukraine

The aim of our work was to study the effectiveness of local enterosorbents’ application in patients with chronic colitis and diarrhoea. Diagnosis of colitis based on clinical data, rectomoranscopical and histological researches of colon mucous biopats. Patients were divided into two groups. One of them received traditional symptomatic treatment, another was treated by polysorb (Si-organic aerosol enterosorbent). Positive clinical effect was marked after pulverisation of colon mucous by polysorb. After the first treatment session diarrhoea and dyspepsia stopped, rectal blood characteristics (erythrocyte deformability and erythrocyt aggregability), regional blood circulation in rectum mucus (pulsing fullness and rectum blood circulation speed) and anometrical data (rectal sphincter force) improved. Far-off results (in a 1–3 months) were better in enterosorbent treated persons as to compare with traditionally treated patients.

**1369** Inflammatory Bowel Disease in Iceland in 1980–1989: An Epidemiological Study
S. Bjôtnsson, J.H. Þórhannsdóttir, E. Oddsdottir. Department of Medicine, City Hospital; Department of Pathology, Department of Medicine, University Hospital, Reykjavik, Iceland

**Aims:** This is a retrospective, nationwide epidemiological study with the main purpose of finding the incidence of IBD in Iceland for the period 1980 to 1989.

**Methods:** Cases were retrieved by a review of all small and large intestine tissue specimens with any type of inflammation submitted to the two departments of pathology in Iceland. All cases with the slightest possibility of IBD were followed by scrutinizing all hospital, out-patient and x-ray records to confirm or exclude IBD.

**Results:** A total of 374 patients with confirmed IBD (Ulcerative colitis, Crohn’s disease or Indeterminate colitis) were found. Of these 281 had UC (M:F ratio 1:4.2), 75 had CD (M:F ratio 0.92) and 18 (4.8%) had IC (M:F ratio 0.5).

For UC the incidence was 10.7 per 105 in the first 5-year period (1980–1984), 12.04 for men and 9.3 for women, and 12.63 per 105 in the second 5-year period (1985–1989), 15.6 for men and 10.08 for women. These figures for UC should be compared to an incidence of 7.4 per 105 in 1970–1979.

For CD the incidence was 2.73 per 105 in the first period, 2.2 for men and 3.27 for women, and 3.48 in the second period, 3.71 for men and 3.25 for women. The figures for CD should be compared to 0.9 per 105 in 1970–1979. The UC/CD ratio remained similar in the two 5-year periods, 3.9 and 3.63 respectively.

**Conclusion:** The study shows a significant and continuous increase in the incidence of IBD in Iceland in the period 1980–1989 as compared to 1970–1979. While the increase in the incidence of UC during these two 10 year periods is less than two-fold, the increase in CD is at least three-fold.

**1370** Association Between Crohn’s Disease (CD) and Myelodysplastic Syndrome (MDS)
K.M. Boberg, L. Birch, M. Vato, P. Sandøe, K. Eilgård, K. Odland. 4 Department of Pathology, Rikshospitalet, Oslo; 3 Medical Department, Halden Hospital, Halden; 2 Department of Pathology, Central Hospital of Østfold, Fredrikstad, Norway

**Background:** The concomitant finding of MDS and CD was recently described in a series of four patients, three of whom had chromosomal abnormalities in bone marrow cells. Whether there is a true association between these disorders, has not been established.

**Methods:** We describe the clinical course and laboratory findings in a 70 year old male who had an inflammatory bowel disease for 20 years, when he presented with signs of a haematological disorder.

**Results:** The bowel disease gave few symptoms until October 1991, when the patient experienced frequent diarrhoea. In July 1992 he presented with severe anaemia (Hb 6.3 g/dl), leucopenia (3.7 x 109/L) and thrombocytopenia (117 x 109/L). A bone marrow smear was consistent with refractory anaemia (MDS type 1) or alternatively, reactive changes. Due to bowel symptoms, treatment with corticosteroids was started. Colonoscopy in December 1992 revealed pronounced inflammatory changes of the descending and sigmoid colon, compatible with CD. The Hb was 7.0 g/dl. The leucocyte- and platelet count decreased to 1.1 x 109/L and 13 x 109/L respectively. The folate and vitamin B12 levels were normal. The marrow smear now showed 25% immature myeloid cells. The dysplastic erythropoiesis constituted 25%, with 30% ringed sideroblasts. The findings were compatible with a myelodysplasia transforming to acute leukaemia. Cytogenetic analysis of bone marrow cells showed no clonal abnormalities. The patient gradually deteriorated and died after 8 weeks. The histological findings in the colon were consistent with CD.

**Conclusion:** The possibility of a MDS should be kept in mind in patients with CD developing cytopenia. Since CD seems to show a peak incidence around the age of 60 and MDS becomes more frequent with age, the association may be coincidental.

**1371** Sucralfate Enema in the Treatment of Ulcerative Proctitis. A Randomized Placebo Controlled Double Blind Study

In an open pilot study we (Carling, Kagevi) in 1985 reported some benefit of treating ulcerative colitis with sucralfate enema, which we now wanted to investigate more thoroughly.

**Aim:** To determine the efficacy of treatment of ulcerative proctitis with sucralfate enemas at a dose of 10 g given 2 times daily for a period of maximally 6 weeks. Assessment of macroscopic healing and secondary aims macroscopic, microscopic and symptomatic improvement after 2, 4 and 6 weeks of treatment. Side effects were registered.

**Methodology:** Patients with ulcerative proctitis restricted to the area reached by sigmoideoscopy max 20 cm, were offered to enter the study which is multicenter randomised, placebo controlled double-blind study. Check-ups are scheduled after 2, 4 and 6 weeks (± 3 days). The study ends when the proctitis is healed or at 6 weeks. The enemas are 50 ml consisting of hydroxypropylcellulose and 10 mg of sucralfate or water. The pH is 4.2.

**Results:** There were 80 patients included, 74 could be investigated for efficacy analyses. In the placebo group (P-G) 17 out of 38 and in the sucralfate group (S-G) 15 out of 36 were cumulative healed after 6 weeks. Concerning macroscopic improvement there were no difference between the two groups. The microscopic (biopsy) differences showed a tendency for better scores in the S-G. Blood in stools at the study start was present in 32 patients in the P-G and 29 patients in the S-G. The corresponding numbers at treatment week 4 and 6 were 14 and 9 respectively for microscopy in the P-G and 17 with 14 respectively for the S-G. The differences in B-Hb between week 0 and 2 week 4 in the S-G compared with the P-G was statistical in favour for the S-G (p < 0.001) which also was a fact comparing the difference of B-Hb week 0 to week 6.
The Role of Transabdominal Ultrasonography in Ulcerative Colitis

I. Dağlı, A. Tezel, S. Boyacioglu, Ç. Baysal, A. Üker, G. Tumecin, Yüksek İhtisas Hospital, Turkey

In order to assess the role of transabdominal ultrasonography (USG) in ulcerative colitis (UC), 40 patients (PTs) with UC (22 active and 18 inactive) were examined by transabdominal USG and compared with colonoscopy. Twenty-eight of the PTs were female, and 19 were male. The average was 35.5 years (range: 2–180). Maximum wall thickness, haustration loss, and localization was searched. USG was found 81% sensitive and 44% specific in terms of detecting wall thickness; and 64% sensitive and 50% specific in terms of detecting haustration loss. The overall diagnostic accuracy was 65% and 55%. The localization was detected correctly in 77% for active and in 64% for inactive PTs.

In conclusion, USG was found highly sensitive but less specific in UC. We think it could not be used as an alternative diagnostic tool but could assist diagnosis.

**1372 High Prevalence of Atopy in Patients with Chronic Ulcerative Colitis (CUC) in Southern Italy**


In order to evaluate the prevalence of atopy in patients with CUC, 50 patients, clinically and morphologically confirmed, (F 18, M 32, mean age 38, range 18–60), consecutively observed, were submitted to an allergologic evaluation based on: (1) familial history; (2) personal history according to the presence of: (a) rhinitis, asthma or acute recurrent urticaria; (b) contact allergic dermatitis (CAD); (c) exposure to an allergen panel constituted by regional pollens, environmental inhalants, regional moulds and food. For each allergen, the result was scored from 0 to 4 comparing the size of papomph to that obtained by a negative (NaCl 0.9% solution) and a positive standard (hystamine cloridrate, 10 mg/ml). A skin reaction was considered positive if the score reached or higher for IgE-mediated reactions and 1 or higher for cutaneous delayed reactions.

Results: 26 patients had an allergic familial history; 31 patients had an allergic personal history: 26 of them reported a history of rhinitis, asthma or acute recurrent urticaria with a consistent DACK syndrome in 4 of them; in 5 patients the UC diagnosis was referred. A total cutaneous positivity was observed in 24 patients (49%): 20 of them presented a clinical allergic history while the remainder were in a preclinical allergic phase. In all the atopic patients a skin positivity to zero allergens was observed. In 11 of them a skin positivity to food allergens was associated. From an our previous analysis on an unscreened group of 50 patients from the general population (same geographic area, similar distribution as regard sex and age) atopy was observed in 21% of them. The difference between the percent of prevalence in the two groups is statistically significant (chi-square = 14.96, p < 0.001). Atopy, so frequent in our CUC patients, could be a further factor conditioning the clinical course of the disease.

**1373 Alcohol, Smoking, Stress and Inflammatory Bowel Diseases**


Smoking has been reported to be more frequent in Crohn’s Disease (CD) than in Ulcerative Colitis (UC) patients (pts). No definitive reports have been published about alcohol and stress. We evaluated the influence of alcohol, smoking and stress on the onset and the course of CD and UC pts of the Padua Gastroenterology Unit. The course of illness was evaluated as number of relapses, hospital admissions and surgery/year. We reviewed the medical records of 646 pts. 402 UC (244 M, 158 F) and 244 CD (133 M, 111 F) followed from 1981 to 1993. Severity at onset, scored by CDAI and Truelove and Witts indices, was: mild 52% CD and 53% UC; moderate 35% CD and 37% UC; severe 13% CD and 9% UC. Results: Alcohol: CD 17 (7.5%) and 36 UC (9%) were drinkers (>1/2 l of wine/day) at the onset; no differences were found regarding severity, extent at onset and clinical course in both diseases. Smoking: 126 CD (55%) and 158 UC (41%) were smokers (>5 cigarettes/day). Smoking habit influences the onset severity in CD: severe (65.5%) vs mild (53%) (X2 p < 0.05). Smoking did not affect the severity of the onset in UC but the percentage of heavy smokers (>10 cigarettes/day) was higher in the group with moderate (61%) and severe (75%) vs mild onset (50%). Smoking status didn’t influence the course of UC and CD. Stress: 49 CD (20.5%) and 102 UC (25%) were permanent ambitious subjects. The stress level was significantly higher in UC than in CD. Stressful events occurred in 52 CD and 72 UC patients, with no relation with illness severity extent and course. Conclusions: our data suggest that alcohol and stress, cannot be considered risk factors for IBD. Smoking does not influence IBD onset but its severity in CD. The course of both diseases doesn’t seem to be modified by the risk factors analyzed.

**1374 The Characteristics of Ulcerative Colitis Cases Seen in Yüksek İhtisas Hospital, Turkey**

K.B. Ateş, A. Üker, Ü Dağlı, A. Tezel, Ç. Baysal, I. Önaran. Yüksek İhtisas Hospital, Ankara, Turkey

A total of 196 cases of ulcerative colitis (UC) were seen and treated in our hospital between 1983 and 1993. One hundred and nine (55.6%) were male and 87 (44.4%) were female. The average age was 38.6 ± 4.4. The disease was most frequent in 25–35 years of age period in males, and 35–44 in females. There was no difference in the distribution of activations with regard to seasonal changes. Fifty nine (30.1%) of the patients (PTS) had distal colitis, 58 (29.6%) had left sided colitis and 72 (36.7%) had pancolitis. The possible cause for the activation was E. histolytica in 34, invasive E. coli in 5, C. difficile in 2, Y. enterococctica in 2, C. jejuni in 1 and S. typhii in 1. No possible cause was detected in the rest.

Sulfasalazine and corticosteroids was given as medication in 59.2% of the PTS, sulfasalazin alone was sufficient in 24.5%. 5-ASA was used in 19.9% of the PTS in the last 2 years because it has been available since 1991. Total parental nutrition was performed during activation in 7.1% of the PTS.

