cyclosporine (OTI), and metronidazole (M). Methods: Treatment I (101 patients): B 5 ml, OTI 500 mg, and M 200 mg all q.i.d. for 14 days. Treatment II (60 patients): B 10 ml and OT 750 mg q.i.d., M 400 mg t.i.d. for 7 days. Treatment III (145 patients): B 10 ml and OT 500 mg q.i.d., M 400 mg t.i.d. for 10 days. Gastroscopy and 14C-urea breath test were performed 4 weeks and 1 year after cessation of therapy. Results: H. pylori eradication rates at 4 weeks were 87.9%, 82.1%, and 95.7% for Treatment I, II and III, respectively, according to the breath test. Having re-examined 100 patients after one year with both gastroscopy and breath test without finding any active ulcer in asymptomatic, H. pylori negative patients, we changed the protocol and did breath test only at one year in these patients. Four (all duodenal ulcer) out of 227 patients (duodenal or pyloric ulcer 177, gastric ulcer 50), who were H. pylori negative at 4 weeks, had become H. pylori positive during one year (H. pylori recurrence rate 1.8%, 95% CI from 0.5 to 4.5%). Only one of these “reinfected” patients had ulcer relapse. Another patient had duodenal ulcer relapse shortly after cessation of treatment in spite of being H. pylori eradicated (ulcer relapse rate 0.9%, 95% CI from 0.1 to 3.1%). Conclusions: Following H. pylori eradication by triple therapy, H. pylori and ulcer recurrence rates are very low during the first year (below 4.5% and 3.1%, respectively).

[80] Randomized Controlled Trial for Helicobacter Pylori Eradication: Dual Therapy (DT) Versus Triple Therapy (TT)

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There is no gold standard treatment for Helicobacter pylori (H. pylori) infection and regimens using TT or DT are currently proposed. The aim of this study was to compare the eradication rate of H. pylori between TT or DT.

Methods: The patients with duodenal ulcer (DU) or non ulcer dyspepsia (NUD) and H. pylori infection assessed by 2 positive methods among CLO-test, histology, culture and PCR were prospectively randomized and received omeprazole (OM) during 2 weeks and antibiotics during the first 10 days. Two regimens were used, DT and two used TT. TT: Ome 60 mg od and amoxicillin (Am) 2 g/d (group OA); OM 60 mg od and clarithromycin (Ca) 500 mg tid (group OC); OM 20 mg od and Am 2 g/d and tinidazole 1 g/d (group OAT); OM 20 mg od and Am 2 g/d and Clo 500 mg od (group OAC). Metronidazole resistance (Me-R) was defined by a MIC > 8 μg/ml (Epsilometer test) and Ca resistance (Ca-R) by a MIC > 2 μg/ml (agar diffusion method). Eradication was defined 4 weeks after the end of the treatment by negative results for all the diagnostic methods. Compliance was defined as inadequate when less than 60% of the prescribed treatment was taken.

Results: Among the one hundred patients enrolled (71 male, median age 45.4, range 20 to 87), eighty-three patients completed the trial and 15 patients were excluded (4 H. pylori negative before treatment, 4 non compliant and 7 lost to follow-up). Pretreatment Me-R was detected in 40/88 (45.4%) and Ca-R in 78/87 (8.8%). H. pylori eradication rate was 36% (8/23) in group OA, 60.9% (14/23) in group OC, 66.7% (12/18) in group OAT and 95.2% (20/21) in group OAC. OAC significantly better than DT (p < 0.01). There was no statistically difference between the 2 triple therapies OAC and OAT (p = 0.06). Me-R, H. pylori strains were eradicated in 58% (n = 19/33), 33% in group OAT (n = 2/6), 70% (n = 14/20) with therapy including Ca of which 88% in group OAC (n = 9/11). There was no difference in side-effects between DT (n = 943 – 20.9%) and TT (9/39 – 23%) with minor gastrointestinal events (diarrhea in 12, metallic taste in 9).

