Abstracts

Inflammatory bowel disease

001 THE USE OF ADALIMUMAB IN REFRACTORY CROHN'S DISEASE: A TERTIARY REFERRAL CENTRE EXPERIENCE

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Introduction: Tumour necrosis factor (TNF-α) blockade is an effective treatment strategy in inflammatory bowel disease (IBD). Currently, only infliximab, a chimeric monoclonal antibody directed towards TNF-α, is licensed in refractory IBD. However, loss of efficacy and hypersensitivity reactions to infliximab have become limitations to its use. Adalimumab is a fully humanised monoclonal antibody targeting TNF-α and recent data have shown its effectiveness in induction and maintenance of remission in moderate to severe Crohn's disease (CD).
Aims & Methods: We aim to audit the use of Adalimumab in the rescue treatment of medically refractory CD at the Western General Hospital, a tertiary centre for IBD serving the Lothian region, Scotland over a 3-year period (2003–6).
Results: 22 (14 females; age at therapy: 32.6 years, IQR 20.9–41.7; 9 patients from previous open-labelled trial) patients with CD were treated with Adalimumab using an induction of 80 mg followed by fortnightly 40 mg regime. 14 (63%), 6 (27%), 1 (5%) and 1 (5%) patients had colonic, ileo-colonic, ileal and oral CD respectively. 20 patients had previous infliximab infusions. All had proven refractory/intolerant to corticosteroids and other immunosuppressants. Of these patients, 8 (36%), 6 (27%), 3 (14%) had previous infusion reactions, no response and lost response to infliximab as indications for Adalimumab therapy respectively. Over a follow-up period of 1.01 years (IQR 0.62–2.48 years), 14 (64%) were considered to be in clinical remission, although 12 (55%) required escalation of therapy to 40 mg weekly with a median time of 0.55 years (IQR 0.22–1.37). 15 (68%) patients were on concomitant immunosuppression. Six (36%) of these patients had had of Adalimumab-free intervals without loss of efficacy on recommencement (1 patient with ileo-colonic CD were successfully re-treated following colectomy). Five (23%) patients had no response to therapy, and required colectomy (median time following initiation of therapy 0.67 years IQR 0.37–2.45). A further three patients required permanent discontinuation of therapy—one patient (female smoker, age at therapy 68.3 years) developed lung cancer after 2.1 years treatment and 2 patients developed serious sepsis-related complications (facial cellulitis and psoas abscess, respectively). No patients developed infusion reactions.
Conclusion: Adalimumab is efficacious in the treatment of patients with refractory CD, with particular benefit in patients who have lost response or developed adverse reaction to infliximab. However, many patients require escalation of dosing regime. Moreover, the treatment carries definite risks of serious adverse events; careful patient selection and continuous monitoring are needed.

002 INFLIXIMAB AS RESCUE THERAPY IN ACUTE SEVERE ULCERATIVE COLITIS: A SURVEY OF THE SCOTTISH SOCIETY OF GASTROENTEROLOGY

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Introduction: As many as 40% of patients with acute severe ulcerative colitis (UC) will fail to respond to first-line medical therapy. Treatment of these patients has been limited to surgery or cyclosporine. Doubts remain about the efficacy of cyclosporine and concerns over its toxicity. Jarnerot *et al* demonstrated that infliximab as ''rescue'' therapy for severe UC was effective with emergency colectomy rates of 29% *v* 67% for placebo ($p=0.017$, NNT<3).[1] We have previously reported on the first 9 patients treated in this setting in Scotland.[2]
Aims & Methods: We aimed to complete a pan-Scotland retrospective audit of infliximab use as rescue therapy for patients with acute severe UC failing first line intensive medical therapy, and determine factors predicting short and long-term outcome. All members of the Scottish Society of Gastroenterology were invited by email to participate in this survey. Responses from 12 hospitals in Scotland were received of which 8 provided sufficient data on 36 patients for inclusion in the study at the time of abstract writing. All data were collected retrospectively by case-note review. All 36 patients met Truelove and Witts criteria for disease severity at admission. There were 20 male and 16 female patients with a median age at diagnosis of 30.7 years (IQR 21.9–43.3).
Results: 25/36 (69.4%) of patients avoided urgent colectomy following infliximab rescue therapy. The median duration from admission to infliximab therapy was 9 days (IQR 6–12 days). Patients treated within 5 days were significantly more likely to undergo colectomy than those treated after 6 or more days (62.5% *v* 28.6%, $p=0.046$). Sex, age at admission, smoking status, disease extent, and drug therapy on admission did not predict colectomy rates. 11/36 (30.6%) of patients underwent urgent colectomy at a median of 5 days (IQR 2–7) following infliximab. Following hospital discharge, only 1 additional colectomy was reported during a median of 130.5 days follow-up (IQR 89.5–303.0). Three months follow-up was available on 18/24; of these 13/18 (72.2%) were in steroid-free remission. One patient, who responded to infliximab and was discharged from hospital, died of septic shock from broncho-pulmonary pneumonia 3 weeks following infliximab therapy. There was one case of varicella-zoster infection, one venflon infection and one acute infusion reaction attributable to infliximab. The only reported postoperative complication was an uncomplicated urinary tract infection.
Conclusion: Infliximab is effective as rescue therapy in acute severe UC, and may act as a bridge to long-term azathioprine immunosuppression, although safety concerns remain paramount.

1. **Jarnerot G**, *et al*. *Gastroenterology* 2005;**128**:1805–11.
2. **Lees CW**, Shand AG, Penman ID, *et al*. *Inflamm Bowel Dis* 2006;**12**:335–7.

Liver free papers

003 A COMPARISON OF SCORING SYSTEMS FOR ORGAN ALLOCATION ON THE LIVER TRANSPLANT WAITING LIST

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Introduction: There is currently discussion as to the most appropriate method of organ allocation for liver transplantation. This occurs on the background of a 38% increase in registrations for liver transplant and 7% fewer liver transplants being performed in 2005/6. Similar problems in the US resulted in the introduction of the MELD system. There are, however, criticisms of this scoring system in that it is not a bedside test and does not take into account significant clinical variables such as ascites. We analysed several scoring systems for end-stage liver disease to assess which predicted survival on the waiting list.
Aims & Methods: All patients listed with UK Transplant (UKT) at our centre, between January 2000 and December 2003, were included in the study. Patients were excluded if they were super-urgently listed, listed for multiple organ transplants, non-NHS entitled for liver transplant or their indication for transplant was amyloidosis. The scoring systems examined were the Child-Pugh (CP) score, MELD score, MELD–Na score and three variants of the CP score incorporating creatinine at the time of listing with UKT. A positive outcome was surviving to transplantation or being delisted due to improvement obviating the need for transplant. A negative outcome was death on the transplant list or being delisted due to the developments of contraindications for transplant. Receiver-operating characteristic (ROC)

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curves were generated for each scoring system based on these outcome measures and the areas under the curve (AUC) were compared using the Hanley–McNeil method.
Results: 787 patients were listed. After exclusions, 490 patients were analysed in the study. The median age of the patients was 55 years and the predominant aetiologies were alcoholic liver disease and hepatitis C. The median CP score was 9 and the median MELD score was 15. There were 416 patients with a positive outcome including 402 transplants. The remaining 74 patients with a negative outcome had significantly higher CPS (11 *v* 9), MELD (18 *v* 14), MELD–Na (38 *v* 16) and modified CP scores (all p values <0.0001). There was no difference in time on the waiting list (64 *v* 68 days; $p=0.18$). The AUC for all scoring systems was >0.705 ($p<0.001$) indicating that they performed well and were clinically applicable. However, MELD–Na was significantly better than the other scoring systems with an AUC of 0.828 ($p<0.001$).
Conclusion: All scoring systems analysed performed adequately in predicting a negative outcome on the transplant waiting list with no difference between CP score and MELD score. However, MELD–Na was significantly better than all the other scoring systems at predicting waiting list mortality and thus any changes in organ allocation warrant comparison with this scoring system.

004 ONE YEAR SURVIVAL IN BUDD–CHIARI SYNDROME TREATED WITH TIPSS: AN INTERNATIONAL STUDY

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Introduction: Hepatic vein thrombosis (Budd-Chiari syndrome, BCS) is a rare cause of liver disease but can lead to liver failure and ascites. Recently we published our treatment algorithm proposing transvenous intrahepatic portosystemic stent shunt (TIPSS) as first line treatment option in patients in whom angioplasty is not possible.
Aims & Methods: We aimed to analyse the outcome of patients with BCS after TIPSS. Case notes of all patients undergoing TIPSS for BCS in 6 European hepatology units were analysed with emphasis on putative factors predicting liver survival (need for liver transplant or death).
Results: From 1993 to March 2006 TIPSS was performed on 122 patients (62% female) including 39 from Birmingham. Aetiology of the syndrome were myeloproliferative disorders (51%, including 30% polycythaemia rubra vera), antiphospholipid syndrome (12%), paroxysmal nocturnal haemoglobinuria (10%) and essential thrombocytopenia (10%). Morbidity pre-TIPSS included ascites (98%), jaundice (52%), hepatic encephalopathy (22%) upper GI bleed (14%) and acute liver failure (8%). TIPSS was performed for portal hypertension (68%), liver failure (22%) and in patients without major complications (10%). A median of 2 stents were placed (range 1–4) and 53% had at least 1 covered stent. During follow-up 8 patients required liver transplantation and 14 died. The main causes of death were liver failure (4), haematological malignancy (4) and sepsis (3). The combined endpoint of death or liver transplant at 1 year was present in 10% of patients. Predictors of this composite endpoint were studied in univariate and multivariate analysis. In multivariate Cox regression analysis patient age, bilirubin and INR were found to be independent predictors of death or transplantation at 1 year. A prognostic score of ''age $\times$ 0.082 + bilirubin $\times$ 0.00924 + INR $\times$ 0.629'' was found to best predict the endpoint with an area under the receiver operator curve of 0.86.
Conclusion: Poor prognosis can be predicted in a subgroup of patients undergoing TIPSS for BCS and this may help in treatment decisions.

005 ISCHAEMIA-REPERFUSION INJURY PROMOTES HEMATOPOIETIC STEM CELL RECRUITMENT TO THE MURINE HEPATIC MICROCIRCULATION IN VIVO

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Introduction: Hematopoietic stem cells (HSCs) can migrate to injured liver and aid repair by differentiating into new and healthy hepatocytes. However, no studies have identified the initial events that govern recruitment of HSCs to hepatic microcirculation. Indeed, it is not known whether HSCs follow a similar recruitment pattern to that described for neutrophils. This study used fluorescent intravital microscopy (IVM) to establish whether hepatic ischaemia-reperfusion (I/R) could promote HSC recruitment. Since the yield of isolated pure HSCs from bone marrow is low, a murine HSC line, HPC-7, which displays many characteristics of ''pure'' HSCs was used.
Aims & Methods: Hepatic I/R injury was induced for 90 minutes in anaesthetised C57BL/6 mice. 100\µl (1×10^6 cells) of fluorescently labelled HPC-7s were administered (i.a) after 5 or 30 minutes reperfusion. Intravital observations were made every 5 minutes for a further 1 hour with cells categorised as adherent (static for >30 seconds) or free flowing. Parallel Stamper–Woodruff assays were conducted on frozen sections of tissue to quantitate HPC-7 adhesion in vitro.
Results: HPC-7 cell adhesion was significantly raised in vivo by 30 minutes post-reperfusion (eg, 13.27 (1.66) in I/R animals at 60 mins *v* 3 (0.94) in sham surgery animals at 60 mins; $p<0.005$). Similar adhesive events were observed at 60 mins regardless of whether cells were introduced at 5 or 30 minutes post-reperfusion. Adhesion was observed predominantly in sinusoidal capillaries rather than post-capillary venules, with ''rolling'' events, typical of neutrophil recruitment, not observed. Similar results were obtained in vitro with significant HPC-7 adhesion to tissue sections isolated from I/R injured animals compared to controls (9.4 (2.5) *v* 4.5 (0.5) respectively; $p<0.05$).
Conclusion: These novel results illustrate that hepatic I/R injury can act as a stimulus for HSC recruitment to sinusoidal microcirculation. Having established this model, future work will aim to identify the molecular mechanisms that govern HSC recruitment. This would allow development of potential strategies to enhance HSC recruitment to injured liver thereby reducing damage and speeding recovery.

006 REPRIORITISATION OF LIVER EXPORT PROTEIN SYNTHESIS IN PATIENTS WITH DECOMPENSATED ALCOHOLIC LIVER DISEASE

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Introduction: Albumin and fibrinogen synthesis appear to account for the majority of protein exported by the liver. In addition, these proteins play an important role in the systemic inflammatory response (SIR) with albumin recognised as a negative acute phase protein and fibrinogen a positive acute phase reactant. The changes in the plasma concentrations have been thought to be due to reprioritisation of liver export protein synthesis. We have previously carried out simultaneous direct measurements of albumin

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	Normal	Baseline (n = 17)	4–6 weeks (n = 10)	p Value
Age (years)	64 (48–69)	50 (38–68)		
Sex (male/female)	4/2	15/2		
Child-Pugh score	NA	12 (9–13)	9 (6–13)	0.007*
Albumin TSR (mg/kg/day)	208 (122–287)	61(29–287)	96 (73–189)	0.011*
Fibrinogen TSR (mg/kg/day)	28 (23–55)	15 (5–55)	23 (12–38)	0.093
APPQ	0.14(0.10–0.25)	0.17(0.10–0.67)	0.22 (0.12–0.42)	1.000

Results expressed as median (range).
*$p<0.05$.

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and fibrinogen in normal subjects and derived a ratio of the total synthetic rate (TSR) of fibrinogen/albumin which is expressed as the Acute Phase Protein Quotient (APPQ).[1] However, to our knowledge there has been no such measurements in disease. The characteristic low albumin seen in patients with decompensated liver disease is an important predictor of outcome and is incorporated into the widely used Child-Pugh scoring system for assessment of disease severity. The aim of the present study was to examine the longitudinal relation between disease severity and total albumin and fibrinogen synthetic rates in patients with decompensated alcohol related liver disease during periods of hospitalisation and recovery.
Aims & Methods: Seventeen patients admitted with decompensated alcohol-related liver diseased and with no evidence of sepsis and GI bleeding were recruited at baseline. Patients underwent measurement of the albumin and fibrinogen synthetic rates using a validated [2H5] phenylalanine flooding dose technique. Routine biochemical parameters of liver function were also measured. Ten patients had these measurements repeated following clinical improvement 4–6 weeks later. The study was approved by the local ethics committee.
Results: Baseline and follow-up results are shown in the table.
Conclusion: On follow-up, there was a significant improvement in the severity of liver disease and this was associated with an increase in both albumin TSR and fibrinogen TSR. However, the relative production of these proteins (APPQ) did not normalise. Therefore, there would appear to be reprioritisation of liver protein synthesis in patients with alcohol-related liver disease. It may be that moderation of the systemic inflammatory response is required to optimise liver function in these patients.

1. **McMillan DC**, *et al.* Simultaneous measurement of albumin and fibrinogen synthetic rates in normal fasted subjects. *Nutrition* 1996;**12**:602–7.

007 PROGNOSTIC FACTORS IN BILIARY TRACT CARCINOMA: MULTIVARIATE ANALYSIS OF 259 PATIENTS

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Introduction: The prognosis of patients with biliary tract cancer (BTC: cholangiocarcinoma (CCA) and gallbladder cancer (GBCA)) remains poor. There is a paucity of adequate prognostic information to guide treatment strategies in the management of BTC.
Aims & Methods: We collated information on patients with a final diagnosis of BTC seen in a joint tertiary referral cancer centre between 1998 and 2005. Patients were identified by searching a prospectively collected hepatobiliary database, as well as oncology, pathology and endoscopy records. Case notes of all identified patients were reviewed. A prognostic evaluation was carried out with survival rate estimates by the Kaplan-Meier method and comparisons by means of log-rank testing. Cox regression analysis was used to determine independent prognosticators.
Results: A total of 259 patients (median age 69 years, range 19–96; F:M: 1.1:1) were identified with either CCA (n = 196; 86% perihilar, 9% distal, 5% intrahepatic) or GBCA (n = 63). 74 (29%) patients underwent surgical intervention. Of the 48 (19%) patients who had surgery with curative intent, R0 resection was achieved in 56%. In the non-surgical patients, 54% were palliated with biliary drainage procedures alone, while 35% received chemo- and/or radiotherapy and (since 2002) 22% received photodynamic therapy (PDT; in 11% plus chemotherapy). Complete follow-up data were available on 237 (92%) patients. The overall median survival was 9 months, with 1-, 2- and 3-year survival rates of 40%, 22% and 11%, respectively. Patients with R0 resections had the most favourable outcome, with a 3-year survival of 56%, compared with 4% for palliative treatment. Univariate survival analysis identified treatment category (surgery with curative intent, PDT, adjuvant therapy and palliative biliary drainage), clinical T-stage, tumour size, vascular invasion, distant metastasis, and serum bilirubin, CA19-9 and CEA levels, as statistically significant ($p<0.01$) prognostic factors. In contrast, Bismuth classification, histological grade, lymph node metastasis, patients' age and gender had no impact on patient survival. On multivariate analysis, treatment category, clinical T-stage and serum bilirubin level at diagnosis became independent prognosticators of survival.
Conclusion: In this large UK series of the surgical and palliative management and outcome of BTC patients, long-term survival was achieved only in surgical patients with R0 resection margins. A normal serum bilirubin level and no mass seen on imaging at the time of diagnosis were independent positive prognostic factors of survival.

008 HEPATITIS E IN SOUTHWEST ENGLAND

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Introduction: Hepatitis E (HEV) is rare in developed countries and has previously been thought to be confined to travellers returning from endemic areas. Recently there have been reports from a number of developed countries of HEV infection in non-travellers. The source of these infections is unknown, but zoonotic transmission from a porcine source has been suggested. The extent and nature of autochthonous (locally acquired) HEV (aHEV) in the UK are unclear.
Aims & Methods: Patients with unexplained hepatitis were tested for HEV over a 7-year period. Cases were defined as: biochemical evidence of hepatitis (serum aminotransferase >500 iU/l) and strong reactivity for anti-HEV IgM (test:cut-off ratio>5), or a rising titre of anti-HEV IgG, or detectable viraemia by RT-PCR. HEV RNA isolated from the cases was amplified, characterised and compared to previously characterised HEV isolates. Cases of aHEV were asked to complete a lifestyle questionnaire to elucidate possible risk factors. The documented incidence of aHEV was compared to that of HAV.
Results: 38 cases of aHEV were identified. Clinical manifestations ranged from asymptomatic infection to subacute hepatic failure. The median index bilirubin was 105 μmol/l (range 3–417 μmol/l), 8/38 were anicteric. 35/38 patients recovered within six weeks. One patient died of an unrelated cause. 3/38 had previously undiagnosed cirrhosis on biopsy, 2/3 developed fulminant hepatic failure and died. 0/38 had travelled to an area endemic for HEV, and all patients were white. Patients were middle-aged/elderly (median age 66, range 35–86 years) and males were more commonly affected (M:F = 29:9). 35/38 cases occurred between March and October. 0/33 were vegetarian and all ate pork. All PCR confirmed cases were HEV genotype 3, which bore close sequence homology to HEV circulating in UK pigs. In 2005 16 cases of aHEV were documented, compared to 9 cases of HAV.
Conclusion: In the UK aHEV is more common than previously recognised, and may be more common than HAV. As has been documented in the Indian subcontinent, aHEV superinfection in patients with cirrhosis carries a poor prognosis. Although the mode of transmission remains to be determined, it may be a zoonosis with pigs as a reservoir. Hepatitis E is a public health issue in the UK.

009 ARE MUC4 AND/OR MUC5AC USEFUL TUMOUR MARKERS FOR BILIARY TRACT CANCER?

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Introduction: Alterations in epithelial mucin expression are associated with carcinogenesis. MUC4 contains an EGF-like domain that can induce cell proliferation and differentiation via the ERBB2 receptor.[1] In pancreatic disease, MUC4 has been proposed as a diagnostic and prognostic marker for malignancy,[2 3] while MUC5AC has been reported to be a sensitive serological marker for biliary tract cancer (BTC).[4]
Aims & Methods: We assessed MUC4 and MUC5AC expression in: (1) 79 archived biliary tissues (69 BTC, 10 benign) by immunohistochemistry (IHC), and (2) bile and serum specimens from 72 patients with biliary obstruction (39 BTC, 8 other malignancies, 9 primary sclerosing cholangitis (PSC), 16 benign), by TaqMan-based quantitative real-time RT-PCR (qPCR) and Western blot, respectively. We used two monoclonal MUC4 antibodies (against transmembrane and secretory unit epitopes) and a mono- and polyclonal MUC5AC antibody. MUC4 and MUC5AC gene primers and probe sets were custom-synthesised according to published reports. mRNA quantification was normalised to the housekeeping gene GAPDH.
Results: In archived tissues, MUC4 and MUC5AC proteins were detected exclusively in 37% and 10% of BTC samples, respectively, vs. in none of the benign samples ($p = 0.02$, $p = 0.4$). In bile, MUC4 protein was detected in 27% of BTC and 29% of PSC cases, but not in other benign disease. qPCR revealed a ~2.5-fold increased expression of MUC4 mRNA in the bile of patients with BTC and PSC compared with other benign disease. No such

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Abstract 009 Biliary tract cancer prediction markers for bile MUC4 and serum MUC5AC by Western blot

	Bile MUC4	Serum MUC5AC	Bile MUC4 or Serum MUC5AC
Sensitivity	27% (9/34)	44% (17/39)	58% (22/38)
Specificity	93% (26/28)	96% (26/27)	87% (20/23)
PPV	82% (9/11)	94% (17/18)	88% (22/25)
NPV	51% (26/51)	54% (26/48)	56% (20/36)

PPV, NPV, positive and negative predictive values.

differences were seen for MUC5AC. In serum, MUC4 was detected in 5% of patients overall, with no significant difference between BTC and non-BTC patients. MUC5AC was found exclusively in BTC and PSC sera (44% and 13%, respectively; $p<0.01$ BTC *v* non-BTC).
Conclusion: Biliary MUC4 and serum MUC5AC are tumour-associated mucins that may prove to be useful in the formulation of strategies for the diagnosis and treatment of BTC.

1. *Nature Rev* 2004;**4**:45–60.
2. *Br J Cancer* 2004;**91**:1633–8.
3. *J Clin Pathol* 2005;**58**:845–52.
4. *Cancer Lett* 2003;**195**:93–9.

010 A NOVEL SIMPLE NONINVASIVE TEST FOR THE PREDICTION OF CIRRHOSIS IN CHRONIC HEPATITIS C: VALIDATION AND COMPARISON OF 707 PATIENTS

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Introduction: Liver biopsy (LB) is no longer required for patients with chronic hepatitis C (HCV) infection as a prelude to anti-viral therapy. Without LB, however, significant fibrosis and cirrhosis may be unrecognised. The long-term effects of achieving a sustained virological response (SVR) in cirrhotic patients, and whether the risk of hepatocellular carcinoma is reduced, is not fully understood. Simple and reliable non-invasive techniques are urgently required by clinicians to identify patients at risk of cirrhosis.
Aims & Methods: The aim of our study was to develop a simple test available from routine clinical data to predict significant fibrosis and cirrhosis in patients with HCV. We performed a retrospective review of all liver biopsies carried out at our institution from 1 January 2001 to 30 June 2006. Consecutive treatment naïve patients were divided into two sequential cohorts to form a training set ($n=602$) and a validation set ($n=105$). A novel index to predict cirrhosis of Age $\times$ AST $\times$ INR/platelets (AAIP) was derived to amplify the opposing effects of factors associated with liver fibrosis. The diagnostic accuracy of the novel test was then compared with pre-existing simple non-invasive tests for hepatic fibrosis of aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio (AAR), cirrhosis discriminant score (CDS), age-platelet index (AP index), Pohl score, and AST-to-platelet ratio (APRI) using receiver operating characteristic (ROC) curve analysis.
Results: In the training set, 602 liver biopsies were reviewed. The AUC for AAIP for predicting significant fibrosis and cirrhosis for AAIP were 0.79 and 0.91. A cut-off of 16.7 gave a sensitivity of 86%, specificity of 80% and a negative predictive value of 95% for the prediction of cirrhosis. In the validation set 105 liver biopsies were reviewed. The AUC for AAIP for significant fibrosis and cirrhosis were 0.89 and 0.94 respectively. On comparison with other simple non-invasive tests AAIP performed best.
Conclusion: Our study showed that an index comprised of simple patient and laboratory data can accurately identify patients with significant fibrosis and cirrhosis. In the new era of antiviral therapy where HCV patients no longer routinely undergo histological assessment, the AAIP may help identify patients at risk of cirrhosis, and thus select those patients to whom HCC surveillance should be offered.

