IBD’s case in the whole country and for a system of alertness with active search in five departments. It was done a retrospective study considering from 1991 to May 2006, and another one prospective from June 2006 to June 2007. It was analyzed the distribution by sex, age, smoke, phenotype and requirement of surgery.

Results: From 335 entered patients, there were analyzed 292 cases (87%). Ulcerative Colitis (UC) 198 (68%), Crohn Disease (CD) 88 (30%) and Indeterminate Colitis (IC) 6 (2%). Is known the place where the disease started in 268 cases, from which are registered in the capital 176; UC 106, and CD 66. The average rate of prevalence in the analyzed departments was a 13/100.000 inhabitants changing from 8.9 to 19.9/100.000 being major in the south of the country, where the capital is located.

Absence of CD was observed in the departments distant to the capital and of minor prevalence of IBD. The 80% of the cases appear after the 80s, being more accelerated the UC at the beginning, but tending to become stable. The CD on the other hand has a constant growth (table). They are more frequent in women (1.4:1). At diagnosis, the middle age in the UC is 34 years (maximum 76 minimal 3), making debut 68% between 20 and 50 years old. Location: proctitis 17.5%, left side 50.8%, pancolitis 27.6%. With the evolution of the disease it is registered an increase of 11% in the pancolitis. Required surgery 11%. Between 16 and 40 years old is debut of 70% of the CD patients. The location is ileum in 40%. Present perianal affection 42%. Required surgery 69% of the patients, of them 48% was ileum affection.

The habit of smoking was registered in 32% of the CD and 13% of UC.

Conclusions: In Uruguay is observed an increase of both diseases, with an initial increase of UC that overcomes the CD, but that tends to become stable whereas continues in ascent the CD. This is similar to what happens in areas of major prevalence.

The average rate of prevalence in the analyzed departments was of 13/100.000 inhabitants; being lower as it was expected compared to countries of the north hemisphere. The majority of CD’s cases are registered in the capital, and all of them appear in the south of the Rio Negro (major population density and urbanization zone).

Both Diseases are more frequent in women. The age of beginning and the location is similar in both sexes.

The percentage of UC with surgery is minor than in other countries and similar in the CD.

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TREATMENT INFLUENCES CARD15 GENE EXPRESSION IN CROHN’S DISEASE PATIENTS

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Aim: Familial aggregations of Crohn’s disease (CD) have suggested the influence of genetic factors in the disease development. CARD15 gene has been the first susceptibility gene known for CD.

Aim of our study was the evaluation of CARD15 gene expression in CD patients living in Lower Silesia, Poland with respect to the treatment strategy.

Material and method: CARD15 gene expression was assessed in 90 individuals: 60 patients with CD (30 females, 30 males) hospitalized in Department of Gastroenterology and Hepatology, Wroclaw Medical University and in the control group (30 healthy volunteers). CD patients were divided into subgroups with respect to method of treatment: steroid, azathioprine or anti-TNFalfa therapy. CARD15 gene expression was measured in peripheral mononuclear cells using real-time RT-PCR. Total RNA was extracted using E.Z.N.A. Total RNA Kit (Omega Bio-Tek). Total RNA was reverse transcribed by the TaqMan Reverse Transcription Reagents (Roche). All quantitative real-time PCR (TaqManTM) primers, probes and Universal master mix were obtained from Applied Biosystems (USA). All PCRs were performed utilizing 5 µl cDNA per reaction in triplicates of 25 µl volume on a ABI Prism 7900HT Sequence Detection System (Taqman) using a 2-step PCR protocol after the initial denaturing of the cDNA (10 min at 95°C) with 45 cycles of 95°C for 15 s and 60°C for 1 min. cDNA aliquots were quantified for target genes using the threshold cycle (Ct) method normalized for the house keeping gene GAPDH.

Results: There was significantly increased CARD15 expression in either steroid or azathioprine CD patients. Contrary, we found significantly decreased CARD15 expression in CD patients treated with anti-TNFalfa agents.

Conclusion: Treatment can influence CARD15 expression in Crohn’s disease patients.

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15 YEARS ON: THE OUTCOME OF THE IRISH EC-IBD COHORT

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Introduction: The formation of the European Collaborative on inflammatory bowel disease, EC-IBD between 1991 and 1993 was a major step in prospectively collecting a population based large cohort for long term follow-up.

Data generated from such study will act as the basis for understanding the nature of chronic diseases (for example IBD) at a local and regional level, in order to formulate future strategies for the evaluation of IBD and it’s management in the pre and post biologics era.

Patients and Methods: A total of 192 Irish patients from the ERBH (Eastern Regional Health Board) were recruited between 1991 and 1993 and were followed for 15 years. 55 patients had a confirmed diagnosis of Crohn’s and the rest (n=137) had Ulcerative Colitis. All patients on records were contacted by telephone over a period of six months. Patients whose contact details were not valid had been traced through either their family general practitioner or their referring hospital or even their family. The cause of death of those deceased since the last contact was identified through reference to the death registry.