Conclusions: (1) Triple therapy is significantly more effective than dual therapy. (2) The OAC regimen is the most effective. (3) In a high level Me-R strains population, the best therapy should be a triple therapy with a proton pump inhibitor and 2 antibiotics including a macrolide instead of Me.

[81] Development of a Quality of Life Index for Patients with Liver Disease and After Liver Transplantation

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Beside morbidity and mortality Quality of Life (QL) is the important outcome parameter following OLT. The purpose of this study was to develop a QL-Index and provide QL data in liver transplant patients.

Between 1982 and 1992 a disease specific QL-index (LSQL) was developed and validated in comparable adult patients with chronic liver disease as well as before and after OLT. Initially, 82 possible relevant items could be reduced to 28 items by analyzing 3 different sets of questionnaires in 147 patients. Item reduction was achieved according to their frequency and ability to discriminate. The questionnaire was validated for testing internal consistency, sensitivity and reliability and by comparison with a known general health index (SF 36).

Internal consistency of the variables as assessed by Cronbach’s α was found to be >0.8 in all dimensions of QL. A strong correlation with the number of associated diseases was found and 14-28 day test-retest reliability in stable patients was r = 0.7. Discrimination among different stages of QL was higher when compared with the SF 36.

The newly developed LSQL-Questionnaire is the first validated disease specific QL-index and allows measurement of QL in liver patients beyond OLT and may become an important tool in assessment of medical or surgical treatment of liver disease/transplantation.

[82] Optimal Timing is Crucial in Liver Transplantation: Experience from the Nordic Waiting List

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From January 1st, 1990, all patients accepted on waiting list for liver transplantation in Finland, Sweden, Norway, Iceland and Denmark are registered and followed (100%) in "The Nordic Liver Transplantation Registry". In the present study we analyzed strategies for organ allocation and outcome for 259 patients accepted on waiting list in 1990 and 1991. The patients have been followed until August 31, 1993, i.e. at least ½ year. For 36 patients with acute liver failure, 5 patients died on waiting list, 2 were taken off the waiting list due to improvement and are still alive. Median time spent on waiting list was 2 days. For 223 non-acute patients, 26 patients died on waiting list (20 due to hepatic failure), 16 left the waiting list alive, but died subsequently (15 due to dissemination of liver malignancies), 6 left waiting list because of improvement and are still alive. Median time spent on the waiting list was 65 days.

Analysis of the strategies for organ allocation was performed by means of Cox’ multivariable regression analysis on the basis of clinical and biochemical variables at the time of acceptance on waiting list: Among patients with non-acute liver disease, and ignoring centre priorities, patients with low MELD at time of listing had a 10 fold higher risk of dying on the waiting list than patients with high MELD. Among non-acute patients, risk factors for dying after liver transplantation were malignancies, high plasma-urea and low plasma-albumin. Waiting time was not of significant importance.

Patients with the most severe impairment of the liver function were given highest priority on the waiting list, but these patients also had a significantly higher risk of dying after liver transplantation. This underlines the importance of referring patients with chronic liver disease to a transplantation centre before the disease has developed into a condition which not only increases the risk of dying while waiting for a new liver, but also increases the risk of dying after transplantation.

[83] Quality of Life Following Liver Transplantation for Alcoholic Liver Disease

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Alcoholic liver disease (ALD) is increasingly an indication for liver transplantation (LTX). With regard to the underlying disease LTX needs further justification in patients with a bad general condition (as e.g. liver incapacity of an incapaciation index) had a significantly shorter waiting time. Survival of the transplantation patients (204) were analyzed by means of Cox’ regression analysis: Increased risk of dying after transplantation was significantly higher in patients with acute liver failure. Among non-acute patients, risk factors for dying after liver transplantation were malignancies, high plasma-urea and low plasma-albumin. Waiting time was not of significant importance.