011 TIPSS IN TREATMENT OF REFRACTORY ASCITES: A SINGLE CENTRE EXPERIENCE

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Introduction: Refractory ascites secondary to cirrhosis has a very poor prognosis. Previous trials utilising TIPSS for ascites have produced inconsistent results, with no survival advantage. We report here the largest single centre series of patients who had TIPSS inserted for refractory ascites.
Aims & Methods: A retrospective study of patients in whom TIPSS was inserted for refractory ascites.
Results: Over 14 years, of 768 TIPSS procedures, 83 (10.8%) were undertaken for ascites (males 72%; mean age 57 (3.7) years). Median follow-up 7.1 (0.1 to 115.8) months. Aetiology: ALD (70%). Mean Child-Pugh (CP) score was 9.6 (1.3) (Child's C, 48%; Child's B, 52%) and MELD score was 15 (5.5). 43% had diuretic resistant ascites and 57% had diuretic intractable ascites. Portal pressure gradient fell from 22.2 (6.04) to 7.2 (2.7) mm Hg post TIPSS. Following TIPSS, there was a complete response in 15%, partial response in 49% and no response in 36%. Factors predicting a favourable response to TIPSS included female sex ($p=0.04$), diuretic refractory rather than diuretic intractable ascites ($p=0.05$) and MELD <17 ($p=0.02$). Patients who responded to TIPSS had lower CP ($p=0.004$) and MELD scores ($p=0.05$). Response was unrelated to type of stent (covered ($n=31$) *v* uncovered ($n=52$)) or creatinine pre-TIPSS. Ascites recurred after initial improvement in 19 (38%) patients at a median of 2.3 (0.1 to 58.1) months. This was related to shunt dysfunction in 10 (52%), and to therapeutic shunt reduction for refractory hepatic encephalopathy (HE) in 3 (15.7%). HE occurred in 47% post-TIPSS, with 4 patients requiring shunt modification. Survival was poorer in Child's C cf Child's B ($p=0.05$), and where MELD >17 ($p=0.001$). On univariate analysis MELD, CP score and sodium <125 were independent predictors of survival, but on multivariate analysis, only MELD was a significant predictor of survival.
Conclusion: TIPSS is effective in the management of refractory ascites, but does not appear to influence the long-term prognosis. Pre-TIPSS MELD <17, female sex, and diuretic refractory ascites predict better response to TIPSS. HE is a significant limitation and patient selection criteria remain to be determined.

012 HISTOLOGICAL PREDICTORS OF OESOPHAGEAL VARICES. A SINGLE BLINDED RETROSPECTIVE ANALYSIS

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Introduction: Clinically significant portal hypertension (CSPH) is defined as a hepatic vein portal gradient of >12 mm Hg and may be complicated by the development of oesophageal varices. Studies have suggested that small nodularity and septal thickness correlates with CSPH[1] and a histological subclassification of cirrhosis has been suggested.
Aims & Methods: The aim of this study was to determine if the nodule size and septal thickness on histology were predictive variables for endoscopic presence of oesophageal varices. Patients with established cirrhosis were randomly selected from an endoscopy and histology database. Biopsies were retrospectively reviewed by two operators (TT and SM) who were blinded to the presence or absence of varices on endoscopy. Nodules were classified as small, mixed or large based on width of the nodule in relation to biopsy size. The septal thickness was classified as thin (<1 mm), medium or thick (>2 mm).
Results: Of the 95 slides reviewed, 8 were excluded as they did not have histologically established cirrhosis leaving 87 slides (males: 54, median age: 53 years (IQR 48–59)) for the final analysis. In 48% of cases the aetiology was alcoholic liver disease. The median biopsy size was 15 mm (IQR 12–20) and the median number of portal tracts was 4 (IQR 3–4). The number of patients with small, mixed and large nodules was 33, 35 and 20 respectively and the number with thin, medium and thick septae was 45, 21 and 22 respectively. There was a significant correlation between presence of oesophageal varices and both the nodule size ($r=0.5$, 95% CI 0.33 to 0.64, two-sided $p<0.001$) and septal thickness ($r=0.36$, 95% CI 0.16 to 0.53, two-sided $p<0.007$).
Conclusion: Small nodule size and thick septae are predictors of the presence of oesophageal varices on endoscopy. Patients with the above

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histological variables should be clinically prioritised to have an early endoscopy.

1. **Nagula S**, Danpat J, Groszmann RJ, *et al*. Histological-haemodynamic correlation in cirrhosis- a histological classification of the severity of cirrhosis. *J Hepatol* 2006;**44**:111–17.

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013 A RETROSPECTIVE ANALYSIS OF GIST MUTATION STATUS IN ONE UK REFERENCE CENTRE

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Introduction: We present a retrospective analysis of intra-abdominal mesenchymal tumours undertaken at University Hospital Birmingham. The aim was to review and classify tumours according to the current criteria and to then proceed with a comprehensive molecular analysis.
Aims & Methods: Cases from the period 1990 to 2004 were retrieved using the SNOMED classification system. Slides were reviewed and immunohistochemistry was performed using an extensive panel of antibodies. GISTs were then tested for KIT or/and PDGFRA gene mutations from paraffin embedded tissue blocks with the following protocol: KIT positive tumours were initially tested for exon 11 of KIT; if wild-type (WT), we subsequently screened exons 9, 13 and 17. Kit negative GISTs were initially tested for exons 11 and 9 of KIT, and exons 12 and 18 of PDGFR-α.
Results: Ninety two tumours were retrieved; 54/92 (59%) were reclassified as GISTs. 52/54 GISTs showed KIT expression by IHC. All 92 tumours were positive with PDGFRA and SCF markers. There were 2 oesophageal tumours, 32 gastric tumours, 7 duodenal tumours, 14 small bowel tumours, 2 colonic tumours, 2 pelvic tumours and 8 liver tumours. Site was not mentioned for 4 lesions. 73 tumours in 68 patients have been analysed for exon 11 and 15 for exon 9 of KIT gene. Exon 11 mutation was detected in 72% of the gastric tumours, 57% of bowel tumours, in 2/2 (100%) of the oesophageal tumours, 2/2 (100%) of the pelvic tumours and in 5/8 (62%) of the liver lesions. Average size of tumours was 5 cm for exon 11 WT tumours and 10 cm for tumours with exon 11 mutations. We have collected 10 very low risk GISTs, all found incidentally in specimens local to either a carcinoma or a large GIST. Only one tumour (from the duodenum) showed a mutation in exon 9.
Conclusion: In conclusion we show that KIT and PDGFR-α mutation analysis is technically feasible from archival material with 100% sensitivity. Our results show that the rate of exon 11 mutation is comparable to other series. As previously shown gastric tumours are more frequently mutated. Exon 9 mutations are rare events and preferentially found in bowel tumours. The absence of mutation in very low risk GISTs overexpressing c-kit protein is an interesting finding. This would suggest that a second molecular event is needed to initiate tumour development.

1. **Grady WM**. GISTs: The revolution continues. *Gastroenterology* 2003;**125**:967–9.
2. **Andersson J**, Bumming P, Meis-Kindblom JM, *et al*. Gastrointestinal stromal tumours with KIT exon 11 deletions are associated with poor prognosis. *Gastroenterology* 2006;**130**:1573–81.

014 THE CHARACTERISATION OF BACTERIAL COMMUNITY DIVERSITY IN CULTURES DERIVED FROM HEALTHY AND INFLAMED ILEAL POUCHES AFTER RESTORATIVE PROCTO-COLECTOMY, USING 16S RIBOSOMAL DNA TERMINAL RESTRICTION FRAGMENT LENGTH POLYMORPHISM PROFILING

M. W. Johnson[1], G. B. Rogers[2], S. McLaughlin[1], K. D. Bruce[2], A. Forbes[3], P. J. Ciclitira[4], J. R. Nicholls[5]. [1]*Gastroenterology, St Mark's Hospital,* [2]*Microbiology, Kings' University,* [3]*Gastroenterology, University College Hospital,* [4]*Gastroenterology, St Thomas' Hospital,* [5]*Surgery, St Mark's Hospital, London, UK*

Introduction: After restorative procto-colectomy 40% develop pouchitis (acute inflammation of an ileal pouch). There are two leading theories regarding the pathogenesis of pouchitis: firstly, that it is a reaction to dysbiosis; and secondly, that it is related to a loss in the immune tolerance towards normal faecal-derived bacteria. We aimed to assess differences between bacterial communities cultured from both healthy and inflamed ileal pouches in patients with ulcerative colitis (UC) and familial adenomatous polyposis (FAP) coli.
Aims & Methods: Pouchitis was determined using an objective pouchitis score (OPS) of $\geqslant$5/12 (endoscopic score of $\geqslant$3/6 and an acute histological score of $\geqslant$2/6). Seven UC patients were diagnosed with pouchitis (P+), 15 UC patients had a healthy pouch (P−), 1 FAP patient had pouchitis (F+), while 9 FAP patients had un-inflamed pouches (F−). Two biopsies were taken per patient and cultured in aerobic and anaerobic conditions. Standardised DNA extraction was performed and PCR products were derived by amplifying the 16S rRNA gene, specific to the domain bacteria. Following digestion with a specific restriction endonuclease, ribosomal gene fragments were resolved by terminal restriction fragment length polymorphism (T-RFLP) profiling. In this way, a ''fingerprint'' of the bacterial community within each of the samples was created. The degree of species richness and evenness was determined from T-RF band lengths and relative intensities.
Results: In total 179 bands representing different species were identified from 64 samples. Of the most prevalent bacteria identified, 39 were consistent with the genera Enterobacter, Citrobacter or Shewanella, 16 were Clostridia, 13 were Lactobacilli and 7 were members of the genus Prevotella. For the F−, F+, P− and P+ groups 96, 29, 124 and 80 species bands were seen, with each sample having an average species richness of 13 (5.6), 17.5 (10.6), 11.9 (6.1) and 14.7 (6.2), respectively. The species diversity was measured at 5.3, 14.5, 4.1 and 5.7, respectively. Similar trends were noted when the anaerobic and aerobic groups were analysed separately. The species evenness was similar throughout all groups, with the average highest/lowest proportions of the anaerobic and aerobic species represented by 33.6/0.02 (F− anaerobes) and 36.9/0.02 (F− aerobes), 18.2/0.08 and 25.8/3.91, 34.5/0.01 and 48.1/0.01, 33.3/0.01 and 45.1/0.01, respectively.
Conclusion: Although dysbiosis is believed by many to be the main cause of pouchitis, no significant differences could be demonstrated between the bacterial cultures derived from inflamed and healthy ileal pouches. Despite this, divergent trends were seen in the species diversity and richness of the two groups. The significance of such data is yet to be fully determined, but would favour the loss of immune tolerance as the primary pathogenic process.

015 STROMAL GENE EXPRESSION MAY BE RESPONSIBLE FOR MAINTAINING MORPHOLOGICAL DIFFERENCES BETWEEN SMALL AND LARGE BOWEL

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Introduction: CDX-1 and CDX-2 regulate gut differentiation in the embryo and are believed to maintain this morphology in the adult by controlling HOX gene expression.[1] However, the molecular mechanisms underlying this regulation are not known. Although it is well established that stroma provides positional information to overlying epithelium,[2] it is unknown whether stromal or epithelial expression of CDX genes is responsible for maintaining gut morphology in the adult human. In addition, a better understanding of the role of CDX genes may allow insight into the molecular mechanisms underlying their association with gastrointestinal metaplasia[3] and adenocarcinoma.[4]
Aims & Methods: The aim of this study was to identify if CDX gene regulation was mediated via stromal signalling, by assessing CDX expression patterns in human gut. Paired samples of full thickness ileum and ascending colon from 3 patients were harvested with 4 unmatched rectal tissue samples, and micro laser dissected into epithelium and stroma. mRNA was extracted using standard techniques, and quality assessed by new 3′:5′ and inhibition assays, prior to quantification by real-time reverse transcription polymerase chain reaction (RT-qPCR).
Results: Expression of CDX-1, 2 mRNA was higher in samples of ascending colon and rectum than small bowel (CDX-1: median 192-fold difference, CDX-2: median 12-fold difference, $p<0.005$). CDX-2 mRNA expression was 1000-fold higher than CDX-1 in both large and small bowel ($p<0.005$). CDX-2 mRNA levels were higher in large bowel stroma compared to the crypt epithelial cells (median ninefold difference; $p<0.005$). CDX-1 mRNA expression levels varied between crypt and stroma in different individuals, and did not reach significance.
Conclusion: Adult human gut expresses CDX-1, 2 in a caudal to rostral gradient, similar to the mammalian embryo. The higher CDX-2 expression in human gut stroma compared with epithelium may indicate a previously unrecognised signalling mechanism for the maintenance of gut morphology. A greater understanding of CDX function in normal differentiated tissue may provide an appreciation of CDX gene involvement in intestinal metaplasia, and provide the basis for novel strategies to monitor risk of associated carcinoma development.

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1. **Deschamps J**, *et al. Int J Dev Biol* 1999;**43**:635–50.
2. **Rawdon BB**. *Cell Biol Int* 2001;**25**:9–15.
3. **Vallbohmer D**, *et al.* 2006;**19**:260–6.
4. **Bonhomme C**, *et al. Gut* 2003;**52**:1465–71.

016 THE EXPRESSION PATTERN OF MCMS, GEMININ AND THEIR RELATION TO TUMOUR DIFFERENTIATION AND PATIENT SURVIVAL DIFFERS BETWEEN GASTRIC AND SMALL BOWEL ADENOCARCINOMA

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Introduction: Gastric adenocarcinoma (GC) is 19 times more common than small bowel adenocarcinoma (SBA), despite the small bowel contributing 90% of the gastrointestinal tract mucosal surface. However, the incidence of SBA is much higher in patients with coeliac disease. Minichromosome maintenance complex (MCM) and geminin are proteins essential for regulation of DNA replication initiation. Deregulation of MCM and geminin function may result in defective DNA replication and thus promote tumorigenesis. The aim of this study was to compare the expression pattern of MCMs and geminin in GC, SBA and coeliac-related SBA.
Aims & Methods: We studied the frequency of expression of MCM2, MCM5, MCM7 and geminin in 160 SBA (including 17 coeliac-related cases) and 163 GC using tissue microarrays and immunohistochemistry (IHC). The relation of individual proteins with clinicopathological data, frequency of Ki67 expression (marker of proliferation) and patient survival was analysed. K-median cluster analysis was performed to compare GC and SBA based on the degree of similarity measured over the 4 IHC markers.
Results: High expression of all MCMs and geminin was associated with poor tumour differentiation in SBA ($p<0.05$) but not in GC. High expression of MCM5, MCM7 and geminin was associated with longer patient survival in GC ($p<0.05$) but not in SBA. High expression of Ki67 was associated with longer patient survival in SBA ($p=0.0286$) and in GC ($p=0.0256$). Expression of the majority of the proteins differed between intestinal-type GC and SBA ($p<0.02$). Cluster analysis showed an excellent (85%) discrimination of GC and SBA using the IHC profile of all markers. MCM2 and MCM5 were expressed more frequently in coeliac-related SBA than in non-coeliac-related SBA ($p<0.05$).
Conclusion: The clear separation of GC and SBA based on their IHC profiles of all markers, and the finding that MCM and geminin expression were related to survival only in GC, plus the different expression pattern of MCMs and geminin in intestinal-type GC and SBA (despite these tumours having similar morphology), suggest that the regulation of DNA replication differs between GC and SBA. However, known additional functions of MCMs and geminin may play a role in the different protein expression patterns seen in these two tumours. Frequent expression of MCMs in coeliac-related SBA may reflect a general increase in cell turnover due to chronic inflammation of the small bowel mucosa in these patients. Further investigations are required to determine whether MCM expression may serve as a marker of an increased risk of malignant transformation in patients with coeliac disease.

017 THE APC1310T/+ MOUSE: A NOVEL MURINE MODEL OF INTESTINAL TUMORIGENESIS ANALOGOUS TO THE APC-1309 MUTATION CAUSING SEVERE INTESTINAL POLYPOSIS IN HUMANS

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Introduction: Mutations in both alleles of the adenomatous polyposis coli (APC) gene result in initiation of intestinal tumorigenesis in patients with familial adenomatous polyposis coli (FAP). In the intestine, the Wnt signalling pathway regulates proliferation and differentiation. The APC protein regulates Wnt activity through interaction with beta catenin. Certain germline APC mutations are associated with a severe disease phenotype in humans, such as the APC-1309 mutation. Commonly used murine models of FAP, such as the ApcMin/+ mouse, carry germline mutations in Apc which are not in sites analogous to those found in humans.
Aims & Methods: To develop a murine model containing an Apc mutation in a site equivalent to that causing severe FAP disease in humans, and compare this with the ApcMin/+ mouse, in order to investigate the functional effects of different apc proteins on Wnt signalling and tumorigenesis.
Methods: We used embryonic stem cell targeting and homologous recombination to create a novel murine model, Apc1310T/+. Molecular characterisation of the Apc1310T/+ was performed with Western and Southern blotting. The phenotype of Apc1310T/+ mice was compared with the most commonly used mouse model of intestinal tumorigenesis, the ApcMin/+, which carries an Apc allele truncated at codon 850. Both mouse lines were compared in terms of tumour burden, site, size and composition. The Wnt signalling pathway was assessed with immunohistochemistry, in situ hybridisation and gene expression arrays. Crypt fission analysis and TUNEL assays were performed to assess tumour development.
Results: Compared with the ApcMin/+, the Apc1310T/+ demonstrates a higher tumour burden (mean number of gastric adenomas, 2; mean number of small bowel adenomas, 186; mean number of large bowel adenomas, 3). Apc1310T/+ adenomas are larger with many tumours showing high grade dysplasia. Tumours develop approximately 20 days earlier than a comparable burden in the ApcMin/+ mouse. In early tumorigenesis, the Wnt signalling pathway is activated to markedly different levels between the two models.
Conclusion: The Apc1310T/+ mouse allows study of intestinal tumorigenesis consequent to germline mutations in Apc that are equivalent to those in humans. Our data suggest this phenotype is analogous to the severe intestinal polyposis seen in FAP patients with APC-1309 germline mutations. Dysregulation of the Wnt signalling pathway relative to that seen in the ApcMin/+ mouse appears to play a central role in producing this more severe phenotype. It is an excellent in vivo model for a comparative study of Wnt signalling control by different portions of the apc protein.

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018 THE IMPACT OF COLORECTAL CANCER FAMILY HISTORY CLINIC ON YIELD OF COLONOSCOPIC SCREENING

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Introduction: Approximately 20% of patients with colorectal cancer (CRC) have a positive family history. Public awareness of CRC is high and there has been an increase in the number of referrals seeking screening in those with a family history of CRC. Guidelines for screening in this group vary and many individuals are screened too early with a resulting low yield of adenomas. In this study, we have compared the yield of screening by colonoscopy in those with a family history of CRC prior to and following the introduction of a CRC family history clinic introducing screening according to agreed guidelines.
Aims & Methods: Cases undergoing colonoscopy between October 1994 and May 2003 prior to introduction of the CRC family history clinic (Group 1) were identified from the endoscopy database. Cases referred subsequently (Group 2) were identified from prospective clinic records and the endoscopy database. Demographic data, adherence to agreed guidelines and adenoma detection rate were compared between the two groups.
Results: 133 individuals were identified in Group 1. 87 (65%) of these were screened earlier than recommended by guidelines with a mean of 7.7 years in advance of these recommendations. This premature screening was more marked in those with lesser familial risk. Only 9 adenomas (6.8%) were detected. Adenoma detection rate increased with age but not with increased familial risk. Of 136 patients referred to the CRCFH clinic in Group 2, 108 attended and were placed into a risk category (average, moderate or high) according to agreed guidelines based on number/degree of relative(s) affected by CRC. 28 were deemed average risk, counselled regarding general population risk screening and discharged from the clinic. A further 11 patients were excluded from analysis because of symptoms ($n=6$) or a previous diagnosis of CRC ($n=5$). Of the remaining 69 patients, 48 have been screened to the time of this review. 10 of these had one or more adenoma (21%) which is significantly higher than yield in group 1 and more in keeping with that found in other studies of screening patients with a family history of CRC. 54% of adenomas were right-sided, 15% were greater than 10 mm in diameter and 40% patients had 2 or more adenomas. Adenoma detection rate increased with age and increased familial risk.

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Conclusion: The introduction of a CRC family history clinic significantly improves the adenoma detection rate in individuals with a family history of CRC. It also eliminates unnecessary endoscopy for those who do not have a significantly increased risk of CRC based on their family history. The high incidence of right-sided adenomas confirms that total colonoscopy is an appropriate screening tool.

019 EARLY EXPERIENCE OF THE MULTIBANDER ENDOSCOPIC MUCOSAL RESECTION: BENEFITS AND SHORT COMINGS

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Introduction: Endoscopic mucosal resection (EMR) is a recent but established method of removing upper GI tract lesions with dysplasia. We have recently started using banding device without submucosal injection, a novel new technique where a pseudopolyp is created by applying a band around the base of the lesion before snaring.
Aims & Methods: To assess the safety, ease of use and effectiveness of this new technique of EMR using banding device without submucosal injection for the removal of dysplastic lesions of the upper GI tract. We collected prospective data of all upper GI tract EMRs carried out by banding device and without submucosal injection in our institution over the last 1 year.
Results: Seventeen cases with mean age of 63.8 years and median ASA status of 2 were included. Conscious sedation was used in 13 cases (midazolam, mean dose 3.4 mg, pethidine mean 44 mg) and GA in 4 cases. The mean duration of the procedure was 41.5 minutes. Excluding GA cases, 9 patients reported no or mild discomfort and 4 moderate discomfort. Before mucosectomy, 9 were intramucosal cancers, 6 high grade dysplasias, 1 hyperplastic polyp and 1 squamous carcinoma. Nine lesions were in the lower oesophagus, 3 at the GOJ, 1 each in the mid oesophagus, cardia and the greater curve. 16/17 lesions were completely resected using this technique. Post-EMR histology showed clear margins in 8, positive lateral margin in 5 and positive deep margin in 2. There were 6 minor bleeds, 1 delayed bleed, 1 perforation and 1 stricture. Two patients with positive deep margins did not have residual lesion after radical surgical resection.
Conclusion: EMR using banding equipment without submucosal injection for the removal of the upper GI lesions appears to be easy, quick and well tolerated by patients. However this new technique is not without complications such as perforation, delayed bleeding and post-EMR stricture. The shortcomings are positive margins and missing the index lesion; both can be avoided if overlapping wide resection is carried out.