The complications seen were as follows: strictures in 6.1%, perianal lesions in 2.8%, dermatologic manifestations in 2.6%, hepatic steatosis in 2.6%, ophthalmologic disturbances in 1.5%, sclerosing cholangitis in 1.5%, perforation in 1.5%, toxic megacolon in 1%, dysplasia in 1% and cancer in 0.5%.

Seventeen (8.7%) of the PTS were referred for surgery for colostomy. The mortality rate was 5.5%.

**1375 Tumour Necrosis Factor Alpha in Stool as a Marker of Intestinal Inflammation**

A. Dobrucali, M. Tuncer, E. Sander, K. Bal, H. Uzunismail, M. Altmn, I. Yardakul, E. Oktay, I. Ding. Gastroenterology Division of Cerrahpaşa Medical Faculty of Istanbul University, Istanbul, Turkey

Measurement of disease activity in patients with inflammatory bowel disease (IBD) is difficult. The best available methods such as endoscopy and radiology are complex, time consuming and specific personal requiring. Tumor necrosis factor alpha (TNF-α) is a cytokine released by mononuclear cells in response to IBD which has been implicated in the pathobiology of IBD. It may be possible to use TNF-α concentration in stool as a marker of disease activity.

In the present study, we measured TNF-α concentrations in stool and blood samples from normal persons (n = 9), patients with active inflammatory disease (n = 13, 7 with ulcerative colitis and 6 with Crohn’s disease) and patients with diarrhea which caused by other reasons (n = 7) such as infection or gluten sensitivity. Stool and blood samples were obtained from patients with active IBD before and after treatment. Single stool and blood were obtained from healthy persons. Stool were collected in sterile containers and weighed. Samples were then suspended in an equal volume of sterile phosphate buffered saline and centrifuged at 15,000 rpm. Supernatants were stored at −70°C until assay. Serum samples were centrifuged at 2000 rpm and supernatants were stored −70°C until assay. TNF-α levels were measured by enzyme-linked immunosorbent assay (ELISA). Results were presented as pg/g stool and pg/ml blood.

The concentration of TNF-α found in the stools of the patients with active IBD (230 ± 294 pg/g) were significantly higher than those detected in the stools of normal persons (2.8 ± 1.2 pg/g) and patients with diarrhea (3.4 ± 1.3 pg/g) (p < 0.001). After the treatment, high concentrations of stool TNF-α levels decreased to the similar levels (2.1 ± 1.5 pg/g) measured in control patients (2.8 ± 1.9 pg/g) (p > 0.05). It was meaningful that patients with Crohn’s disease with small and large bowel involvement had higher stool TNF-α levels than patients without colonic involvement. There was no correlation between the serum concentrations of TNF-α and disease activity in both groups (2.1 ± 2 pg/ml in patients with active IBD, 2.7 ± 1.9 pg/ml in treated IBD, 2.3 ± 1.8 pg/ml in patients with diarrhea and 2.5 ± 2.3 pg/ml in controls) (p > 0.05).

Measurement of stool TNF-α concentrations may provide a simple way to monitor disease activity in IBD and selective inhibition of TNF-α may be beneficial in the treatment of IBD.
Utility of Abdominal Ultrasound for Inflammatory Activity Assessment in Crohn’s Disease

J.M. Segura, J.C. Erdozain, M. Pesa, A. Herrera, E. Molina, P. González Sanz Agero, J. Lizasoain, F. Muñoz. Digestive Endoscopy Unit, Gastroenterology Section, Hospital “La Paz,” Madrid, Spain

Introduction: The imaging techniques to evaluate the degree of inflammatory activity in Crohn’s disease are those that allow us to visualize the intestinal wall, mainly the wall thickness.

Objective: To investigate by abdominal ultrasound the morphology of the intestinal wall in patients with Crohn’s disease, before and after treatment (preliminary study).

Subjects and methods: We used an ultrasound catheter 5 MHz considering a normal diameter of the intestinal wall at the ileum being less than 4 mm. Inflammatory activity was assessed by the CDAI index. We present the echographic findings in two patients with involvement of ileum and the right colon.

Patient 1: Lady 32 yo with high inflammatory activity, CDAI: 297.6 and a echographic wall thickness of 12 mm. After 1 month of treatment the diameter descended to 7 mm. Three months later the CDAI was 104.4 and the wall thickness was 4 mm.

Patient 2: Lady 34 yo with severe inflammatory activity, CDAI 327.24 and a echographic diameter of 7 mm. Two months after treatment the wall thickness was 4 mm and the CDAI 81.24.

Comment: (1) The echographic changes at the intestinal wall are a fast and effective diagnostic method to follow the Inflammatory Activity in Crohn’s disease.

(2) The use of ultrasound may be an easy method to evaluate clinical response to treatment.

A Multicentre Trial of Methotrexate (MTX) for Chronically Active Crohn’s Disease (CD)

B. Feagan, North American Crohn’s Study Group Investigators. University Hospital, 607F, 339 Windermere Road, London, Ontario, Canada

We conducted a multicentre randomized, double-blind, placebo-controlled trial to assess the ability of MTX to induce remission and spare steroids in CD.

Methods: One hundred and forty-one patients whose CD was active for a minimum of 3 months despite prednisone treatment were randomized in a 2:1 ratio to either 25mg MTX IM once weekly or placebo. All participants received 20mg of prednisone which was tapered over 10 weeks. Other treatments for CD were not allowed. The primary measure of efficacy was the proportion of patients able to discontinue prednisone and remain in remission (CDAI ≥ 150) at week 16. Secondary outcomes were the mean prednisone dose, mean CDAI and quality of life (IBDQ) scores, and physician and patient global ratings.

Results:

Baseline Demographics

<table>
<thead>
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<th>MTX (n = 94)</th>
<th>Placebo (n = 47)</th>
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<tbody>
<tr>
<td>age ± SD (range)</td>
<td>33.7 ± 5 (19-58)</td>
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<tr>
<td>male gender (%)</td>
<td>54</td>
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<tr>
<td>colonic disease (%)</td>
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<tr>
<td>CDAI mean ± SD (range)</td>
<td>162 ± 108 (0-602)</td>
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<tr>
<td>IBDQ mean ± SD (range)</td>
<td>162 ± 33 (72-224)</td>
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<td>Patient global mean ± SD (range)</td>
<td>2 ± 1.3 (1-7)</td>
</tr>
<tr>
<td>Physician global mean ± SD (range)</td>
<td>3.0 ± 1.2 (1-6)</td>
</tr>
</tbody>
</table>

p > 0.10 all comparisons.

Complete followup is available on 115 patients (82%), 36 patients (26%) have been withdrawn for the following reasons; lack of efficacy 20, possible drug toxicity 15, non-compliance 1. Based on a placebo response rate of 23% (17/71), this study has 89% power to detect a 25 percent difference in the proportion of patients with a primary outcome event.

Conclusions: The analysis of this trial, which provides valuable new data on the efficacy of MTX for the treatment of CD will be available March 1st, 1994.

Interactivity Indicial Correlation in Crohn’s Disease

H. Holloway 1, W. Mullins 2, J.F. Fielding 1. 1 Dept. of Medicine and Gastroenterology, Royal College of Surgeons in Ireland, Dublin, Ireland; 2 Beaumont Hospital, Dublin and Dept. of Statistics, Trinity College, Dublin, Ireland

Introduction: The Crohn’s disease activity index (CDAI), the Van Hee’s activity index (Al), the Harvey and Bradshaw index (SI) and the Fielding index. The purpose of this study was to determine the relationship between the clinical assessment of disease activity with each index.

Methods and results: A total of 194 clinical assessments were performed on 56 (26 male and 30 female) patients. Following history and examination the activity of the disease was independently graded by two of the authors (H.H. and J.F.F.). Quiescent disease was designated 1, mildly active disease 2, moderately active 3 and severely active 4. Following assessment blood was taken for haematocrit, ESR and albumin and the four indices were calculated. The relationship between the clinicians grading of disease activity and the four calculated indices was displayed using a box and whisker plot.

Results: The agreement between clinicians grading of activity was excellent with both giving the same rating in 81% (157) of estimates. A good relationship was observed between the median index values and the clinical gradings for the CDAI, the Al and the SI. The Harvey index showed a closer agreement with the Al with a central 50% overlap between increasing grades of disease activity.

Conclusion: There was excellent correlation at clinical assessment. All four index medians showed good correlation with clinical assessment. The Al showed the best correlation for both clinicians. The degree of correlation may be user dependent.

The Systemic Load and Efficient Delivery of Active 5-ASA in Patients with Ulcerative Colitis on Treatment with Dipentum (Olsalazine) and Mesalazin (mesalazine)

J. Flintholmen. Laboratory of Gastroenterology, Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway

The purpose of this study was to compare the efficacy of delivery of active 5-ASA to the colon and the systemic load as basis for potential long term toxicities during treatment with Dipentum (Olsalazine) and Mesalazin (mesalazine) in patients with inactive ulcerative colitis. Nephrotoxicity has been reported with mesalazine (5-ASA) therapy and the risk of this may be greater with high systemic levels of 5-ASA. The study was an open, randomized, cross-over design; and 15 patients, 8 males and 7 females, 24 to 66 years old were included. The daily dose of Dipentum and Mesalazin was 500 mg twice and 500 mg thrice, respectively, for 7 days each. The concentration of 5-ASA and Ac-5-ASA in plasma (morning, predose) and urine (24 hours collection) was determined by HPLC from samples at day 6 and day 7 in each treatment period. The mean value of the two determinations of the plasma and the urine concentrations was calculated. The ratio Mesalazin/Dipentum differed significantly from 1 both for 5-ASA (5.1) and Ac-5-ASA (3.6) in plasma; and for 5-ASA (9.9), Ac-5-ASA (2.6), total 5-ASA (2.9) and equimolar total 5-ASA (% of given dose) (1.7) in urine. The plasma concentration of 5-ASA was 1.2 (range 1.0-2.0) for Dipentum and 7.5 (range 3.1-33.5) for Mesalazin. The equimolar urine concentration of total 5-ASA was 23% (range 13-44%) for Dipentum and 39% (range 21-68%) for Mesalazin. Some of the subjects on Mesalazin treatment showed unexpected high levels of plasma and urinary 5-ASA concentrations which may have long term safety impli-
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1383 Does Dietary Fat Deteriorate Crohn's Disease?
Y. Fukuda, T. Kosaka, I. Yamamoto, M. Okui, H. Hirakawa, T. Shimoyama. Department of Internal Medicine 4, Hyogo College of Medicine, Mukogawa, Nishinomiya, Hyogo 663 Japan

Introduction: Nutritional treatment for Crohn’s disease was focused on the therapeutic use of elemental diets, which contain low fat, in patients with active disease. However, why elemental diets exert therapeutic effect is not clear. To evaluate the dietary fat may have compared the therapeutic action of low dietary fat intake and high dietary fat intake.

Patients and methods: Ninety-two patients with inactive Crohn’s disease after the nutritional treatment were divided into two maintenance feeding groups. All patients were given in isocaloric quantities. One was an elemental diet plus low dietary fat (low fat group: n = 44; average fat intake 16.4 g/day), and the other was an elemental diet plus high dietary fat (high fat group = 48; average fat intake 45.3 g/day). Clinical remission was defined as Crohn’s Disease Activity Index lower than 150 and/or IBD score lower than 1.

Results: Thirty-eight of low fat group maintained clinical remission for long period, however, 40 of high fat group got flare-up in 24 months (logrank test; p < 0.01). In conclusion, it is supposed that dietary fat has potency to promote flare-up.

1384 Anorectal Fistulas in Ulcerative Colitis: A Prospective Difaecographic Study
F.I. Habib, A. Alvino, C.M. Camasta, A.M. Pronio 1, C. Montesan 2, G. Ribotta 1, A. Torosli. Cattedra di Gastroenterologia 1, I.V Clinica Chirurgica, Universita’ “La Sapienza”, Roma, Italy

Ano-rectal fistulas (ARF) are uncommon in ulcerative colitis (UC). The presence of ARF may, however, adversely affect the outcome of restorative proctocolectomy in these patients. Since previous personal observations have showed the ability of difaecography in detecting asymptomatic ARF, a prospective study was undertaken with the aim of determining by difaecography the frequency of ARF in UC. Method: Fifty-one UC patients (32 M, 19 F), mean age 39.2 ± 16.5 years, age range 14-71 years were enrolled, 26 of them undergoing a restorative proctocolectomy. Fifty one age and sex matched subjects (32 M, 19 F, mean age 39.1 ± 16.3 years, age range 13-71 years) with non-inflammatory disorder of the GI tract were studied as control. Diagnosis of UC was made by the usual clinical, radiologic, endoscopic and histologic criteria. Diagnosis was confirmed at laparotomy and by pathology on the resected specimen in all the 25 pts who underwent proctocolectomy. Difaecography usually included 6 frames (antero-posterior, latero-lateral and oblique in both rest and during straining, to better opacify the fistulous tract). Results: ARF were detected in 9 (17.6%) UC patients and in no subject belonging to the control subjects. There were 12 fistulas in the 9 pts, 3 were recto-vaginal, 5 intersphincteric, 3 transsphincteric and 1 extraspincteric. Of the 9 patients with ARF, two were submitted to restorative proctocolectomy. In one patient who had a rectovaginal fistula, a fistula from the pouch to the pre-sacral space was found in both groups. A lower 24 h amplitude of C and higher 24 h amplitude (p < 0.05) were found. In conclusion, administration of alpha-blockers, individualized corticoid regimen and application of SMS should be considered in UC treatment.