Results: Of the initial 192 patients recruited at the inception phase, 6 were found not to have IBD. 11 were unwilling to complete the study and therefore were excluded. Of the remaining 175 patients 25 deceased over the study period (22 had none IBD related death). At 15 years 91 patients were contactable and the rest were excluded due to incomplete data entry (30) or untractability due to change of address (29).

Of those who were contacted, 42 patients were in clinical remission on medical therapy for inflammatory bowel disease and further 31 patients in remission without current IBD maintenance therapy and 18 patients were having relapses. The total number of patients in remission was 73 (17 in the CD group and 56 in the UC group).

Conclusion: This cohort evaluated one of the biggest and longest prospective follow up studies undertaken in Ireland for a chronic condition, of unknown aetiology.

The presence of a large cohort is essential to evaluate disease outcome and response to treatment modalities over time.

This is an objective way of evaluating our practice and the natural history and treatment methods of IBD in Ireland during the evolution of medical therapy.

One of the identified limitations of this study was the incomplete data entry and loss of patients follow up over long period of time. This limitation needs to be taken into account when considering new long term follow up studies in order to minimise the level of non health related attrition.

Therefore, we propose the formation of a national registry for IBD patients in Ireland. This will facilitate research in this chronic disease particularly in view of recent advances in clinical management.

P245

ASSOCIATION OF SEROTONIN TRANSPORTER GENE POLYMORPHISMS WITH CROHN’S DISEASE (CD) PHENOTYPES

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Background and Aims: Serotonin (5-HT) is key mediator in intestinal peristalsis, secretion, vasodilatation and sensory signalling. The serotonin-selective reuptake transporter protein (SERT) terminates the action of 5-HT. Human SERT is encoded by a single gene on chromosome 17q11; 2 important polymorphic sites in the SERT gene are: variable number tandem repeats in the gene’s second intron (SERTi2), and an insertion/deletion in the promoter region (SERTPR). Regarding to behaviour, CD has 3 different phenotypes: inflammatory, penetrating and strictureting. The reason for this differentiation isn’t understood. Consistent with the effects of 5-HT in the gut, SERT polymorphisms could potentially be involved in the development of different phenotypes. The aim of this study was to assess the correlation between SERT polymorphisms (SERTPR, SERTi2) and CD phenotypes.

Methods: According to Vienna classification 114 CD patients were phenotyped in three groups: inflammatory (group 1), penetrating (group 2), and strictureting (group 3). SERT genotyping was performed by the PCR method. A test for Hardy-Weinberg equilibrium as well as linkage-disequilibrium likelihood-ratio test was performed. Haplotype frequencies were estimated using Expectation-Maximization algorithm, leading to maximum likelihood estimates of haplotype frequency. Chi squared test was used for comparisons of the allele and genotype frequencies among groups. Log likelihood-ratio tests were performed to compare distributions of the estimated haplo-
types among groups. All statistical analyses were carried out using SPSS 11.0 (SPSS Inc., Chicago, IL, USA) statistical software package.

Results: Genotype frequencies of the SERTPR LL, LS and SS in the sample were 35, 62 and 17, respectively and of the SERTII LL, IS and ss genotypes were 50, 48 and 16, respectively. No significant deviations from the expected Hardy-Weinberg proportions were observed. Test result for linkage disequilibrium between loci was significant in total sample (p<0.018, x² = 5.525, d.f.=1), group 1 (p<0.02, x² = 5.35, d.f.=1), although not in group 2 (p=0.09, x² = 2.80, d.f.=1) and group 3 (p=0.88, x² = 0.03, d.f.=1). Statistical differences were found in distributions of the estimated haplotypes among those groups for both loci (x²=14.8, d.f.=6, p<0.022). Subsequent analyses showed statistical differences in distributions of the estimated haplotypes between groups 1 and 3, and 2 and 3 (Group 1 vs. group 3: x²=11.14, p=0.012, d.f.=3). Group 2 vs. group 3: x²=11.4, p=0.01; d.f.=3). Those results remained positive also after correction for multiple testing. In subsequent analyses, SS vs. others, Ss haplotype was found to be significantly different distributed among groups (x²=7.16, p=0.028, d.f.=2), due to differences between groups 1 and 3, and 2 and 3 (H4 vs. others, group 1 vs. group 3: x²=4.97, p=0.026; d.f.=1, group 2 vs. group 3: x²=4.45, p=0.035; d.f.=1). These significances were last after correction for multiple testing.

Conclusion: Polymorphisms of SERT gene could be associated with development of different phenotypes of CD.

P246 UNIQUE ROLE OF JUNCTIONAL ADHESION MOLECULE-A IN MAINTAINING MUCOSAL HOMEOSTASIS IN INFLAMMATORY BOWEL DISEASE

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Junctional adhesion molecule-A (JAM-A) is a protein localized at the tight junctions of epithelial and endothelial cells. JAM-A is involved in the control of transcytosis of cytokine and infiltration into the tissues, and in regulating cell junction assembly.