Patients with the most severe impairment of the liver function were given highest priority on the waiting list, but these patients also had a significantly higher risk of dying after liver transplantation. This underlines the importance of referring patients with chronic liver disease to a transplantation centre before the disease has developed into a condition which not only increases the risk of dying while waiting for a new liver, but also increases the risk of dying after transplantation.

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Evidence for Recurrence of Primary Sclerosing Cholangitis (PSC) After Orthotopic Liver Transplantation (OLT)

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The aim of the present study was to elucidate the incidence of pre-OLT disease in post-OLT bile physiology. We included 35 patients into 4 groups: I Alcohol cirrhosis (ALC); II Colitis (COL); III Posthepatic cirrhosis (HEP); IV Acute Liver Failure (ALF). The aim was to determine whether PSC can recur after OLT by comparing biliary strictures, their possible etiologies and liver histology in PSC patients with control groups of primary biliary cirrhosis (PBC) patients and non-PSC OLT patients with Roux-en-Y (RY) reconstruction. For OLT performed from 2/88 to 10/92, 96% of PSC, 79% of PBC and 100% of RY patients were alive with a median graft follow-up of 735, 467 and 454 days respectively. Biliary strictures occurred in 9 PSC, 8 PBC and 1 RY grafts (Table).

<table>
<thead>
<tr>
<th>No.</th>
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<th>No. (%)/Grafts with Strictures</th>
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<tr>
<td>Pts</td>
<td>Grafts</td>
<td>Anatomic (AS) Nonanatomic (NAS)</td>
</tr>
<tr>
<td>PSC</td>
<td>27</td>
<td>33</td>
</tr>
<tr>
<td>PBC</td>
<td>23</td>
<td>96</td>
</tr>
<tr>
<td>RY</td>
<td>9</td>
<td>11</td>
</tr>
</tbody>
</table>

In the 8 PSC grafts with NAS ( hilar + intrahepatic), 2 were associated with vascular occlusion, 2 with ischemia time >15 h and 1 with CR. The remaining 3 patients had no apparent risk factors and one required retransplantation. In the 4 PBC grafts with NAS, 2 were associated with CR, one with an ischemia time of 12 h, and one with no apparent risk factors. Histological changes of pericholangitis and periductal edema with post-OLT biliary strictures were seen in 4 PSC but no in PBC patients.

Summary: (1) There was a higher incidence of NAS in PSC compared to PBC, but this difference was not significant (p > 0.2). (2) RY was not per se associated with an increased risk of NAS. (3) More PSC than PBC patients developed diffuse NAS without identifiable risk factors. (4) Histological changes consistent with recurrent PSC were observed only in PSC with biliary strictures.

Conclusion: In PSC following OLT, there is evidence suggestive of recurrent primary disease. However, this evidence is not conclusive because of its lack of specificity and the overall prognosis of patients with PSC after OLT is excellent.

Colchicine in Alcoholic Cirrhosis – Preliminary Results of a Double-Blind Randomized Trial

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The potential role of colchicine in the treatment of cirrhosis is still uncertain. These are preliminary results of a double-blind randomized controlled trial to evaluate the efficacy of colchicine in alcoholic cirrhosis both on clinical and histological parameters. Consecutive patients with biopsy proven alcoholic cirrhosis were included. Exclusion criteria included: bilirubin >170 mMol/L, Child-Pugh class C, gastrointestinal bleeding in the period of 15 days prior to randomization, renal failure or cancer. Colchicine, 1 mg or a placebo were administered orally, on a daily dose, 5 consecutive days a week. Forty-three patients were assigned either to colchicine (C = n = 20) or placebo (P = n = 23); mean age was 54 and 56 years respectively. There were 18 males and 2 females in C and 18 males and 5 females in P; at randomization, Child-Pugh score was 5.8 ± 1.0 and 5.4 ± 0.5, respectively. The time elapsed between clinical diagnosis and inclusion was 48 months for C and 37 months for P (NS). Data concerns results obtained after a mean follow-up of 19.5 ± 9 (C) and 16.1 ± 1 (P) months. Medication was well tolerated, compliance was excellent. Fifty-seven percent of patients in C and 45% in P remained abstinent. Laboratory evaluation did not show any significant changes in albumin, bilirubin, prothrombin time or transaminases values. Serum levels of the N-terminal propeptide of procollagen type III (RIIA) decreased in a similar way in both groups (P = 0.03), mainly in abstinent patients. Child-Pugh score remained stable in both groups throughout the study. Cumulative survival was similar, 82% in C and 94% in P (NS). Colchicine is well tolerated and does not appear to have any significant benefit, however this may be confounded by the small number of patients and the short period of follow-up.

