

dietary supplementation in patients with IBD, and particularly Crohn's disease. Subject numbers are relatively small and statistical significance was not achieved, but no other study on the subject is placebo controlled and double blinded, or has dietary oral calcium intake data for subjects. Although tolerability of the medication was good, results do not provide enough evidence to support the use of oral calcium and vitamin D supplements in all patients with inflammatory bowel disease.

**P102**  
**THYROID DISORDERS IN A POPULATION OF ULCERATIVE COLITIS (UC) PATIENTS**

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**Introduction:** The prevalence of thyroid disorders is 2-4 times more frequent in patients affected by Ulcerative Colitis (UC) than in general population (1). We have screened for these disorders our population of UC patients.

**Materials and Methods:** We have studied 140 patients (100 females-F and 40 males-M) affected by UC. UC was classified in mild, moderate and severe activity disease according to Truelove classification and the site of disease was specified. Mean age is 43 year (range 18-80). Blood thyroid hormones dosage (FT3, FT4, TSH) was performed in every patient and, only in case of alterations suggestive for thyroid disorders, blood thyroid autoantibodies (anti thyroglobulin and anti microsomal for hypothyroidism, anti TSH receptor for hyperthyroidism) were studied in association with ultrasound and scintigraphy study.

**Results:** 30 patients (22 F and 8 M) showed a severe UC, 52 (33 F and 19 M) a moderate UC and 58 (45 F and 13 M) a mild activity disease. 22 patients (15 F and 7 M) had a pancolitis, 60 patients (51 F and 9 M) a left colitis, 30 patients (20 F and 10 M) a proctosigmoiditis and 28 (14 F and 14 M)(2.8%) only a rectal involvement. 4 patients (2 F and 2 M) (2.8%) had thyroid disorders. All patients were affected by severe UC; 3 (1 F and 2 M) with left colitis and 1 F with pancolitis. A clinical picture compatible with hyperthyroidism (blood suppression of TSH, marked blood increase of FT3, FT4 and anti TSH receptor > 15 mU/L n.v.0-1) was present in a female 60 year old and a surgical resection for was needed for histological diagnosis of severe dysplasia; only medical therapy (metimazole to step down from a starting dose of 30 mg/day) for 2 years was needed and, actually, the patient is well. 2 M and 1 F had a diagnosis of autoimmune hypothyroidism (Increased blood level of TSH (mean 10 MU/L range 5-15 n.v. 0.6-5), low blood level of FT4 (mean 7 ng/ml range 3-8.5 n.v. 9-18) and presence of anti thyroglobulin and anti microsomal antibodies) and they actually are treated with L-Tiroxine therapy (mean dosage 75 mcg/day range 50-200). In all patients ultrasound didn't reveal thyroid nodules, but a marked ultrasound pattern alteration.

**Conclusion:** Thyroid function should be considered in patients affected by UC and, particularly, in patients with left colitis and pancolitis associated to severe disease activity.

**References:** [1] Snook L.A., De Silva H.J., Jewell D.P.: The association of autoimmune disorders with inflammatory bowel disease. *Q.J.Med.* 1989; 72: 835-40.

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**P103**  
**QUANTITATIVE EXPRESSION OF CD64 ON POLYMORPHONUCLEAR NEUTROPHILS: A NEW DIAGNOSTIC TOOL IN IBD**

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**Background:** Intestinal bacterial infections and non-inflammatory intestinal disorders, such as lactose or fructose intolerance (LFI), may present with symptoms similar to active inflammatory bowel disease (IBD). However, there is currently no discriminative laboratory marker available. Here, we investigated the utility of CD64 as a tool in differential diagnosis of IBD.

**Patients and Methods:** Expression of CD64 by PMN was determined by FACS analysis using a fluorescence quantitation kit (Quantibrite™ PE, BD Biosciences). We investigated patients with active (n=27) or inactive (n=49) IBD, infectious enterocolitis (n=24, i.e. Campylobacter [n = 13], Salmonella [n = 7], Shigella [n = 1], and Clostridium difficile [n = 3]), LFI (n=32), and healthy subjects (n=28). (Clinical measures of disease activity included the Crohn's disease activity index (CDAI) for patients with Crohn's disease (n=52), and the colitis activity index (CAI) for patients with ulcerative colitis (n=24). Active IBD was defined as CDAI > 150 and CAI > 6, respectively. Statistical

comparisons of means were done by t-test. Correlations were assessed by means of Spearman's correlation coefficient. Receiver operating characteristic curves were generated in order to define discriminative cut off values of CD64 expression. Data are given as median and range from the 25th to the 75th quartile (IQR).

