P102
Altered epithelial tight junction expression and elevated IL 6 levels in pouchitis
J. Landy1, H. Omar Al-Hassi2, E. Ronde3, E. Mann2, S. Peake1, R. Man1, E. Ciclitira4, R.J. Nicholls5, S.K. Clark6, S. Knight2, A.L. Hart1 *
1St Mark’s Hospital, IBD Unit, London, United Kingdom, 2Antigen Presentation Research Group, Imperial College, London, United Kingdom, 3St Mark’s Hospital, Endoscopy Department, London, United Kingdom, 4St Thomas’ Hospital, Gastroenterology, London, United Kingdom, 5Imperial College, Department of Biosurgery and Surgical Technology, London, United Kingdom, 6St Mark’s Hospital, Colorectal Surgery, London, United Kingdom

Background: Intestinal epithelial barrier function limits the interactions between microbial antigens and the mucosal immune system. In IBD, epithelial barrier function is impaired with altered expression of tight junctions. We aimed to assess epithelial tight junction expression and mucosal cytokines in acute and chronic pouchitis and non-inflamed pouches of patients with ulcerative colitis.

Methods: Mucosal biopsy samples were taken from ulcerative colitis patients with pouchitis (chronic pouchitis n = 9, acute pouchitis n = 4) and those without pouchitis (n = 11). Epithelial cells were isolated from biopsy tissue after incubation with DTT and EDTA. Epithelial cell expression of ZO-1, claudin 1 and claudin 2 were measured by multicolour flow cytometry. Cytokines were assessed by multiplex ELISA of biopsy supernatants. The t-test was used for statistical analysis.

Results: In acute pouchitis ZO-1 was elevated compared with both chronic pouchitis and non-pouchitis (p = 0.008), whilst in chronic pouchitis ZO-1 expression was reduced compared with non pouchitis (p = 0.006). Claudin 1 expression was reduced in chronic pouchitis (p = 0.04), but not significantly reduced in acute pouchitis. In acute pouchitis, claudin 2 expression was elevated (p < 0.001), but was not increased in chronic pouchitis. IL6 levels were elevated in chronic pouchitis compared with non pouchitis patients (p = 0.01).

Conclusions: Epithelial tight junction expression was altered in pouchitis in association with increased IL6 levels. Increased claudin 2 expression in acute, but not chronic pouchitis may represent early pathological changes in the development of pouch inflammation. In chronic inflammation the tight junction complex was deranged with reduced expression of both claudin 1 and ZO-1. Increased epithelial barrier permeability due to altered tight junction expression may be a critical mechanism in the development and perpetuation of pouch inflammation.

P103
Adding fuel to the fire – neutrophils as antigen presenting cells in Crohn’s disease
R. Somasundaram1 *, C.J. van der Woude1, M. Peppelenbosch1, G. Fuhrer1. 1Erasmus mc, Gastroenterology and Hepatology, Rotterdam, Netherlands

Background: Neutrophils (PMN) are the first line of defence against bacterial infection. However, they may also act as antigen-presenting cells (APCs), as is observed in inflammatory diseases like rheumatoid arthritis and bacterial infections. During inflammation, PMN are exposed to proinflammatory cytokines which not only influence PMN survival, but upon prolonged exposure can also lead to their dedifferentiation towards an APC-like phenotype. PMN influx at the site of inflammation in Crohn’s disease (CD) has been described. However, the functional consequences of their presence remain controversial. Here, we show that PMN in mucosa from CD patients acquire APC characteristics.

Methods: Freshly isolated peripheral blood PMN from healthy volunteers (HC) and CD patients were cultured for 3 days in the presence of GMCSF 50U/ml, IFNγ 100U/ml, IL4 3 ng/ml.

Expression of CD80, CD86, MHCII on CD66b+ PMN were measured by flowcytometry in peripheral blood and single cell suspensions from biopsies. PMN expression of MHCII at the site of inflammation was determined by double labelling of biopsies.

Results: PMN present in the peripheral blood from CD patients and HCs did not express the co-receptors for antigen presentation. However, mucosal PMN from fresh CD biopsies did express APC co-receptors, both at site of inflammation and in non-inflamed regions (n = 5, 13±2% of PMN vs 15±6%). In contrast, mucosal PMN from healthy control biopsies did not express CD80, CD86 or MHC II. As a confirmation of the flowcytometric data, biopsies from CD patients and HCs were stained for MHCII in conjunction with the PMN marker CD66b. Double positive cells were found only in active CD colonic and small intestinal biopsies. To investigate whether the propensity to dedifferentiate was intrinsically enhanced in CD PMN, peripheral blood PMN were cultured in the presence of a cytokine cocktail, inducing dedifferentiation and expression of CD80, CD86, MHC II. However, similar percentages of PMN expressed APC markers in CD (9±6%, n = 8) and HC (15±10.6%, n = 11) in vitro.

Conclusions: We show for a first time that a subset of PMN in active CD patients expresses APC co-receptors. Induction of redifferentiation of PMN from CD and HC in vitro is not different, indicating that in all likelihood, the local presence of pro-inflammatory cytokines induces this dedifferentiation of mucosal PMN in CD patients. This may serve to enhance presentation of bacterial antigens to T cells, thereby adding fuel to the already over-activated T cell response in CD.

P104
Adalimumab for induction of clinical remission in moderately to severely active ulcerative colitis in Mexican population
F. Gonzalez1 *, T. Cortes1, M. Ramos1. 120 de Noviembre National Medical Center, ISSSTE, Gastroenterology, Mexico City, Mexico

Background: Despite the available treatments for ulcerative colitis (UC), a big number of patients relapse. Adalimumab (ADA) is a human monoclonal antibody targeted to TNF-α. It has been recently approved in Europe, and in the United States the use of ADA in UC is based on the ULTRA-1 and ULTRA-2 trials.

Methods: Retrospective, cross-sectional trial.

Determine the location and activity of the disease prior to the use of ADA and evaluate the clinical response obtained by week 12 using the mayo score, the endoscopic activity index and C reactive protein (CRP) in patients naïve to treatment with biologics, and in patients previously treated with biologics (Infliximab) who did not achieve remission of the disease after 24 weeks of treatment.

Results: 20 patients were analyzed. 11 had prior treatment with biologics and 9 were naïve to biological treatments. In the group treated with biologics, 36% were males, mean age 44.7 years; females represented 63% with a mean age of 46 years. In the biological treatment naïve group 67% were females, mean age 50.6 years; 33% for males and mean age of 61.3 years. The location of the disease measured by the Montreal classification for the biological treatment naïve group was 66% in E3, E2 22%, and E1 11%. For the pretreated patients with biological treatment the extension of the disease was of 36% in E2 and E1, and 28% in E3. The clinical activity evaluated according to the Mayo Score in the biological treatment naïve group was in average 9 for the pre-treatment, and 6 post-treatment (p = 0.001). In the group treated with biologics an average Mayo Score of 9 in the pre-treatment, and 6 post-treatment (p = 0.001) were observed. The endoscopic index evaluated in both groups showed no statistically significant difference in the biologics naïve patients group (p = 0.63). With respect to CRP no statistically significant difference was