Abstract 019

Paris type	Lesions	EMR success	Complications
I s	7	7/7	3
I sp	2	1/2	1
II a	1	1/1	0
II b	7	7/7	5

020 WHAT ARE THE SENSITIVITY AND SPECIFICITY OF ENDOSCOPIC PHOTOGRAPHS IN DOCUMENTING COMPLETION OF COLONOSCOPY? RESULTS FROM AN ONLINE QUESTIONNAIRE

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Introduction: There is no consensus as to the best method for documenting complete colonoscopy and little is known about which methods are actually used. Two studies have examined the use of endoscopic photographs. Both studies asked reviewers to determine whether images taken of caecal landmarks documented complete colonoscopy. A combination of different views was most convincing but there was considerable disparity between reviewers as to whether the photographs confirmed completion of colonoscopy. For endoscopic photographs to be useful for documentation reviewers must be able to distinguish between incomplete and complete colonoscopy.
Aims & Methods: The aims were to assess current methods of documenting colonoscopy completion and to calculate the diagnostic specificity and sensitivity of a pair of photographs in confirming complete colonoscopy. 80 pairs of photographs were taken from completed colonoscopies. Two photographs, including at least one view of the ileo-caecal valve, were taken of caecal landmarks and/or the terminal ileum. Colonoscopy completion was independently validated using video clips. 20 pairs of photographs were also taken from another site in the colon that could potentially be misinterpreted as the caecum, for example hepatic flexure. Using an online questionnaire, experienced endoscopists were asked which method they used most frequently to document complete colonoscopy. Each reviewer then assessed the 100 photographic pairs and was asked ''Taking both photographs into account are you convinced that complete colonoscopy has been performed?''
Results: Thirty four endoscopists completed information on their current practice; 19 (56%) did not routinely use any objective method to document colonoscopy completion; 13 (38%) most frequently used single or multiple photographs for documentation. 32 endoscopists reviewed the 100 pairs of photographs. This generated review of the equivalent of 2560 (32×80) images of completed colonoscopy and 640 (32×20) images of incomplete colonoscopy. Using a pair of endoscopic photographs to document colonoscopy completion had a sensitivity of 51.4% (CI 49.5–53.3%) and a specificity of 89.2% (CI 86.8–91.6%).
Conclusion: Endoscopic photographs are not routinely used to document completion of colonoscopy. Both the sensitivity and the specificity of a pair of endoscopic photographs are too low to be used for reliably documenting colonoscopy completion.

1. **Rex DK**. Still photography versus videotaping for documentation of cecal intubation: a prospective study. *Gastrointest Endosc* 2000; **51**:451–9.
2. **Marshall JB**, Brown DN. Photodocumentation of total colonoscopy: how successful are endoscopists? Do reviewers agree? *Gastrointest Endosc* 1996;**44**:243–8.

021 BOTOX PREDICTS THE OUTCOME OF ENDOSCOPIC SPHINCTEROTOMY IN POST-CHOLECYSTECTOMY BILIARY PAIN DUE TO SPHINCTER OF ODDI SPASM

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Introduction: Muscle spasm of the sphincter of Oddi (SO) can cause post-cholecystectomy biliary pain. Sphincter of Oddi hypertension (SOH) is classically diagnosed using endoscopic SO manometry (EBM). This procedure is associated with a high incidence of pancreatitis and does not accurately define the patients whose symptoms are due to SO spasm. Botulinum toxin (Botox) injected into the SO muscle will relax the sphincter for 2–3 months.
Aims & Methods: To study whether relief of pain following Botox injection predicts the outcome of endoscopic sphincterotomy in post-cholecystectomy biliary pain due to SO spasm.
Methods: Over a 3-year period, 78 patients underwent 4 injections of 25 units each of Botox into their SO muscle at duodenoscopy.
Results: Fifty eight (50 females) of these 78 patients were referred with post-cholecystectomy biliary pain and no physical abnormality of the biliary tree. Thirty three of these 58 patients underwent EBM prior to Botox treatment. Forty one of the 58 patients (71%) experienced temporary relief from their pain following Botox treatment. Thirty nine of these 41 patients have undergone endoscopic biliary sphincterotomy (ES) with relief of pain in 36 patients (92%). All 25 patients with positive EBM and relief of pain following Botox achieved pain relief following ES compared with an 85% response for those patients who did not undergo EBM prior to Botox treatment. This compares with a 75% pain relief rate when ES was based on EBM results alone.
Conclusion: Botox relaxation of the SO is a highly sensitive indicator of the response to endoscopic sphincterotomy in patients likely to have biliary pain from SOH.

022 DETERMINATION OF SAFETY OF DRINKING BEFORE GASTROSCOPY

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Introduction: Traditionally patients have fasted for 6 hours (food and fluid) before routine endoscopy. A number of guidelines have endorsed shorter fluid fasts for elective surgical procedures. The findings of one small randomised controlled trial comparing a shortened fluid fast of 90 minutes before endoscopy with traditional 6-hour fast suggests similar residual

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gastric volume and pH, but conditions were very controlled.[1] An unpublished survey of endoscopy units in NW England in 2000 revealed only 4 of 21 units with a fluid fasting policy of 2 hours.
Aims & Methods: To determine the clinical equivalence of a shortened and conventional fluid fasting time in endoscopy patients on levels of gastric volume and pH. Study design: double blind randomised controlled clinical equivalence trial. Study population: patients aged 18–80 years and ASA grade 1 or 2 undergoing routine gastroscopy performed by a nurse endoscopist. Setting: one endoscopy unit in NW England. Study period: June 2002 to June 2006. Randomisation: central off-site computer-generated randomisation stratified by age and sex. Intervention: intervention group: 6 hours from appointment time food fast and 2 hours clear fluid fast. Control group: standard 6 hours from appointment time fast for food and fluid. Main outcome measure: residual gastric volume. Other outcome measure: pH. Subsidary outcome measures: thirst, headache, anxiety, adverse events.
Results: Of the 440 subjects randomised, 218 were in the intervention group and 222 in the control group. Sixteen subjects were on acid suppressants at time of endoscopy. With the exception of smoking, baseline characteristics were similar between the groups. The median time from last drink to procedure was estimated to be 2.7 hours and 6.9 hours for the intervention and control group respectively. A total of 418 subjects had a residual gastric volume collected. The mean residual gastric volume in the intervention group was 24.5 ml (SD 18.83) and 24.0 ml (SD 17.05) in the control group (difference = 0.5 ml, 95% CI −2.95 to 4.00). There were no adverse events. Compared to the control group, intervention group subjects were more satisfied with fasting time and had less thirst but were more anxious. The difference in mean residual gastric volume in smokers was 0.9 ml (−5.9 to 7.7) and in non-smokers was 1.3 ml (−2.9 to 5.4).
Conclusion: A policy advising a shortened fluid fast before gastroscopy does not appear to substantially increase the residual gastric volume.

1. **Greenfield SM**. Assessment of residual gastric volume and thirst in patients who drink before gastroscopy. *Gut* 1996;**39**:360–2.

Oesophageal free papers

023 LARGE-SCALE PROSPECTIVE STUDY REVEALS NOVEL RISK FACTORS FOR BARRETT'S OESOPHAGUS

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Introduction: Barrett's oesophagus (BO) is the precursor lesion for oesophageal adenocarcinoma (AC), which is rapidly rising in incidence. Most patients with AC present de novo without the opportunity for surveillance as their BO has not been diagnosed. Hence the epidemiological risk factors associated BO could be clinically useful in determining a Barrett's predictor model, to determining which patient group to screen. To date symptom nomograms have not been sensitive or specific enough for clinical use.
Aims & Methods: A modified validated questionnaire was used to prospectively investigate the epidemiological factors that may be associated with BO in consecutive patients attending upper gastrointestinal endoscopy for all indications. Unselected patients between 18–75 years were recruited prospectively in 3 UK centres: Addenbrooke's Hospital, Cambridge, Oldchurch Hospital, Essex and UCLH, London following MREC approval.
Results: 1823 patients were recruited, 904 were male (M) and 919 female (F). 119/1823 (6.5%) patients were found to have a new diagnosis of BO, 78M and 41F. The significant findings on univariate analysis and multivariate logistic regression analysis are summarised in the table. Smoking at various time points was not associated with BO.
Conclusion: This is the largest prospective epidemiological study to date. Multivariate analysis showed that increasing age, male sex, duration of reflux symptoms and nocturnal symptoms were associated with a diagnosis of BO. Although current alcohol consumption was not associated with an increased OR of BO, at age 30 this was associated with an astonishing OR of 30.32 on univariate analysis, supporting the hypothesis that this may act as an initiator of BO. Interestingly, eating smaller meals more often was associated with a reduced OR of BO, suggesting that adopting this lifestyle measure may be efficacious in reducing reflux and prevention of BO. Risk factors for BO are multifactorial and large patient numbers are required to demonstrate factors with relatively small odds ratios.

Abstract 023 Significant risk factors for Barrett's oesophagus on uni- and multivariate analysis

	Univariate analysis (OR)	p Value	Multivariate Log regression (OR)	p Value
Sex (M:F)	2.01	<0.001	2.04	0.004
Age	1.03 per year	<0.001	1.03	0.001
Heartburn >5 years	1.88	0.003	1.80	0.013
Acid regurgitation >5 years	3.31	0.028		NS
Noctural awakening heartburn	1.80	0.034	1.96	0.022
Nocturnal acid regurgitation	1.70	0.034		NS
Heartburn: some bothersome sx	1.97	0.009	1.84	0.01
Alcohol >10 units aged 30	30.52	0.006		NS
Eating smaller meals	0.51	0.005	0.48	0.004

NS, not significant; OR, odds ratio.

024 MAPPING CLONALITY IN INDIVIDUAL GLANDS FROM HUMAN BARRETT'S OESOPHAGUS

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Introduction: Barrett's oesophagus is am important pre-malignant condition. Work on clonal expansion in Barrett's suggests that in some patients a single clone can expand to populate an entire Barrett's segment. This work was largely completed on lysate obtained from whole biopsies.
Aims & Methods: We aimed to re-examine the clonality of Barrett's dysplasia using p53 gene mutations and microsatellite markers to assess for loss of heterozygosity (LOH) in the lysate obtained from single Barrett's glands. Individual glands from across dysplastic patches from paraffin embedded Barrett's tissue were isolated by laser capture microdissection. Gland lysate underwent microsatellite marker analysis for three tumour suppressor genes (APC, p53, p16), and nested PCR amplification to allow p53 gene sequencing. Individual gland mutations were compared with the results obtained from whole biopsy lysates.
Results: Dissected tissue was classified histologically. LOH patterns for the three different markers were analysed for each of the histological tissue grades present in oesophagectomy and biopsy blocks. p53 gene mutations and LOH patterns showed a great deal of clonal diversity between individual glands in oesophagectomy blocks, suggesting a greater degree of clonal heterogeneity than expected. No LOH or gene mutations were found in neo-squamous islands. Individual gland dissection also allowed detection of LOH not detectable from whole biopsy analysis.
Conclusion: Individual gland dissection and analysis reveals clonal diversity within Barrett's segments not detectable by whole biopsy analysis. Gland-to-gland clonal heterogeneity suggests that previous models of mutational selective sweeps across entire Barrett's segments may be oversimplifications. Neo-squamous islands appear to have a different clonal origin from the surrounding mucosa and may originate from oesophageal gland ducts.

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025 LOW INCIDENCE OF OESOPHAGEAL ADENOCARCINOMA FOLLOWING OPTIMAL REGIMEN OF AMINOLAEVULINIC ACID PHOTOFRIN PHOTODYNAMIC THERAPY FOR HIGH GRADE DYSPLASIA IN BARRETT'S OESOPHAGUS

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Introduction: Photofrin photodynamic therapy (PDT) has recently been licensed to treat high grade dysplasia (HGD) for the prevention of adenocarcimoma in Barrett's oesophagus. Aminolaevulinic acid (ALA) PDT is a potentially attractive alternative because of the short light photosensitivity (24 hours) and lack of oesophageal stricture formation. Many different ALA regimens have been suggested in the literature for the eradication of dysplasia in Barrett's oesophagus including varying light dose, drug dose and wavelength of the activating light. The optimal regimen of ALA PDT remains unknown.
Aims & Methods: Seventy two patients were treated for high grade dysplasia with different parameters of ALA PDT to determine the optimal regimen. All patients were hydrated with intravenous fluids prior to the oral administration of ALA to prevent systemic hypotension. Three groups of patients were studied: Group A: high dose ALA (60 mg/kg) activated by high dose red light (1000 J/cm), Group B: high dose ALA activated by lower doses of red light (500–750 J/cm), and Group C: low dose ALA (30 mg/kg) activated by high light dose. Additionally, 24 patients in groups A and C were randomised to either red (1000 J/cm) or green laser light (1000 J/cm) activation. Success was determined by regular endoscopic follow-up and quadrantic biopsies every 2 cm through the treated area. The primary outcome was development of adenocarcinoma.
Results: One patient was lost to follow-up. Kaplan Meier analysis demonstrated that patients treated in group A, with high red light and high drug dose, had a very significant decrease in cancer risk at 36 months at 3% compared with 34% in those treated with other regimens (Log rank statistic = 0.002). In patients randomised to either red or green light activation the difference in adenocarcinoma rates were also significantly different in favour of red light at 8% versus 45% (p value <0.05). No patients suffered photosensitivity reactions or developed oesophageal strictures.
Conclusion: This case series of 72 patients demonstrates a statistically significant difference in the cancer rates between ALA regimens. The adenocarcinoma incidence rate following ALA PDT with the most effective regimen was low at 3% compared to the other regimens at 34%. This data compare favourably to the cancer rates in the randomised trial of PPI versus photofrin PDT at 28% and 14% respectively at two years' follow-up. These data would support the use of the optimal regimen of ALA in a randomised controlled trial of ALA versus photofrin PDT.

026 INTEROBSERVER VARIATION IN THE DIAGNOSIS OF DYSPLASIA IN BARRETT'S OESOPHAGUS

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Introduction: Riddell *et al*[1] described ''dysplasia'' as an unequivocal neoplastic alteration of the epithelium. Six studies have assessed the interobserver variation in the diagnosis of dysplasia in Barrett's oesophagus (BO), mostly based on Riddell's method of classification in IBD. There are no studies based on the accepted Vienna system.
Aims & Methods: The primary aim of the study was to assess the interobserver variation in the diagnosis of dysplasia (in particular, indefinite for dysplasia) in BO using the revised Vienna classification. Histology database was searched for lists of cases diagnosed with BO (SIM on histology), dysplasia and adenocarcinoma in the time period 1 April 1984 to 31 December 2004. 42 cases with a diagnosis of IND for dysplasia and 15 time-matched controls, each with a diagnosis of BO without dysplasia, LGD, HGD and ADO were thus identified and 137 slides retrieved. Three GI histopathologists (P1, P2 and P3) reassessed the slides independently based on the revised Vienna classification. Interobserver agreement between individual GI pathologists was determined by Cohen's Kappa statistics.
Results: Twenty one of 42 cases (50%) were reclassified as IND by at least one of the three histopathologists—14 by pathologist 1 (P1), 3 by pathologist 2 (P2) and 12 by pathologist 3 (P3). Thus P1, P2 and P3 were in agreement with the original diagnosis of IND in 14/42 (33%), 3/42 (7%) and 12/42 (29%) cases respectively. P1 and P2 agreed on the diagnosis of IND in a single case, P2 and P3 in none and P1 and P3 in 7 cases. A consensus diagnosis of BO in 11 of 42 cases (26%) originally diagnosed as IND. The kappa for the cases with an initial diagnosis of IND (n = 42) between P1 and P2 was 0.15 (poor), between P2 and P3 was 0.03 (poor) and between P1 and P3 was 0.35 (fair). The kappa on all cases between P1 and P2 was 0.26 (fair), between P2 and P3 was 0.13 (poor) and between P1 and P3 was 0.36 (fair).
Conclusion: This is the first study looking at interobserver variation in the diagnosis of indefinite for dysplasia in Barrett's oesophagus using the revised Vienna criteria. This is the most difficult group to identify histologically due to the overlap with inflammatory changes, but causes surveillance and clinical conundrums. The kappa for the diagnosis of IND was fair at best in this study (0.15, 0.03 and 0.35 respectively).

1. **Riddell RH**, Goldman H, Ransohoff DF, *et al*. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. *Hum Pathol* 1983;**14**:931–68.

027 DYNAMICS OF UNBUFFERED POSTPRANDIAL ACID POCKET AND ROLE IN ACIDIC GASTROESOPHAGEAL REFLUX

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Introduction: An unbuffered pocket of highly acidic juice is observed in the proximal stomach after a meal in healthy subjects using pull-through pH studies.
Aims & Methods: (1) To confirm that postprandial acidification of the proximal stomach occurs using a novel static high resolution pH catheter. (2) To determine whether the characteristics of this acid pocket change with time. (3) To establish whether discrete episodes of oesophageal acid reflux originate from the postprandial acid pocket. Fifteen healthy subjects were studied. A custom made high resolution 12 sensor pH catheter (sensors 1–12 located 172; 138; 127; 116; 105; 94; 83; 72; 61; 50; 30; 0 mm from the distal tip) was attached to the oesophageal mucosa at the proximal margin of the gastric folds using endoclips through prolene loops between sensors 4 and 5. After a 2-hour rest period following endoscopy, fasting pH was recorded for 30 minutes, during a standardised meal and for 90 minutes after completion of the meal. The % time pH $\geqslant 4$ for the 90 minute postprandial period in every sensor was calculated for each subject and episodes of postprandial acidic oesophageal reflux recorded.
Results: The median % time pH $\geqslant 4$ for the 90 minute postprandial period was reduced in the sensors immediately distal to the proximal margin of the gastric folds. The median difference (in median % time pH $\geqslant 4$) between sensors 6 and 10 (the area of most consistent intragastric buffering) was 29.3% (p = 0.045) with a strong trend also seen in sensors 7 (median difference 21.5% *v* sensor 10; p = 0.055) and 12 (median difference 15.5% *v* sensor 10; p = 0.09).The proximal stomach showed the least duration of buffering after completion of the meal. The duration of buffering progressively increased on moving distal to the proximal stomach. 60 reflux events (oesophageal pH$<$4) were recorded in the postprandial period in the 15 subjects. 43/60 (71.7%) acid reflux events could be attributed to a source within the proximal stomach.
Conclusion: Postprandial buffering is of least duration in the proximal stomach and this provides a source of highly acidic gastric juice available for reflux into the oesophagus.

Abstract 027

Sensor	1	2	3	4	5	6	7	8	9	10	11	12
Median % time pH $\geqslant 4$	99.9	99.4	98.8	97.5	79.9	41.9	55.8	98.9	99.7	99.6	85.5	69.2
Distance proximal (−) or distal (+) to folds (mm)	−61.5	−27.5	−16.5	−5.5	5.5	16.5	27.5	38.5	49.5	60.5	80.5	110.5

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028 THE PREVALENCE OF LARYNGOPHARYNGEAL REFLUX IN A POPULATION WITH GASTRO-OESOPHAGEAL REFLUX

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Introduction: Laryngopharyngeal reflux (LPR) is a syndrome associated with a constellation of symptoms usually treated by ENT surgeons. It is believed this is caused by the retrograde flow of stomach contents into the laryngopharynx; this being a supra-oesophageal manifestation of gastro-oesophageal reflux (GORD).[1] It has been cited that LPR and GORD can be considered as separate entities.[2] Our hypothesis was that LPR is a supra-oesophageal manifestation of GORD and therefore that patients with GORD should have a degree of symptoms suggestive of LPR due to the reflux of the gastric contents. We examined a population of patients with both UGIE and symptom-proven GORD and using a questionnaire looked at their existing symptoms to help assess the prevalence of LPR. We also looked at whether, as expected, that with more severe GORD (suggestive of increased gastric contents reflux) the degree of symptoms suggestive of LPR would be increased.
Aims & Methods: A population of patients with endoscopically-proven GORD were recruited and divided into groups depending on the severity of their reflux disease. A questionnaire was then administered examining both LPR and GORD scoring criteria. The relationship between GORD and LPR was then analysed.
Results: 1383 subjects with GORD were recruited; those with severe GORD had significantly higher LPR scores compared with those with mild ($p<0.01$), moderate ($p<0.05$) and inactive disease ($p<0.001$).
Conclusion: The condition of LPR is likely to represent a supra-oesophageal manifestation of GORD. This study has examined a large number of patients with endoscopically-proven GORD and has demonstrated a correlation between severity of GORD and the prevalence of LPR. LPR and GORD remain common and interlinked conditions. Most patients with GORD have LPR but tend only to complain of the dominant symptoms. The subsequent diagnosis of LPR in the population with GORD is therefore likely to be dramatically underestimated.

1. **Koufman JA**. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): A clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. *Laryngoscope* 1991;**101**(Suppl 53):1–78.
2. **Koufman JA**, Belafsky PC, Daniel E, *et al*. Prevalence of oesophagitis in patients with pH-documented laryngopharyngeal reflux. *Laryngoscope* 2002;**112**:1606–9.

029 LASER AND RADICAL CHEMORADIOTHERAPY FOR OESOPHAGEAL CARCINOMA

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Introduction: The incidence of oesophageal carcinoma is rising with rates in the UK the highest in the EU. Most patients present with locally advanced disease and 5-year survival rates are poor. The median survival even after neoadjuvant chemotherapy and surgery is only 17 months. Further, most patients are elderly, present with dysphagia and may be unfit for surgery. Minimally invasive approaches are needed.
Aims & Methods: To determine whether endoscopic laser followed by radical chemoradiotherapy resulted in acceptable survival and morbidity. We retrospectively reviewed the notes of all patients with oesophageal carcinoma treated with laser followed by radical chemoradiotherapy at UCH between January 1999 and November 2004. All patients had palliation of dysphagia before starting chemoradiation. Mitomycin C and 5-fluouracil were then administered during weeks 1 and 4 of external beam radiotherapy (median 55 Gy, range 45–60 Gy) which was given in divided daily doses over 6 weeks.
Results: Thirty one patients, (21 male, 10 female), median age 69 (range 51–88) were treated. 19 patients had squamous cell carcinoma and 12, adenocarcinoma. Two patients had stage T2N1, 12 had T3 disease and 15, T3/4 or T4 disease. Dysphagia was adequately palliated in all apart from 4 who had a PEG placed. 28 of 31 patients completed treatment. Overall median survival was 15 months which did not change after exclusion of patients who had had less than 50 Gy radiotherapy. Median survival among patients with adenocarcinoma was 22 months compared with 12 months for squamous cell carcinoma. Early toxicity was mild with radiation-associated dysphagia in only 4 patients. Late toxicity included a benign oesophageal stricture in 50% which responded to dilatation. Local recurrence occurred in at least 50% of patients.
Conclusion: Laser followed by radical chemoradiotherapy appears to be a viable treatment for locally advanced oesophageal carcinoma which causes minimal morbidity compared to surgery. It is generally well-tolerated and provides a median survival similar to neoadjuvant chemotherapy followed by resection. A randomised controlled trial comparing these approaches is warranted.