1385 Influence of Hormonal Changes – New Way of Treatment of Ulcerative Colitis?
M. Huerka, J. Payer, Jr., I. Őrbi, M. Mikulecky, H. Kratochvilová, P. Ondrejka. 1st. Dept. Int. Med. Comenius University, Faculty Hospital, Michalikovcova 13, 913 69 Bratislava, Slovakia

Hormonal changes are supposed to play a role in the pathogenesis of ulcerative colitis (UC). According to empirical knowledge stress could be the triggering and keeping up factor in UC (catecholamines, cortisol). Somatostatin (SMS) with its inhibitory effect on intestinal motility and secretion, cellular proliferation and splanchic blood flow may be beneficially involved in the course of UC. The urinary catecholamines (CA) levels were determined in 30 patients (P) with UC, blood cortisol (IC) in 16 P and SMS in 10 P All P were in active phase of the disease. Control group was formed for CA by 30, for CA by 15 and SMS by 12 healthy subjects (HS). In UC urinary adrenaline and VMA were enhanced (p < 0.05). Noradrenaline and dopamine levels were comparable in both groups. A lower 24 h amplitude of C and higher 24 h amplitude (p < 0.05) were observed. The patients with UC had a higher mesor (p < 0.05) and longer acrophase (p < 0.05) of SMS in P were found. In conclusion, administration of alpha-blockers, individualized corticoid regimen and application of SMS should be considered in UC treatment.

1386 Lidocaine Gel Treatment for Refractory Distal Ulcerative Colitis
B.A. Jacobsen, S.N. Rasmussen. Dept. of Medical Gastroenterology, Aalborg Hospital, Denmark

Lidocaine gel has recently been suggested as treatment to patients with ulcerative colitis (UC). Lidocaine gel has been suggested to inhibit nerve reflexes and block neuroimmune response in UC. Patients with distal UC resistant to conventional topical therapy has been reported to respond well to lidocaine gel treatment.

 Aim: To evaluate the efficacy of lidocaine in treatment of resistant distal ulcerative colitis.

Design: Open trial.

Material: 9 patients (male/female 3/6; age 44 years (27-58) (median (range)) receiving lidocaine gel 400 mg x 2 daily. All patients had distal UC at the beginning of treatment resistant to conventional topical treatment (5-ASA/steroids). All patients remained on the same peroral medication during the lidocaine gel treatment.

Efficacy parameters: The physician scored the patient as improved, unchanged or worsened concerning clinical and endoscopic appearance after ending lidocaine gel treatment and stated if remission was obtained.

Results: Patients were treated for 28 days (3-63), median (range). Clinically 2 patients improved, 5 were unchanged and 2 worsened. 1 patient was considered in clinical remission after lidocaine gel treatment. Endoscopically 2 patients improved, 5 were unchanged and 2 patients were not evaluated. 1 patient was considered in endoscopic remission.

Conclusion: In this open trial in patients with resistant distal ulcerative colitis only minimal therapeutic effect was seen after lidocaine gel treatment.

1387 Cyclosporin A Enema Treatment for Refractory Distal Ulcerative Colitis
B.A. Jacobsen, S.N. Rasmussen. Dept. of Medical Gastroenterology, Aalborg Hospital, Denmark

Treatment of distal ulcerative colitis (UC) unresponsive to conventional topical therapy is a continuous challenge. Cyclosporin A (CyA) enema treatment has been suggested to these patients, but the results reported so far are conflicting which further evaluation of this modality is necessary.

Aim: To evaluate the efficacy of CyA in treatment of resistant distal ulcerative colitis.

Design: Open trial.

Material: 10 patients (male/female 4/6; age 44 years (27-58) (median (range)) receiving CyA enema 250 mg in 100 ml once daily. All patients had distal UC at the beginning of treatment resistant to conventional topical treatment (5-ASA/steroids). All patients remained on the same peroral medication during the CyA enema treatment.

Efficacy parameters: The physician scored the patient as improved, unchanged or worsened concerning clinical and endoscopic appearance after CyA enema treatment and stated if remission was obtained.

Results: Patients were treated for 32 days (16-70), median (range). Clinically 2 patients improved, 6 were unchanged and 2 worsened. In 1 patient CyA was considered in clinical remission after CyA enema treatment. Endoscopically 2 patients improved, 6 were unchanged and 1 worsened. 1 patients were considered in endoscopic remission.

Conclusion: In this open trial in patients with resistant distal ulcerative colitis only minimal therapeutic effect were seen after CyA enema treatment.

1388 Surgical Management of Crohn’s Disease
F. Jelenc, S. Repše, R. Juvan. Department of Gastroenterologic Surgery, Clinical Centre Ljubljana, Slovenia

The aim of our study was to analyse the surgical treatment of Crohn’s disease in 84 patients, who were operated from January 1978 to December 1992. There were 38 females and 46 males. The indications for surgery were as follows: chronic obstruction, fistulizes and abscesses and acute abdominal pain, ileus and symptoms as extensive peritonitis in acute patients. The most common procedure was ileocolic resection (27 cases). Resection of the small intestine was performed in 22 patients, resection of the colon in 31, proctocolecotomy with ileostomy in 3 and strictureplasty in one patient. Emergency procedures for acute complications included small intestinal resection, ileocecal resection and subtotal colectomy.

Recurrent of Crohn’s disease was observed in 17 patients treated by small intestinal and ileocecal resection. In our series there was one death: a 78-year old woman died of cardiac failure. 1 patient was operated on 18 times.

Crohn’s disease is a relatively common disease in Slovenia. Surgical management of this disease is limited on treating of the complications.
1389 Connective Tissue Metabolites (CTM) in Patients with Crohn's Disease (CD). Increased Turnover of Collagen I

J. Kjeldsen, P. Junker, O.B. Schaffalkitzky de Muckadell. Dept. of Medical Gastroenterology and Rheumatology, Odense University Hospital, Denmark

Measurement of CTM has emerged as a useful tool in the assessment of disease activity and prognosis in some fibroproliferative disorders. The procollagen peptides [N-terminal propeptide of type III procollagen (PIIINP) and C-terminal propeptide of type I procollagen (PICP)] reflect the synthesis rate of the parent collagens. The C-terminal telopeptide of type I collagen (ICTP) is derived from cross-linked collagen I and provides an estimate of its degradation. CTM is accompanied by stricture formation due to deposition of large amounts of collagen type I, III, and IV, and we have previously shown that ICTP is increased in active CD as compared to controls (7.7 µg/L vs. 2.8 µg/L p < 0.001), s-PICP decreased [109 µg/L vs 140 (p > 0.004)], and PIIINP unchanged. Aim: to relate changes in the clinical state and effect of antiinflammatory treatment with the course of CTM. Methods: PIIINP, PICP and ICTP were measured by recently developed radioimmunoassays in 29 patients (13 newly diagnosed) with active CD who entered a treatment protocol with prednisolone. 20 achieved clinical remission, and 16 were tapered off prednisolone, 9 were withdrawn from the protocol due to failure of the treatment. Results: s-ICTP was in the majority of patients continuously elevated before, during, at end of treatment, and in the period of follow-up. s-PIIINP and s-PICP were in the majority of patients continuously elevated before, during, at end of treatment, and in the period of follow-up. Clinical remission s-PICP increased significantly. No significant changes in CTM took place in patients where the treatment with prednisolone failed. Conclusion: This study provides evidence of a persistently increased collagen I turnover in CD irrespective of clinical disease activity as reflected by the finding of elevated levels of crosslinked C-terminal telopeptide of collagen I. The well-established markers of collagen I and III formation were normal or low normal perhaps due to the fact that PICP and PIIINP are cleared by the liver endothelial cells.

1390 A Dimeric, Non-Ionic Contrast Medium (Iotrolan) as Intestinal Permeation Marker in Active Crohn's Disease

F. Lærum 1, O. Fausa 1, S. Ferstad 1, I. Nordøy 1, K.E. Solheim 2, A. Stordal 3, L. Aabakken 1, E. Aaldøen 1, S. Aasen 1, R. Lysholm 1, 2, and H. Sch磊 1, 2, 4, 5

Purpose of the study was to investigate the effect of the iso-osmolar contrast agent (CM) iotrolan (Iotrovis®, Schering AG) to a well established permeation marker (51Cr-EDTA) in patients with well characterized Crohn's disease and normal control persons. (2) To determine the effect of the CM on clinical activity of the disease. The study was performed as a prospective follow-up study, comparing clinical activity parameters over 2 weeks in 22 patients with verified Crohn's disease (activity index, simple score ≥ 60) and 10 healthy controls (activity index ≤ 5). The healthy controls were matched for age, sex, and weight. The CM was administered orally to the patients and controls (100 µCi 51Cr-EDTA) and blood samples were collected 0.5, 1, 2, 12, 24, 48, 72, and 96 hours post-administration. Results: No significant changes were observed in the blood concentrations of the CM between the two groups. Conclusion: Iotrolan is an effective and safe permeation marker in patients with Crohn's disease and can be used to evaluate the effect of treatment on the clinical activity of the disease.

1391 Impaired Gastric Secretory Capacity in Crohn's Disease: A Study of Gastric Function and Morphology

Th. Lingenfeller, Walter Renn, D. Overkamp, Willi Daiss, W. Dölle

Department of Medicine, Eberhard-Karls-University Tübingen, Germany

Patients with overt Crohn's disease (CD) of the lower gastrointestinal (GI) tract may suffer from concomitant disease in the upper GI tract. Gastric acid hypersecretion and bile acid reflux are well-established nosologic factors for the mucosa in the upper GI tract.

We tested the hypothesis that CD would modify gastric acid secretion and bile reflux, we recruited 27 patients, 14 men and 13 women, age 34.2 ± 3.7 years (mean ± SD) with histologically proven CD of the lower GI tract for 9.5 ± 1.6 years, and 10 age- and gender matched controls. Classification of mucosal lesions based on standardized upper GI endoscopy and careful histological examination of healthy and diseased areas. One week later, acid secretory studies were performed in all patients determining basal acid output (BAO) and peak acid output (PAO). 3a-bile acids thought to represent total bile acids were measured enzymatically in the gastric juice.

Patients with CD had a significantly decreased BAO (23.7 ± 0.4 vs. 63.0 ± 1.1 mM, p < 0.001) and peak acid output (42.4 ± 0.6, 26.0 ± 0.6, and 36.0 ± 0.6, 18.0 ± 0.7, 7.7 ± 0.3 mEq/p, p < 0.1), particularly those with CD in the upper GI tract (BAO 0.35 mM, PAO 12.70 ± 6.99 mM). Oral steroids did not increase acid secretion (BAO 1.37 ± 0.34 mM, PAO 23.58 ± 7.66 mM). Ileocecal resection resulted in an increased PAO (21.78 ± 3.22 vs. 32.95 ± 12.18, p < 0.05), decreased gastric level (40.0 ± 49.55 µEq/mL, p < 0.05), and reduced bile acid reflux (150.8 ± 65.13 vs. 5.33 ± 4.78 µEq/mL, p < 0.05). Total bile acid reflux is not increased in patients with CD (118.48 ± 51.76 vs. 174.29 ± 114.93 µEq/mL).

In conclusion, gastric acid hypersecretion and increased bile acid reflux do not occur in CD, and thus, are not responsible for the high frequency of mucosal lesions in the upper GI tract. Impaired gastric secretory capacity in most patients with CD points to generally compromised gastric function as an alternative mechanism.