Human colonic, Crohn’s disease (CD) and ulcerative colitis (UC) specimens were studied for JAM-A expression by confocal microscopy and western blot, as well as in healthy and colitic mice undergoing dextran sulphate sodium (DSS) treatment.

JAM-A is involved in the control of transcytosis of cytokine and infiltration into the tissues, and in regulating cell junction assembly. The activity of JAM-A is influenced by several factors, including cytokines, growth factors, and cell-cell interactions.

Conclusion: JAM-A is involved in the control of transcytosis of cytokine and infiltration into the tissues, and in regulating cell junction assembly.

P247 CHRONIC TRICHURIASIS: A NOVEL MURINE MODEL OF INFLAMMATORY BOWEL DISEASE

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Background: Murine experimental models of colitis have contributed greatly to pathophysiological and therapeutic advances in Inflammatory Bowel Disease (IBD). Models permit correlation of phenotype, histology, immune response, and conserved mucosal gene expression. However, due to the heterogeneity of IBD, no single model can integrate all pathogenic or clinical features. Thus multiple models, with individual strengths and weaknesses, have developed. Trichuris muris nematode infection induces chronic colitis in susceptible mouse strains. This model displays both a polarised Th1 response and a histological similarity to IBD. Conversely, resistant mouse strains exhibit transient infection, inflammation quickly resolving with a presiding Th2 response. These pivotal strain differences may therefore provide novel clues to the genomic determinants of susceptibility or resistance to chronic colitis.

Aim: 1) Assess colonic mucosal gene expression in resistant and susceptible mouse strains following T.muris infection. 2) Compare the gene expression profile of T.muris induced chronic colitis to published data, both IBD and other murine models.

Method: Susceptible (AKR) and resistant (BALB/c) mice were administered 300 T.muris ova by oral gavage. Naive animals were compared to day 35, a chronically infected time-point in AKR mice. Worm count, serum IgG, colonic histology and mRNA were analysed. Gene expression was quantified using PCR microarrays, targeting innate and adaptive immune pathway transcripts (Superarray®). Genes differentially expressed between naive and infected animals were regarded as potentially significant if increased or decreased >2-fold.

Results: Colonic inflammation, with focal thickness lymphocytic infiltration, was only seen in infected AKR mice. A dominant Th1 immune response was highlighted in AKR mice, and a Th2 immune response in BALB/c’s, by serum IgG-isotype profiling.

Of 160 genes analysed, 30 were significantly up-regulated and 38 down-regulated in infected AKR mice. Expression of these 68 genes was similarly polarised in infected BALB/c mice for 29 genes (16 up, 13 down); yet oppositely polarised in 39 (14 up AKR vs down BALB/c; 25 down AKR vs up BALB c). Of these 39 strain-discriminating genes, the expression profiles of 13 tracked IBD findings, whereas 3 differed from IBD in their direction of change. For the remaining 23 genes, no data regarding expression in IBD currently exist, providing novel candidates for further study.

Comparison with other published murine model data shows T.muris colitis gene expression in AKR mice is closer to human IBD than DSS or TNBS colitis, and similar to CD4CD45R0+ induced colitis.

Conclusion: Chronic Trichuriasis offers a validated, immuno-competent and reproducible tool for colitis research. Showing clear biological commonalities with human IBD, this antigen-driven natural model of colitis may allow identification of the differential mechanisms governing outcome, potentially highlighting genes that determine whether or not resolution of mucosal inflammation occurs. Further comparative analysis of the chronic colitis vs resolution phenotypes may highlight new disease markers or therapeutic targets, and additionally inform future human genetic studies.

P248 ATTENUATED TNF-α RELEASE FOLLOWING TOLL-LIKE RECEPTOR STIMULATION OF MACROPHAGES IN CROHN’S DISEASE

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Introduction: Although the aetiology of Crohn’s disease (CD) remains an enigma, strong evidence suggests that microbial components are involved in the pathogenesis. Recent work provides compelling evidence of a failure of acute inflammation in CD and suggests that the primary defect operates at the level of the macrophage. Macrophages play a major role in the induction of inflammatory responses to microbes via Toll-like receptors (TLRs), producing a variety of pro-inflammatory chemokines and cytokines. Tumour necrosis factor-α (TNF) is a pivotal pro-inflammatory cytokine and a major target of biologic therapy. Elevated TNF levels have been well described during the T cell-driven chronic inflammatory phase of CD, but little is known about levels during the preceding acute inflammatory response in these patients.

Aims/Methods: To assess whether the TR2 and/or TR4 response is defective in CD, TNF release by peripheral blood-derived macrophages was measured following challenge with the bacterial ligands Pam3Cys (TLR2) and LPS

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