**Results:** The quantitative expression of CD64 was significantly higher in patients with IBD (1125, 621-2083), than in healthy subjects (569, 387-756, p<0.01), or in patients with LFI (531, 435-605, p<0.001). In patients with active IBD the CD64 expression was significantly higher (2158, 1230-7709) than in patients in remission (755, 438-2109, p<0.0001). CD64 correlated with the CDAI (110, 44-197; 0.55, p<0.0001), the CAI (2, 0-5; 0.63, p<0.0001), and with serum of levels of CRP (0.93, 0.4-2.67; 0.65, p<0.0001). With a cut off point of 800 CD64 had a 96% sensitivity and a 97% specificity in discriminating between LFI and active IBD. In patients with infectious enterocolitis (15209, 11410-22965) the quantitative expression of CD64 was significantly higher than in patients with active IBD (4058±3590, p<0.001). With a cut off point of 10000 CD64 had a 88% sensitivity and a 93% specificity in discriminating between infectious enterocolitis and active IBD.

**Conclusion:** Assessment of the quantitative expression of CD64 on PMN allows to discriminating between active and remitting IBD, infectious enterocolitis, and LFI. Thus, CD64 may serve as a valuable diagnostic tool for the differential diagnosis and monitoring of IBD.

**P104**  
**THE ROLE OF ANORECTAL MANOMETRY IN ULCERATIVE COLITIS PATIENTS AFTER RESTORATIVE PROCTOCLECTOMY**

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**Introduction:** Patients after restorative proctocolectomy with pouch formation often present anorectal dysfunction that can be due to motility disorders. AIM OF THE STUDY: The aim of the study was to evaluate the changes in anorectal manometry in patients after restorative proctocolectomy.

**Material and Methods:** Anorectal manometry was performed in patients suffering from ulcerative colitis after final stage of restorative proctocolectomy with pouch formation. The study group consisted of 12 patients (8 females, 4 men), mean age 44,5 (21-72). Anorectal manometry was performed with 4-channel water perfused probe with latex balloon. After manometric evaluation the volumetric examination was performed using the balloon.

**Results:** Anorectal manometry: in 5 patients we found normal manometric features- normal resting and squeeze pressures. In 2 patients we found lower pressures of anal sphincters- in one resting and squeeze in other just squeeze pressure. In 5 (42%) squeeze pressures were far above normal (above 250 mmHg). Volumetric findings: In 2 patients the examination was not performed due to technical reasons. In 7 patients the volumetric finding were within normal: RAIR (recto-anal inhibitory reflex) was seen with mean volume of 60ml, first sensation with mean volume of 62ml, urge to defecate with mean volume of 80ml. In 3 patients (25%) first sensation nor RAIR was found to the volume of 100ml.

**Conclusion:** In patients after restorative proctocolectomy the adaptive changes can be seen due to prevent the involuntary defecation. In 25% changes in volumetric examination was found, probably due to innervation damage after the surgical treatment.

**P105**  
**SURGERY AT DIAGNOSIS OF CROHN'S DISEASE REDUCES THE NEED FOR STEROIDS AND IMMUNOMODULATORS**

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**Background:** The severity of clinical activity of Crohn's disease (CD) is high during the first year of the disease after diagnosis and subsequently declines. Half of patients requires steroids and immunomodulators and three quarters need for surgery. Surgery leads to a much more durable remission than that induced by medications, raising the possibility that early surgery may be more cost-effectiveness than the continued use of expensive medications.

**Aims:** Aim of the study is to evaluate whether surgery at diagnosis may reduce the subsequent need for medical and surgical therapy.