1392 Toxic Megacolon in Patients with Inflammatory Bowel Diseases

M. Lukšá, K. Lukšá, J. Šváb. 2nd Medical Department, Charles University, Prague, Czech Republic

The clinical features and outcome of 11 patients treated for toxic megacolon between 1985 and 1991 in the 2nd Med. Dept. were determined.

Results: There were 6 women and 5 men a mean age 34.8 and 43.4 years. Only 1 patient had Crohn's colitis, in the remaining 10 patients had ulcerative colitis. Predisposing factors we have determined in 7 patients (colonscopy, barium enema and antiinflammatory medication). 3 patients without preliminary intensive medical treatment required emergency surgery on the day of admission. 8 patients had a history of medical management. This was successful in only 2 cases. Medical treatment failed in 6 patients and urgent surgical treatment was required after a mean delay of 3 days. In our series 11 patients nobody died from toxic megacolon. There is a lot of patients we referred two-stage procedures. In the first time we performed colotomy, terminal ileostomy with preservation of the rectum and in the second time definitive procedures were made. In 1 patient subsequent proctectomy was performed, in 3 patients ileorectal anastomosis and in 1 patient ileostomy. An anastomosis was constructed successfully.

Conclusions: Toxic megacolon is a serious complication, mainly, of ulcerative colitis and requires immediate care in the special unit. Surgery may be delayed for 48–72 hours to allow a trial intensive medical and resuscitative treatment to improve the patients chance of survival. According to our experience the best approach for patients with toxic megacolon is a surgical procedure in time.

1393 Development and Clinical Application of a New Activity Index for Ulcerative Colitis


As a simple and objective measurement of disease activity is generally available in ulcerative colitis (UC), we developed from clinical data of 148 patients with UC a novel activity index (AI). According to endoscopic findings and extent of inflammation patients were classified into 3 groups (remission/slightly active n = 31); moderate/active disease and severe colitis n = 50). Independently from the characterization 17 different laboratory and clinical variables were evaluated by factor analysis and 3 "supervariables" with highest statistical power could be calculated. These 3 laboratory variables, erythrocyte sedimentation rate (ESR), hematocrit (HCT), and gamma-globulins (GG) as well as body weight by Broca-index (BI) and stool frequency (sf) were subsequently weighted by discriminating functions. According to this statistical procedure 81.4% of the patients were correctly classified.

2.8 × ESR + 2.6 × HCT + 71 × sf − 0.2 × BI − 9.2 × GG

sf = 1: 0–5 stools/day, 2: 6–8 stools/day, 3: >8 stools/day. The novel AI was subsequently applied and validated in a prospective study in 85 patients with UC of different severity. The AI was correlated to morphological findings and

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Comparison of Pharmacokinetics and Colonic Transit Time in Quiescent Ulcerative Colitis on Mesalazine and Olsalazine – A Cross Over Study

V. Mani, P. Gotch. 1 Department of Gastroenterology, Leigh Infirmary, Leigh, Gr. Manchester, UK. 1 Pharmacia Ltd, Milton Keynes, UK

Background: It has been shown that Acetyl-5-aminosalicylic acid (Ac-5-ASA) in the stools after oral Mesalazine (Asacol) in quiescent ulcerative colitis (QUC) correlated with colonic transit time (CTT). We have compared the kinetics and CTT after oral Asacol (ACL) and olsalazine (OLS). Method: 10 patients (3 males: 7 females) with QUC were randomised to receive ACL (1.2 g/day) or OLS (1 g/day) orally for 2 weeks and then crossed over to the other drug. CTT was estimated at 26 ± 4 weeks. Plasma, urine and stool levels of 5-aminosalicylic acid (5-ASA) and Ac-5ASA were estimated at 0.26 ± 4 weeks. Results: Plasma levels of both 5-ASA and Ac-5-ASA were consistently lower during the OLS period compared with the ACL (83.7 ng/ml and 713.3 ng/ml vs 339.6 ng/ml and 1374.8 ng/ml). CTT was quicker with OLS than ACL the difference being 0.34 days (p = 0.06). The proportion of Ac-5-ASA to total 5-ASA (ACPR) appeared to correlate with CTT on both ACL and OLS. The difference between ACPR within OLS and ACL was significant (p < 0.05). Conclusion: Our study further confirms lower plasma 5-ASA levels on OLS. CTT correlated with faecal Ac-5-ASA proportion on ACL and OLS. CTT was quicker with OLS which may be beneficial in distal disease.

Antineutrophil Cytoplasmic Antibodies in Greek Patients with Inflammatory Bowel Disease, Coeliac Disease and Infectious Colitis

G.J. Mantzaris, M. Economou, A. Tsiorianni, Ch. Zografos, G. Triantafylly, I. Economou. 1 Dept of Immunology & Gastroenterology, Evangelismos H., Athens, Greece

It has been suggested that serum perinuclear antineutrophil cytoplasmic antibodies (pANCA) identify a genetically distinct subset of UC patients possibly related to the clinical course of UC. This hypothesis was tested in this study, because UC is supposed to be rather milder in Greek than northern Europeans patients. Using an indirect immunofluorescence assay, the prevalence of pANCA and cANCA were detected in Greek patients with UC (N = 50), Crohn’s disease (CD; N = 30), infectious colitis (IC; N = 30), coeliac disease (CD; N = 25), ex-colectics (ileoanal pouch, N = 24) and healthy controls (HC, N = 30). cANCA were not detected in any patient group. pANCA were detected in two patients with active CD (7%), one had also PSC and one patient with UC (4%) but in none with quiescent CD, UC or IC. pANCA were detected in 25/45 patients with active UC (56%) and in only 6/20 patients with quiescent UC (30% p < 0.01) and 2/20 (10%) ex-colectics. Three ex-colectics had pANCA at the time of testing, but only one was pANCA positive. Ten patients were sequentially tested with active and quiescent UC, five of pANCA positive patients, when UC was active, remained positive when disease activity had settled. Despite the higher incidence of serum pANCA in patients with active UC, no clear correlation was found between pANCA positivity and UC extent, severity, duration or the presence of extraintestinal manifestations. Thus, the prevalence and pattern of serum pANCA is not different in Greek UC compared to patients reported in other countries and may not be related to the milder course of UC in Greece.

Estimated Incidence of Inflammatory Bowel Disease in Panama (1987-1993)

C. Cantón 1, M. Pérez-Miranda, J. Maté. 1 Endoscopy Unit, Hospital M.A. Guerrero, Colón, Panamá. 1 Gastroenterology Department, Hospital de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain

Aim: To estimate incidence figures for Inflammatory Bowel Disease (IBD) in an area of Central America, namely the “Distrito de Colón” in Panama.

Materials and methods: The population data have been obtained from the Contaduría Nacional (national census for 1980). The Distrito de Colón is 4,890 square km in area and has a predominantly urban population of 169,294 inhabitants (Colón capital town: ±140,000 inhabitants; the remaining 28,000 living in rural areas). Most of these people are ethnically blacks and half-breeds from Indian and black, although there exists a minority of pure indians, asians and causasians. Diet largely consists of unelaborated vegetal products. Hospital M.A. Guerrero is the only reference centre within this zone and the only in which endoscopy, pathology and radiology are available. Population under risk of IBD was obtained from the clinical files of Endoscopy, Pathology and Radiology reviewing records from January 1987 to December 1993. Suspected cases of IBD were reevaluated. For a positive diagnosis to be established, consistent clinical course, endoscopy and histology were needed and at least two negative fecal cultures. Incidental rates were carried out by dividing the number of diagnosed cases for the first time by the number of inhabitants in the studied area.

Relative to IBD cases were pre-selected and in 14 of them a diagnosis could be firmly established, all of them being ulcerative colitis (UC) patients. This represents an annual mean incidence of 1.2/100.000. Patients characteristics: mean age at diagnosis was 38; sex ratio M/F was 2.2; and all were half-breeds from Indian and black. There were no caucasians amongst patients with a positive diagnosis of UC. Not a single case of CD was identified.

Conclusion: These preliminary results show how rare a condition is UC in Central America and that Crohn’s Disease is almost unknown there. To our knowledge, these are the first reported incidence figures for IBD in Central America, and are in keeping with those published for ethnically similar populations in other geographical areas.

Randomized Clinical Trial of 4-Aminosalicylic Acid (4-ASA) and 5-Aminosalicylic Acid (5-ASA) Enemas in Distal Ulcerative Colitis

Ph. Marteau, A. Lavergne-Slove, M. Halphen, M. Barthet, M.A. Bigard, A. Bitoun, J.F. Colombel, J.F. Contou, R. Copé, J.C. Grimaud, P. Guyot, F. Klotz, G. Naudin, H. Partier, J.F. Rey, J. Villette, Paris, Marseille, Nancy, Lille, Lyon, St Laurent de Var, France

Aim: A multicentre, randomized trial was performed to evaluate the efficacy and tolerance of 4-ASA (Quadras®) enemas 2 g/d versus 5-ASA enemas 1 g/d in the treatment of distal ulcerative colitis.

Patients and methods: Fifty patients in 13 centres with mild to moderately active ulcerative colitis, endoscopically limited below the splenic flexure, were randomized to receive nightly for 4 weeks enemas in 100 ml suspension of either 4-ASA (Quadras®, 2 g, n = 26), or 5-ASA (1 g, n = 24).

Clinical and endoscopic evaluation were performed at baseline and after 2 and 4 weeks with laboratory (safety) testing at baseline and week 4. The subjects filled a daily questionnaire on enema duration, and efficacy was measured (on a 0–3 scale, 0: perfect tolerance, 3: very poor tolerance).

Results (means ± SD): The two groups did not differ at baseline for age (±4.13 ± 13 years), extent of disease, and symptoms. Both treatment were significantly effective to achieve clinical and endoscopic remission, and efficacy did not differ between 4-ASA and 5-ASA.

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The combination of macroscopic appearances and biopsy result is completely accurate in diagnosing of Crohn's disease, but, the relationship between the endoscopic appearance of the mucosa of the ileum and disease activity is often unclear.

1399 Postoperative Course Does Not Differ in Patients with Primary and Recurrent Crohn's Disease

Surgery is often delayed in Crohn's disease (CD) for the high recurrence rate and the operative mortality and morbidity reported to be an unacceptable high after surgery for recurrent disease. Aim of the study was to compare the early p.o. course for primary and recurrent CD in a consecutive series of pts. operated in a short period in the same Clinic. Methods: between Jan. and Dec. 1993, 38 pts. were admitted to the II Surgical Clinic, University "La Sapienza" Rome for CD. 2 pts. were not operated, another 2 underwent perianal procedures under general anesthesia. Of the remaining 34 pts., 16 underwent laparotomy for primary (group A) and 18 for recurrent (group B) CD. Age, localization (duodenum, ileum, colon, ileo-colon), type of disease (perforating, non perforating) and pts. on long term steroid therapy were comparable in the 2 groups. Emergency and urgent surgery was needed twice in primary and three times in recurrent CD. All but one pt. were operated by the same team. No excisional surgery (loop ileostomy) was employed only once in a pt. with proctocolitis and severe perianal disease. Results: no mortality was observed in either groups. Minor complications (p.o. fever, wound infection) did not differ in the 2 groups. One pt. in group A needed 3 units of blood for lower g.i. bleeding on the 7th p.o. day after ileocolic resection and 3 stricturoplasies. Major morbitity requiring reoperation was seen once in group A (anast. dehiscence in a pt. operated by another on call team) and twice in group B (anast. dehiscence 1, pancreatitis 1). Both pts. who developed anastomatic dehiscence had been operated upon as an emergency. We conclude that in the presence of recurrent, complicated CD surgery is indicated just as for primary CD.

1400 The Incidence of Inflammatory Bowel Disease (IBD) in South-Eastern Norway 1990-1992
1 Pratid Sentralbykehus, Fredrikstad, Norway; 2 Rikshospitalet, Oslo, Norway; 3 Akademiska Sjukhuset, Upsala, Sweden; 4 IBSEN Study Group, Norway.

There is a great variation in the incidence rates of IBD in different parts of the world. Western and northern Norway have the highest incidence rates of IBD reported during the last decade.

In a prospective incidence studies of IBD we were able to compare the incidence rates in three separate geographical areas in south-eastern Norway with other Norwegian studies. Furthermore, the study included one year follow-up of all incident cases which enabled us to systematically verify the initial diagnosis.