Pre-Transplantation-Liver Affects in Patients Recovery of Bile Secretion After OLT in Man

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Restitution of bile secretion is one of the most important hepatic processes after liver transplantation (OLT). The aim of the present study was to elucidate the influence of pre-OLT disease on post-OLT bile physiology. We included 35 patients into 4 groups: I Alcohol cirrhosis (ALC); II Colitis (COL); III Posthepatic cirrhosis (HEP); IV Acute Liver Failure (ALF). The aim was to determine whether PSC can recur after OLT by comparing biliary strictures, their possible etiologies and liver histology in PSC patients with control groups of primary biliary cirrhosis (PBC) patients and non-PSC OLT patients with Roux-en-Y (RY) reconstruction. For OLT performed from 2/88 to 10/92, 96% of PSC, 79% of PBC and 100% of RY patients were alive with a median graft follow-up of 735, 467 and 454 days respectively. Biliary strictures occurred in 9 PSC, 8 PBC and 1 RY grafts (Table).

Lipid Peroxidation and Acetaldehyde-Derived Protein Adducts in Alcoholic Livers

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Excessive alcohol consumption has been suggested to induce aldehyde-derived protein modifications in the liver. We have previously demonstrated that both acetaldehyde (AA), the first metabolite of ethanol, and malondialdehyde (MDA), a product of lipid peroxidation, may be involved in such modifications.

In the present work, we have extended this study to examine cova lent chemical addition products (adducts) of proteins and AA, MDA and 4-hydroxynonenal (HNE) in liver specimens obtained from ethanol-fed mic r o g r o w n rats and from human alcoholic. Specific antibodies recognizing the different adducts of proteins were used in immunoperoxidase and double immuno fluorescence stainings. Collagen was demonstrated using Weigert von Gieson collagen staining.

Aldehyde-derived adducts were found in the alcoholic livers, the centrilobular region of the liver being the most site of their occurrence. Centrilobular fibrosis was also frequently present at this site. With continuing inflammation and scarring the positive staining for the peroxidation-derived products, including 4-HNE, became more frequent. The protein adducts were found to colocalize with the areas of fatty infiltration, focal necrosis and fibrosis. Peroxidation-derived adducts were also present in the fibrous septa.

The studies suggest that the aldehyde-derived protein modifications may be involved in the adverse effects of ethanol in the liver. Species and dietary differences should be considered when evaluating the role of lipid peroxidation in this process.

Non-Alcoholic Hepatic Steatosis: In Vivo Study of Hepatic Mitochondrial Dysfunction

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The physiopathology of non-alcoholic hepatic steatosis remains largely unclear: triglycerides accumulation within hepatocytes may be due in part to a defect in mitochondrial fatty acid oxidation. 14C-keto-isocaproic acid breath...
### Urinary Cyclic S'-Guanosine Monophosphate (c-GMP) and Hemodynamic, Neurohumoral and Renal Function Changes in Cirrhosis

C.M. Fernández-Rodriguez, A. Andrade, J. Zozaya, J. Quiroga, D. Rodriguez, S. Pereira, A. Papadakis, J.S. Pallarés. Gastroenterology and Dept. of Internal Medicine. Hospital Xeral de Vigo. Clinica Universitaria de Navarra, Pamplona, Spain

Intracellular accumulation of c-GMP in response to extracellular signals such as endothelial nitric oxide and natriuretic peptides has been proposed to underly peripheral arteriolar vasodilation in cirrhosis. Total cGMP urinary excretion (UcGMPV) represents the systemic and renal production. Furthermore, variation of this excretion reflects the changes of plasma cGMP concentration.