030 CLINICAL OUTCOME OF CASES WITH INDEFINITE FOR DYSPLASIA IN BARRETT'S OESOPHAGUS OVER A 20 YEAR PERIOD

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Introduction: The American College of Gastroenterology and the British Society define Barrett's oesophagus (BO) as a change in the oesophageal epithelium of any length that can be recognised at endoscopy and is confirmed or corroborated to have intestinal metaplasia on histology. Two yearly surveillance is recommended for non-dysplastic BO, more often for cases with dysplasia. No study has looked at clinical outcome of cases with the diagnosis of indefinite (IND) for dysplasia in BO-clinically important but the most difficult group to survey.
Aims & Methods: The aim was to study the clinical outcome of the cases diagnosed as IND for dysplasia over the last 20 years at our institution. This was a cohort analytical study. Histology database was searched for the words ''dysplasia'', ''Barrett's oesophagus'', ''specialised intestinal metaplasia'' and ''oesophageal adenocarcinoma'' to generate lists of cases diagnosed with Barrett's oesophagus (SIM on histology) and dysplasia in the time period 1 April 1984 to 31 December 2004. Demographics were collected from case notes, endoscopy and histology records. All cases had slides reviewed by three GI histopathologists. Progression was defined as a diagnosis of LGD, HGD or ADO while regression was defined as a diagnosis of BO. For the cases that progressed, progression was correlated with the re-diagnosis of IND, and consensus diagnosis between the three histopathologists.
Results: Follow-up information was available on all 42 cases originally diagnosed as IND for dysplasia. They were followed up for a median of 38.7 months (range 6–122 months). 31 cases (73%) did not progress but 11 cases (27%) progressed. Of these 11 cases, 5 (45%) to LGD, 3 (28%) to HGD, 2 (18%) to suspicious for invasive carcinoma and 1 (9%) developed intramucosal cancer. The 11 cases which progressed did so after a median follow-up of 31.4 months (range 6–104 months). All three histopathologists agreed on a common diagnosis of BO in 2 of these 11 cases but in neither of these did they all agree on a common diagnosis of IND. However, P1 and P3 agreed on a diagnosis of IND in 3 of the 11 cases. The 9 cases that progressed and had no consensus diagnosis were reclassified by P1 as BO (2), IND (3), LGD (2), HGD (1) and CIS (1) by P2 as BO (1), LGD (2), HGD (4) and IMCA (2) and by P3 as BO (1), LGD (3) and HGD (5) respectively. There was a non-significant negative correlation with progression and a consensus diagnosis of IND (8 cases (7 between P1&P3 and 1 between P1&P2) ($r=-0.308$, $p=0.809$)), but a significant positive correlation between a diagnosis of IND by at least one histopathologist (21 cases) and progression ($r=0.485$, $p=0.01$). On Kaplan–Meier analysis, there was no significant association between a consensus diagnosis of IND, or a re-diagnosis of IND with progression.
Conclusion: A second opinion from an experienced histopathologist does not necessarily predict cases with an initial diagnosis of IND for dysplasia, which might progress. Patients with a diagnosis of IND for dysplasia should be offered surveillance similar to other dysplasia grades as a proportion of these progress to higher grades, though there is no correlation between a consensus agreement and progression.

031 THE SAINT TRIAL (STEM CELL ANALYSIS AND IDENTIFICATION BY IUDR LABELLING OF NEOPLASTIC TISSUE): IDENTIFICATION OF BARRETT'S STEM CELLS

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Introduction: A gastrointestinal epithelial cell will be shed from the epithelial surface into the lumen and replaced from below by the progeny of a somatic stem cell. Since stem cells are the only long-residing cells

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within the gastrointestinal epithelium, it is logical that they are the target for mutations that may lead to the aberrant epithelial biology seen in Barrett's metaplasia, a pre-malignant condition that can lead to oesophageal adenocarcinoma. To date, the identification of the putative stem cell within the epithelium of the Barrett's metaplastic lesion remains elusive.
Aims & Methods: We used iododeoxyuridine (IUdR) a nucleoside and a thymidine analogue which is incorporated into the DNA of replicating cells, as a marker to identify the putative Barrett's stem cell. Since transit amplifying cells are lost from the lumen and replaced from below in about 3–7 days, we expect the label retaining cells (LRC) to contain the putative Barrett's stem cell.Two patients diagnosed with oesophageal adenocarcinoma having previously undergone chemotherapy were scheduled to undergo oesophagectomy. These two patients were recruited to the SAINT clinical trial. Seven days prior to their surgery each patient was infused with IUdR. After resection, tissue samples of normal oesophagus, Barrett's, normal stomach and tumour were extracted and fixed in neutral buffered formalin for approximately 8 hours. Routine immunohistochemistry was performed on 6 micron sections of all tissue types.
Results: Infusion three days or less in vitro in transformed cells and explants revealed appropriate abundant staining of the proliferative compartments. However labelling at 7 days days in both patients ex vivo showed positive discrete staining of LRCs within various gastrointestinal tissue types including Barrett's metaplasia. These label retaining cells were seen in the parabasal layer and basal layer of the squamous epithelium, this is in line with the current dogma of the location of the oesophageal stem cell. LRCs were seen at several locations in metaplastic tissue both at the base of the gland and in the neck region.
Conclusion: This is the first report of LRCs within the human oesophagus. Our findings correlate with the hypothesised location of stem cells in the squamous epithelium. More importantly LRCs were also located in the basal and neck region of the Barrett's gland, implying that these are the locations of Barrett's stem cells. Future studies underway include looking at 14 days post-IUdR infusion pre-surgery as well as molecular characterisation of the stem cells and their niche.

032 ELASTIC SCATTERING SPECTROSCOPY TO GENERATE AN IMAGE OF PATIENT RISK IN BARRETT'S OESOPHAGUS

G. D. Mackenzie, M. Yong, B. Clark, M. R. Novelli, S. M. Thorpe, S. G. Bown, L. B. Lovat. *National Medical Laser Centre, University College London, London, UK*

Introduction: Elastic scattering spectroscopy (ESS) is a real-time in vivo technique which detects changes in the physical properties of cells. We have previously demonstrated a sensitivity for detecting high grade dysplasia (HGD) in Barrett's oesophagus of 92% and a specificity of 60%. ESS is a point measurement but readings are extremely fast offering clinicians the opportunity to virtually ''scan'' an area of Barrett's mucosa.
Aims & Methods: This was a preliminary study to prospectively test our previously published algorithm for the detection of HGD and aneuploidy in Barrett's oesophagus. Four measurements per site and quadrantic sites every centimetre were measured throughout a patients Barrett's segment. An optical image was created by interpolating the spectral scores following analysis to define the risk of HGD and aneuploidy. This was then compared to quadrantic biopsies every 2 cm taken for histology. One biopsy at each level was processed for aneuploidy using image cytometry. The time taken for the measurements to be collected was recorded in order to assess practicality.
Results: Forty patients had their Barrett's oesophagus scanned. Twenty four had HGD on subsequent biopsies and 16 had either low grade dysplasia or no dysplasia. Of these 16 patients without HGD, 7 were found to have aneuploidy in all of their biopsies. All 24 patients with HGD and all 7 with aneuploidy had positive scans and 4/9 low risk patients with no dysplasia or aneuploidy had entirely negative scans. If biopsies were directed only at suspicious areas on the scans, 17 instead of 80 biopsies would have been required in the low risk patients and only 7 instead of 19 would have been necessary to exclude aneuploidy. Scanning the oesophagus optically was performed by four different operators and took an average of 4 minutes and 22 seconds for a 6 cm segment of Barrett's, with no significant difference between operators.
Conclusion: Scanning patients Barrett's oesophagus is fast without interobserver variability and can be used to identify high risk patients with either HGD or aneuploidy. It could reduce the number of biopsies required to detect HGD by over a half and reduce the number of biopsies processed for aneuploidy by over 60% in a surveillance population. The findings also suggest that no biopsies would be needed in a half of all patients undergoing endoscopic surveillance. In this series, no patients with HGD or aneuploidy had negative scans. This study requires completion followed by confirmation in multisite testing on a surveillance population.

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033 RANDOMISED CONTROLLED TRIAL OF PATIENT CONTROLLED SEDATION FOR COLONOSCOPY: ENTONOX VERSUS PATIENT-MAINTAINED, TARGET-CONTROLLED PROPOFOL

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Introduction: Intravenous sedation for colonoscopy is associated with cardiorespiratory complications and prolonged drowsiness and we have previously shown that Entonox is superior to intravenous sedation.[1] Moreover, patient controlled sedation has shown to be effective for various procedures. We aimed to compare patient-controlled Entonox inhalation with patient-maintained, target-controlled Propofol infusion for colonoscopy, in terms of analgesic efficacy, psychomotor recovery, patient and endoscopist satisfaction.
Aims & Methods: All patients undergoing elective colonoscopy were included. Ethics committee approval was obtained and patients were randomised (with adequate allocation concealment) to receive either Entonox or target-controlled infusion of propofol. Patients in entonox group inhaled gas for 60 seconds before procedure and then as required. Patients in propofol group were administered the drug with target of 1.2 μg/ml loading dose and then allowed to sedate themselves using handset. Sedation scoring was done every 5 minutes during procedure and every 10 minutes subsequently. Patients completed anxiety score, baseline letter-cancellation test and pain score on 100 mm-visual analogue scale (VAS) before procedure and repeated letter-cancellation tests and marked pain on VAS immediately after procedure and at discharge. All patients completed satisfaction survey at discharge and 24-h post-procedure, when they also marked pain assessment. Secondary end-points measured were completion rates, nurse and endoscopist satisfaction and complication rates. An anaesthetist was present throughout procedure.
Results: 100 patients were randomised to receive Entonox ($n=50$) or Propofol ($n=50$). The median dose of propofol was 174 mg and median time to reach target concentration was 3 minutes. There was no difference in two groups in terms of pain recorded (Entonox group mean score 20 *v* 15, $p=0.3$; Mann–Whitney U test) with similar pre-procedure anxiety scores ($p=0.1$). There was no difference between two groups in terms of completion rates, total colonoscopy time and endoscopist and nurse satisfaction. Patient satisfaction was similar in both groups. The depth of sedation was higher in propofol group (median 3/5 as compared to 1/5 in entonox group), with more patients needing assistance for change of position as compared to Entonox group (6 *v* 0; $p<0.05$). Psychomotor recovery and hence discharge was faster in entonox group, though differences were not statistically significant. There were no complications in both groups.
Conclusion: Patient-controlled sedation using target-controlled Propofol provides greater depth of sedation as compared to Entonox; however both techniques are safe and effective for colonoscopy, providing excellent patient satisfaction and facilitating early discharge. We believe that Entonox should be used in all patients undergoing colonoscopy but with patient-controlled Propofol used instead of midazolam/analgesia for those cases where Entonox is unsuitable.

1. **Maslekar S**, Hughes M, Skinn E, *et al.* Entonox is superior to intravenous sedation: proof from randomised controlled trial. *Gut* 2006;**55**(Suppl 2):a1–a119.

034 HIGH PROFICIENCY READING OF 3D VIRTUAL COLONOSCOPY BY EXPERIENCED OPTICAL ENDOSCOPISTS AND ENDOSCOPY NURSES: A NEW ERA IN COLONOSCOPY?

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Introduction: V3D (Viatronix Inc) virtual colonoscopy (VC) is currently the only CT colonoscopy application which presents the reader with a primary 3D animated image of the colon. The virtual reality image resembles a conventional optical colonoscopy (OC) and the mouse control closely replicates the tip-control of a video-endoscope. A large screening study conducted by radiologists has indicated that V3D VC is at least as sensitive as optical colonoscopy for detecting cancer, and polyps >5 mm in size 1. In this study, we have tested the hypothesis that experienced endoscopists and endoscopy nurses are able to accurately read and interpret 3D VC.

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Aims & Methods: Fifty symptomatic gastroenterology outpatients aged 45 and older underwent same-day VC and OC. The VC image included matched supine and prone views. An experienced GI radiologist (JB) provided initial training to two advanced gastroenterology trainees (AP, SE) and an experienced endoscopy nurse (LJ). The radiologist and three non-radiologists independently inspected both the prone and supine VCs from rectum to caecum and caecum to rectum. All readers were blinded to the colonoscopy result. The 2D view was only referenced when the 3D view was equivocal. The endoscopist performing the OC was unaware of the V3D result until the withdrawal phase of the endoscopy when segmental unblinding occurred. The VC and OC findings were compared using the unblinded OC as the reference standard.
Results: Three cancers were found on OC, all of which were detected by the four VC readers. On unblinded OC, six polyps >5 mm in diameter were reported in five patients. The radiologist and one gastroenterology trainee detected all 6 polyps on VC. The second trainee and the endoscopy nurse correctly identified five polyps. Both failed to identify the same polyp localised at the anal margin, abutting on the non-occluding rectal inflation catheter. The mean reporting time for the radiologist was 21.0 (SD 4.99) minutes. The mean reading time for non-radiologist ranged from 25.8 (SD 9.37) to 44.1 (SD 12.43) minutes with the nurse reading the quickest. The endoscopy nurse, gastroenterology trainees and the radiologist reported preference or equivalence for the 3D, as opposed to 2D image in 100%, 85%, 84% and 80% of the VC images respectively.
Conclusion: After a short period of training, experienced endoscopists and endoscopy nurses can be taught to read animated VC to a similar standard as radiologists. It is well established that distal rectal polyps abutting on the rectal catheter are easily missed on VC and this accounted for the single polyp not identified by two of the non-radiologists. Accurate VC reporting by experienced colonoscopists and endoscopy nurse raises the possibility of non-radiologists reporting 3D VC, and if positive, immediately progressing to a targeted therapeutic or diagnostic colonoscopy on the pre-prepared bowel. This paradigm offers a new model for colon imaging and colon cancer screening.

1. **Pickhardt PJ**, *et al*. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 2003;**349**:2191–200.

035 ENDOSCOPIC MUCOSAL RESECTION FOR FLAT NEOPLASIA IN CHRONIC ULCERATIVE COLITIS: CAN WE CHANGE THE ENDOSCOPIC MANAGEMENT PARADIGM?

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Introduction: No studies have addressed the potential of EMR for treating flat dysplastic lesions (Paris 0-II) in chronic ulcerative colitis (UC). Historically, such lesions were referred for colectomy. There are only limited data to support endoscopic resection of exophytic (Paris I) adenoma-like mass lesions in UC.
Aims & Methods: To evaluate the safety and clinical outcomes of patients with chronic UC undergoing EMR for Paris class 0-II and class I adenoma-like mass as compared to sporadic controls. Secondary aims: to re-evaluate the prevalence, anatomical ''mapping'' and histopathological characteristics of both Paris class 0-II and class I lesions in the context of UC. Prospective clinical, pathological and outcome data of patients with colitis-associated Paris class 0-II and Paris class I adenoma-like mass treated with EMR (primary end-points being colorectal cancer development, resection efficacy, metachronous lesion rates and post-resection recurrence rates) were compared to sporadic controls.
Results: 204 lesions were diagnosed in 169 UC patients throughout the study period. 82% (167/204) were diagnosed at ''entry'' colonoscopy with 36/204 (18%) at follow-up. A total of 170 ALMs, 18 DALMs and 16 cancers were diagnosed. 4316 colonoscopies were performed throughout the study period (median per patient 6; range 1–8). The median follow-up period for the complete cohort was 4.1 years (range 3.6–5.21). 1675 controls were taken from our prospective database of non-colitis patients who had undergone EMR of sporadic Paris class 0-II and Paris type I lesions from 1998 and considered to be at ''moderate'' to ''high'' lifetime risk of colorectal cancer. 3792 colonoscopies were performed in this group (median per patient 4; range 1–7), median follow-up period 4.8 years (range 2.9–5.2). There were no statistically significant differences observed between the UC group and controls with respect to age, sex, median number of colonoscopies per patient, median follow-up duration, post-resection complications, median lesional diameter or interval cancer rates. LST recurrence rates were higher in the UC cohort (1/7 (14%)) as compared to controls (0/10 (0%); $p=0.048$). There was a significant between-group difference regarding Paris class 0-II lesion prevalence in the UC group (82/155 (61%)) as compared to controls (285/801 (35%); $p<0.001$).
Conclusion: Flat dysplastic Paris class 0-II adenoma like mass, similarly to Paris class I lesions, can be managed safely by EMR in chronic UC with no increase in colorectal cancer incidence at medium-term follow-up. A change in management paradigm to include EMR for the resection of flat dysplastic lesions in selected UC cases is proposed.

036 MORTALITY FOLLOWING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: RESULTS OF THE NATIONAL CONFIDENTIAL ENQUIRY INTO PATIENT OUTCOME AND DEATH

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Introduction: Percutaneous endoscopic gastrostomy (PEG) is an accepted method of placing a feeding tube to enable enteral feeding in patients with swallowing difficulties. However the factors associated with morbidity and mortality following PEG have not been studied in detail. We describe the largest audit of mortality following PEG tube insertion in the UK.
Aims & Methods: Deaths occurring within 30 days following PEG tube insertion in the UK between April 2002 and March 2003 were identified and a questionnaire sent to the consultant endoscopist for completion.
Results: 719 patients (391 male, median age 80 years; range 26–98 years) who died within 30 days following PEG insertion were identified. 97% of patients had coexistent neurological disease. PEG tubes were inserted by specialised GI physicians in 522 cases (73%). Seventy two patients (10%) required reversal agents following sedation. Following PEG tube insertion 309 patients (43%) died within one week. Death was due to cardiovascular disease (n=175), respiratory disease (n=508), central nervous system disease (n=358), renal disease (n=38) and hepatic failure (n=11). In 136 cases (19%) the NCEPOD expert panel regarded the procedure as futile.
Conclusion: Mortality and morbidity following PEG tube insertion is not insignificant. Selection of patients is paramount to good patient outcomes. Multidisciplinary team assessment should be performed on all patients being referred for PEG tube insertion. Attention to pre-procedural baseline investigations may also reduce morbidity and mortality.

037 ELECTRONIC CHROMOENDOSCOPY IN BARRETT'S OESOPHAGUS USING NARROW BAND IMAGING: A STUDY TO VALIDATE MUCOSAL MORPHOLOGY FINDINGS AND INTER/INTRAOBSERVER AGREEMENT

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Introduction: High resolution magnification endoscopy (HRME) with narrow band imaging (NBI) improves visualisation of mucosal surface without the need for dye spray (electronic chromoendoscopy).[1] Our aim was to validate the mucosal morphology findings and inter/intra-observer agreement in detecting cardia mucosa (CM), specialised intestinal metaplasia (SIM), dysplasia (D) and early cancer (EC) in Barrett's oesophagus (BO).
Aims & Methods: After inspecting BO in white light overview mode, NBI endoscopy in overview and magnification mode every 1–2 cm was performed by four expert endoscopists (RS, GKA, KY, KR) and a minimum of one biopsy taken from each quadrant imaged. Magnified NBI endoscopic findings were classified as: (A) round pits with regular microvasculature, (B) villous/ridge pits with regular microvasculature, (C) absent pits with regular microvasculature and (D) irregular pits with irregular microvasculature. The endoscopic findings and the corresponding biopsies were recorded and blinded histopathological analysis performed. The sensitivity, specificity, and predictive values of the various patterns for the prediction of CM, SIM and D/EC were then calculated. Reproducibility of this classification was assessed by four non-NBI expert endoscopists (HK, PF, AS, KG). 210 digital images of each pre-biopsy specimen were selected and the predominant pattern agreed upon by the expert endoscopists. Forty of the images were first shown as a reference guide followed by the remaining images which were graded based on the above classification. This was repeated after one week, with the same images but in a different order.

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Results: 100 patients (71 males, mean age 61.7, mean length 4.3 cm) of which 890 biopsy specimens were taken. The sensitivity, specificity, positive and negative predictive values for round pits (type A) (1) corresponding to CM was 97%, 100%, 100%, and 100% respectively; (2) types B-C for the prediction of SIM were 100%, 60%, 86% and 100% respectively and (3) type D for the prediction of HGD/EC was 94%, 100%, 90%, and 100% respectively. The mean kappa value for interobserver agreement in assessing the various patterns were 0.711 (SD 0.042) and the intraobserver agreement was 0.869 (SD 0.031).
Conclusion: HRME with NBI can clearly visualise the mucosal morphology in BO without dye spray. It has a high level of inter- and intraobserver agreement, further demonstrating its potential to be useful in routine clinical practice.

1. **Anagnostopoulos GK**, *et al*. High resolution magnification endoscopy with narrow band imaging in Barrett's oesophagus. *Gut* 2006;**55**:A105.

038 ACHIEVING R0 RESECTION IN THE COLORECTUM USING ENDOSCOPIC SUBMUCOSAL DISSECTION: FIRST FEASIBILITY STUDY IN THE UK

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Introduction: EMR permits resection of Paris type 0-II, Is and LSTs of the colorectum. However, piecemeal EMR has raised concern given default staging to Rx. Endoscopic submucosal dissection (ESD) using a gastroscope and distal transparent cap attachment allows en bloc knife dissection for lesions >20 mm. There are no data regarding ESD technical feasibility in the UK.
Aims & Methods: A prospective technical feasibility study of cap assisted ESD for curative intent in selected Paris 0-II, LST and Is lesions. Primary endpoints were R0 resection status, safety and recurrence rates. Patients with Paris 0-II adenoma or LSTs >20 mm were recruited (EUS pre-resection). Lifting of the submucosal plane from the muscularis was achieved using a 1% solution of 1900 kDa sodium hyaluronic acid (HA). Circumferential mucosal incisions were made at 5–6 mm intervals around the lesion using an Olympus KD 630 L ''flex knife'' (total cutting vertical length 1 mm) using a 40 W pure cut. Submucosal dissection was then initiated from the most proximal lesion aspect using the IT knife in an oblique 30–40 degree axial position. Complications of all resections were recorded in addition to 30-day mortality and re-admission rates.
Results: 42/56 (75%) patients with 42 lesions fulfilled criteria. En bloc resection was achieved in 33/42 (78%) with 9 (22%) requiring a piece meal approach. Median time for ESD completion was 48 mins (range 18–240). Median inpatient stay was 22 hours (range 4–120). Perforation occurred in 1 patient (1/42 (2.4%)). Three patients (3/42 (7%)) required admission due to post resection ileus (median stay 46 hours; range 26–58). Bleeding complications occurred in 5/42 (12%) of cases. There were no significant differences observed regarding the frequency of bleeding complications, lesion diameter or anatomical location between Paris type 0-II lesions as compared to LSTs (G or NG-type). 36 patients (36/42 (86%)) completed a median of 6 months surveillance (range 3–18 months). Recurrent disease criteria were met in 4/36 (11%). At 6 months follow-up overall ''cure rates'' for the ESD cohort was 34/42 (81%).
Conclusion: This is the first UK and largest cohort study addressing the technical feasibility, safety and short-term efficacy of ESD for R0 intent in the colorectum. ESD achieves high endoscopic cure rates using both endoscopic and EUS recurrence criteria. Furthermore, we have extended the technical feasibility of ESD to include en bloc dissections proximal to the splenic flexure. These data may change the management paradigm of selected Tim/T1/N0 neoplastic lesions to one of primary endoscopic versus surgical resection.

039 RANDOMISED TRIAL OF NARROW BAND IMAGING FOR ADENOMA DETECTION AT COLONOSCOPY IN HIGH RISK GROUPS

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Introduction: Comprehensive adenoma detection at colonoscopy is important for carcinoma prevention, risk stratification and as a quality indicator. Back-to-back studies of colonoscopy indicate a miss rate for adenomas of 22%.[1] Flat adenomas are more difficult to detect and may have enhanced pre-malignant potential. Narrow band imaging (NBI) is a novel, push-button, optical technology that enhances contrast for superficial capillaries and may improve adenoma detection.
Aims & Methods: High definition (HDTV) white light colonoscopy was compared with narrow band imaging for ''wide-field'' adenoma detection during colonoscope withdrawal in groups at high risk for adenomas defined as: surveillance following a diagnosis of colorectal cancer; or had at least 3 adenomas or 1 adenoma ⩾10 mm at last colonoscopy; or had a positive faecal occult blood test. Patients were randomised at the caecum if bowel preparation was adequate in a 1:1 ratio. A third generation prototype NBI system (Olympus, Japan) with narrow band filters centred on wavelengths 415 and 520 nm was used. Two experienced colonoscopists who each had over 100 procedures experience with NBI performed the examinations. Minimum withdrawal time was 8 minutes.
Results: Eighty two patients (of a planned 214) were randomised, 41 to each arm. Groups were generally well matched for baseline demographics, but there was an excess of men in the white light arm, p = 0.04. There was a 30% increase in the number of patients with at least 1 adenoma in the NBI arm, p = 0.17 (Fisher exact). More polyps were found in the NBI arm, p = 0.01, with a trend towards more adenomas detected p = 0.06 (Mann–Whitney). There was a trend towards a higher proportion of flat adenomas in the NBI arm, p = 0.08 (Fisher exact). Twice as many patients had 5 or more adenomas in the NBI arm, p = 0.22 (Fisher exact).
Conclusion: In a population at high risk of further adenomas, NBI increased adenoma detection overall by over 40%, driven partly by an increase in the numbers of flat adenomas. NBI may have a role for improving wide field adenoma detection in screening and surveillance of these and other higher risk groups.
ClinicalTrials.gov Identifier: NCT00279357.