The study included 183,222 and 195 patients during the three years of registration translated to an annual incidence rate of 19.1, 23.1 and 20.3 and a mean annual incidence rate of 20.8 per 10^5 inhabitants. The majority of cases were diagnosed as ulcerative colitis (UC) (112 2 per 10^5 inhabitants) followed by Crohn's disease (CD) (5.3) and indeterminate colitis (INC) (3.3). Two mixed urban/rural areas entailed higher incidence rates (26.6 and 20.3) than the urban area (17.6 per 10^5 inhabitants), and this difference was present during all three years. UC was more common in men (14.4 per 10^5 inhabitants) than in females (10.8) and the opposite relation existed for CD (4.4 and 5.7 per 10^5 inhabitants respectively). There was a peak in age-specific incidence between 25-34 years for UC and 15-24 years for CD.

At the follow up one year after diagnosis so far 251 patients with UC, 103 with CD and 52 with INC have participated. Among UC patients the diagnosis were unchanged for 93% of cases, re-evaluated to CD in 3%, 3% were deemed to have INC and in 1% the patients initial diagnosis of CD was ruled out. Among CD patients 91% were unchanged, 4% were re-evaluated to UC and 3% were ruled out. Finally, in the case of INC, 42% were assigned a diagnosis of UC, 15% CD, 35% still classified as INC and for 8% an initial diagnosis of IBD was ruled out.

Conclusion: In this study we were able to confirm the high incidence of IBD in Norway. There were differences in the annual incidence in different areas participating in the study. At follow-up one year after diagnosis the diagnosis was unchanged in the great majority of patients. However, among patients initially diagnosed as INC the majority could be either classified as either UC or CD at the follow-up one year after diagnosis.

1401 Anemia of Inflammatory Bowel Disease in Children
S. Nousia-Arvanitakis, V. Sidi, F. Athanasiodou-Piperopoulos, E. Kosmidou, C. Demirakopoulos, D. Katriou-Nicolakaki. Department of Pediatrics, University of Thessaloniki, Greece.

Anemia of Inflammatory Bowel Disease (IBD) is multifactorial. The aim of this study is to determine the frequency of refractory anemia resulting from chronic disease in children with IBD. Thirty four patients with IBD, 27 boys and 7 girls, 6 to 16 (median 12) years were investigated. The findings were compared to those of normal individuals matched for sex and age. The following parameters were examined: hemoglobin (Hb), erythrocyte indices (MCV, MCH, MCHC), serum iron (Fe), ferritin (Ft), erythropoetin (EPO), folates (Fo) and B12. Twenty two patients (62%) had iron deficiency anemia (mean values) as shown below:

<table>
<thead>
<tr>
<th></th>
<th>Hb</th>
<th>MCV</th>
<th>MCH</th>
<th>MCHC</th>
<th>Fe</th>
<th>EPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>10.6</td>
<td>72</td>
<td>25</td>
<td>30</td>
<td>38</td>
<td>10</td>
</tr>
<tr>
<td>Remission</td>
<td>13.4</td>
<td>82</td>
<td>28</td>
<td>33</td>
<td>88</td>
<td>29</td>
</tr>
<tr>
<td>Normal</td>
<td>13.5</td>
<td>84</td>
<td>28.5</td>
<td>34</td>
<td>92</td>
<td>57</td>
</tr>
</tbody>
</table>

Seven patients (24%) had megaloblastic anemia.

<table>
<thead>
<tr>
<th></th>
<th>Hb</th>
<th>MCV</th>
<th>MCH</th>
<th>MCHC</th>
<th>Fe</th>
<th>EPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>8.7</td>
<td>93</td>
<td>23</td>
<td>34</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>Remission</td>
<td>11.9</td>
<td>85</td>
<td>29</td>
<td>30</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td>Normal</td>
<td>13.5</td>
<td>84</td>
<td>28.5</td>
<td>31</td>
<td>10</td>
<td>620</td>
</tr>
</tbody>
</table>

Five patients with CD (14%) had refractory anemia which resolved only after remission.

Conclusion. In children with IBD anemia is mainly due to iron deficiency. Megaloblastic anemia and refractory chronic anemia are less common. EPO values are low both in active disease and remission. EPO appears to be a useful index in the evaluation of IBD. In patients with long standing active disease and refractory anemia, EPO treatment might be considered in order to improve anemia, nutrition and, perhaps, induce remission.

1402 Longstanding Ulcerative Colitis (UC) and Cancer: Surveillance
A. Penna, G. Buongiorno, G. Di Matteo, O. G. Manghisi. IRCCS, "De Bellis" Castellana Grotte (Ba), Italy.

The risk of colorectal carcinoma is increased among patients with Ulcerative Colitis (UC) of more than 10 years duration. The development of cancer in UC is hypothesized to evolve by many factors, such as the diffusion and the subsequent development of pseudopolyposis and epithelial dysplasia. Aim of this study was to evaluate the significance of clinical, biochemical, endoscopic and histologic surveillance for early diagnosis of severe dysplasia → colorectal cancer evolution in UC of more than 10 years duration.

Material and Methods: 50 patients with UC of more than 10 years duration (28 M, 22 F; mean age 52.3. range 45-68) were studied in 3 years. All the 50 patients were randomized with clinical and biochemical controls every 3 months and with endoscopic and histologic surveillance every year. 18 (10 M, 8 F) patients with extensive pseudopolyposis and moderate dysplasia were evaluated with endoscopic and histologic controls every six months.

Results: In the 18 patients with UC and extensive pseudopolyposis and moderate dysplasia, 3 patients with recurrence of the acute inflammation of colonic mucosa are developed a cancer after 12 years of disease at an early curable stage. 5 patients are involved in severe epithelial dysplasia with an increase of the number and the size of the pseudopolyps. These are colectomized. 1 is died for extraintestinal complication of UC. The last 10 patients are in clinical, endoscopic and histologic surveillance every six months.

Discussion: The object of surveillance in patients with longstanding UC is an early diagnosis of evolution to severe dysplasia at cancer at a curable stage.

1403 Subgroups Classification in Crohn's Disease: Treatment and Outcome in Long-Term Follow-up
A. Musso, M.T. Fiorentini1, R. Sostegni, A. Sambataro, F. Balzola, M. Astegiano, Angelo Pera. 1 Division of Gastroenterology Mauriziano Hospital; Sperimential Department of Gastroenterology, Molinette Hospital, Turin, Italy.

A classification of patients subgroups in Crohn's disease (CD), based upon different clinical behaviour and outcome, has been recently proposed. We have
retrospectively evaluated the clinical history of our CD patients followed-up for more than 10 years. The clinical data of 141 patients with a mean follow-up of 14 (range 10–34) were reviewed. In 59 cases (42%) the disease was confined to the small bowel, in 22 (15%) to the large bowel, 54 (38%) had ileo-colonic involvement. Surgery was most frequent in ileal localization (90% of patients operated) compared with colonic (10% operated). A “fibrostenotic” behaviour was present in 57 patients (40%); 30 (21%) had a “penetrating” disease. 44 (31%) had “inflammatory” disease, one case was unclassifiable. The 3 subgroups significantly differed for length of steroid therapy and number of surgical resections. 89% of patients with “fibrostenotic” disease needed surgery with 1.7 resection per patient and steroid therapy for an average of 10.5 months per patient; 100% of “penetrating” forms underwent surgery (2.2 patient) and needed longer steroid therapy (17 months/patient). Subjects affected by “inflammatory” disease had the most prolonged steroid therapy (36 months/patient), but only 9% of these underwent surgery. If CD, as many authors believe, is not a single pathogenetic and clinical entity, our data allow us to retrospectively differentiate, in more than 90% of cases, clinical subgroups characterized by different clinical behaviour and outcome. A prospective classification might be of prognostic value and allow different therapeutic protocols in CD.

1404 Gallbladder Disease (GD) in Inflammatory Bowel Disease (IBD): A Prospective Multicentre Investigation


Prevalence of GD (Gallstone) or history of previous cholecystectomy, Cx, has been evaluated in 484 IBD patients (317 ulcerative Colitis, UC: 189 male and 128 female, mean age at 41 ± 2.5 ± 5.2 S.D.; 167 Crohn’s Disease, CD: 86 male and 72 female, mean age 37.7 ± 14.6 ± 4.7 S.D.). 374 patients diagnosed for irritable bowel disease (IBS) matched as to sex and age and served as controls. Patients with IBD had a prevalence of GD higher than controls (9.71% vs 5.08%, p = 0.01). No difference was shown between UC and CD (9.15% vs 10.78%). Frequency of either GS or Cx was as follows:

<table>
<thead>
<tr>
<th>s age</th>
<th>IBS n°</th>
<th>UC n°</th>
<th>CD n°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>tot Gd</td>
<td>Cx</td>
<td>tot Gd</td>
</tr>
<tr>
<td>M &lt;41</td>
<td>108</td>
<td>1</td>
<td>101</td>
</tr>
<tr>
<td>&gt;40</td>
<td>84</td>
<td>5</td>
<td>86</td>
</tr>
<tr>
<td>F &lt;41</td>
<td>30</td>
<td>1</td>
<td>31</td>
</tr>
<tr>
<td>&gt;40</td>
<td>84</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>

UC/CD vs IBS (p =): 0.04 vs 0.003

Women with IBD have a higher prevalence of GD and they develops GS at a younger age with respect to women with IBS. IBD patients with GD have a higher frequency of Cx in CD rather than in UC (p = 0.04). Cx might be performed more frequently in CD patients because it is difficult to discriminate between abdominal pain due to GS or disease activity.

In conclusion, bile acid metabolism should be evaluated more carefully in IBD patients.

1405 Calprotectin in Feces (FeCal test): A Granulocyte Protein Reflecting Disease Activity in Ulcerative Colitis

A.G. Reseth, E. Aalldian, J. Jahnsen, N. Raknerud. Dept. of Medicine, Akers University Hospital, Oslo, Norway; 1 Dept. of Pathology, Akers University Hospital, Oslo, Norway

In ulcerative colitis (UC) the disease activity (DA) is determined on the basis of clinical symptoms and/or the colonicoscopic findings. Correct estimation of DA is important as a guideline for medical therapy. We have therefore studied the faecal excretion of the granulocyte protein calprotectin (FeCal test) in 50 patients with UC. All participants were unslected out-patients and brought faecal samples when arriving for colonoscopy. Disease activity was assessed on colonscopic and histologic findings and scored from 0-3.43 of the 50 patient (86%) had a total colonscopy; In addition traditional biochemical marker of DA were assessed. Of the 50 patients, there were 25 females and 25 male, mean age 41 years, range 24-86. FeCal test values from 50 healthy subject served as controls (median = 3 mg/l, upper ref. limit: 10). In control subjects the excretion of calprotectin were significantly lower than in UC-patients in remission (p < 0.0001).

FeCal test values (mg/l) in patients with UC:

<table>
<thead>
<tr>
<th>Remission</th>
<th>Active disease</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Median</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Range</td>
<td>1.2-70</td>
<td>3.2-140</td>
</tr>
</tbody>
</table>

The correlation between the endoscopic and histologic scores were significant (r = 0.67, p = 0.001).

In conclusion; the present results show that the FeCal test separates well between patients with inactive and active ulcerative colitis and can therefore be used as a objective marker of disease activity in patients with this disease. In addition, the test might be useful to identify patients with ulcerative colitis.

1406 Calprotectin in Feces (FeCal Test); A Granulocyte Protein Reflecting Disease Activity in Crohn’s Disease?

A.G. Reseth, E. Aalldian, H. Schjonsby, M.K. Fagerhol 1. Dept. of Medicine, Akers University Hospital, Blood Bank, Oslo, Norway; 1 Department of Immunology, Ullevål University Hospital, Oslo, Norway

The difficulty of estimating disease activity (DA) in patients with Crohn’s disease (CD) is generally acknowledged. Calprotectin, is a prominent neutrophil leukocyte protein which is both stable and can be accurately assessed in small samples (5 g) of stools. Previously we have found that the faecal calprotectin concentration was higher in patients with CD than in healthy controls (p < 0.0001). In the present study we wanted to assess whether the FeCal test is a measure of disease activity in such patients. We have studied 53 unslected patients with CD, 31 females and 22 males, mean age 41 (22-78) years; 12 patients had ileitis, 29 ileocolitis and 14 colitis. 27 had intestinal resections and 32 were on medical therapy for CD. Faecal calprotectin was measured using an ELISA technique, DA was assessed by the Harvey & Bradshaw’s simple index, by measuring acute phase reactants and α1(1)-antitrypsin (A1-AT) in plasma and stools.

Correlation between FeCal test and the other parameters of DA.

