used for quantitative real-time PCR, with multiparameter flow cytometry utilised to measure hydrogen peroxide levels, apoptosis, DNA damage and cell proliferation.

**Results** DUOX2 is expressed throughout the colonic epithelium, is upregulated in active compared to quiescent ulcerative colitis and also in areas of UC associated dysplasia. In the setting of intestinal inflammation, but not in quiescent disease, 5-ASA enhances DUOX2 expression in vivo and ex vivo. As expected, 5-ASA was found to suppress cytokine (IL-6 and IL-8) production during an inflammatory flare and to maintain low cytokine levels during remission. The addition of 5-ASA in vitro led to upregulation of DUOX2 and elevated levels of hydrogen peroxide, DNA damage and apoptosis. These effects were further enhanced in a setting of hypoxia.

**Conclusion** We have shown that 5-ASA over stimulates DUOX2 expression in the setting of inflammation and hypoxia, but not in quiescent disease. Importantly, this suggests that during a flare 5-ASA could act as a carcinogen rather than a chemo-preventative drug. Further investigations to confirm the functional relevance of DUOX2 up-regulation in the colonic mucosa of patients with active UC is indicated.

**Competing interests** None declared.

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**PWE-256**

**INTESTINAL INFLAMMATION REGULATES RETINOIC ACID DEPENDENT IMPRINTING OF GUT TROPISM BY DENDRITIC CELLS INDEPENDENTLY OF RALDH EXPRESSION**

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T J Sanders,* 1N E McCarthy, 1E Giles, 2J O Lindsay, 1A J Stagg. 1Centre for Immunology and Infectious Disease, Blizard Institute, London, UK, 2Digestive Diseases Clinical Academic Unit, Barts & The London School of Medicine & Dentistry, London, UK

**Introduction** In the mouse, tissue-specific expression of retinaldehyde dehydrogenase (RALDH) enzymes by CD103+ intestinal dendritic cells (DC) enables them to generate all-trans retinoic acid (RA) and thereby imprint a gut-tropic phenotype on T cells via induction of homing receptors including CD103. In contrast, the ADH enzymes Clinical Academic Unit, Barts & The London School of Medicine & Dentistry, London, UK

**Methods** Conditioned media (CM) were generated by culture of intestine-derived DC or CD103+ non-inflamed tissue. CM were added to naïve allogeneic CD4+ T cells in a 1:1 ratio and RALDH activity assessed using the Aldefluor assay. Induction of 4β7 following activation of naïve allogeneic CD4+ T cells was determined by flow cytometry.

**Results** Activation of naïve CD4+ T cells by human monocyte-derived DC resulted in RA-dependent upregulation of 4β7. These DC possessed retinal-inhibitable Aldefluor activity and expressed both alcohol dehydrogenase (RDH10) and RALDH (RALDH1,2,3) enzymes required for the generation of RA from retinol via retinal. Aldefluor activity was regulated by GM-CSF and RA, and reflected predominately the activity of RALDH2 as suggested by qRT-PCR analysis of sorted Aldefluor+ DC. CM significantly suppressed Aldefluor activity (p<0.0001) irrespective of whether generated from healthy or IBD tissue (inflamed or non-inflamed). The inhibitory effect of CM generated from healthy tissue could be partially reversed with the prostaglandin E2 (PGE2) EP-2 receptor antagonist AH6809 but this effect was less marked with CM from IBD tissue suggesting the involvement of distinct RALDH regulators. Although the effects of inflamed and non-inflamed CM on Aldefluor activity were similar, DC differentiated in the presence of inflamed CM induced significantly higher (p<0.05) levels of CD4 T cell 4β7 expression.

**Conclusion** Factors generated in the human intestinal mucosa limit RALDH activity in DC and may thereby impact upon their generation of RA. Factors other than PGE2 are involved particularly in inflamed tissue. Intestinal mediators influence the imprinting of gut tropism independently of effects on RA-generating enzymes. Manipulation of RA availability may offer new therapeutic options in IBD.

**Competing interests** None declared.
“downstream” RALDH enzymes. These data imply that RA availability is regulated differently in mice and men, with expression of RDH10 providing an important control point in humans.

**Competing interests** None declared.

**PWE-258** THIOPURINE MONITORING IN INFLAMMATORY BOWEL DISEASE PATIENTS AT A DISTRICT GENERAL HOSPITAL

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1 T Jowitt,* 1 C Bowman, 2 M Ahmed, 3 S Singh, 2 C H Lim. 1 Medical School, University of Birmingham, Birmingham, UK; 2 Department of Gastroenterology, Good Hope Hospital, Sutton Coldfield, UK

**Introduction**

Thiopurines are an unlicensed but recognised therapy for Inflammatory Bowel Disease (IBD). These drugs interfere with cell signalling and have significant side effects including leucopaenia, pancreatitis and hepatotoxicity. Therefore routine monitoring of blood is mandatory. We have a Trust guidelines (based on BSG guidelines) for the monitoring of Thiopurine therapy. Patients are monitored by an IBD Nurse specialist using a simple electronic database.

**Methods**

**Objective:** To determine the effectiveness of the IBD Nurse database in ensuring that patients on Thiopurines are monitored according to Trust guidelines. A total of 900 patients with IBD attend our gastroenterology clinics. Of these 204 are on Thiopurines. Trust guidelines recommend weekly blood test monitoring for the first month starting Thiopurines. This is followed by monthly for the next 3 months and every 3 months subsequently. Patients latest blood results were collected over a two consecutive days in July 2011 for 204 patients. Patients more than 7 days late for blood tests were considered non-compliance with the guideline.