### Aim and Methods:
To determine UcGMPV and investigate its relationship to systemic hemodynamics, neurohumoral and renal function changes in cirrhosis. Five healthy subjects and twenty cirrhotic patients were studied. Systemic vascular resistance (SVR) was calculated as (mean arterial pressure−RAP)/cardiac output. Cardiac output was determined by pulsed Echo-Doppler. Plasma atrial natriuretic factor (ANF), plasma levels of the endothelium-dependent vasodilator substance P (SP) and UcGMP were measured by RIA.

### Results:
Cirrhotic patients had higher blood volume, cardiac output, plasma renin activity (PRA), plasma aldosterone concentration (PAC), plasma norepinephrine (NE), ANF, SP and lower SVR and fractional excretion of sodium (FENa) than patients of the control group. UcGMPV was higher in the group with cirrhosis than in the control (861 ± 69 vs. 147 ± 69 pg/mL/min. xUVOL ± SD; p < 0.01). In the group with cirrhosis, the UcGMPV inversely correlated with the SVR (r: −0.51; p < 0.03) and EFNa (r: −0.53; p < 0.02) and directly with right atrial pressure (RAP) (r: 0.52; p < 0.02), PRA (r: 0.49; p < 0.05), NE (r: 0.5; p < 0.05), SP (r: 0.66; p < 0.01), ANF (r: 0.57; p < 0.02) and Pugh’s score (Spearman, r: 0.57; p < 0.02). With stepwise multiple linear regression analysis, only plasma levels of SP and RAP remained independently associated to UcGMPV (r²: 0.53; p < 0.001 and r²: 0.15; p < 0.01, respectively).

### Conclusions:
Results indicate an excessive cGMP excretion in cirrhosis and suggest that this messenger may mediate the hemodynamic and renal function changes in these patients. Plasma SP probably through endothelial nitric oxide and RAP by way of natriuretic peptides release, account for most of the urinary cGMP production in cirrhosis.

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### Red Cell Ferritin as a New Marker of Chronic Alcoholism

U. Schmidt, L. Senf, A. Neumeister. Medical School of Erfurt, Germany

The influence of chronic alcoholism on the red cell ferritin (RCF) was investigated.

**Patients:** 22 with alcoholic liver disease without cirrhosis (NC), 28 with alcoholic cirrhosis (AC), control group (CG): 51 (21 female, 20 male).

**Methods:** From the heparinized venous blood the supernatant with buffy coat was removed, the sediment suspended in isotonic saline, washed three times and an aliquot prepared for cell counting. The erythrocyte preparation was lyzed by freezing at −20 °C for at least 12 hours. After thawing and homogenization the ferritin contents was determined by an immunoradiometric assay (human liver antibodies, Behring).

Results are shown in the table. MCV mean corpuscular volume of the red cells, GGT gamma glutamyl transerase. The numbers on the table show the persons with elevated values. The statistical values are meant for the whole collective. M median.