<table>
<thead>
<tr>
<th>Median</th>
<th>Range</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FeCal test</td>
<td>37.5</td>
<td>2.5-350</td>
<td>-</td>
</tr>
<tr>
<td>A1-ATfaeces</td>
<td>0.24</td>
<td>0.0-1.95</td>
<td>0.51</td>
</tr>
<tr>
<td>A1-ATplasma</td>
<td>1.8</td>
<td>1.0-2.6</td>
<td>0.90</td>
</tr>
<tr>
<td>Oromucoid</td>
<td>1.0</td>
<td>0.37-8.6</td>
<td>0.47</td>
</tr>
<tr>
<td>Hepotoglobin</td>
<td>2.5</td>
<td>0.11-7.8</td>
<td>0.51</td>
</tr>
<tr>
<td>CRI</td>
<td>2.0</td>
<td>0.0-114</td>
<td>0.21</td>
</tr>
<tr>
<td>ESP</td>
<td>13.0</td>
<td>1.0-107</td>
<td>0.26</td>
</tr>
<tr>
<td>Simple index</td>
<td>3.0</td>
<td>0.9-16</td>
<td>0.16</td>
</tr>
</tbody>
</table>

The FeCal test was increased in 48/53 patients whereas A1-AT in stools in only 4. There was a significant correlation between the FeCal test and the concentration of A1-AT in stools. A1-AT has been shown to correlate well with DA in CD assessed by radiolabelled leucocytes. Calprotectin, found only in leucocytes, should reflect the degree of migration of such cells over the gut wall and hence, might be a better marker of inflammation than faecal-A1-AT. We therefore suggest that the FeCal test could be a useful test, both in estimating disease activity and to identify new patients IBID.

1407 Reticulocytes in Inflammatory Bowel Disease

T. Salomone, A. Guariano 1, P. Tomassetti 2, C. Serra, R. Lamedica 1, A. Morselli Labate 2, M. Rombo 1, G. Sprovieri 1, M. Miglioli. Medicina dell’Invenza, Bologna, Italy; 1 Laboratorio Centrallizzato, Bologna, Italy; 2 Clinica Medica Policlinico 1, Crema, Bologna, Italy

Reticulocyte (RC) count gives direct information on erythropoesis and indirectly reveals an inflammatory state in patients (pts). Cytometric results (O-Auramine) can determine the RC absolute number and the percentages of RC fractions, and also their degree of maturity according to the intensity of fluorescence, related to the RNA content. We have evaluated RC in pts with inflammatory bowel disease (IBD) and related RC count to HB, WBC, PLT, biochemical indices of activity (BAI), blood loss, extension and activity degree of the disease, assessed by endoscopy and pathology. We studied 11 pts, 9 had active ulcerative colitis (UC), 2 had active Crohn’s disease (CD). The 2 CD pts and 4 pts with diffuse UC did not show clear blood loss, they had normal HB, high total RC, PLT and BAI positively related to RC count. In the CD pts RC fractions were not modified while young RC were increased in the UC pts. The 2 pts with ulcerative proctosigmoiditis had blood-stained stools but normal RC number and fractions; HB, PLT, BAI were also normal. The 3 pts with diffuse UC and bloody diarrhea had moderate-severe anaemia, and a large increase in total and young RC; increase enhanced by iron therapy, positively related to PLT and BAI.
Our data suggest that quantitative and qualitative RC analysis is useful in the IBD assessment. It not only reveals the presence and the amount of blood loss and the response to iron therapy, but may also be an indirect index of the disease activity and extension. A larger number of pts is required to support our suggestion and to confirm that RC modifications may be different in UC and in CD; presumably because in CD clear blood loss is not as closely related to the disease activity as in UC.

**1408 Platelet Density, Size and Release Reaction in Patients with Inflammatory Bowel Disease**
Hanna Sandberg-Gertzen 1, Petter Järems 2, Gunnar Jämerot 1, 1 Division of Gastroenterology, Department of Medicine, Örebro Medical Center Hospital, Örebro, Sweden; 2 Department of Clinical Chemistry, Örebro Medical Center Hospital, Örebro, Sweden

Several studies have reported an increased risk of tromboembolic manifestations in patients with inflammatory bowel diseases (IBD), and small vessel thrombosis has been postulated as an etiological factor in Crohn's disease. Increased platelet sensitivity to low concentrations of aggregating agents and spontaneous aggregation of platelets have been demonstrated in patients with IBD as well as elevated plasma levels of Beta-thromboglobulin (β-TG). The aim of the present study was to investigate platelet characteristics in patients with IBD. Peak platelet density served as an indicator of platelet granularity content and consequently platelet reactivity and plasma levels of β-TG were used to estimate platelet in vivo activation.

**Material and methods:** Twenty two patients with IBD were investigated, 15 of whom had active disease as judged by clinical symptoms and findings. Eleven healthy blood donors served as controls. Patients on drug treatment for their IBD were not excluded from the study.

Platelet counts and mean platelet volume (MPV) were determined using a Coulter Counter S Plus 6 (Coulter, UK). Peak platelet density was determined after centrifugation on a Percoll density medium (Pharmacia, Sweden). Platelet distribution in the gradient was monitored by measuring light transmission through the test tube. Density marker beads (Pharmacia) were used as an internal standard making it possible to determine peak platelet density. Plasma levels of β-TG were determined using a commercial radioimmunoassay (Kodak, UK). Standard procedures were used for determining plasma hapto globulin and orosomucoid levels. The one way analysis of variance was used for statistical evaluation.

**Results and discussion:** The patients with active IBD had an augmented peak platelet density (p < 0.05), a lower MPV (p < 0.001) and elevated plasma levels of β-TG (p < 0.01). No significant differences were found between the three groups regarding platelet counts and haptoglobin or orosomucoid levels. The results suggest that enhanced platelet in vivo activation is associated with active IBD. Furthermore, the present study indicates increased platelet reactivity in patients with active IBD as estimated from platelet density monitoring.

**1409 5-Aminosalicylate Related Renal Dysfunction in IBD**
S. Schreiber, A. Raeder, S. Howaldt, W. Zehnter 1, W.H. Daer, W. Kruis 1, Med Departments, Universities Hamburg, Germany; 1 Cologne, Germany

**Background:** Oral treatment of IBD patients with slow release 5-Aminosalicylic acid (5-ASA) leads to partial systemic resorption. The purpose of this study is to evaluate the risk of kidney damage by assessing parameters indicating early renal dysfunction (tubular protein excretion pattern, urine concentrations of tubular enzymes [alkaline phosphatase (AP) and γ-glutamyl transferase (GGT)]).

**Methods:** 208 outpatients with chronic IBD were evaluated. In addition to routine kidney function tests (creatinine and phosphate clearances), the excretion of protein (quantitatively and qualitatively by SDS-PAGE), albumin, α1-microglobulin, IgG and tubular enzymes were assessed. The lifetime 5-ASA exposure history was obtained by a questionnaire.

**Results:** 19% of IBD patients were on no 5-ASA therapy, 32% received 1.5 g 5-ASA or less and 49% received more than 1.5 g 5-ASA (41% 3 g or more/d). The patients in the high dose group (≥3 g/d) had a significantly higher incidence of a tubular protein excretion patterns in the SDS-PAGE as well as a higher occurrence rate of enhanced levels of AP. The incidence of tubular protein excretion and elevated AP, resp., correlated with the lifetime intake of 5-ASA. No correlation between disease activity, patient age, disease duration or disease history and the incidence of tubular protein excretion or elevated urine AP levels, resp., could be found. Creatinine and Phosphate clearance were not decreased in the high 5-ASA group. No differences between normal controls, and IBD patients with or without 5-ASA were seen in α1-microglobulin excretion, IgG excretion or urine electrolytes.

**Discussion:** Although no impairment of renal clearance functions was induced by 5-ASA we found an increased incidence of a pathological tubular protein excretion pattern with both increasing lifetime and actual dosages of 5-ASA. Together with a simultaneous increase in alkaline phosphatase excretion our findings may be indicative for early tubular damage by the drug. We conclude that careful monitoring of renal function is warranted when further increasing the recommended daily dosage of 5-ASA to treat IBD.

**1410 Recombinant Erythropoietin for the Treatment of Anaemia in Active Inflammatory Bowel Disease. Final Results from a Double-Blind Cross-Over Prospective Trial**
S. Howaldt, A. Raeder, S. Schreiber. Medical Department, University of Hamburg, Germany

**Background:** The anaemia in patients with active inflammatory bowel disease (IBD) is often caused by chronic inflammation and refractory to treatment.

**Methods:** 34 patients with active IBD and Hb levels <100 g/l were enrolled in a prospective trial of 24 weeks duration. Vitamin/iron deficiency as reason for anaemia were excluded. Patients receive iron substitution and either r-Epo (150 Ud/kg body weight, 2 × weekly s.c.) or placebo with a cross-over after 12 weeks. Patients are seen every three weeks for physical exam, and complete laboratory. Primary efficacy parameter is a rise in the Hb level, study end points are completion of the protocol or Hb levels falling >20 g/l (primary treatment failure). In addition, peripheral blood monocytes were cultured for 24 h (± PWM) and the release of pro-inflammatory cytokines (TNFα, IL1β) was assessed by ELISA.

**Results:** Serum erythropoietin levels at the beginning of the study were increased in the anemic IBD population with no differences between Crohn's disease and ulcerative colitis, respectively, but (compared to non-IBD anaemic patients) not adequately high for the degree of anaemia. The degree of anaemia correlated to the immunologic activity of the disease (IL1β, TNFα secretion levels). After 12 weeks the mean Hb-concentration increased by 22.3 ± 2.3 g/l under r-Epo, compared to a mean difference in Hb-concentrations under placebo treatment (beginning vs. after 12 weeks) of −3.7 ± 1.4 g/l (p < 0.01, n = 34). The mean Hb level before rEPO therapy was 82.3 ± 3.2 g/l and increased to 102 ± 5.1 g/l (p < 0.01). Only three primary treatment failure (Hb <80 g/l) were seen in 34 IBD patients receiving rEPO, whereas eight placebo patients needed transfusions because of Hb levels <80 g/l. The response time to rEPO treatment correlated with the immunologic activity of the intestinal inflammation.

**Discussion:** Endogenous erythropoietin production in IBD patients is not adequately high in comparison with the degree of anaemia. Supplemental medication with r-Epo increases Hb-concentrations in anaemic IBD patients. The use of r-Epo helps to reduce the number of necessary blood transfusions.

**Conclusion:** The immunologic activity of IBD patients assessed by the capacity of peripheral monocytes to secrete TNFα and IL1β correlates to the degree of anaemia and is predictive for the response to rEPO treatment.

**1411 Functional Results After Hand Sewn or Stapled Ileo Pouch-Anal Anastomosis**
J.E. Thoresen, E.H. Myrvold. Department of Surgery, Trondheim University Hospital, Trondheim, Norway.

The aim of the present investigation was to evaluate the functional results after ileo pouch-anal anastomosis and to compare hand sewn with stapled anastomosis.


Material and methods: During the period 1984–1993, 112 restorative proctocolectomies were performed. Ninety patients were followed up in the outpatient clinic with a median observation time of 36 months (range 3–108 months). Fifty-one patients were hand sewn, median observation time 49 months (range 8–108) and in 39 patients a stapled anastomosis were performed, median observation time 19 months (range 3–43). Fifty-six patients were operated with a J-pouch, 29 patients with a K-pouch and 5 patients with a 5-pouch.

Results: Median bowel movements was 5 (range 2–10). For the hand sewn group the median bowel movement was 5 (range 2–10) and for the stapled group median 4 (range 3–9). During night time median bowel movements was 0 (range 0–2) and there was no difference between hand sewn and stapled anastomosis. Involuntary bowel movements occurred in 12 patients. Of these, 10 had a hand sewn and 2 a stapled anastomosis. Seepage day time occurred in 15 patients, 12 hand sewn and 3 stapled anastomosis, and seepage night time occurred in 19 patients, 13 hand sewn and 6 stapled anastomosis. There was no difference in functional results between the different types of reservoir.

Conclusion: In the present material the number of regular bowel movements day and night was not influenced by the type ofileo pouch anal anastomosis performed, i.e. hand sewn or stapled. However, involuntary bowel movements during night time occurred more frequently in the handset sewn group as did seepage, both day and night indicating a slightly poorer functional result in the hand sewn group.