Abstract 039

	White light (n = 41)	NBI (n = 41)
Mean age (range)	63 (37–82)	63 (40–84)
Sex , male	31 (76%)	21 (51%)
Extubation time, mins	11	11
At least 1 adenoma	23 (56%)	30 (73%)
Total adenomas	57	81
Flat adenomas	7	20
Advanced adenomas	2	5
Total polyps	86	142
3+ adenomas	12 (29%)	19 (46%)
5+ adenomas	4 (10%)	9 (22%)

1. **van Rijn**, *et al*. *Am J Gastroenterol* 2006;**101**:343–50.

040 STUDY OF SERUM ELECTROLYTES FOLLOWING SODIUM PHOSPHATE BOWEL PREPARATION AND COLONOSCOPY IN PATIENTS WITH NORMAL CREATININE

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Introduction: Sodium phosphate (NaP) is widely used as bowel preparation for colonoscopy. It can cause serum electrolyte abnormalities sometimes severe enough to cause fatalities. The occurrence of these abnormalities in a UK population with normal creatinine is not known.
Aims & Methods: To study the changes in sodium, potassium, magnesium, calcium, and phosphate following NaP bowel preparation and subsequent colonoscopy. Second, to examine the risk factors associated with these changes. Patients undergoing elective colonoscopy between April 2003 and March 2004 with normal creatinine were invited to take part after ethics committee approval. Blood samples were obtained from patients one week before the procedure (baseline, B), before colonoscopy (BC) and after colonoscopy (AC).
Results: Seventy seven patients were included after informed consent. The median age was 58 years (range 22–97) and male/female ratio was 0.97 (38/39). All patients had normal creatinine with a median of 85 μmol/l (range 46–140). The means of serum electrolyte changes in the three time frames are shown in the table. The prevalence of changes was hyperphosphataemia in 50.6%; hypernatremia in 11.7%; hypokalaemia in 9.1% and hypocalcaemia in 2.6% patients following bowel preparation. Post colonoscopy, the prevalence of hyperphosphataemia was in 54.5%; hypokalaemia in 15.6%; hypernatremia in 6.5% and hypocalcaemia

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persisted in 2.6% of patients. No changes in magnesium levels were noted. Analysis of variance found significant relationships between baseline creatinine (>100 μmol/l) and BC sodium (p=0.02), potassium (p<0.01) and phosphate (p=0.03); as well as AC potassium (p=0.02) and phosphate (p=0.01) values. There was also a significant relation between side effects and BC sodium (p<0.01) values. None of the patients had any apparent clinical adverse effects from these disturbances.
Conclusion: Significant changes in phosphate, sodium and potassium occur following NaP bowel preparation and after colonoscopy. Rising creatinine levels and presence of side effects were observed to be risk factors. However, these electrolyte changes did not have any undesirable clinical events in this group.

1. **Curran MP**, Plosker GL. Oral sodium phosphate solution: a review of its use as a colorectal cleanser. *Drugs* 2004;**64**:1697–714.
2. **Azzam I**, Kovalev Y, Storch S, *et al*. Life threatening hyperphosphataemia after administration of sodium phosphate in preparation for colonoscopy. *Postgrad Med J* 2004;**80**:487–8.
3. **Markowitz GS**, *et al*. Renal failure due to acute nephrocalcinosis following oral sodium phosphate bowel cleansing. *Hum Pathol* 2004;**35**:675–84.

041 DIAGNOSIS OF PANCREATICOBILIARY MALIGNANCY BY DETECTION OF MINICHROMOSOME MAINTENANCE 5 PROTEIN IN BILE ASPIRATES

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Introduction: Brush cytology (BC) is the most commonly used method of sampling a biliary stricture but has a low sensitivity (20–40%) for the detection of malignancy. We have shown that minichromosome maintenance (Mcm) replication proteins can be utilised as novel proliferation markers for the diagnosis of cervical and bladder cancer.[1, 2]
Aims & Methods: To determine if Mcm proteins are dysregulated in malignant pancreaticobiliary disease and their detection in bile is a sensitive marker of malignancy. In 30 biopsy/resection specimens from malignant/benign biliary strictures we studied Mcm expression by immunohistochemistry. Bile aspirates were collected prospectively from 102 consecutive patients (mean age 66 years, range 33–103 years; M:F 1:1) with biliary strictures of established (n=42) or indeterminate aetiology (n=60). Biliary Mcm5 levels were analysed in a blinded fashion using monoclonal anti-human Mcm5 antibodies in an automated immunofluorometric assay. Patients with indeterminate strictures also underwent BC as part of standard practice. A diagnosis of malignancy was made by positive cytology/biopsy, or evidence of disease progression on imaging. Benign disease was confirmed by negative pathology during a median 22 (range 6–32) months follow-up.
Results: In benign biliary strictures, Mcm protein expression was confined to the basal epithelial proliferative compartment—in contrast to malignant strictures where expression was seen in all tissue layers. The percentage of nuclei positive for Mcm protein was higher in malignant tissue (median 76.5%, range 42–92%) than in benign tissue (median 5%, range 0–33%) (p<0.0005). Among the 102 patients, 63 (62%) had malignant disease: cholangiocarcinoma (n=28) pancreatic cancer (n=23), or other malignancies (n=11). Benign strictures (n=39) were attributed to gallstone disease (n=14), primary sclerosing cholangitis (n=9), or other conditions (n=16). Operating characteristics at maximal sensitivities for Mcm5 in bile and BC sampled from the 60 indeterminate strictures are given in the table. The sensitivity and specificity of Mcm5 test in strictures with established diagnoses was 62% and 92% respectively.
Conclusion: Elevated levels of Mcm5 in bile are significantly more sensitive than brush cytology for the diagnosis of pancreaticobiliary malignancy, with a comparable specificity.

1. **Williams**, *et al. PNAS* 1998.
2. **Stoeber**, *et al. JNCI* 2002.

042 NARROW BAND IMAGING FOR COLONOSCOPIC SURVEILLANCE IN HEREDITARY NON-POLYPOSIS COLORECTAL CANCER

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Introduction: Standard colonoscopic surveillance has recently been shown to reduce cancer death rates in patients with hereditary non-polyposis colorectal cancer (HNPCC)[1]; however some of the ''successes'' represent early stage detection of cancer rather than prevention through polypectomy. Chromoendoscopy has recently been shown to detect significantly more additional adenomas than white light endoscopy alone in HNPCC surveillance.[2, 3] Narrow band imaging (NBI), nicknamed ''digital chromoendoscopy'', uses optical filters in the light source to highlight superficial blood vessels and may improve polyp detection. We aimed to test this in HNPCC surveillance.
Aims & Methods: Patients who met revised Amsterdam II or genetic criteria for HNPCC were examined twice from the caecum to sigmoid-descending junction, first with high definition white light, and then with NBI. All polyps were biopsied or resected immediately when seen and assessed by an experienced gastrointestinal pathologist. Examination was performed by three endoscopists, each with over 100 NBI cases experience, with a high definition (HDTV) colonoscope and NBI system (Olympus Medical System Corporation, Tokyo, Japan) with a minimum extubation time of 6 minutes for each pass. NBI illumination was with blue and green narrow band filters centred on 415 and 540 nm respectively.
Results: Fifty four patients (of a planned 60) were examined, mean age 47 (range 33–80), 20 (37%) male. The proportion of flat adenomas was significantly higher in NBI pass, p=0.02 (Fisher exact). The median extubation time was longer in the NBI pass by 16 seconds, p=0.002 (Wilcoxon signed-rank). A further 5 adenomas in 3 patients, all with proximal adenomas, were found in the segment from sigmoid descending junction to rectum with white light alone.

Abstract 042 Results proximal to sigmoid-descending junction

	Initial white light pass	Second NBI pass additional findings	Combined white light + NBI
At least 1 adenoma	15 (28%)	15 (28%)	23 (43%)
Total adenomas	23	19	42
Flat adenomas	3	9	12
Total polyps	51	47	98
Average adenoma size (mm)	3.3	3.2	3.3
Withdrawal time (mins)	6:33	6:49	13:22

Conclusion: The use of NBI after meticulous HDTV white light examination and polyp removal almost doubled the yield of adenomas in the right colon. The overall proportion of patients with at least one adenoma is higher than a previous series from our instiution (43 *v* 27%).[4] These results exceed those seen in a similar trial using pan-chromoendoscopy.[2] NBI looks promising as a tool to improve adenoma detection in HNPCC surveillance.

ClinicalTrials.gov Identifier: NCT00313755

1. **Dove-Edwin I**, *et al. BMJ* 2005;**331**:1047.
2. **Lecomte T**, *et al. Clin Gastroenterol Hepatol* 2005;**3**:897–902.
3. **Hurlstone DP**, *et al. Am J Gastroenterol* 2005;**100**:2167–73.
4. **Gaglia P**, *et al. Gut* 1995;**36**:385–90.

Abstract 041

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Area under curve (95% CI)
Mcm 5 cut-off point >1000	66% (50–79)*	94% (70–100)†	97% (90–100)	50% (32–68)	80% (70–91)
Brush cytology	20% (7–35)*	100% (75–100)†	100%	31% (18–44)	60% (40–76)

*p=0.004 Mcm5 *v* cytology.
†p=NS.

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Service development free papers

043 HOW TO ACHIEVE AN ''A'' IN TIMELINESS: CAPACITY AND DEMAND MANAGEMENT IN ENDOSCOPY SERVICES

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Introduction: Our endoscopy unit was able to achieve the national waiting time target (6 weeks for routine and 2 weeks for all urgent referrals) by September 2006 with the following strategy.
Aims & Methods: *Capacity management*: in 2002, a new purpose built endoscopy unit with three available suites was commissioned and an electronic endoscopy reporting system was installed (Endosoft, Utech Inc). Based on national endoscopy pilot, a capacity and demand data recording system was put in place. Utilisation of lists was monitored for each endoscopist. All lists were pooled and generic work initiated. The booking system was centralised. Full booking was introduced (outpatients choosing the appointment from available slots before leaving hospital). Nurse pre-assessment was introduced to assess risk, handout information leaflets and provide bowel prep with instructions. Patients were sent postal reminders to attend. Protocols were developed after multispecialty consultation, for diabetic and anticoagulated patients, to maximise day case procedures. Sessions cancelled due to leave and on-call commitments were offered to other endoscopists with financial remuneration. Capacity was improved by adding two evening lists. Upper and lower GI nurse endoscopists were trained. Trained locum endoscopists were occasionally used. *Demand management*: A retrospective audit of surveillance colonoscopies based on BSG guidelines showed that 60% of the performed procedures were either premature or not needed. Based on this a prospective programme was initiated for future booked procedures and those not conforming to guidelines were managed appropriately (by cancellation or appropriate timing). NICE Dyspepsia Guidelines were introduced and implemented in April 2005. Stool antigen test for H pylori was introduced in hospital and community. All upper GI alarm symptoms referrals were triaged, telephone pre-assessed and brought straight to endoscopy into dedicated slots. A web-based referral system was introduced to assure quality and adherence to guidelines. All endoscopy requests were triaged using this web-based system.
Results: The waiting times improved to a mean of 7.3 weeks in September 2003 (median 7.5 weeks, range 3–12 weeks), 6.2 weeks in September 2004 (median 7 weeks, range 4–8 weeks), 7.2 weeks in September 2005(median 7 weeks, range 5–13 weeks). In September 2006 mean waiting times of 3.5 weeks (median 3 weeks, range 2–6 weeks) were achieved for routine procedures. For urgent procedures the waiting time improved to 2 weeks.
Conclusion: Ensuring timelines requires a corporate work model. Flexible working is advantageous. Dissemination and easy availability of information to referring doctors is necessary. Regular and ongoing quality assurance is important.

044 ONE WEEK RAPID IMPROVEMENT OF QUALITY AND THROUGHPUT IN ENDOSCOPY

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Introduction: We planned to create a rapid improvement in quality and throughput in Endoscopy in one week by shortening room turnaround time as a result of introducing ''lean'' operation methodologies to frontline staff and embedding these methodolgies into the culture thus creating a nucleus for further improvement.
Aims & Methods: Working with the Trust's Service Improvement Team and McKinsey Management Consultants, a number of methodologies were applied to improve the efficiency of the department. Overall Equipment Effectiveness (OEE) methodology was applied in that the theoretical maximum production limit for Endoscopy would be the continous use of endoscopes. Any activity other than endoscope usage time reduces the actual number of patients seen from the theoretical maximum. OEE analysis and Single Minute Exchange of Die (SMED) helped staff to understand aspects of productivity and all the specific activities involved in turnaround that decreased time spent with patients and focussed problem solving efforts on the best areas of opportunity. Areas focussed on examined how to reduce turnaround times through creating a more consistent and efficient approach. These included defining clear roles, responsibilites, pre-procedure preparation and room realignment to reduce unnecessary movement identified by using a spaghetti diagram and applying the ''5S'' principles. The ''5S'' priniples provided a structured approach to establish and maintain a well organised workplace and involved Sorting, Straightening, Shining, Standardising and Sustaining. Idle time, due to reasons including patient flow, was tackled by dialogue and the use of visual management boards.
Results: During the observation period the mean turnaround time was 12 minutes and following initial implementation of the above, there was a reduction of 2.5 minutes (21%) per procedure. There was an agreement that any time saved was to be used to embed methodology into the unit culture to improve patient care. Problem solving discussions with external parties were initiated and high motivation of frontline staff to improve quality of patient care and productivity was achieved.
Conclusion: In the course of one week rapid improvement was achieved. However, sustainable improvements require regular team performance discussions and active problem solving with consideration given to the following three intersecting elements. Operating systems involving equipment, activites and information flows needed to treat patients. Mindsets and behaviours involving active engagement of all staff, to improve the system through problem solving and sustaining changes through adherence to standards. Management infrastructure involving performance metrics and management activities required to monitor amd continuously improve the system and engagement of staff.

045 GLOBAL RATING SCALE REQUIREMENTS FOR PATIENT COMFORT IN ENDOSCOPY: A SOLUTION

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Introduction: It is a Global Rating Scale (GRS) requirement to collect patient comfort data for endoscopic procedures and to provide anonymised data on this to individual endoscopists at least three times a year, to ''enable endoscopists to review their technique or sedation practice if comfort levels are suboptimal''. How this is achieved remains a challenge. One suggestion, using nurse-reporting of patient comfort, is subject to bias. We report our solution to the problem.
Aims & Methods: As we believed that only the patient could comment on their level of comfort, a simple discharge questionnaire was devised. All patients complete this before leaving the endoscopy unit. To the question ''How comfortable did you find your procedure?'' patients circle one of four responses: comfortable (3), acceptable level of discomfort (2), uncomfortable (1), very uncomfortable (0). The procedure, endoscopist and sedation type/dose is also recorded by the discharging nurse. Data are anonymised and collated into a broader 4-monthly audit of quality and safety indicators in endoscopy. Each endoscopist can view their own data along with anonymised data for their colleagues. Comfort is presented as a mean score for each procedure that each endoscopist performs (see table). An in-house policy has been devised and ratified for what is considered an unacceptable level of discomfort (mean <2.0), and what action should be taken if this occurs.
Results: See table (note: data are illustrative).

Abstract 045

Endo code	N	G	C	FS	E	Comments
1	15	2.8	2.0	2.9	2.6	
2	10	2.2	2.4	2.6		
3	24	2.9	2.9	2.4		

Conclusion: By implementing the survey, our Unit improved its GRS comfort rating from C to A. We believe the survey provides a simple and accurate snapshot of patient comfort levels. By collecting the responses at a standardised time (on discharge), variation in recollection of comfort over time is minimised. Although use of higher doses of sedation could distort recollection, we also monitor endoscopists' sedation practices/use of reversal agents to ensure a safe sedation practice.

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046 NEW GLOBAL RATING SCALE SHAREWARE: ENDOSCOPY AUDIT AT A KEYSTROKE

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Introduction: Endoscopy units joining the National Bowel Cancer Screening Programme are required to score level B or above on the Global Rating Scale (GRS) for quality and safety. The data recorded on our department's endoscopy reporting system are insufficient for this purpose.
Aims & Methods: Using Microsoft Access, a comprehensive database was constructed to record quality and safety data for use with the GRS in patients undergoing endoscopy. The programme included auditable outcomes and quality standards for all endoscopies as defined by the British Society of Gastroenterology. An initial version was piloted over 6 months in two endoscopy units. The system was developed further using feedback from endoscopists and nurses. Data were entered prospectively on one screen per procedure alongside the endoscopy reporting system. Oucome data were entered retrospectively.
Results: This programme provides: annual or biennial audits for endoscopic procedures in one keystroke; comfort data by endoscopist; 6-monthly safety data; quality outcomes by endoscopist. A live demonstration will be given.
Conclusion: A successful collaboration between the hospital IT department, endoscopists and nurses has produced a comprehensive endoscopy governance system which is fully transferable to other units.

047 EFFECT OF HELICOBACTER PYLORI ERADICATION ON DYSPEPSIA, QUALITY OF LIFE AND UTILISATION OF HEALTHCARE RESOURCES IN THE EASTERN ENGLAND HELICOBACTER PYLORI PROJECT: RANDOMISED CONTROLLED TRIAL

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Introduction: Helicobacter pylori (H pylori) infection can contribute to the development of diseases, such as dyspepsia, gastritis and ulcers in the stomach and duodenum. H pylori infection is most likely acquired by ingesting contaminated food and water and through person to person contact. The purpose of this paper is to determine the impact of a community based H pylori screening and eradication programme on the incidence of dyspepsia, quality of life and resource utilisation, including a cost consequences analysis.
Aims & Methods: Ten general practices and one community hospital in Eastern England participated in the study. 12 504 people aged 21–65 years were screened for H pylori infection (13C urea breath test); 1639 of the 1794 participants who tested positive were randomised to H pylori eradication treatment or placebo, and 1606 (98%) were followed up for two years. The treatments given were Ranitidine bismuth citrate 400 mg and clarithromycin 500 mg twice daily for two weeks or placebo. Clinical care consultation rates for dyspepsia (defined as epigastric pain) two years after randomisation, with secondary outcomes of dyspepsia symptoms, quality of life, utilisation of resources and health cost were evaluated.
Results: In the eradication group, 37% fewer participants consulted for dyspepsia over two years compared with the placebo group (56/793 *v* 79/784; odds ratio 0.66, 95% confidence interval 0.47 to 0.95; $p=0.022$; number needed to treat 32) and 30% fewer participants had regular symptoms (odds ratio 0.72, 0.57 to 0.91; $p=0.06$). NHS costs were £87.45 (£76.70 to £95.56) greater per participant in the eradication group over two years, of which £86.20 ($148; €123) was the cost of eradication treatment. No difference in quality of life existed between the two groups.
Conclusion: Screening and eradication of H pylori is feasible in the general population and contributed to significant reductions in the number of people who consulted for dyspepsia and had symptoms two years after treatment. These benefits have to be balanced against the costs of eradication treatment, so a targeted eradication strategy in dyspeptic patients may be preferable.

048 ENDOSCOPY 30 DAY MORTALITY: A RETROSPECTIVE AUDIT OF DIAGNOSTIC AND THERAPEUTIC ENDOSCOPY AT A SINGLE UNIT

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Introduction: The publication from NCEPOD ''Scoping our Practice'', 2004, provides nationwide 30 day mortality data for all therapeutic endoscopic procedures. It is important for all centres to perform mortality audits on their own endoscopic practices and compare this to NCEPOD data. This enables assessment, maintenance and improvement of standards in endoscopy.
Aims & Methods: We aimed to retrospectively assess 30 day mortality for the following diagnostic and therapeutic endoscopic procedures—OGD, colonoscopy and percutaneous endoscopic gastrostomy (PEG) for a 1 year period between March 2005 to March 2006 and compare this to the published NCEPOD data. Our secondary aim was to document the causes of death and assess which deaths may have been contributed to by endoscopy. This was done using our Trust clinical information coding system and examination of patient records, postmortem reports and endoscopy reports.
Results: Of 7698 endoscopies performed between March 2005 and March 2006, 89 patients in total died within 30 days of their procedure. Endoscopy directly contributed to death in only 3/7698 total endoscopies performed (0.04%). These were peritonitis secondary to a PEG leak ($n=1$), perforated duodenal ulcer during therapeutic endoscopy ($n=1$) and haemorrhage post colonoscopy with polypectomy in a patient with end stage renal failure ($n=1$). Causes of death not attributable to endoscopy ($n=86$) were invasive malignancy ($n=42$), COPD ($n=9$), sepsis ($n=9$), cardiac disease ($n=8$), GI bleed ($n=6$), chronic liver disease ($n=5$), stroke ($n=3$) and other ($n=4$). Rates of postmortem examination and reporting of deaths to the coroner at GSTT were 16/89 (18%) and 39/89 (44%) respectively, compared with 9% and 27% respectively from NCEPOD.
Conclusion: The 30-day mortality rates after endoscopy at GSTT over a 1-year period compare favourably with those of NCEPOD. Only a small percentage of deaths were directly contributed to by endoscopy. In each of these a systematic review of care was undertaken and appropriate changes where necessary were implemented. Rates of postmortem examination and deaths within 30 days of endoscopy reported to the coroner were superior to those of NCEPOD but were still well short of the recommendation from NCEPOD that all deaths following a medical procedure should be reported to the coroner. This highlights the need for greater vigilance by gastroenterologists in the reporting of deaths to the coroner after endoscopy.

Abstract 048 30-day mortality after endoscopy

	GSTT (diagnostic) 2005–6	GSTT (therapeutic) 2005–6	NCEPOD (therapeutic) 2002–3
OGD	64/4188 (2%)	7/238 (3%)	2200/47,931 (5%)
Colonoscopy	9/2851 (0.3%)	1/256 (0.4%)	102/40,378 (0.3%)
PEG		8/165 (5%)	986/16,648 (6%)

049 COLONOSCOPY WAITING LISTS: REVALIDATION BY GENERAL PRACTITIONERS IS COST EFFECTIVE AND REDUCES UNNECESSARY ENDOSCOPY COMMISSIONING

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Introduction: The advent of colorectal screening highlights the need for accurate colonoscopy waiting lists. The Endoscopy Global Rating Scale (GRS) states that the appropriateness of an endoscopic investigation is central to patient safety and service provision quality. It also highlights timeliness as a patient centred endpoint in rating customer care. Failure of endoscopy units to comply with GRS quality standards precludes their participation in colorectal cancer screening programmes and endoscopy training. By December 2008 all patients in the NHS will require effective

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treatment within 18 weeks of original referral, adding further impetus to the need for reduction of endoscopy waiting lists.

Aims & Methods: This study aimed to assess the positive impact of clinical revalidation on a Primary Care Trust non-urgent colonoscopy waiting list. The Bath and North East Somerset Primary Care Trust (BANES PCT) covers a population of 182 000 patients and consists of 227 GPs. Patients on the colonoscopy waiting list for over three months were identified from the Primary Care Trust and Royal United Hospital Bath clinical databases. Their general practitioner revalidated the need for a colonoscopy by reviewing their clinical records (66%), contacting the patient by phone (25%) or seeing the patient in clinic (9%). A proforma to help guide this revalidation was produced after consultation with clinical leads in endoscopy, colorectal surgery, gastroenterology, general practice and medical management. The form categorised patients and their symptoms into the need for a barium enema, flexible sigmoidoscopy, colonoscopy or no further action. Results were returned by post. The study took four weeks to complete.