<table>
<thead>
<tr>
<th>NC</th>
<th>AC</th>
<th>CG</th>
<th>Normal range</th>
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<tbody>
<tr>
<td>RCF</td>
<td>21 (95.5%)</td>
<td>26 (92.9%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>M: 108 (51.0%)</td>
<td>M: 165 (10-691)</td>
<td>M: 15 (4-50)</td>
<td>S: 39 ng/cell</td>
</tr>
<tr>
<td>MCV</td>
<td>16 (72.7%)</td>
<td>18 (64.3%)</td>
<td>76 (13.7%)</td>
</tr>
<tr>
<td>MGT</td>
<td>15 (88.2%)</td>
<td>23 (92.1%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>M: 3.8 (0.35-38)</td>
<td>M: 2.40 (24-32)</td>
<td>M: 0.28 (0.10-0.77)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In alcoholicics the sensitivity of RCF is higher than GGT and MCV RCF is also suitable for the differential diagnosis of several liver diseases (but not in cases of primary iron overload, iron deficiency anemias, haemolysis and anemias with disorders of iron utilization). In cases with a longer period of abstinence the RCF will be normal after ca. 4 months. In patients with prospective liver transplantation the RCF is suitable for the evidence of their abstinence.

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### Comparison of Ultrasonographic Score and Histology in Patients with Chronic Liver Disease

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In patients with chronic liver disease, ultrasonography (US) is routinely used to assess the appearance of early signs of cirrhosis and portal hypertension, but its role at this regard is not clearly defined. In this prospective study, 137 consecutive patients (pts) with chronic liver diseasecandidate to liver transplantation were studied to determine liver biopsy in the period January-July 1993. Histology was classified as: chronic active hepatitis (CAH = 59 pts), chronic active hepatitis with bridging necrosis and fibrosis (CAH+ = 43 pts), and liver cirrhosis (LC = 35 pts). US features were evaluated by a score, based on liver size, morphological analysis, edges and echogenicity, portal vein caliber and flow velocity, and spleen size. This score differed significantly among the 3 histological groups (CAH 23 ± 19, CAH+ 39 ± 31, LC 83 ± 26; ANOVA p < 0.0001). US score correctly detected CAH in 485/59 pts (81.4%). In the CAH+ group, US score suggested the diagnosis of CAH in 25 pts and LC in 10 pts, while 9 pts had an intermediate dotting. US score correctly diagnosed LC in 27/36 pts. The US diagnosis of LC was supposed in 13 other pts, classified as CAH+ (10 pts) and CAH (3 pts) at histology. The overall accuracy of US score in detecting LC was 64.7%, with a sensitivity of 77.1%, and a specificity of 67.3%. A stepwise logistic regression analysis identified 4 parameters as independently associated with LC: liver echogenicity (p < 0.0001), liver morphology (hypertrophy of the left lobe) (p < 0.0003), portal flow velocity (p < 0.05) and spleen size (p < 0.05).

On the basis of these data there is no complete agreement between US and histology in detecting cirrhosis in patients with chronic active hepatitis. The absence of specific signs at US cannot exclude the diagnosis of cirrhosis. On the other hands, US may suggest cirrhosis even without a typical histological picture. If this might depend on a US overestimation, or an underestimation at histology (i.e. related to inadequate liver samples) is unclear.
In these cases repeated liver biopsy may be advised in order to recognize cirrhosis before starting interferon therapy.

93 IL-6, TNF-α and Soluble TNF-α Receptor Serum Levels in Crohn’s Disease

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Crohn’s disease (CD) is associated with an activation of macrophages. TNF-α and IL-6 are produced by macrophages and their serum levels seem to be increased in active CD. However results remain controversial. Soluble TNF-α receptor (sTNF-α-R) serum level has never been evaluated in CD. The aim of our study was to measure IL-6, TNF-α and sTNF-α-R serum levels in active and inactive CD and to compare it with normal controls.

We measured by ELISA the IL-6, TNF-α and sTNF-α-R serum level in 26 patients with inactive CD (CDAI < 150), 32 patients with active CD (CDAI > 150) and 80 normal controls. Results were compared using a t-test of Significant difference if p < 0.05.