1412 Quality of Life and Inflammatory Bowel Diseases

G.A. Lanfranchi, A. Tragnone, D. Valpiani1, F. Miglio2. Div. Internal Medicine Bellaria Hospital, Univ. of Bologna, Bologna, Italy; 1 Div. Internal Medicine; 2 Div. Internal Medicine Malpighi Hospital, Bologna, Italy

Purpose and Methods: We recently investigated the Quality of Life (QL) in pts. with Inflammatory Bowel Disease (IBD) demonstrating a reduction of QL during phases of relapse by employing the index of Grogono-Woodgate. Then we used the Duke-Und Health Profile, that, modified for our purposes, gives more detailed information about the global QL, the physical and emotional status, social relations and working capacity. The study was carried out in 45 pts. with Ulcerative Colitis (UC) (40±14.2 years; 67% M, 33% F) and 48 with Crohn’s Disease (CD) (34.8±11.5 years; 65% M, 35% F). Results. A significant correlation between the QL and the severity of the disease was found in both UC (p < 0.05) and UC (p < 0.01). QL decreases during relapses and returns to the mean value of the year when in remission (UC: Relapse 68.4±32.4 vs Remission 97.1±11.7; CD: Relapse 67.2±32.7 vs Remission 92.6±21.7)<0.001. The evaluation of the different categories included in the Duke-Und Profile is shown in the Table.

<table>
<thead>
<tr>
<th>U.C.</th>
<th>C.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical score</strong></td>
<td><strong>Social relations</strong></td>
</tr>
<tr>
<td>Relapse</td>
<td>123.6±7.1</td>
</tr>
<tr>
<td>Remission</td>
<td>22.7±2.1</td>
</tr>
<tr>
<td><strong>Working capacity</strong></td>
<td><strong>Emotional status</strong></td>
</tr>
<tr>
<td>Relapse</td>
<td>46.6±2.8</td>
</tr>
<tr>
<td>Remission</td>
<td>60.0±1.2</td>
</tr>
</tbody>
</table>

**P < 0.001.**

As far as the emotional status is concerned, all pts showed a heavy impairment during relapses with a persistence also in remission only in CD and mostly in the operated than in non operated pts (p < 0.05).

<table>
<thead>
<tr>
<th>CD</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Operated</td>
<td>Non operated</td>
</tr>
<tr>
<td>35.1±11.4</td>
<td>37.5±5.9</td>
</tr>
<tr>
<td>35.1±10.8</td>
<td>(n.s.)</td>
</tr>
<tr>
<td>29.3±16.1</td>
<td>(n.s.)</td>
</tr>
</tbody>
</table>

In conclusion, either UC and CD an important alteration of psychological and social dimension exists and the physician should always take it into consideration.

1413 Chorea Movements and Ulcerative Colitis

G.N. Dalekos, D.I. Anastasopoulos1, M.H. Merkouropoulos, E.V. Tsianos. Department of Internal Medicine (Hepato-Gastroenterology Division), School of Medicine, University of Ioannina, Greece; 1 Department of Neurology; School of Medicine, University of Ioannina, Greece

Central nervous system (CNS) involvement is well known to complicate many systemic diseases in particular with an autoimmune background. CNS involvement as cerebral vasculitis has been already reported in patients with ulcerative colitis (UC). We report a patient with well defined UC and a movement disorder resembling Huntington's disease. The diagnosis of Huntington's disease is not probable as there was no positive family and/or past history of the patient, as well as no mental changes. In addition, saccadic eye movements were not slow or delayed. T-weighted axial MRI showed high-intensity multiple, small subcortical lesions bilaterally in the parietal lobes and no atrophy of the caudate nuclei.

The association of the two conditions prompted us to report this case considering that this involuntary movement disorder may represent another rare systemic manifestation of UC possibly due to CNS involvement.

1414 Diagnostic Sensitivity of Immune Scintigraphy Compared to Leucocyte Scintigraphy in Inflammatory Bowel Disease

L. Udby, J. Marving, P.F. Hellund-Carlson, A. Veje, M. Villen. Dept. of Medicine, Holbæk Hospital, Holbæk, Denmark; Dept. of Clinical Physiology/Nuclear Medicine, Holbæk Hospital, Holbæk, Denmark

Immune scintigraphy (IMSC) using a Tc-99m labelled granulocyte-monoclonal monoclonal antibody (BW 250/183) was compared to conventional leucocyte scintigraphy (LSC) using Tc-99m-HMPAO labelled autologous leucocytes. The study included 11 patients with clinically active inflammatory bowel disease. Scintigrams taken 3 h, 5 h and 24 h after antibody injection or 2 h and 3 h after leucocyte reinjection were evaluated blindly. The results of LSC were confirmed by colonoscopy and biopsy.

Five patients with ulcerative colitis all had positive LSC (and endoscopy) for at least one segment of colon. Only 3 of these patients had positive IMSC. In the remaining 2 patients IMSC showed no sign of inflammation and was thus considered false negative.

Three of 6 patients with Crohn's disease (CD) had positive LSC (and endoscopy). Only 1 of these 3 patients had positive IMSC, leaving 2 false negatives. In the other 3 CD patients both IMSC and LSC were negative although 1 showed sign of inflammation by endoscopy.

This small sample study indicates that the simple and time-saving IMSC method cannot be recommended for routine use in ulcerative colitis or Crohn's disease due to too many false negative results.

1415 Autonomic Neuropathy as an Extraintestinal Manifestation in Inflammatory Bowel Disease

N. Erol, C. Ulasoglu, Z. Mungan, S. Kaymakoglu, O. Yejmiscli, R. Szej. Section of Gastroenterology, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey

A number of extraintestinal manifestations (EM) are being described in ulcerative colitis (UC) and Crohn's disease (CD). Even to some symptoms attributable to autonomic neuropathy (AN) it hasn't been listed as an EM of inflammatory bowel disease (IBD). In this study, autonomic functions of 44 patients with UC, 32 patients with CD and 24 healthy subjects are analyzed and scored by five cardiac autonomic reflex tests (resting pulse, valsalva manoeuvre, heart rate response to breathing, postural changes of heart rate "30:15 ratio" and blood pressure). Positivity of at least three tests is accepted as autonomic abnormality. Disease activities are scored according to Harvey (Lancet, 1980) and Seo (Ann J Gastroenterol, 1992). AN was present in 23/32 (71.8%) of CD, 10/44 (22.7%) of UC and none in control group. AN was present in 98% of UC, 67% in UC and 50% in colonic CD. In UC cases, AN was present in 11% of rectosigmoiditis, 25% of left sided colitis, 37% of pancolitis and none in proctitis cases. Symptomatic or vagal predominance was not significantly different in UC or CD. Nocturnal diarrhea was present in 46%, orthostatic hypotension in 38%, tachycardia attacks in 32%, sweating disorders in 25%, mouth dryness in 22%, syncope in 14% and impotence in 1% of cases, as AN related symptoms. None of the patients had diabetes, peripheral neuropathy, hyperthyroidism or severe anemia.

With these results, it can be concluded that AN is a frequent accompanying extraintestinal manifestation in nonspecific IBD, irrelevant with sex, age, drugs being used, activity, onset age and duration of diseases.

1416 Clinical Aspects of Inflammatory Bowel Disease

P Varmann, A. Koldits. Estonian Institute of Experimental and Clinical Medicine, Central Hospital of Tallinn; Tallinn, Estonia

We studied the occurrence of inflammatory bowel disease (IBD) according to the hospitalization data. The Department of Gastroenterology of the Central Hospital of Tallinn serves as a gastroenterological centre for North-Estonia. From 1991 to 1993 IBD was diagnosed in 83 patients. Ulcerative colitis was diagnosed in 77 patients, 62.3% of them male (48 persons) and 37.7% female (29 persons); male to female ratio 1.85. Crohn's disease was diagnosed in 6 patients. The diagnosis of IBD was based on clinical history, rectoscopy, radiology of the large bowel and colonoscopy with histopathological reports. From 310 colonoscopies performed in 1992 ulcerative colitis was diagnosed in 11.9% (37 cases) and Crohn's disease in 0.65% (2 cases). Of all the hospitalized cases 49% appeared to be severe, 25% medium and 26% mild. Various complications occurred in 27% of the severe cases, 2 patients were operated.
on. The mean age of the patients was 44 (range from 16 to 77) years with two distinct peaks from 20 to 30 and 50 to 60 years. In 1990 the mean duration of hospital treatment was 29.4 days for IBD and 19.5 days for the whole department. These figures have decreased to 19.2 and 12.4 days respectively in 1993. The reason of this tendency lies first of all in the socioeconomic changes as well as in the possibility of continuous ambulatory maintenance therapy for the IBD patients during the last few years. Although today IBD is significantly less frequent in Estonia than in other northern countries, it needs serious attention. The gradual adoption of the western lifestyle and nutritional habits among the Estonians will probably affect the occurrence of IBD in the future.

Colon Function in the Diabetes Mellitus Patients and Efficacy of Lactulose Administration

V. Vдовиченко, V. Danilitchenko, S. Eliseeva, S. Kravets. Medical Institute, Lviv, Ukraine

24 patients (13 males 11 females, mean age 43, 2 years) with diabetes mellitus were observed (10 of the 1st type and 14 of the 2nd type). The range of disease duration was from 2 to 23 years. At the same time general clinical and traditional laboratory tests also bacteriologic researches were executed. As it was found, all patients had dyspeptic complaints and 14 (58.3%) colon dyskinesia: 6 constipation, 3 diarrhea, 5 alteration of constipation and diarrhea. Dysbiotic disorders were moderate: 13 (54.1%) patients had reduced quantity of Escherichia, 5 (20.8%) – Bifidum; in 2 (8.3%) patients lactobacillus were absent. The conditionally-pathogenic flora was offered by Enterobacter in 10 (41.6%), Escherichia hemolytic in 5 (20.8%), Staphylococcus in 2 (8.3%) and association of 2–4 bacteria in 4 (16.8%) patients. All patients received sugar-reduced drugs and Lactulose (Inalco/Molteni) 45 ml a day. In 8–10 days general state of 22 (91.7%) patients was better, dyspeptic disorders reduced in 13 (54.1%) and disappeared in 9 (37.5%) patients. 22 patients had a formed stool and in 18 (75%) patients meteorism and abdominal pains were absent. Only in 2 (8.3%) patients administration of Lactulose intensified diarrhea and the drug was abolished. Lactulose didn’t influence at the traditional bacterial flora and reduced number of patients with the association of conditionally-pathogenic bacteria. We didn’t remark any influence of Lactulose at the 24-hours glycemia level. We recommend Lactulose administration in complex treating of the diabetes mellitus patients.

Test Item Bias in Crohn’s Disease (CD) Activity Indices

P. Vedtofte, J. Brynskov, S. Kreiner. Copenhagen County Hospital Glosstrup, Denmark

Clinical activity indices are essential instruments in the evaluation of CD activity and form the basis for scientific evaluation of different treatments. Indices must meet several requirements if they are to be regarded as objective and valid measures of activity. One of the most important of these is that there is no item-bias or differential item functioning – i.e., item-responses are conditionally homogenous across different subgroups or subpopulations, given disease activity. We have tested if this is the case for three different index scales. 71 patients (25 men, 46 women) with a median age of 30 years (range 16–68 years) with chronic active CD (CDAI) score greater than 150 were studied. The following indices were calculated at 5 consecutive visits: Crohn’s Disease Activity Index (CDAI), Activity Index (AI), and Simple Index (SI). Item bias of the components of these three different index scales were examined by statistical tests of conditional independence of separate items versus sex, age, duration of disease, and localization, given the level of disease activity as measured by the respective indices. Evidence of differential item functioning were disclosed in several of these tests as shown below.

<table>
<thead>
<tr>
<th>Index</th>
<th>Number of items in index</th>
<th>Items with no evidence of bias</th>
<th>Items with evidence of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDAI</td>
<td>8</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>AI</td>
<td>9</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>SI</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

*Item "sex" was not tested.

As shown in the table, we have found that indices commonly used to standardize CD activity are subject to considerable item bias against basic demographic features such as age, sex, etc. This means that these indices are not generally applicable in patients with CD. We conclude that there is a need for revision of existing indices and recommend that an item bias detection strategy is included as an early and essential step in the development of new indices.