Results: 769 patients were identified on the waiting list. Ages ranged from 18–100 years old. 11 patients had waited 7 years,13 patients 6 years, 17 patients 5 years, 28 patients 4 years and 682 less than 3 years. All GP practices in the PCT participated, and no cost was charged by GPs for conducting the revalidation. Of the 769 forms sent out, 92 were incomplete as patients were not contactable due to moving out of the PCT area. Of the remaining 677 patients 328 (48%) no longer required the examination due to a full recovery from symptoms or not wanting the investigation. 52 patients (7%) were redirected to a flexible sigmoidscopy and 14 (2%) to a barium enema. 283 (41%) still required a colonoscopy and of these 133 (19%) were colorectal cancer surveillance patients. If the original numbers of procedures on the waiting list are taken into account a saving of £154,100 in endoscopy commissioning was achieved.

Conclusion: The striking reduction in colonoscopies required after this revalidation (48%) not only brings into question the accuracy of other waiting lists for endoscopic procedures but perhaps more importantly referral practices by clinicians. For planning in endoscopy services to be efficient and cost effective, accurate waiting lists are a necessity. This survey has demonstrated that through cooperation between commissioning agents, GPs and the local service providers, a more accurate record of waiting lists can be achieved, and service provision for the patient optimised with minimal cost being incurred.

050 AN AUDIT TO UNDERSTAND OUTCOMES OF CRITCALLY ILL GASTROENTEROLOGY PATIENTS AND THE SELECTION CRITERIA USED BY CRITICAL CARE TO IMPROVE SERVICES

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Introduction: The mortality of patients admitted to Critical Care (High Dependency or Intensive Care) with gastroenterological diagnoses such as chronic liver disease (CLD) and upper GI haemorrhage (UGIH) is high. Consequently, patient selection by Critical Care (CC) may be an important factor contributing to outcomes of critically ill patients referred by gastroenterologist. There are no data on patient selection and outcomes in non-select gastroenterology patients referred to CC.

Aims & Methods: To understand outcomes in critically ill gastroenterology patients and the selection criteria used by CC for service development. University Hospital Aintree (UHA) is a large teaching hospital with a 72 bedded gastroenterology unit covered by a 7 consultant gastroenterologists on a specialist on-call rota. CC consists of 20 ventilated and non-ventilated beds covered by 9 consultant intensivist. This was a prospective audit, where all Gastroenterology ward referrals to CC were identified and the medical case notes audited using a standard proforma over a 12-month period (22/8/05 to 21/8/06). 30-day mortality from referral was used as the measurable outcome. Comparisons were made using χ^2 and Mann–Whitney Analysis between accepted (ACC) and rejected (REJ) patients by CC with $p<0.05$ as the significance level.

Results: Forty nine referrals were made in 38 patients with 66% accepted by CC. Overall 30-day mortality was 61%, but 48% in those accepted for intervention (ACC) compared to 85% in those rejected (REJ) ($p=0.007$). There were no differences in average age (ACC; 51 (14.4) years *v* REJ 56 (8.3) years, $p=0.3$), ASA grade (ACC 2.8(0.7) *v* REJ 3.4(1) ($p=0.12$)) or comorbidities ($p=0.7$). 58% of patients had either CLD and/or UGIB. Diagnoses were similar with patients with alcohol related problems (36% *v* 53%) and decompensated CLD (48% *v* 53%) in ACC and REJ ($p=0.3$ and $p=0.7$ respectively). Patients with UGIB were more likely to be ACC (32% *v* 8%) but this was not significant ($p=0.1$). Furthermore, the reasons for requiring CC including; acidosis, hypoxia, ventilatory support and haemodynamic instability, severe sepsis and intensive monitoring/care were also similar in both groups ($p>0.2$ in all). In REJ patients, the commonest reason for non-acceptance was that ''care ward would be sufficient'' (54%) in whom the mortality was 71%.

Conclusion: The outcomes of critically ill patients referred by gastroenterologist following acceptance by CC (ACC) were superior to those that were not (REJ). However, we did not find any clear differences between the two populations to suggest patient selection was a contributory factor. Although these results need be viewed cautiously because of the small numbers, this audit does suggest that all patients referred to CC may have potentially benefited. Following this audit, service improvements suggested (1) introduction of gastroenterology/CC patient proforma/pathway, (2) improved dialogue between CC physicians and gastroenterologists and (3) potential high dependency area within Gastroenterology.

051 TOWARDS A BETTER OUTPATIENT SERVICE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Outpatient (OP) services for inflammatory bowel disease (IBD) patients must alter to meet changing patient expectations and required reduction in New:Follow-Up ratios while maintaining a safe quality service. We have initiated a flexible, responsive service using dedicated email (ibdbarnsley@nhs.net) or SMS text messaging plus blood tests to reduce unnecessary OP attendance and free slots for new patients.

Aims & Methods: IBD patients under one medical consultant were identified by review of all OP letters from 2005. Analysis identified which visits appeared to have involved no alteration in management or therapy or useful discussion. All patients were offered (by letter) the option of future follow-up, when they were stable, by SMS/email link plus routine blood test to monitor disease activity and for therapy related adverse effects. Where judged from these that an OP visit was not needed the OP slot was cancelled and re-booked and further blood forms supplied. Informal comment on the proposals was requested. Patients first seen in 2006 were subsequently included. The system uses NHS net for email and SMS.

Results: 278 patients were identified, average age 51 years (range 17–88). 40% had Crohn's disease and 56% had ulcerative colitis. 33 (12%) were taking azathioprine. 160 (37%) of 429 OP attendances in 2005 appeared to have been non-contributory to patient care. Response rate by 8 weeks was 41% (113 of 278). Of these 50% wanted to use email, 34% SMS (5% either) and 12% wanted to stay on current system (average age 62). 8% wanted a phone contact (average age 65), which we accommodated although not originally intended. Above age 40 use of SMS: email was fairly even at 46%:54%, Nine aged 60+ (max 79) used SMS. Younger patients favoured email (68%) over SMS (32%). Comments were uniformly enthusiastic ''self-employed, will save time and money'', ''avoids two bus journeys each way'', ''mutually beneficial'', ''such a change is long overdue'', etc. SMS/email contacts currently run at about 25/month

Conclusion: The new system is liked and beneficial to patients. It saves them time and frees OP slots for others. Patients also use it as a ''hot line'' for rapid advice and when a major flare-up requires an earlier OP slot. Flexibility is required for those (predominantly elderly) wanting to avoid visits but needing phone contact. All age groups use SMS and email, Compared with those over 40 younger patients preferred email over SMS which was not anticipated. Current extra management work load is a few minutes/week. Long-term there will be a benefit on New:Follow-Up ratios. We are extending the system to those with haemochromatosis, PBC and CAH.

052 DEVELOPMENT OF AN ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION CYTOLOGY SERVICE: A REVIEW

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Introduction: Endoscopic ultrasound fine needle aspiration (EUS-FNA) is an established technique for obtaining diagnostic material for cytological (and histological) analysis. BSG guidelines suggest that the target yield for diagnostic material using this technique should be 90%. After earlier experience in radial EUS, we introduced this technique to our cancer network in 2004 and review here our outcome data.

Aims & Methods: EUS-FNA was done with a Hitachi FG38X echoendoscope and 22G Wilson-Cook Echotip needles. Air-dried smears were used for cytology and any solid material was fixed in formalin. Specimens were

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Abstract 052

Site of FNA	Number	Diagnostic material	Malignancy	Benign	True positive	True negative	False negative
Lymph nodes	23	20	11	9	11	7	2
Pancreas	27	26	18	8	18	6	2
Other masses	10	9	5	4	5	3	1

Results of EUS-FNA from various sites.

reported by a pathologist with expertise in GI malignancy and cytopathology. A review of all case notes was done, with pathology reports classified as: inadequate, malignant or benign. Validity of reports was judged by case note analysis.
Results: Sixty patients underwent EUS-FNA from various sites, classified here as lymph nodes (mediastinal/coeliac), pancreas, or other masses (table). There were no procedure related complications. Median follow-up was 9 months. Adequate samples were obtained in 55/60 cases (92%). Overall sensitivity and specificity for malignancy were 85% and 100% respectively. Other diagnoses obtained included lymphoma and sarcoidosis.
Conclusion: EUS-FNA had a good safety record and diagnostic yield in this case series, and has become an invaluable diagnostic aid in our management of suspected cancer.

Neurogastroenterology/motility free papers

053 ISOLATION, CHARACTERISATION AND TRANSPLANTATION OF HUMAN ENTERIC NERVOUS SYSTEM STEM CELLS

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Introduction: Hirschsprung's disease (HSCR) is a congenital defect affecting 1 in 5000 births per year. It is caused by a failure of the enteric nervous system (ENS) to develop in a variable region of terminal bowel, which is therefore aganglionic. Current treatment is surgical, but long-term morbidity often ensues. A possible future therapy is the use of ENS stem cells to replenish the deficient ENS in the aganglionic segment. Embryonic and early postnatal mouse, rat and human gut have all been shown to contain a source of ENS stem cells that are contained within neurospheres generated in cell cultures of dissociated gut. We have used the chick chorio-allantoic membrane (CAM) as a model gut culture system to maintain recipient gut following ENS stem cell transplantation.
Aims & Methods: Our aims were: (1) to isolate and characterise ENS stem cells from embryonic and postnatal (early and late) human gut and (2) to transplant the ENS stem cells into recipient chick gut maintained on the CAM. Cell cultures were generated by dissociating human gut, including the ganglionic portion of HSCR gut. ENS stem cells, contained within neurospheres, were characterised using molecular markers for neural crest progenitors and differentiated neurons and glia. ENS stem cells were labelled using a nuclear marker Hoechst 33342 and then transplanted into recipient ganglionic (E6 and E12) and aganglionic (E5) embryonic chick gut maintained on the CAM. ENS and smooth muscle development was subsequently assessed in recipient guts using immunohistochemical staining with markers for tubulin, glial fibrillary acidic protein and alpha-smooth muscle actin.
Results: Neurospheres were successfully generated from embryonic (n = 11, range 6–12 weeks' gestation, mean 8.5 weeks' gestation) and postnatal (n = 18, range 0.5–18 years, mean 5.9 years) human guts, including 3 children with HSCR. Those generated from embryonic gut contained cells positive for neuronal and glial markers, as well as ENS progenitors, as shown by p75 and Sox10 immunostaining. Transplanted ENS stem cells derived from embryonic human gut were shown to survive, migrate, and integrate within the host myenteric and submucosal plexi of the ENS in recipient chick gut (n = 3).
Conclusion: Neurospheres can be generated from human embryonic and postnatal gut, beyond the age of 1 year. Characterisation shows that they contain cells positive for markers of neurons, glia and ENS stem cells. When transplanted into recipient gut, ENS stem cells migrate to the appropriate gut layers. Current work is directed towards further characterisation of the fate of transplanted neurospheres within recipient guts including the generation of mature neuronal subtypes. These findings provide a significant basis for future work towards a possible stem-cell-based therapy for HSCR.

054 IRRITABLE BOWEL SYNDROME SHOWS AN ACTIVATED AND EFFECTIVE IMMUNE SYSTEM

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Introduction: Irritable bowel syndrome (IBS) is a heterogeneous condition characterised by abdominal pain or discomfort and alterations in stool frequency and consistency. The aetiology is unknown although low-grade mucosal inflammation has been described by ourselves and others. Alterations in the IL-12/IL-10 balance have been reported[1] and genetic polymorphism studies suggest a deficiency in interleukin-10 production may be important.[2]
Aims & Methods: Our aim was to assess deficiencies in inflammatory responses between IBS patients and healthy controls. 65 IBS patients satisfied Rome II criteria for IBS: 29 diarrhoea-predominant IBS (D-IBS), 10 constipation-predominant (C-IBS) and 26 post-infective IBS (PI-IBS). 21 normal healthy controls (HC) were recruited. Peripheral blood mononuclear cells (PBMCs) were isolated over a Histopaque gradient and incubated for 24 hours, with and without LPS stimulation. Supernatant cytokine levels were assayed by Becton Dickson cytometric bead array.
Results: Unstimulated PBMC incubations from D-IBS and PI-IBS had significantly elevated IL-1β, IL-10 and TNF-α levels compared to healthy controls, $p<0.05$. LPS-stimulated incubations showed no significant differences between HC and IBS subgroups, $p>0.05$. IL-12 was undetectable in most cases.
Conclusion: IBS differ from healthy controls in producing elevated TNF-α, IL-1β and IL-10 from unstimulated PBMC incubations, suggesting that most IBS patients have an inflammatory component to their illness. The immune

Abstract 054 Cytokine results as median

	HC (n = 21)	D-IBS (n = 29)	PI-IBS (n = 26)	C-IBS (n = 10)	p v HC
−LPS					
IL-1β	8	577*	820**	650	*0.04,**0.008
TNF-α	6	120*	186**	88	*0.04,**0.008
IL-10	5	206*	292**	266	*0.03,**0.002
+LPS					
IL-1β	3137	2547	3395	2595	p = 0.5
TNF-α	274	391	316	199	p = 0.3
IL-10	1307	1020	1032	991	p = 0.3

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system in IBS patients is activated compared to healthy controls and is equally responsive to LPS stimulation. These data suggest an activated rather than a deficient immune system.

1. **O'Mahony L**. *Gastroenterology* 2005;**128**:541–51.
2. **Gonsalkorale WM**. *Gut* 2003;**52**:91–3.

055 INCREASED TRPV1 EXPRESSING NERVE FIBRES IN COLONIC BIOPSIES FROM IRRITABLE BOWEL SYNDROME PATIENTS CORRELATE WITH THE DEGREE OF ABDOMINAL PAIN

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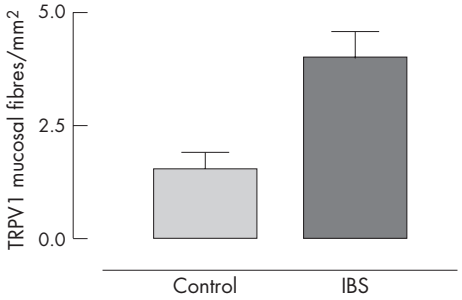
Introduction: TRPV1 is the heat and capsaicin receptor expressed by nociceptor fibres, which on activation leads to burning pain and local release of the neuropeptides CGRP and substance P (SP). It has been linked to GI disorders including painful IBD and rectal hypersensitivity, where increased TRPV1 fibres correlated with rectal hypersensitivity to distension and heat. Our objective was to characterise molecular basis of visceral hypersensitivity in IBS patients by quantifying TRPV1 and SP fibres, and relating these to pain severity.
Aims & Methods: Patients were defined as suffering from IBS using Rome II criteria. Daily pain diaries (using the SF-MPQ) were recorded for 1 week after colonoscopy by IBS patients and controls. All subjects had normal mucosa at colonoscopy/flexible sigmoidoscopy. Recto-sigmoid biopsies were taken for histological analysis to exclude inflammation, and immunostained with antibodies to TRPV1, nerve markers (Neurofilaments and Peripherin PGP 9.5) and SP. TRPV1- immunoreactive nerve fibres were expressed as fibres/mm^2, while PGP 9.5 and SP fibres were analysed by computerised image analysis. The area of TRPV1 immunoreactivity was correlated with abdominal pain.
Results: Fine mucosal TRPV1-immunoreactive fibres were seen in all control (n = 22) and IBS (n = 23) biopsies. There was a significant increase in TRPV1 fibres in IBS (fibres/mm^2, mean (SEM), 4.0 (0.6)) compared to controls (1.6 (0.3); $p<0.0001$). TRPV1 fibres/mm^2 including both groups correlated with pain score VAS (max) (Spearman $r = 0.61$; $p<0.0002$). A subset of control (n = 5) and IBS biopsies (n = 6) were used to study SP and PGP 9.5 fibres. SP was significantly increased in IBS (% area, 1.78 (0.5); controls 0.37 (0.08); $p<0.05$). PGP 9.5 fibres were also significantly increased IBS patients (4.03 (0.91); controls (1.38 (0.2)). No biopsies showed evidence of inflammation.
Conclusion: We have demonstrated significantly increased TRPV1 and SP nerve fibres, and total number of nerve fibres, in IBS patients. The TRPV1 fibres correlated with pain, providing a rationale for the treatment of IBS with TRPV1 antagonists.



Abstract 055

056 FUNCTIONAL EVIDENCE FOR HEMISPHERIC ASYMMETRY IN THE CORTICAL CONTROL OF HUMAN SWALLOWING: A ''VIRTUAL BRAIN LESION'' STUDY

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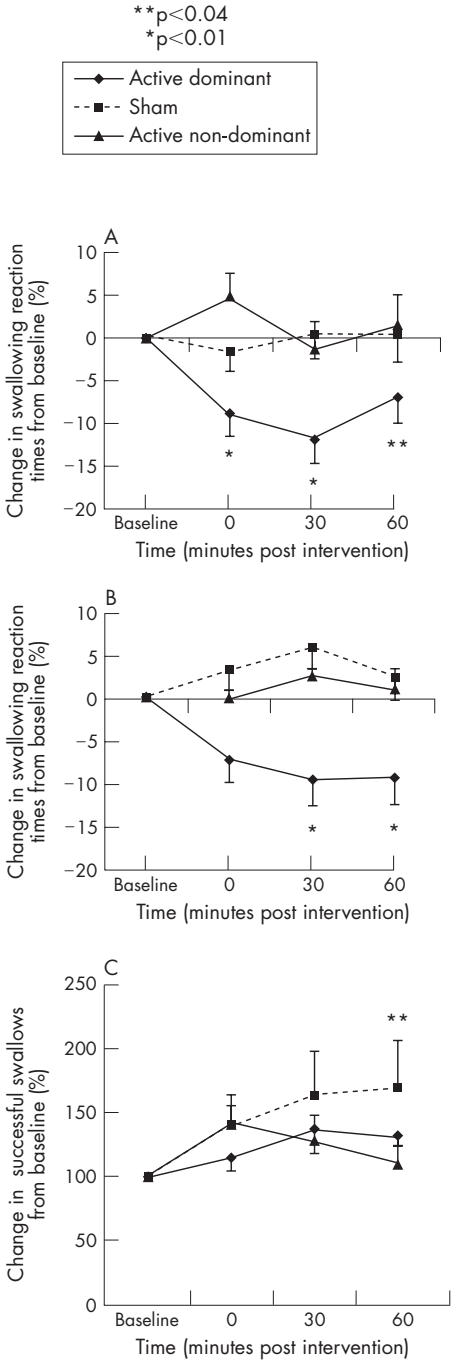
Introduction: Cortical control of swallowing is bilateral but displays inter-hemispheric asymmetry, with dominant and non-dominant projections. However, the precise relationship between these pathways remains unclear. 1Hz repetitive transcranial magnetic stimulation (rTMS) can be used to induce ''virtual lesions'' of targeted brain regions.
Aims & Methods: Our study applied 1Hz rTMS to the bilaterally represented motor cortex system for human swallowing to establish the existence of functionally relevant asymmetry. Eight right-handed healthy subjects (5M/3F; range 26–47 years) participated in this study. Single pulse TMS combined with pharyngeal motor evoked potentials (PMEPs), recorded via a swallowed intraluminal catheter, were used to assess swallowing motor cortex (SMC) of both hemispheres. The hemisphere evoking the largest PMEPs was termed dominant SMC (D-SMC), the other,



Abstract 056 Changes in (A) normal, (B) fast and (C) challenge swallow reaction times from baseline following a 1 Hz rTMS-induced ''virtual lesion'' to swallowing motor cortex.

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contralateral ''non-dominant'' SMC (ND-SMC). A swallowing reaction time task was used to assess swallowing behaviour and comprised 3 cued tasks: normal, fast and challenged swallows (within a 150 ms time window). Baseline swallowing measurements were followed by 10 minutes of 1Hz rTMS (active to D-SMC or ND-SMC and sham, randomised to separate days). Behavioural measurements were then re-acquired, immediately (0), 30 and 60 minutes after rTMS. Baseline *v* hemispheric intervention data (active and sham) were then analysed with ANOVA.
Results: RTMS to D-SMC was associated with a reduction in both normal ($-12\pm3\%$, $p<0.01$) and fast ($-9\pm4\%$, $p<0.018$) swallow reaction times compared to baseline. By contrast, active rTMS to ND-SMC and sham had no effect. Moreover, challenge swallows showed an expected rise in successful ''hits'' following sham ($p<0.041$) but showed no change following active rTMS of either hemisphere.
Conclusion: Our data show clear differences in swallowing behaviour to a virtual lesion of each hemisphere, providing compelling evidence for functionally relevant asymmetry in the cortical swallowing motor system.

057 NORMAL RECTAL SENSORY FUNCTION: EVALUATION USING FOUR DIFFERENT MODALITIES IN HEALTHY VOLUNTEERS

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Introduction: Intact rectal sensory function is integral to normal defaecation and maintenance of faecal continence. Aberrant rectal sensitivity (both heightened and blunted) has been implicated in the genesis of symptoms in patients with functional hindgut disorders. Assessment of rectal sensory function is most widely measured using simple intrarectal balloon distension. However, although quick and easy to perform, results are susceptible to misinterpretation in the presence of altered rectal wall properties (for example, compliance, capacity). Hence, different sensory stimuli (pressure, thermal, electrical) have also been used for evaluating rectal sensation. Irrespective of technique however, defining abnormal rectal sensory function is entirely dependant upon robust normative data, which are currently lacking.
Aims & Methods: To provide robust normal ranges for rectal sensation using different sensory modalities, and to asses their degree of correlation with volumetric balloon distension. 91 healthy volunteers (50 F, mean age 39 years, range 18–63) underwent assessment of rectal sensory thresholds (ml) to balloon distension. Sensory thresholds to electrical (mA: bipolar electrode mounted on a Foley catheter) and thermal (heat °C: customised thermal probe) stimuli were evaluated in 89 and 59 volunteers, respectively. 45 subjects underwent all of the above, and also barostat assessment of pressure thresholds (mmHg). Correlations between different sensory modalities were assessed using Pearson's test.
Results: Normal ranges (mean $\pm$2 SD) for rectal sensory thresholds using the different modalities are presented in the table. There were strong correlations between MTV on balloon distension and electrosensory ($r=0.296$, $p=0.005$), thermosensory ($r=0.612$, $p<0.001$)and volume thresholds on barostat ($r=0.530$, $p<0.001$).Similar correlations were observed between DDV on balloon distension and the other sensory modalities.
Conclusion: Normative data for four tests of rectal sensation in a large cohort of healthy volunteers are presented, and can be adopted by other centres using these techniques. Normal ranges are wide, indicating care must be taken not to ''overdiagnose'' sensory dysfunction. The positive correlation between sensory thresholds obtained by balloon distension and particularly thermal stimulation suggests a common afferent pathway for these stimuli. All tests should be regarded as complimentary.

Abstract 057

Modality	Female	Male
Balloon distension		
FCS	31 (21–108 ml)	48 (15–151 ml)
DDV	87 (38–199 ml)	116 (40–192 ml)
MTV	148 (75–291 ml)	200 (74–326 ml)
Electrosensitivity	12.0 (3.8–20.2 mA)	13.4 (4.9–36.3 ml
Thermosensitivity	45.3 (41.3–50°C)	46.2 (42.4–50°C)
Rectal barostat		
FSP	7 (4–12 mmHg)	9 (4–14 mmHg)
DDP	16 (8–24 mmHg)	13 (8–24 mmHg)
MTP	28 (10–44 mmHg)	26 (9–36 mmHg)

FCS, DDV and MTV (first sensation, desire to defaecate and max tolerated volumes).