**Patients and Methods:** The records of 490 consecutive CD patients admitted at our GI units from 1980 to 2005 were reviewed. Patients were classified according to Vienna criteria. Gender, age at diagnosis, localization and clinical behaviour of the disease, extraintestinal manifestations, family history of IBD, appendectomy, smoking habit and therapies (salicylates, antibiotics, corticosteroids, immunosuppressives, infliximab, surgery) performed during

the follow up period were assessed. Out of the 490 patients, 115 (23.5%) underwent intestinal resection at diagnosis of CD; the remaining 375 patients (76.5%), not operated at diagnosis, served as controls.

**Results:** Patients with surgery at diagnosis of CD had lower need for steroids and immunomodulators during the follow up period compared to controls (OR 0.3,  $p < 0.0001$ ; OR 0.6,  $p < 0.004$ , respectively). Time to first operation was longer in the patients with surgery at diagnosis compared to controls (10.8 years vs 5.8,  $p < 0.01$ ). The stricturing disease and the penetrating disease were found to be risk factors for surgery at diagnosis of CD (OR 19.7,  $p < 0.0001$ ; OR 20.0,  $p < 0.0001$ , respectively).

**Conclusions:** Surgery performed at diagnosis of CD was associated to a lower need for steroids and immunomodulators compared to controls. The time to first operation was longer in the patients with surgery at diagnosis compared to controls. These data suggest that in CD the early surgery could be more cost-effectiveness than long term medical therapies.

#### P106

##### 5-AMINOSALICYLIC ACID (5-ASA)-MEDIATED BLOCK OF COLON CANCER CELL GROWTH IS ASSOCIATED WITH DEGRADATION OF CDC25A AND ACCUMULATION OF CELLS IN S-PHASE

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**Background and Aim:** Epidemiological observations indicate that 5-aminosalicylic acid (5-ASA) reduces the risk of developing CRC in patients with ulcerative colitis. However, the molecular mechanism underlying the antineoplastic effect of 5-ASA remains poorly characterized. In this study we have examined whether 5-ASA modulates CRC cell growth and analyzed its effects on cell cycle checkpoints.

**Methods:** CRC cell lines (i.e. HCT-116, HT-29 and CT-26) were treated with graded doses of 5-ASA (5–30 mM) for 48 hrs, and then cell cycle and proliferation were evaluated by FACS. Both phosphorylated and total CDC25A, CHK1 and CHK2 were evaluated in total extracts of 5-ASA-treated cells by Western blotting. Moreover, we evaluated the effect of 5-ASA on the development of CT-26-derived xenografts in mice.

**Results:** 5-ASA dose dependently inhibited CRC cell growth. The 5-ASA-mediated anti-mitogenic effect was reversible and associated with no change in CRC cell survival, and accumulation of cells in S-phase. Consistently, 5-ASA enhanced phosphorylation and degradation of CDC25A, a phosphatase necessary for promoting the G1-S phase transition and S-phase progression. Time-course analysis showed that CDC25A phosphorylation was preceded by activation of the upstream kinase CHK2. Finally we showed that administration of 5-ASA to Balb/c mice markedly reduced the development of CT-26-derived colon cancers.

**Conclusions:** These data support further the notion that 5-ASA negatively regulates CRC cell growth, thus bringing new insights into the molecular mechanism underlying the antineoplastic action of this drug.

#### P107

##### BENIGN INTRACRANIAL HYPERTENSION AND INFLAMMATORY BOWEL DISEASE. A NEW EXTRAINTestinal MANIFESTATION OR AN ADVERSE EFFECT OF THERAPY?

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Benign intracranial hypertension (BIHT) is a rare condition, of unknown cause, in which intracranial pressure is risen without an organic cause, and with a normal cerebrospinal fluid (CSF) composition. The use of some drugs, most notably steroids, can be associated to the production of such condition. We present three cases of BIHT observed in inflammatory bowel disease (IBD) patients, that rise the possibility of BIHT being an extraintestinal manifestation of the disease. Case 1: 28-year-old woman diagnosed of Crohn disease Montreal A2 L2 B1 since November 2002. In September 2002 she underwent neurological evaluation for the subacute appearance of headache and impaired vision. The ophthalmologic examination revealed a bilateral papilloedema. At that time she was receiving a weaning off steroids therapy and mesalazine. Lumbar puncture identified an opening pressure of 50cm H2O. The cranial CT and MRI were normal. Case 2: 64 year-old man diagnosed of left-sided ulcerative colitis since June 2002. In January 2006 he underwent neurological evaluation for the acute appearance of impaired vision without headache. At that time he was receiving a weaning off steroids therapy and mercaptopurine. The CSF composition was normal. Lumbar puncture revealed an opening pressure of 45cm H2O. The cranial CT and MRI were nor-