**Results**

182 (89%) patients were having their bloods monitored as per trust guidelines. However, 22 patients (11%) were being monitored incorrectly, with a median of 68.5 (32.25–269.25) days overdue. 16 of these patients have a diagnosis of Crohn’s Disease, the remaining six have Ulcerative Colitis. 14 (7%) patients had either deranged liver function tests or were neutropaenic.

**Conclusion**

The current manual database is reliable as the majority of thiopurines patients were being monitored as per hospital guidelines. However, 7% of abnormal blood results may not be recognised promptly and no action was taken. An automated database with automated reminder to patients who passed their blood test due date and electronic notice to the doctor responsible for the patient is needed to reduce the potential risk of harm to the patients.

**Competing interests** None declared.

**REFERENCE**


**PWE-259** THE EFFICACY OF METHOTREXATE IN CROHN’S DISEASE: A CLINICAL PERSPECTIVE

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T T Gordon-Walker,* M W Stahl, M Groome, J Todd, N Reynolds, C Mowat. Department of Gastroenterology, Ninewells Hospital, Dundee, UK

**Introduction**

Methotrexate (MTX) has been shown in clinical trials to be effective in the induction and maintenance of remission in Crohn’s Disease (CD). It is predominantly used in patients intolerant of, or whose disease is refractory to, thiopurine treatment. It was our aim to examine, in a clinical setting, the efficacy and side-effect profile of MTX in patients with CD.

**Methods**

A retrospective audit was performed by casenote review of all patients with CD attending the clinical investigations unit at Ninewells Hospital to commence parenteral MTX during the period 1 January 2007 to 31 December 2010. A total of 53 patients were identified, for whom casenotes were available in 52 (26 male/26 female). Intramuscular MTX treatment was initiated at a dose of 25 mg once weekly for 16 weeks, followed by oral MTX at a dose of 15 mg once weekly. Clinical response by physician’s global assessment was recorded at 3, 6 and 12 months. Clinical response was defined as complete response (absence of IBD symptoms or complete healing of fistulae); partial response (symptomatic improvement but ongoing symptoms); or no response (no improvement or deterioration from baseline). Relapse was defined as deterioration in symptoms necessitating additional medical or surgical intervention.

**Results**

Median age of starting MTX was 32 (range 15–73). 51 of 52 patients had previously received thiopurine treatment. 12-month follow-up data were available for 46 patients. 34 patients were taking steroids at the time of initiating MTX. At 12 months, complete response was reported in 8 patients (17%), partial response in 6 patients (12%), no response in 21 patients (44%) and drug withdrawal due to side effects in 15 patients (27%). Relapse was reported in 17 patients (35%). 10 patients (21%) required additional medical therapy (steroids or biological therapy). Surgical intervention was required in seven patients (13%). Steroid withdrawal at 1-year, without recourse to biological or surgical therapy, was reported in only 11 of 34 patients (32%). MTX-associated side effects were reported in 25 patients (48%). Reported side effects included: LFT abnormalities (9), nausea (8), lymphopenia (5), lethargy (3) and mouth ulceration (1). Monitoring of FBC/LFTs was performed at 97% of scheduled weekly intervals for patients receiving parenteral MTX and at 74% of scheduled monthly intervals for patients on oral MTX.

**Conclusion**

In this cohort, the clinical effectiveness of MTX in the induction and maintenance of remission of CD was limited. Only 29% of patients had either a complete or partial response to therapy at 1-year. The clinical effectiveness of MTX was limited by side-effects in 27%. On the basis of these results we should re-consider the position of MTX in the management of CD.

**Competing interests** None declared.

**PWE-260** OPTIMAL C REACTIVE PROTEIN CUT-OFF POINT FOR PREDICTING HOSPITALISATION IN PATIENTS WITH MODERATELY ACTIVE CROHN’S DISEASE

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1 J-F Colombel, 2 W J Sandborn, 3 E Louis, 4 R Panaccione, 5 R B Thakkar, 6 M M Castillo, 5 M Yang, 6 Finney-Hayward, 5 J Zhao, 5 P M Mulani. 1 Centre Hospitalier Universitaire de Lille, Lille, France; 2UCSD, La Jolla, California, USA; 3U of Lübeck, Lübeck, Belgium; 4U of Calgary, Calgary, Alberta, Canada; 5Abbott Laboratories, Abbott Park, Illinois, USA; 6Abbott Laboratories Ltd, Maidenhead, Berkshire, UK

**Introduction**

To identify high risk patients among patients with moderately active CD and identify CRP concentration and hospitalisation risk for patients with moderately active CD and identified the optimal CRP cut-off point as a marker to predict CD-related hospitalisation. CRP is a well-studied and commonly used laboratory marker of inflammation in CD. The relationship between CRP and hospitalisation risk given the same Crohn’s Disease Activity Impairment (CDAI) score in patients with moderate CD has not been studied.

**Methods**

Data from CHARM, a 56-week (wk), randomised, placebo-controlled trial of adalimumab maintenance therapy, were analysed. All patients received adalimumab during a 4-wk, open-label induction period; patients were then randomised to adalimumab or placebo for a 52-wk double-blind period. For this analysis, only patients who were randomised to placebo at Wk 4 and had
PWE-257 The role of RDH10 and RALDH enzymes in retinoic acid-mediated immune regulation by antigen presenting cells in the human intestine
T J Sanders, N E McCarthy, E M Giles, J O Lindsay and A J Stagg

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