Results:

<table>
<thead>
<tr>
<th>IL-6 (pg/ml)</th>
<th>TNF-α (pg/ml)</th>
<th>sTNF-α-R (ng/ml)</th>
</tr>
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<tbody>
<tr>
<td>Normal controls</td>
<td>3.20 ± 8.62</td>
<td>10.35 ± 5.84</td>
</tr>
<tr>
<td>Inactive CD</td>
<td>10.23 ± 12.02</td>
<td>13.00 ± 4.48</td>
</tr>
<tr>
<td>Active CD</td>
<td>28.62 ± 26.50</td>
<td>24.77 ± 33.12</td>
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</table>

IL-6 and sTNF-α-R were significantly higher in CD than in controls and in active than in inactive disease. For TNF-α, there was a significant difference only between active CD and controls.

In conclusion IL-6, TNF-α and sTNF-α-R serum levels are increased in active CD, reflecting macrophages activation and might be useful in the monitoring of the disease.

94 A Controlled Randomized Trial of Beclomethasone Dipropionate (3MG) Versus 5-Aminosalicylic Acid (1G) Versus Combination of Both (3MG/1G) as Retention Enemas in Active Distal Ulcerative Colitis

Chris J.J. Mulder 1, Paul Fockens 2, Herbert van der Heide 3, Guido N.J. Tytgat 4, E.H.H. Willot 1, 1 Hepatogastroenterology, Rijnstate, Arnhem; 2 AMC, Amsterdam; 3 Martini, Groningen

Sixty patients with active distal ulcerative colitis participated in a multicentre, randomized, double-blind trial to compare the effect of beclomethasone dipropionate (BDP) enema (3 mg/100 ml), with 5-aminosalicylic acid (5ASA) enema (1 g/100 ml), and enema’s with a combination of BDP/5ASA (3 mg/100 ml). The patients were treated for 4 weeks, and the efficacy of the drugs were evaluated by sigmoidoscopy and subjective symptoms after 4 weeks.

After 4 weeks of treatment 7 of 19 patients (37%) receiving BDP/5ASA had healed endoscopically, compared with 6 of 20 receiving BDP (30%), compared with 2 of 21 receiving 5ASA (10%) (p < 0.05).

The overall results after 28 days of treatment were: clinical improvement: 100% (BDP/5ASA) vs 70% (BDP), 76% (5ASA), endoscopic improvement: 100% (BDP/5ASA), vs 75% (BDP), vs 71% (5ASA). Two patients on 5ASA and three on BDP had a marked deterioration during treatment. The combination of BDP/5ASA was superior to single agent therapy in terms of both significantly improved sigmoidoscopic and subjective symptoms (p < 0.05).

No significant differences in improvement between the 5ASA vs BDP treated patients were recognized.

No side effects were recognized.

The results of our study show that topical treatment of active disease with either 5ASA or BDP is equally efficacious. So far no data on topical combination therapy have been described. However combination therapy of BDP/5ASA seems superior to single agent therapy and causes no adverse reactions.

Becloventhason versus 5ASA versus combinete Becloventhason-5ASA-clysmaat bij Proctitis Ulcerosa.

95 Bone Alterations in Crohn’s Disease (CD): A Comparison Between Active and Quiescent Disease

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We have previously shown that although bone mineral density (BMD) is decreased in about 30% of patients with quiescent CD (QCD) no sign of increased bone resorption or decreased formation is detectable, thus suggesting that besides steroid intake and nicotine consumption other factors are likely to contribute. Aim of this study was to compare the osteometric features of a group of CD patients during flare up (ACD) with a group of QCD. Methods: 28 patients, QCD = 20, ACD = 8 and 12 controls (C) were studied. Half of ACD patients were on steroids at the time of the study. BMD expressed as the Z-score and the lifetime prednisone dose (l.p.d.) were determined, as well as serum, PTH, osteocalcin (BGP), and minerals were measured. The calcium/creatinine (Ca/Crea) ratio was determined in fasting urine. Results (mean values ± SEM; ANOVA and unpaired t-test): a Z-score < -2 was present in 25% of QCD patients and in 50% of patients with ACD (Mean Z-score C: 0.06 ± 0.03; QCD: -1.29 ± 0.29, p < 0.05; ACD: -1.68 ± 0.36, p < 0.002). l.p.d. was similar in QCD and ACD, but while in QCD there was a significant correlation between l.p.d. and Z-score, this was absent in patients with ACD. PTH was significantly lowered in ACD (4: 53 pg/ml ± 2; QCD: 48 ± 2; ACD: 27 ± 7, p < 0.029). PTH correlated in ACD with urinary Ca/Crea. BGP was significantly lowered only in ACD (11 ng/ml ± 1; QCD: 11 ± 1; ACD: 6 ± 1, p < 0.05). In ACD patients BGP levels were similar in those taking or not taking steroids. No differences were found in serum minerals and the urinary Ca/Crea ratio.