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058 AN INVESTIGATION INTO THE PREVALENCE OF OSTEOPOROSIS AND THE RELATIVE CONTRIBUTION OF GENETIC AND ENVIRONMENTAL FACTORS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Low bone mineral density (BMD) and osteoporosis are recognised complications of inflammatory bowel disease (IBD). The aetiology of low BMD in IBD is multifactorial encompassing genetic and environmental factors.
Aims & Methods: In this study we have investigated the role of genetic factors—vitamin D receptor (VDR) variants, NOD2/CARD15 variants and IBD5 variants, and a number of environmental factors on the prevalence of osteoporosis in patients with IBD. DEXA scans were performed using a Hologic QDR4500A machine on 286 patients with Crohn's disease (CD): 107 males, 179 females, median age at DEXA 42.3 years; 153 patients with ulcerative colitis (UC): 74 males, 79 females, median age at DEXA 43.0 years. 240 healthy controls were also genotyped. Phenotypic data were collected by case note review and cumulative steroid data were calculated by the number of months on corticosteroids. A T score of <-2.5 at the lumber spine was classified as osteoporosis and a T score between -1.5 and -2.5 was classified as osteopenia. VDR gene polymorphisms Taq1 and Apa1 were genotyped using PCR-RFLP, IBD5 variants IGR2096, IGR2198, IGR2230, OCTN1 variant (SLC22A4 1672C→T), OCTN2 variant (SLC22A5 -207G→C) and NOD2/CARD15 variants R702W, and 1007fsinsC were genotyped using the Taqman system. NOD2/CARD15 G908R genotyping was performed by PCR-RFLP.
Results: 16% of the CD patients and 13% of the UC patients were found to have osteoporosis. 18% of the CD patients and 19% of the UC patients were osteopenic. Univariate analysis showed that low body mass index (BMI) (<18.5), smoking status and being postmenopausal ($p=0.008$, 0.005 and 0.007 respectively) were associated with osteoporosis and osteopenia in CD patients. Low BMI was also associated with osteoporosis on multivariate analysis ($p=0.021$, OR 5.83, CI 1.31 to 25.94) in CD. No variable was associated with osteoporosis in UC and cumulative steroid dosages were not associated with osteoporosis. No difference was observed between Taq1 and Apa1 VDR polymorphisms in IBD, CD, UC and controls. However, CD males were more likely to carry the mutant Taq1 allele than healthy control males ($p=0.0018$, OR 1.94, CI 1.28 to 2.92) and female CD patients ($p=0.0061$, OR 1.60, CI 1.17 to 2.44). No association between VDR, IBD5 and NOD2/CARD15 variants and osteoporosis was observed in the Crohn's disease cohort.
Conclusion: In this well phenotyped cohort of IBD patients, low incidences of osteoporosis were observed compared to previously published series.

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Low BMI was the strongest risk factor associated with osteoporosis. Taq1 VDR variants were more prevalent in the male CD population suggesting a sex specific effect.

059 ADALIMUMAB MAINTAINS CLINICAL REMISSION AND RESPONSE, INDUCES AND MAINTAINS HEALING OF DRAINING FISTULAS IN PATIENTS WITH ACTIVE CROHN'S DISEASE

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Introduction: This study assessed the efficacy and safety of adalimumab (ADA), a fully human anti-TNF monoclonal antibody with demonstrated efficacy in the induction of remission in Crohn's disease (CD), in the maintenance of clinical remission and of response in patients with active CD.
Aims & Methods: In CHARM, a double-blind (DB), placebo-controlled, multicentre study, patients with moderately to severely active CD (CDAI 220–450) received open-label (OL) induction dosages of ADA sc, 80 mg/40 mg at Wk 0 (BL)/Wk 2. All patients were randomised at Wk 4 to placebo (PBO) or 40 mg ADA every other wk (EOW) or 40 mg weekly (W), through Wk 56. Clinical response was defined as a decrease from BL CDAI ⩾70 or 100 (CR-70/100). Co-primary endpoints were remission (CDAI<150) at Wks 26 and 56 in Wk-4 responders (randomised responders (RR), CR-70). Patients with draining fistulas at both screening and BL visits were evaluated for healing at Wks 26 and 56 and at their last 2 blinded study visits. Safety was routinely assessed.
Results: Characteristics at BL were similar across treatment arms; mean CDAI = 313. Of 854 patients enrolled, 778 patients were randomised at Wk 4. Of these, 499 (58%) were stratified as RR. Significantly higher rates of remission and response were maintained in RR with ADA *v* PBO at both Wk 26 and Wk 56 (table). Maintenance ADA therapy significantly increased percentages of all randomised patients with complete fistula healing at their last 2 visits (33% combined ADA groups *v* 13% PBO, $p<0.05$) and at both Wks 26 and 56 (33% combined ADA groups *v* 13% PBO, $p<0.05$). In the 4-wk OL induction period, serious adverse events (SAE) were reported in 5% of patients. In the 52-wk DB period, significantly lower rates of SAE were reported in the ADA 40 mg EOW/W treatment groups, 9% and 8% respectively, *v*15% in the PBO group ($p<0.05$).
Conclusion: Adalimumab, EOW or W, was more effective than PBO in maintaining ADA-induced clinical remission and response in patients with moderately to severely active CD. Patients receiving ADA therapy achieved and maintained significant and complete fistula healing. Adalimumab was well-tolerated, with significantly lower rates of SAE with ADA maintenance compared with PBO.

060 PREGNANCY OUTCOME AND FERTILITY IN INFLAMMATORY BOWEL DISEASE IS INFLUENCED BY DISEASE PHENOTYPE

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Introduction: The incidence of the chronic inflammatory bowel diseases, Crohn's disease (CD) and ulcerative colitis (UC) peaks between the ages of 10 and 40 years. Subsequently many females have IBD during their reproductive years and have concerns surrounding fertility, pregnancy, and childbirth. CD patients have fewer babies than expected; the most important determinant of fecundity is disease activity at conception. In UC there is a threefold increase in subfertility in women with previous ileal pouch anal anastamosis.
Aims & Methods: We aimed to describe pregnancy outcome, subfertility rates, and menstrual health in a large population of accurately phenotyped Scottish women whose IBD was diagnosed while they were of child-bearing age. Furthermore, we aimed to explore women's perception as to how their IBD has affected their decisions regarding their family planning. A detailed questionnaire was sent to 554 female IBD patients from a single tertiary referral centre in Lothian, Scotland. All women were less than 50 years old at diagnosis (median 26.4 years; IQR 21.3–33.2). Data from 272 fully completed responses were analysed, comprising 137 patients with UC and 135 with CD. The median age at enrolment was 40.5 years (IQR 33.0–49.8). Control data on over 95% of the childbirths in Scotland were available for comparison (http://www.isdscotland.org/isd/1022.html). These data are recorded back to 1976 and include over 8000 births in Lothian from 2005.
Results: 58.8% of women reported attempting pregnancy, with 90.6% of these successful. 36/160 (22.5%) of women attempting to be pregnant were referred for fertility treatment. 172/272 (63.2%) of respondents had been pregnant, with data available on a total of 365 pregnancies. 27/172 (15.7%) patients had at least one unplanned pregnancy; 12.2% were taking the oral contraceptive pill at the time of conception. Although women with CD took longer to conceive for each pregnancy than those with UC (6.64 months *v* 3.83 months, $p=0.03$), they had equivalent numbers of pregnancies. The proportion of low birthweight infants was more than expected in the background population (11.2% *v* 7.2%, $p=0.01$). Women with IBD during their pregnancy years had shorter gestations than those diagnosed after all pregnancies (38.9 *v* 39.7 weeks, $p=0.0023$) and more preterm babies (16.2% *v* 6.8%, $p=0.021$). Detailed phenotyping demonstrated that patients with ulcerative proctitis (E1) had significantly heavier birthweights than those with left sided or extensive colitis (E2 and E3) (3.43 kg *v* 3.20 kg, $p=0.03$). Women reported that IBD made their periods heavier and more painful, especially during periods of disease activity.
Conclusion: Women with IBD in Lothian have pregnancies of shorter duration and babies of lower birthweight than the background population. However, women with limited ulcerative proctitis appear to be protected from these problems.

061 IDENTIFICATION OF GLI-1 AS AN IBD2 SUSCEPTIBILITY GENE

C. W. Lees[1], E. R. Nimmo[1], A. Tenesa[2], C. L. Noble[1], J. Loane[3], H. Campbell[2], S. E. M. Howie[4], M. G. Dunlop[2], J. Satsangi[1]. [1]*Gastrointestinal Unit;* [2]*MRC Human Genetics Unit, University of Edinburgh;* [3]*Department of Pathology, Western General Hospital;* [4]*MRC Centre for Inflammation Research, QMRI, University of Edinburgh, Edinburgh, UK*

Introduction: There is compelling evidence for a genetic susceptibility locus determining ulcerative colitis (UC) susceptibility/phenotype within 12q13 (IBD2), outwith the NOD2/CARD15 gene in the IBD1 region that is implicated in Crohn's disease (CD) pathogenesis. However, the causative IBD2 gene has yet to be identified. The hedgehog (HH) signalling pathway plays vital roles in gastrointestinal tract development, homeostasis and disease,[1] Paneth cell differentiation,[2, 3] T cell immunology, and inflammation. The major HH pathway effector, *GLI-1*, lies within the IBD2 linkage region, leading us to hypothesis that *GLI-1* might play a role in disease causation.
Aims & Methods: We aimed to analyse the contribution of inherited *GLI-1* variation and dysregulated HH signalling to IBD susceptibility. A total of 19 SNPs were typed, including 4 *GLI-1* tagging SNPs, and 8 tSNPs that

Abstract 059 ADA efficacy at Weeks 26 and 56, % of patients

Endpoints	Wk	PBO (n = 170)	ADA 40 mg EOW (n = 172)	ADA 40 mg W (n = 157)
Remission	26	17	40*	47*
	56	12	36*	41*
CR-100	26	27	52*	52*
	56	17	41*	48*
CR-70	26	28	54*	56*
	56	18	43*	49*

*$p<0.001$ *v* PBO.

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defined adjacent haplotype blocks. Three common and five rare *GLI-1* haplotypes were present in the Scottish healthy control (HC) population (n = 1374). SNPs were assayed by Taqman in a Scottish IBD population (335 cases of CD and 474 of UC) for case-control analysis. Log-likelihood testing assessed the overall contribution of *GLI-1* variation to disease susceptibility. Haplotype and variant analysis was performed using χ^2 testing. Expression of key HH signalling components were analysed by microarray, real-time PCR and immunohistochemistry in a large panel of formalin-fixed and fresh frozen colonic tissues from CD (n = 53), UC (n = 67) and HC (n = 31).
Results: A gene-wide haplotype-tagging strategy was employed to determine whether *GLI-1* is the IBD2 gene. We have demonstrated a strong association with *GLI-1* variation and inherited susceptibility to UC (OR = 35.8; $p<0.0001$), particularly with severe disease ($p = 3.55\times10^{-5}$), extensive disease ($p = 0.014$), and requirement for colectomy ($p = 1.45\times10^{-6}$). UC patients homozygous for the risk haplotypes had increased rates of severe disease (88.9% *v* 48.2%, p = 0.002, OR = 8.61), colectomy (55.6% *v* 16.7%, p = 0.0001, OR = 6.25) and more extensive disease (E3 72.2% *v* 41.0%, p = 0.02, OR = 3.74) than other UC patients. Haplotype tagging of adjacent blocks shows that *GLI-1* is located in a haplotype block spanning 10Kb that does not extend into neighbouring genes. In detailed expression studies, we have shown that Indian hedgehog-Patched-1-GLI-1 signalling is downregulated in UC, regardless of inflammation, supporting a causal role for hedgehog dysregulation in disease pathogenesis. In contrast Sonic hedgehog is induced by colonic inflammation, consistent with recent reports that it is downstream of NF-κB.
Conclusion: These findings implicate common genetic variation in a key component of the HH signalling pathway in the pathogenesis of IBD, providing evidence that *GLI-1* is the IBD2 gene.

1. **Lees C**, Howie S, Sartor RB, *et al. Gastroenterology* 2005;**129**: 1696–710.
2. **Lees CW**, Satsangi J. *Gastroenterology* 2006.
3. **Varnat F**, *et al. Gastroenterology* 2006;**131**:538–53.

062 NATALIZUMAB MAINTAINS CORTICOSTEROID-FREE REMISSION FOR 2 YEARS IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE AND IN THOSE WITH PRIOR INFLIXIMAB EXPOSURE: RESULTS FROM AN OPEN-LABEL EXTENSION STUDY

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Introduction: Natalizumab has been demonstrated as effective therapy for moderately to severely active Crohn s disease (CD) in both induction and long-term maintenance trials. Fifty five per cent of patients who responded to natalizumab induction therapy were in remission (Crohn's Disease Activity Index (CDAI) score <150) after 15 months of continuous natalizumab therapy in the ENACT trials, compared with 22% in the placebo group ($p<0.001$). This analysis was undertaken to assess the ability of natalizumab to maintain long-term corticosteroid-free remission.
Aims & Methods: Patients who completed the ENACT-2 trial were eligible to enroll in an open-label extension (OLE) study. The primary objective of this 2-year study was to examine the long-term safety and tolerability of natalizumab. Secondary efficacy endpoints included evaluation of the ability of natalizumab to maintain remission. This analysis includes patients who were in remission after 15 months of continuous natalizumab therapy in the ENACT trials who enrolled in the OLE study and received an additional 12 months of natalizumab therapy. Eighty seven patients met the criteria for analysis, 22 of whom had previous exposure to, and 11 of whom had previously failed therapy with, infliximab. Remission rates were calculated using last observation carried forward.
Results: Ninety three per cent (81/87) of patients who were in remission at Month 12 of ENACT-2 were in remission following 6 additional natalizumab infusions in the OLE study. After 12 additional infusions, 86% (75/87) were in remission. 91% (73/80) of the patients who were corticosteroid-free and in remission on entry maintained corticosteroid-free remission after 6 additional natalizumab infusions in the OLE, and 85% (68/80) did so after 12 additional infusions. In the subpopulation of patients with prior exposure to infliximab, 85% (17/20) and 90% (18/20) were in corticosteroid-free remission after an additional 6 and 12 infusions of natalizumab in the OLE study. Similarly, 80% (8/10) who had previously failed therapy with infliximab were in corticosteroid-free remission at the same timepoints.
Conclusion: Natalizumab maintained remission for >2 years (27 months) when administered as continuous therapy. Patients who entered remission with natalizumab induction therapy were highly likely to maintain long-term corticosteroid-free remission, including patients who had previously failed therapy with infliximab.

063 REPLICATION OF CROHN'S DISEASE MUCOSAL *E COLI* ISOLATES WITHIN MACROPHAGES AND THEIR SUSCEPTIBILITY TO ANTIBIOTICS

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Introduction: At least five independent studies have shown that Crohn's disease (CD) mucosae commonly contain *E coli.*[1–5] These *E coli* have an adherent phenotype and can be found within CD tissue macrophages suggesting a role in pathogenesis.
Aims & Methods: We aimed to investigate the ability of CD mucosal *E coli* to replicate within macrophages and their susceptibility to antibiotics. Replication of CD *E coli* isolates within J774-A1 murine macrophages and human monocyte-derived macrophages (HMDM) was assessed by lysis and culture after gentamicin killing of non-internalised bacteria and verified by transmission electron microscopy (TEM). The antibiotics: ampicillin, azithromycin, clarithromycin, ciprofloxacin, rifampicin, tetracycline and trimethoprim, were assessed for their efficacy against macrophage-internalised CD *E coli*.
Results: All three CD isolates studied: HM580, HM605 and HM615, replicated within J774-A1 cells (170.8 (6.8)%, 230.3 (15.9)% and 274.3 (33.8)% respectively by 3 h) more than non-pathogenic *E coli* strain K12 (127 (16.3)%; $p<0.05$). Similar replication was seen within HMDM (HM605: 395.2 (74.3)% by 3 h) also exceeding that seen for K12 (138.8 (20.0)%, p = 0.03). TEM showed replicating *E coli* within macrophage phagolysosomes. The table shows killing of HM605 within J774-A1 cells following 3 h incubation with antibiotics at published peak serum concentrations (C_{max}) and 10% of C_{max}. At 10% C_{max}, combinations of ciprofloxacin, trimethoprim and tetracycline (97 (0)% killing) and of ciprofloxacin, rifampicin and tetracycline (94 (1)%) were able to kill a higher proportion of HM605 within macrophages compared with ciprofloxacin alone (86 (2)%), $p<0.01$.
Conclusion: Clinical trials are now indicated to assess the efficacy in CD of combination antibiotic therapy with ciprofloxacin, tetracycline and trimethoprim.

1. **Swidsinski A**, *et al.* Mucosal flora in inflammatory bowel disease. *Gastroenterology* 2002;**122**:44–54.
2. **Darfeuille-Michaud AJ**, *et al.* High prevalence of adherent-invasive *E. coli* associated with ileal mucosa in Crohn's disease. *Gastroenterology* 2004;**127**:412–21.

Abstract 063

Antibiotic	% killing of HM605 at C_{max} Mean (SE)	% killing of HM605 at 10% of C_{max} Mean (SE)
Ampicillin	11.2 (2.5)	7.8 (4.5)
Azithromycin	41.0 (10.5)*	28.5 (9.1)
Clarithromycin	50.8 (4.3)*	32.2 (3.6)*
Ciprofloxacin	100.0 (0.0)*	87.2 (9.5)*
Rifampicin	76.0 (11.5)*	16.0 (12.5)
Tetracycline	69.3 (11.5)*	61.7 (6.6)*
Trimethoprim	57.2 (4.9)*	44 (8.8)*

*$p<0.05$.

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3. **Alpern J**, *et al*. Invasive *E. coli* strains are increased in Crohn's disease. *Gastroenterology* 2006;**130**:A–362.
4. **Martin HM**, *et al*. Enhanced *E. coli* adherence and invasion in Crohn's disease and colon cancer. *Gastroenterology* 2004;**127**:80–93.
5. **Kotlowski R**, *et al*. High prevalence of *Escherichia coli* belonging to the B2+D phylogenetic group in inflammatory bowel disease. *Gut* 2006 (in press).

064 ADALIMUMAB MAINTAINS CLINICAL REMISSION IN PATIENTS WITH CROHN'S DISEASE WITHOUT CONTINUED STEROID USE AND REGARDLESS OF ANTI-TNF HISTORY OR CONCOMITANT IMMUNOSUPPRESSANT THERAPY

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Introduction: This study evaluated the efficacy of adalimumab (ADA) in sustaining clinical remission in patients with active CD (1) without continued corticosteroid use and (2) with a history of anti-TNF treatment or concomitant immunosuppressant (IMM) therapy.
Aims & Methods: In CHARM, a Phase III, double-blind, placebo-controlled study of the efficacy and safety of ADA, patients with active CD (CDAI 220–450) received open-label induction dosages of ADA sc, 80 mg/40 mg at Wk 0 (BL)/Wk 2. At Wk 4, all patients were randomised to placebo (PBO) or 40 mg ADA, every other week (EOW) or weekly (W), through Wk 56. Patients with clinical response (decrease from BL CDAI ⩾70 [CR-70]) at Wk 4 were classified as randomised responders (RR). Steroid tapering was permitted at/after Wk 8 for patients with clinical remission (CDAI<150). The % of patients with CDAI<150 at Wks 26 and 56 who had been off steroid therapy for ⩾90 days were calculated for each treatment arm. The % of patients with CDAI<150, stratified by either concomitant IMM use or anti-TNF history, were also calculated at Wks 26 and 56.
Results: Clinical characteristics at BL were similar across the 3 arms: mean CDAI = 313; corticosteroid use, 44%; concomitant IMM use (AZA, 6-MP, or MTX), 47%; history of anti-TNF therapy, 50%. Of 854 patients receiving induction therapy, 778 were randomised. Of these, 499 (58%) were RR. Significantly greater percentages of patients receiving ADA achieved steroid-free remission for ⩾90 days (19% EOW, 15% W, 3% PBO at Wk 26; 29% EOW, 20% W, 5% PBO at Wk 56 ($p<0.05$ each ADA group *v* PBO)). The proportions of RR achieving CDAI<150 at Wks 26 and 56 by history of prior anti-TNF or concomitant IMM therapy are shown (table).
Conclusion: Adalimumab therapy allowed a significant percentage of patients to maintain steroid-free remission for ⩾90 days at both Wk 26 and Wk 56. Adalimumab was also significantly superior to PBO for the long-term treatment of CD irrespective of concomitant IMM or prior anti-TNF therapies.

065 FURTHER EXPERIENCE WITH THE USE OF 6-THIOGUANINE AS AN ALTERNATIVE IMMUNOSUPPRESSANT IN PATIENTS WITH CROHN'S DISEASE

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Introduction: 6-Thioguanine (6-TG) has been used as an alternative thiopurine in patients with Crohn's disease (CD) resistant to, or intolerant of conventional immunosuppression, with evidence of good clinical efficacy. However, recent reports have questioned its safety with respect to hepatotoxicity but experience remains limited. In this study we report our experience of the safety and efficacy of 6-TG in a series of patients with Crohn's disease.
Aims & Methods: A retrospective study of 29 patients with CD who had failed thiopurines +/− methotrexate between 2001 and 2006 was performed. Indications for treatment with 6-TG were active disease (n = 15), ability to withdraw infliximab (n = 8), steroid sparing (n = 3) and fistula closure (n = 3). All patients underwent regular clinical review, liver function tests (LFTs) and full blood counts (FBC). 20/29 patients underwent imaging of the liver and those on treatment for longer than 1 year were advised to undergo liver biopsy.
Results: The median dose of 6-TG used was 40 mg daily (range 20–60 mg). Median duration of 6-TG treatment was 22 months (range 0–60 months). Initial clinical response was achieved in 17/29 (59%). Of these, 12 (41%) remained in remission at a median of 44 months follow-up. Six of 29 (21%) patients discontinued 6-TG due to adverse effects (hepatotoxicity (n = 3), gastrointestinal upset (n = 2), and rash (n = 1)). In total, 9/29 (31%) patients developed abnormal LFTs during thioguanine therapy. These were mostly transient and mild (up to 2× normal). One patient developed a sinusoidal syndrome with splenomegaly and pancytopenia resolving on cessation of 6-TG. FBCs were normal in all other patients. MRI and US imaging showed mild splenomegaly in one other patient. All other liver images were normal. Of 11 liver biopsies, none showed evidence of nodular regenerative hyperplasia. Positive findings at liver biopsy were focal areas of thickened liver cell plates (but no fibrosis) (n = 1), granuloma (n = 1), mild portal tract inflammation (n = 2) and mild steatosis (n = 6).
Conclusion: 6-TG is moderately well tolerated with acceptable clinical efficacy for third line immunosuppression in CD. Hepatotoxicity remains a concern and the occurrence of an acute sinusoidal syndrome emphasises the need for vigilance. Mild LFT abnormalities are common and of uncertain significance. However, reports of significant NRH as summarised by a recent European 6-TG Working Party have not been substantiated by this well-studied UK cohort.

066 MEDIUM-TERM RESULTS OF ORAL TACROLIMUS TREATMENT IN REFRACTORY INFLAMMATORY BOWEL DISEASE

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Introduction: Oral tacrolimus, a macrolide immunosuppressant, approved for the prophylaxis of kidney and liver transplant rejection, has been shown to be effective in refractory inflammatory bowel disease.
Aims & Methods: This study aimed to evaluate the efficacy of oral tacrolimus in patients with inflammatory bowel disease refractory to conventional therapy, including azathioprine, 6-mercaptopurine and infliximab. Retrospective review of all patients with inflammatory bowel disease treated with oral tacrolimus. Tacrolimus was administered at an initial dose of 0.05 mg/kg twice daily, aiming for serum trough levels of 5–10 ng/ml. We evaluated clinical response, a retrospective ''estimated Crohn's Disease Activity Index'' (CDAI) for Crohn's disease (CD), modified Truelove-Witts index for ulcerative colitis (UC), and modified Pouch Disease Activity Index (mPDAI) for pouchitis. Patients had been monitored clinically for benefit and side effects, and by whole blood tacrolimus level, approximately each 4 weeks for the duration of treatment. Clinical remission was defined as an ''estimated CDAI'' <150 (CD), an inactive disease score on the Truelove-Witts index (UC) and mPDAI <5 (pouchitis).
Results: Twelve patients with CD, six with UC and one with pouchitis, all resistant to previous therapies, were treated for a median of 5 months. After four weeks 10 CD (83%), four UC (67%) patients and one pouchitis patient had a clinical response. There was a median reduction of the

Abstract 064 Randomised responders in remission by concomitant therapy, n/N (%)

Week	Therapy	PBO	ADA, EOW	ADA, W
26	IMM	14/83 (17)	32/77 (42)	32/79 (41)
	No IMM	15/87 (17)	36/95 (38)	41/78 (53)
	Prior anti-TNF	13/81 (16)	28/86 (33)**	30/71 (42)*
	No prior anti-TNF	16/89 (18)	40/86 (47)*	43/86 (50)*
56	IMM	10/83 (12)	30/77 (39)	28/79 (35)
	No IMM	10/87 (12)	32/95 (34)	37/78 (47)
	Prior anti-TNF	8/81 (10)	26/86 (30)***	24/71 (34)*
	No prior anti-TNF	12/89 (14)	36/86 (42)*	41/86 (48)*

Statistical significance: *$p<0.001$; **$p<0.05$; ***$p<0.01$, all *v* PBO.