mal. Case 3: 17-year-old man diagnosed of Crohn disease Montreal A1L3B1 since May 2003. In September 2004 he developed orbital headache of moderate intensity without blurred vision. At that time he was receiving a weaning off steroids therapy. An ophthalmologic evaluation identified bilateral papilloedema. Cranial CT and MRI excluded both the presence of a mass in the brain and venous thrombosis. These three cases were observed along three years and represent a 0.004% of 690 patients followed in our outpatient IBD Clinic.

**Conclusions:** 1. Although aminosalicylates are the most frequent cause of headache in IBD patients, one should be aware to exclude other causes, such as BIHT. This is specially true in patients treated with steroids, perhaps more so during weaning. 2. Our findings highlight even more the fact that impaired vision must be evaluated with care in IBD patients, because they can be the manifestation of significant and treatable causes (uveitis, BIHT).

#### P108

##### VISILIZUMAB THERAPY IN SUBJECTS WITH MODERATE-TO-SEVERE, REFRACTORY CROHN'S DISEASE

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**Purpose:** We evaluated the safety and clinical activity of visilizumab, a humanized anti-CD3 monoclonal antibody in an open-label, phase I study in moderate-to-severe inflammatory non-fistulizing Crohn's Disease (CD).

**Methods:** Subjects with a CDAI more than 250, a CRP more than 4 mg/L, and endoscopic evidence of active disease were administered i.v. bolus injections of visilizumab 10 µg/kg on 2 consecutive days (Days 0 and 1). Clinical response was defined as a decrease in the CDAI of more than 100 points below the subjects' baseline value, and remission as a CDAI less than 150 at D59. Biopsies from a subset of 6 subjects were evaluated by immunohistochemistry at pre-therapy and Day 59.

**Results:** Seventeen of 18 enrolled subjects received both doses (1 subject withdrew after the first dose); 13 treated subjects were followed through to Day 89. The median baseline CDAI was 396 (271–516), and the median baseline CRP was 28 mg/L (2–70). Nine subjects were oral or IV steroid-resistant, 6 were oral or IV steroid-dependent, and 3 were steroid-independent. Seventeen subjects had received prior infliximab (IFX); 5 were primary IFX non-responders, 2 had had intolerable infusion reactions, and 10 had discontinued IFX due to loss of activity. By Day 29, responses were seen in 11/18 subjects, clinical remission in 5/18. More than half (13/18) of the subjects had a clinical response to visilizumab at Day 59, and 5 were responders at 6 months. Remission by Day 59 was achieved in 6/18 subjects. The median D59 CDAI was 266 (69–570). On average, in visilizumab responders, the CRP decreased by more than or equal 50% by or before Day 15. By Day 59, all 6 subjects for whom paired biopsies were available showed evidence of mild to moderate histological improvement. Mild to moderate cytokine release syndrome (CRS) occurred in the majority of subjects. The adverse event (AE) profile, including their severity, incidence, and drug relatedness were similar to that previously seen in IVSR-UC subjects who had received an equivalent dose of visilizumab (10 µg/kg × 2). No lymphoproliferative, malignant or life-threatening AEs were reported.

**Conclusion:** Two 10 µg/kg visilizumab doses administered as IV bolus injections on consecutive days were tolerated and produced a rapid and sustained improvement in 11/18 subjects with moderate-to-severe, refractory CD.

#### P109

##### DOSE-DEPENDENT INFLUENCE OF 5-ASA ON THIOPURINE METABOLISM

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**Introduction:** Thiopurines are frequently administered immunosuppressive drugs in the treatment of inflammatory bowel disease (IBD). A substantial number of patients is unable to benefit from thiopurine therapy due to the development of inadequate metabolites levels. Several studies indicated that 5-aminosalicylates (5-ASA) may influence the metabolism of thiopurines but conclusions were restricted due to the number of patients or study design.

**Aims & Methods:** We prospectively investigated the influence of two