Conclusions: 1. In ACD there is a reduced bone formation also in patients who are not treated with steroids. 2. In ACD, bone demineralization is not correlated to the amount of steroids taken. 3. The greater impairment of the Z-score in ACD compared to QCD may indicate that some recovery of bone mineralization is possible when disease activity subsides. 4. These data are consistent with the hypothesis that active inflammation per se might affect bone metabolism.

96 Inflammatory Bowel Disease and Domestic Hygiene in Childhood

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Early environmental experience may predispose to intestinal disease.

The purpose of this study was to explore the hypothesis that improvement in domestic hygiene has contributed to the unexplained increased incidence of Crohn's disease. 364 patients with inflammatory bowel disease (IBD), 231 with ulcerative colitis, 133 with Crohn disease were compared with an equal number of healthy age and sex matched controls from the same population. Patients and controls underwent a short structured interview about housing and domestic facilities in childhood and a history of appendectomy recorded. The results were analysed by conditional logistic regression for matched sets.

Crohn’s disease was significantly more common in subjects whose first home had hot tap water (odds ratio = 5.09 95% CI 1.4-17.3) and separate bathroom (or 3.39 95% CI 1.34-8.3; in contrast ulcerative colitis showed no clear relationship to the provision of these household amenities. Ulcerative colitis however showed a strong negative association with a flush toilet and mains drainage.

These data support the proposed hypothesis. The incidence of Crohn’s disease in as yet under-developed countries may therefore increase as domestic hygiene improves. The fact that there is no clear association between ulcerative colitis and household facilities suggests that different factors may predispose Crohn’s disease and ulcerative colitis.

97 Quality of Life in Inflammatory Bowel Disease and the Effect of Smoking


Smoking is positively correlated with the frequency of hospital admission and bowel surgery in Crohn’s disease (CD). No comparable data are available for ulcerative colitis (UC). To evaluate potential differences in quality of life (QoL) in CD and UC between smokers and non-smokers we used a mailed version of the inflammatory bowel disease questionnaire (IBDQ, Guyatt et al, 1991). The IBDQ consists of 32 questions clustered in 4 categories covering bowel symptoms, systemic symptoms, emotional function and social function, all scored on a 7 point scale: range 1 (worst) to 7 (best). The Wilcoxon rank sum test was used for statistical evaluation.

The response rate was 92%. The questionnaire was returned by 458 patients with CD (mean age 38.7, females 59%, smokers 52%) and 441 with UC (mean age 43.8, females 43%, smokers 23%). The categories systemic symptoms and emotional function were scored lower in CD compared to UC (p < 0.005 and p < 0.05).

In CD smokers had a lower score in all four categories compared to non-smokers: bowel symptoms 5.36 vs 5.69*, systemic symptoms 4.77 vs 5.20*, emotional function 5.9 vs 6.2* (p < 0.005 **: p < 0.0005). In UC no difference between smokers and non-smokers was observed (bowel symptoms 5.61 vs 5.63, systemic symptoms 5.16 vs 5.18, emotional function 5.55 vs 5.61, social function 6.11 vs 6.07).

Summary and conclusion: in the patient group with CD, smokers had a QoL inferior to that of non-smokers, whereas there was no such a difference