Emergency Subtotal Colectomy in Acute Colitis with Intra Pelvic Closure of the Rectal Stump

M. Wiedemann, A. Wettergren, A. Hartvigsen, L.B. Svendsen, S. Bulow. 1 Department of Gastrointestinal Surgery C, Rigshospitalet, County Hospital of Hvidovre, University of Copenhagen, Copenhagen, Denmark; 2 Department of Gastrointestinal Surgery, County Hospital of Hvidovre, University of Copenhagen, Copenhagen, Denmark

147 consecutive patients (71 women 76 men with a median age of 40 years, range 19-95) underwent acute subtotal colectomy for acute ulcerative, Crohn’s or unclassified colitis leaving the rectal stump in the pelvis. In all patients the rectal stump was transacted with a linear stapler, oversewn with 3/0 vicryl sutures and left in the pelvis. This method, without the use of subcutaneous “rectal closure” when the retained distal bowel is placed at the caudal end of the abdominal incision in the subcutaneous or fascial layer, appears to be just as safe and nor higher morbidity was observed.

Indication for surgery was failure of medical treatment (84/147), toxic megacolon 41/147, perforation 4/147, hemorrhage 3/147 other 12/147. 110 patients had ulcerative colitis, 31 Crohn’s disease and 6 other colitis. Median duration of disease until operation was 24 months, range 0-360 and 99 patients were treated by high doses (median 75 mg, range 20-160 mg) of steroid preoperatively.

The risk of perforation, sepsis and problems with locating the rectal stump in subsequent surgery seems overestimated and hard data are lacking. We found a mortality of 3% and none of the deaths related to the rectal stump, pelvic abscess in 4%, leakage/bleeding from rectal stump in 3%, activity or retention in the rectal stump were seen in 4% and could easily be treated with colotomy. Wound infections requiring operation was seen in 8%. Subsequent operations could easily be performed (pouch or ileorectal anastomosis), a total of 80% underwent later surgery, 20% had no indication for, or interest in later surgery.

Usefulness of PGA and PGC Determination in Evaluating Helicobacter Pylori Eradication

M. Ferrana, F. Vianello, M. Pleban, S. Salandin, P. Dotto, M. De Boni, M. Rugge, N. Dal Bo, T. Del Bianco, G. Battaglia, F. Di Mario. Dept. of Gastroenterology, University of Padua, Italy; 1 Dept. of Biochemistry, University of Padua, Italy; 2 Dept. of Pathology, University of Padua, Italy; 3 Dept. of Gastroenterology of Feltre, Italy; 4 Dept. of Gastroenterology of Venice, Italy

Different methods have been proposed to verify Helicobacter Pylori (HP) eradication, with variable accuracy. Recently, preliminary papers focused the role of serum Pepsinogen A (PGA) and C (PGC) as markers of HP eradication. Aim of the paper was to study the relationship between HP-eradication and PGA, PGC levels.

259 patients with peptic disease (159 DU; 28 GU; 15 DU + GU; 57 Gastritis; 177 M; 82 F; mean age 50.1 yrs; range 29–90 yrs) entered the study. The patients were all positive for HP infection by two tests: histological examination of two antral and/or two body biopsies (Giemsa modified stain), the urease test (Clio test, Delta West Ltd, Bentley, Western Australia).

In order to eradicate the bacterium, the patients were treated with different schedules of Omeprazole, Amoxicillin or Azithromycin and Metronidazole for two week. Two months later an endoscopic control was performed in order to verify the HP eradication: 158 out of 259 patients were found free of infection. Venous blood samples for PGA and PGC determination were performed at every endoscopic examination (PGA: RIA method, Pepsik I Sorin Biomedica, Salugia Italy; μg/ml; normal range 30–100; PGC: RIA method, Pepsik II, Sorin Biomedica, Salugia, Italy; μg/ml; normal range 4–24). Statistical analysis was performed by means of Student’s test.

<table>
<thead>
<tr>
<th>Eradicated patients (x ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA levels</td>
</tr>
<tr>
<td>before 139.5 ± 72.2</td>
</tr>
<tr>
<td>after 85.4 ± 42.9</td>
</tr>
</tbody>
</table>

Conclusions: our data evidence that HP eradication caused a statistically significant reduction of PGA and PGC levels possibly related to the known improvement of the inflammatory picture.
section. In the rest of the patients only different types of palliative procedures could be performed.

Overall morbidity rate amounted to 6%, while hospital mortality could be kept as low as 3.4%. The retrospective analysis covered the diagnostic procedures – ultrasonography, computed tomography, ERCP tumor marker CA 19-9 and fine needle aspiration biopsy – pre- and postoperative staging. 85% of the patients in the nonresected group had stage III and IV pancreatic cancer, 15% were classified as stage II, and were considered unresectable because of local spread. In the resected group it was surprising to find upon pathologic examination, that in spite of the resectability of the tumor 8% of the patients were classified having stage III-IV, 35% stage II and 57% stage I cancer, respectively. Overall mean survival of the resected group was 16 months. It seems that early pancreatic cancer is a rare clinical finding. This might be due to the lack of characteristic symptoms and the uncertainty of the diagnostic procedures in our experience.

1918 Endoscopic Treatment of Pancreatic Diseases
A. Vavrečka, Ľ. Jančula, I. Novotný. Clinic of Gastroenterology, Postgraduate Medical Institute, Bratislava, Slovak Republic

Introduction: Strictures, stones and pseudocyst impair the normal outflow of pancreatic juice in chronic pancreatitis (CP) and may cause pain and/or recurrent attacks of acute pancreatitis (AP). Patients with these problems must be treated. One of the possibilities is a surgical intervention a second is endoscopic treatment: pancreatic papillosphincterotomy (PPS) stenoses dilatation, stones extraction, lithotripsy and stenting. In this non-randomised single centre study evaluated the endoscopic management of these problems.

Materials and methods: In the Clinic of Gastroenterology 40 PPS have been done. There were 27 men and 13 women with a mean age 56.6 years (range 25-86). Indication for PPS was CP 34 times (from this PPS of papilla duodeni minor was done 4 times). Stenosis of pancreatic duct with major prestenotic dilatation was seen in 16 patients with CP After PPS was done extraction of stones or drainage (pancreatic duct or pseudocyst). The attempt of drainage of pancreatic duct was done 16 times and was successful 12 times.

Results: In 10 patients with CP after pancreatic duct drainage the pain significantly decreased in 1 patients only mild change of the pain could be seen and in 1 patient the pain was very strong and did not decrease after the drainage. Therefore he was indicated for surgery.

Conclusion: Our experiences with a small number of patients with painful CP demonstrated good results after pancreatic duct drainage. Recurrent attacks of AP after the drainage were not seen in 83.3% of our patients and their pain decreased significantly. In some patients could be seen dilatations of pancreatic three after removing of pancreatic stent.

1919 Prostenone: Preconditions for its Usage in Treatment of Chronic Pancreatitis
N.M. Budagov, A.V. Yegoda, V.D. Pasechnikov. Department of Internal Diseases #1, Medical Institute, Stavropol, Russia

The cytoprotective action of prostaglandins (PG) in inflammatory lesions of pancreas, along with their ability to modulate exocrine pancreatic secretion prompted us to examine the effects of Prostenone (P), PGE2 derivate, in chronic pancreatitis (CP).

52 patients with mild manifestations of CP recurrence and 19 healthy volunteers were studied. The effects of intravenous P (Tallinn pharm. factory; 0.08 mg/kg/min for 40 min) on basal and Enzprostat F-stimulated (PGF2α; 0.4 mg/kg/min) gastric HCl secretion, pancreatic enzymes’ activities, Na bi-carbonate output, pancreatic juice (PJ) volume, and cyclic nucleotides (CN) levels in PJ were tested.

Administration of P in volunteers resulted in quick (in 20 min) but short-term (for 40 min) increase in Na bicarbonate production and PJ volume (p < 0.05). Enzymes activities, CN contents in PJ and HCl secretion did not change. Pretreatment with Enzprostat F caused growth of enzymatic activity in PJ and HCl secretion in both groups. This effect was abolished by P (p < 0.05), which, however, did not suppress Enzprostat-stimulated rise in PJ output and bicarbonate production. P was also found to relieve pain. Analgesia started 20–30 minutes after the beginning of stimulation, lasted for up to 1–3 days and was most likely related to relaxation of smooth muscles verified by ultrasonographic examination.

Thus, P appears to stimulate directly (without CN involvement) H2O and bicarbonate secretion, relieve pain and provide a "functional relaxation" for the acinar cells under stimulation. These properties of the drug may be helpful in treatment of CP patients.

1920 Vagal Tone and Antral Size in Duodenal Ulcer and Functional Dyspepsia Patients
T. Hauskén, S. Svebak, A. Berstad. Medical Department, Haukeland University Hospital, Department of Biological and Medical Psychology, University of Bergen, Norway

Patients with functional dyspepsia (FD) are characterized by low vagal tone and wide gastric antrum compared to healthy controls (C) (Scand J Gastroenterol 1992; 27: 427–432, Psychosomatic Medicine 1993; 55: 12–22). The aim of the present study was to investigate vagal tone and antral size in patients with duodenal ulcer (DU). Methods: Sixteen consecutive patients with endoscopically verified DU and Helicobacter pylori infection were investigated the day after endoscopy. No patients received any ulcer treatment. All subjects were investigated fasting in the morning. The antral width was measured ultrasonographically in a standardized vertical section, and measurements of respiratory sinus arrhythmia (RSA) was calculated to index vagal tone. The results were compared to those in 25 patients with FD and 25 C similarly examined previously. Results: Vagal tone was significantly higher in DU (7.2) and C (5.7) compared to FD (1.9) (p < 0.001). DU patients tended to have higher vagal tone than C (p = 0.07). Fasting antral area was significantly wider in DU (4.8 cm2) and FD (4.6 cm2) than in C (3.4 cm2) (p = 0.01). Conclusions: DU patients are characterized by high vagal tone compared to functional dyspepsia patients. Both groups have a wide gastric antrum; possibly due to a functional disorder in FD and to a mechanical outlet obstruction in DU.

1376 Does Systemic Absorption of 5-Aminosalicylic Acid from Olsalazine (Dipentum®) and Mesalazine (Asacol® and Pentasa®) Differ Significantly in Ulcerative Colitis?
T.K. Daneshmend, M. Hendrickse, M. Salzmann, D. Daneshmend. Dept. of Medicine, Royal Devon & Exeter Hospital, Exeter EX2 5DQ, Devon, England, Dept. of Pathology, Royal Devon & Exeter Hospital, Exeter EX2 5DQ, Devon, England

5-Aminosalicylic acid (5-ASA), the active moiety of sulphasalazine, formulated as the azo-bonded analogue olsalazine (Dipentum), or as delayed release or slow release mesalazine (Asacol (A) and Pentasa (P)), is effective in prevention of relapse in ulcerative colitis. However, significant systemic absorption of 5-ASA may make it less effective and may increase adverse effects. Method: We compared the systemic absorption of D, A and P at steady state. 15 patients (age 21–69 y, 6 female) with ulcerative colitis in remission were given in a randomised block design 7-day courses of D 1.0 g/d, A 1.2 g/d, and P 1.5 g/d. Plasma and urine were collected on days 6 and 7 of each course and analyzed for 5-ASA and its main metabolite, acetyl-5-ASA, by HPLC. Results: Mean (SEM) plasma and urine 5-ASA and Acetyl-5-ASA in 15 patients

<table>
<thead>
<tr>
<th>Plasma</th>
<th>Dipentum</th>
<th>Asacol</th>
<th>Pentasa</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-ASA (μmol/L)</td>
<td>1.48 (0.35)</td>
<td>3.76 (1.27)</td>
<td>1.35 (0.21)</td>
</tr>
<tr>
<td>Ac-5-ASA (μmol/L)</td>
<td>3.51 (0.57)</td>
<td>7.90 (1.39)</td>
<td>5.29 (1.26)</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-ASA (μmol/24 h)</td>
<td>53.1 (22.8)</td>
<td>149 (40.8)</td>
<td>252 (66.7)</td>
</tr>
<tr>
<td>Ac-5-ASA (μmol/24 h)</td>
<td>1180 (136)</td>
<td>1730 (132)</td>
<td>3190 (266)</td>
</tr>
<tr>
<td>Total 5-ASA (μmol/24 h)</td>
<td>1230 (151)</td>
<td>1880 (155)</td>
<td>3450 (272)</td>
</tr>
<tr>
<td>Equimolar 5-ASA (% dose)</td>
<td>21.2 (3.5)</td>
<td>24.0 (1.98)</td>
<td>35.1 (2.77)</td>
</tr>
</tbody>
</table>

*p < 0.01 compared with A, #p < 0.001 compared with P

Conclusions: 5-ASA and acetyl-5-ASA in plasma and urine during olsalazine (Dipentum) treatment were significantly lower than with the two mesalazine formulations (A and P). At therapeutic doses olsalazine appears to have the least systemic absorption at steady state.