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''estimated CDAI'' of 108 points (range 35–203; p = 0.002) and stool frequency of three per day at week 4. Remission was achieved in 42% (5/12) of CD and 50% (3/6) of UC patients at the end of follow-up. Side effects included temporary elevated creatinine (n = 1), tremor (n = 3), arthalgia (n = 1), insomnia (n = 1) and malaise (n = 1). Four patients discontinued treatment due to side effects.
Conclusion: Oral tacrolimus is well tolerated and effective in patients with refractory inflammatory bowel disease, in the short to medium term. Further controlled, long-term evaluation is warranted.

067 TOLERABILITY OF 6-MERCAPTOPURINE IN AZATHIOPRINE-INTOLERANT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Azathioprine (AZA) and 6-mercaptopurine (6-MP) are both effective immunosuppressive agents for the induction and maintenance of remission in both Crohn's disease (CD) and ulcerative colitis (UC). At present, AZA therapy is prescribed in preference in Europe, while 6-MP is favoured as first-line therapy in N America. Azathioprine intolerance (AZA_{INTOL}) is a common clinical problem, requiring drug withdrawal in up to 30% of patients. The subsequent use of 6-MP in these patients is described, but data to support this are lacking.
Aims & Methods: The aim of this study was to assess the tolerability of 6-MP therapy in IBD patients previously intolerant of AZA, and determine factors that predict tolerability. 61 AZA_{INTOL} patients who were subsequently treated with 6-MP at a single tertiary referral centre for IBD between 1993 and 2005 were identified. Data were extracted by retrospective case-note review. Phenotypes were analysed by the Montreal classification. The median age at diagnosis was 34.9 years (IQR 24.7–46.8). There were equal numbers of each sex (male 31/61, 50.8%), and disease type (CD 31/61, 50.8%; UC 30/61, 49.2%). The median duration of 6-MP treatment was 733 days (IQR 328–1127) in AZA_{INTOL}6-MP_{TOL}, and 54 days (IQR 13.5–105) in AZA_{INTOL}6-MP_{INTOL} patients.
Results: 6-MP was tolerated by 59% (36/61) of AZA_{INTOL} patients overall, 60.7% (17/28) in patients in whom nausea and vomiting was the primary reason for AZA withdrawal, 61.1% (11/18) for flu-like illness, 33.3% (3/9) with hepatotoxicity, 100% (1/1) with neutropenia, 100% (3/3) with rash and 0% (0/1) with pancreatitis. It was noteworthy that the primary intolerance of 6-MP was frequently different to that for AZA. The median age at diagnosis was significantly younger in the AZA_{INTOL}6-MP_{INTOL} group (28.4; IQR 22.5–38.1) compared with AZA_{INTOL}6-MP_{TOL} (37.0; IQR 27.8–56.5; p = 0.014). 6-MP was tolerated more frequently in males (22/31; 71.0%) than in females (14/30; 46.7%; p = 0.048, OR 2.79, CI 0.97–8.04). The maximum AZA dose in the two groups was equivalent (AZA_{INTOL}6-MP_{TOL} 1.48 mg/kg vs. AZA_{INTOL}6-MP_{INTOL} 1.39 mg/kg, p = 0.80), as was the median duration of AZA treatment (50.0 days (IQR 24.0–157.0) *v* 76.0 days (IQR 26.5–197.0), p = 0.93). 6-MP tolerance was not affected by diagnosis, disease location, disease behaviour, surgery, smoking status, family history, extra-intestinal manifestations, or TPMT activity.
Conclusion: 6-MP should be considered in AZA_{INTOL} patients, particularly those in whom nausea and vomiting, flu-like illness or rash was the major reason for AZA withdrawal.

Colorectal free papers

068 POLYPOSIS FAMILIES WITHOUT MUTATIONS HAVE A LESS SEVERE PHENOTYPE

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Introduction: Familial adenomatous polyposis (FAP) is an autosomal dominant condition predisposing to multiple polyps of the large bowel. However, not all patients with polyposis carry germline mutations in the APC (adenomatous polyposis coli) gene or other known genes which predispose to this condition.
Aims & Methods: The genotype-phenotype relationship of polyposis kindreds without identified mutations in known genes was determined in order to characterise features of a previously undescribed polyposis syndrome. The yield using stringent mutation detection methods was also determined. A cohort of sixty two unrelated patients recorded at St Mark's Hospital did not have mutations in the APC or MYH genes identified using standard techniques in diagnostic genetics laboratories. The coding and splice site regions of the APC gene were directly sequenced. Exon copy number changes were detected using a relatively new technique called multiplex-ligation probe amplification (MLPA). Haplotype analysis was performed using six flanking microsatellite markers, and two intronic single-nucleotide polymorphisms (SNPs) within APC. The MYH gene was screened for mutations using single-stranded conformational polymorphism (SSCP) analysis and sequencing.
Results: Nineteen kindreds were found to have either previously undetected APC mutations or exon copy-number changes. Four patients were found to carry a biallelic MYH mutation. Therefore approximately 37% of patients had mutations found not previously identified by diagnostic genetics laboratories. Five novel mutations of APC were identified, including a duplication of exon 4 of APC found using MLPA. Duplication mutations have not previously been identified. Genotype-phenotype analysis revealed a difference in polyp number between mutation positive (n = 23) and mutation negative (n = 39) groups ($p<0.003$, *t* test). Tumour genotype did suggest an aetiology not involving the Wnt signalling pathway. A subgroup analysis of the mutation negative group (based on family history) shows that there is a less penetrant condition among those with evidence of recessive inheritance of the trait. There is a later age of diagnosis of polyposis (41 years *v* 31.8 years, p = 0.007, t test), lower rate of colorectal and extra-colonic cancers (p = 0.002 and 0.017 respectively, Fisher's exact), and lower rate of duodenal polyposis ($p<0.0001$, Fisher's exact).
Conclusion: The mutation negative group is likely to consist of a heterogeneous group of patients with mutations in different predisposition genes for polyposis. A subgroup analysis indicates that those kindreds with a recessive type of inheritance pattern have a less severe phenotype and may represent a distinct syndrome.

069 DETERMINANTS OF COMPLIANCE TO A COMMUNITY COLORECTAL CANCER SCREENING PROGRAMME IN LECCO PROVINCE (ITALY)

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Introduction: Compliance to the first round of the colorectal cancer screening programme in the Lecco province (21 654 invitations), based on faecal occult blood test (FOBT) + colonoscopy in FOBT-positive individuals, was 47%. In order to assess major determinants of compliance, we evaluated differences of scholarity, profession, age, sex and motivations in two randomised groups of participants (P) and non-participants (NP) to the programme. We also studied the overall impact of different promotional interventions on the compliance to the programme.
Aims & Methods: 400 postal questionnaires were sent by ordinary mail in June 2006 to the two groups (200 P and 200 NP) randomly selected from the Health trust population database. Since NP had also a very low response rate, they were then contacted by phone. Concerning the different promotional interventions, other than a campaign on local media, specific interventions were classified as A, B, C and D: A personal invitation letter + information of GPs, Pharmacists and Health trust personnel; B as for A + involvement of voluntary associations (Red Cross and other local associations) particularly to facilitate collection and transportation of stool samples from remote areas to the central laboratory; C as for B + providing the test kit with the invitation letter; D as for B + a second invitation letter (recall).
Results: Responders in the P group were 119 (59.5%) as compared to only 19 (9%) in NP group. By telephone, we could find only 100 further individuals (50%) of the NP group. The main differences between groups were: female sex: 54% in the P group *v* 46% in NP group; scholarity, 16% of NP had a high school level, while the latter was 41% in P group ($p<0.001$); mean age of NP was higher than NP 61 *v* 59; $p<0.01$); professions: labourer or housewife had a lower participation rate than employee manager or professional (32% *v* 67%).Compliance rate did also differ according to the different degree of intervention: A = 44%; B = 42%; C = 62%; D = 52%. Approximately 90% of P and NP judged the information received on the campaign as complete and exhaustive. The main reasons for non participation were: ''scare'' of a possible problem (17%), no time to participate (21%). 84% of NP stated that they are willing to participate in the future. The most effective means of information were in order: letter of invitation (60%), information from GPs, friends and neighbours (22%), role of Pharmacists, media and associations (14%). Time, language, explanations, logistic problem with the test kit and, in general, the level of satisfaction concerning the programme were around 90% for P group.

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Conclusion: Major determinants of compliance to mass colorectal cancer screening in our province are: age, level of scholarity, type of profession, type of intervention. In order to increase population compliance to this programme we should work on better communication, by promoting the advantages of early diagnosis; another useful concept could be to outline a message like ''take time for yourself and your health''. We should consider sending the kit by the ordinary mail, as this strategy had a higher level of participation, and also to send a recall letter for those who did not participate initially.

070 MASS SCREENING OF COLORECTAL CANCER WITH AN IMMUNOCHEMICAL FAECAL OCCULT BLOOD TEST IN ITALY. PRELIMINARY RESULTS IN A PILOT PROVINCE

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Introduction: Mass screening of colorectal cancer with faecal occult blood test (FOBT) every two years has been recommended by health organisations in Italy. Lecco province is one of the first pilot areas which were selected in order to implement screening for the general population. We report herein the preliminary results of this program which started in November 2005.
Aims & Methods: The campaign has been organised according to the schedule of conditions defined by regional health authorities. The target population comprised 78 464 men and women aged between 50 and 69 years, before exclusion: individuals with history of colorectal adenoma or cancer, known inflammatory colonic disease or those who underwent a complete colonoscopy in the last 5 years were excluded. The campaign started in November 2005; general practitioners (GPs) were trained in small groups before starting up. Study population was contacted by mail; the faecal test was distributed by pharmacists and GPs. When necessary, reminder letters were sent 2 months after the first contact. Immunochemical faecal tests were processed with an automated reading technique by a single analysis centre.
Results: Up to October 2006, 21 654 asymptomatic individuals have been screened. The participation rate was equal to 47.6%. The FOBT positivity rate was 5.2%. A complete colonoscopy was performed in 93.3% of people referred for a positive test. On colonoscopy cancer was diagnosed in 23 cases (4.2%), an advanced adenoma in 111 cases (20.5%), a non-advanced adenoma in 137 cases (25.3%). The subsite of cancer was the rectum or the sigmoid colon in 57% of cases; 71.1% of screen-detected cancers were stage 0 or I, and 33.3% were diagnosed by histology of resected adenomatous polyps. The rate of caecal intubation at colonoscopy was 97.6%; perforation rate after colonoscopy was equal to 1.8 per 1000 examinations.
Conclusion: These positive results of mass screening for colorectal cancer in the Lecco province by means of an immunochemical FOBT followed by colonoscopy in FOBT-positive individuals should lead Italian authorities to gradually implement this campaign all over Italy.

071 EXPRESSION OF COLONIC STEM CELL MARKERS IN COLORECTAL CANCER CORRELATES WITH A POOR PROGNOSIS

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Introduction: It is known from previous research that adult stem cells in the colon reside in the colon crypt base. However, to date no reliable colonic adult stem cell marker(s) have been identified. The identification of such a marker will have far-reaching implications in many aspects of medicine and biology, especially in identifying the true origins and behaviour of colorectal cancer. Changes in the expression of A-type lamins have been described in a number of cancers. However, until now these changes in expression have not been directly linked to disease progression.
Aims & Methods: The aims of this study were to identify a unique colonic adult stem cell marker and to delineate its role, if any, in colorectal cancer. Tissue samples were taken from resected colon cancer specimens. These included normal colonic tissue. The samples were oriented and fixed in formalin before being embedded in paraffin blocks. Serial sections were stained with an antibody specific to lamin A/C. Serial sections were also stained with known proliferation markers and also markers for differentiation in colonic epithelial tissue. Subsequently a study was carried out, looking at the expression of A-type lamins in tumours of 656 incident colorectal cancer patients participating in the Netherlands Cohort Study on diet and cancer. The downstream implications of lamin A expression in a Dukes' B cell line known to express no endogenous lamin A were also investigated. GFP-lamin A constructs were stably transfected into SW480 colon cancer cells (SW480-lamA). GFP was transfected as a control (SW480-cntl). A cell motility assay and RNA profiling were used to compare differences between these cell lines.
Results: Lamin A was shown to be a reliable marker for adult stem cells in the human colon. Furthermore lamin A/C expression was associated with an increase in colorectal cancer mortality. This association pertained to Dukes' stages A through C. Cell motility was found to be markedly increased in SW480-lamA cells versus SW480-cntl after 24 hours. Additionally RNA profiling indicated an upregulation of T-plastin, concomitant with a downregulation of E-cadherin in SW480-lamA cells which was subsequently confirmed by semiquantitative RT-PCR.
Conclusion: These findings indicate a potential mechanism by which lamin A/C may impose a less adherent, more motile and consequently more aggressive phenotype on colon cancer cells. Cancers exhibiting lamin A/C expression may be more aggressive because they acquire a stem cell-like phenotype.

072 COLORECTAL STENTING IN MALIGNANT LARGE BOWEL OBSTRUCTION USING COMBINATION FLUOROSCOPY AND DIRECT ENDOSCOPIC PLACEMENT: A PROSPECTIVE 5-YEAR EVALUATION

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Introduction: Malignant colorectal obstruction can be managed with self-expanding metal stents. Palliation of non-operable neoplastic disease can be achieved in addition to providing a ''bridge to surgery''. This management facilitates optimisation of preoperative clinical parameters, which improve outcome in this group. Small case numbers and predominant retrospective study designs limit current data. We describe our prospective experience of combination fluoroscopic and ''through-the-scope'' (TTS) self expandable metallic stent placement over a 5-year period.
Aims & Methods: All patients presenting with clinical or radiological evidence of colorectal obstruction between January 2001 to November 2006 at a tertiary referral colorectal unit were recruited to the study. Combination fluoroscopic and TTS endoscopic placement under conscious sedation was used for all stent placements. The primary clinical end-point was technical success of stent placement. Secondary end-points included in the analysis were procedure related complications (stent migration, re-occlusion, perforation, stent fracture and fistualisation).
Results: Sixty six patients were recruited to receive combination fluoroscopic/TTS stent insertion. Complete colorectal luminal obstruction was radiologically evident in 30% of patients pre-procedure using water-soluble contrast ''road mapping''. 3/66 (4.5%) of stents were placed proximal to the splenic flexure. Technical success was achieved in 89% (59/66) cases. Complications (early/delayed) occurred in 10/66 (15%) of the cohort. Stent migration occurred in 3%, luminal re-occlusion 6%, acute ''on table'' perforation 1.5%, stent fracture 1.5% and stent related fistualisation in 1.5%.
Conclusion: This is the largest prospective UK experience of combination TTS/fluoroscopic colorectal stenting. We have shown the combination approach provides a highly effective clinical outcome when used as a clinical tool both for palliative and preoperative ''bridging'' therapy with a threefold reduction in complication rates when compared to previous published retrospective UK data.[1]

1. **Suzuki N**, *et al*. Colorectal stenting for malignant and benign disease: outcomes in colorectal stenting. *Dis Colon Rectum* 2004;**47**:1201–7.

Endoscopy videos

073 ENDOSCOPIC MUCOSAL RESECTION TECHNIQUES FOR UPPER GASTROINTESTINAL NEOPLASMS: VIDEO REVIEW

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Introduction: Endoscopic mucosal resection (EMR) is a standard minimally invasive treatment for early gastric and oesophageal neoplasms in Japan. However, there are very few centres in the UK performing EMR on a regular basis. We have been treating all early upper GI neoplasms by EMR at our centre. The EMR techniques are rapidly evolving but there are four common techniques that are widely used. Most centres use one of these

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techniques to treat all cases but we believe that all these techniques are complimentary and a centre performing EMR should have expertise in all these techniques.

Aims & Methods: We have recorded small (60–90 seconds) video clips of the common EMR techniques and will present them with the aims: (1) to demonstrate the technical feasibility of each technique and (2) to discuss the strengths, weaknesses and clinical applicability of each technique. All patients undergoing EMR have chromoendoscopy to identify the exact margins of the abnormal area which is then premarked using diathermy. Once the dissection field has been identified then submucosal injection is performed (if indicated) prior to EMR.

Results: We have performed EMRs on 40 upper GI lesions using four different techniques as listed below. We have had excellent clinical outcome and cure rates with only a single patient developing delayed bleeding at 48 h (which was controlled very effectively by endoscopic therapy). None of our patients developed perforation or required emergency surgery. We have recorded small clips demonstrating the technical aspects of each of the following techniques: video clip of strip biopsy (conventional) using a double channel gastroscope; video clip of cap and snare technique (Olympus); video clip of Duette (Ligation) technique (Cook); video clip of endoscopic submucosal dissection (ESD) using an IT knife and Neddle knife (Olympus). We feel that Cap and Snare technique is well suited to remove single small and raised (<1.5 cm) lesions with or without surface inflammation/erosions but is time consuming requires two operators. Duette is very effective in treating large flat lesions and is very quick requiring only single operator but is not suited for polypoid lesions and lesions with surface erosions/minor ulcerations. Strip Biopsy is an excellent technique to remove residual islands left behind using any of the above techniques. ESD is an excellent technique which meets the basic onco-surgical principle of one piece resection of cancers. However it is time consuming and has a long learning curve.

Conclusion: EMR is an effective technique to treat early upper GI neoplasms. All four techniques demonstrated above are not mutually exclusive but are complimentary and the technique should be chosen depending on the site and size of the lesion. We recommend that clinicians performing EMR should acquire expertise in all these techniques as more then one techniques are commonly used to effectively remove a large lesion in upper GI tract.

074 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY OESOPHAGEAL CANCER: TECHNICAL FEASIBILITY AND CLINICAL APPLICABILITY

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Introduction: Conventional EMR techniques are well suited for tiny (<1.5 cm) gastric and oesophageal lesions. However, when used to resect large lesions then these techniques are associated with high risk of recurrence.[1] In order to overcome this problem, a new technique of endoscopic submucosal dissection (ESD) has been developed and has become a standard treatment for early gastric cancers in Japan.[2] The primary aim of ESD is to obtain one piece resection of cancers. However, ESD using endoscopic knives is not routinely used in UK. We have been performing ESD for all early gastric cancers at our centre in Portsmouth for the last 2 years. We now report the first case of ESD of early oesophageal cancer in UK.

Aims & Methods: A 74-year-old male with known Barrett's oesophagus was found to have high grade dysplasia on a non-targetted biopsy taken during surveillance OGD. We performed chromoendoscopy to identify the lesion and removed it using Insulated Tip (IT) knife assisted ESD. It starts with identification and demarcation of the lesion margins which are marked by a needle knife. This is followed by submucosal injections at the margins before performing a circumferential mucosal incision around the lesion. Subsequent submucosal dissection is performed using an IT knife. We will demonstrate a video clip of IT knife assisted ESD in oesophageal adenocarcinoma.

Aims: (1) To demonstrate the technical feasibility of ESD in early oesophageal cancer. (2) To discuss the strengths and clinical applicability of ESD. (3) To demonstrate the common complications and there management during ESD

Results: We identified and removed a 4.5 cm large oesophageal lesion extending 3 cm above and 1.5 cm below the cardia involving half the oesophageal circumference. On histology this was primarily high-grade dysplasia but a very tiny focus of adenocarcinoma with superficial submucosal invasion was identified. The procedure took 150 minutes. Some intraoperative haemorrhage was noted and effectively treated. No other complication was seen and patient was discharged home after overnight observation.

Conclusion: We have demonstrated that it is technically possible to remove large oesophageal lesions using IT knife assisted ESD. It is safe and feasible but is time consuming. ESD provides a large single piece resection specimen for accurate histological staging to predict the risk of lymph node metastasis and decide the need for additional treatment. We feel that in our case the focus of submucosal invasion was so minute that it would have been easily missed by conventional multiple piece EMR techniques and patient might have received inadequate treatment with risks of delayed recurrence. We suggest that ESD is an ideal technique to remove oesophageal lesions bigger then 2 cm in size.

1. **Egguchi T**, Gotoda T, Oda I, *et al.* Is endoscopic one piece resection essential for early gastric cancer ? *Dig Endosc* 2003;**15**:113–16.
2. **Oda I**, Gotoda T, Hamanaka H, *et al.* Endoscopic submucosal dissection for early gastric cancer: technical feasibility, operation time and complications from a large consecutive series. *Dig Endosc* 2005;**17**:54–8.

075 AN EMERGING ''GOLD STANDARD'' FOR THE COLONOSCOPIC ASSESSMENT OF ULCERATIVE COLITIS: HIGH MAGNIFICATION CHROMOSCOPY PROVIDES A VALID IN VIVO OPTICAL BIOPSY AND EXTENT ASSESSMENT TOOL

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Introduction: Colonoscopy with mucosal biopsy is currently considered the ''gold standard'' investigation for the evaluation of disease activity and extent in UC. Conventional colonoscopic criteria alone are inadequate for disease extent assessment and in predicting clinical relapse. Histopathological markers of relapse such as microscopic crypt abscess formation and mucin depletion cannot be identified using conventional resolution white light endoscopy.

Aims & Methods: To evaluate the efficacy of high-magnification-chromoscopic colonoscopy for the in vivo prediction of histopathological inflammation and disease extent using standardised endoscopic and histopathological criteria. Total colonoscopy using the Olympus CF240Z magnifying colonoscope was performed prospectively on 325 consecutive patients with a known diagnosis of ulcerative colitis. A ''bi-phasic'' examination of all 5 colonic segments and rectum using conventional endoscopy followed by magnification imaging and biopsy was performed. Disease activity was documented using the Baron classification, modified Saitoh criteria for magnification imaging and Matts criteria for histopathology.

Results: 1800 images were analysed from 300 patients (25 excluded). The K coefficient of agreement between magnification Saitoh grade 1/2, 3/4, 5/6 and histopathological Matts grade 1/2, 3a/b and grade 4/5 disease was 0.96, 0.62 and 0.51 respectively. Mild, moderate and severe histopathological disease (Matts grade 1/2, 3a-4 and 5) was represented more accurately using Saitoh criteria than conventional Baron scores for all clinical parameters ($r=0.976$; $p<0.001$). Magnification imaging was significantly better than conventional colonoscopy when predicting in vivo extent of disease ($p<0.0001$).

Conclusion: This is the largest prospective study and only Western group to report on this application of magnification imaging. Using a simplified modification to the HMCC Saitoh criteria we demonstrated a more accurate in vivo representation of disease activity as compared to conventional colonoscopy using Baron criteria for all parameters ($p<0.001$). These data may have major clinical implications, as HMCC grade 2/3 disease is associated with epithelial defects and an increase in mucosal inflammatory cellular traffic—a significant independent predictor of disease relapse. These data are therefore clinically useful for targeting patients at ''high risk'' of clinical relapse where medical therapy could be augmented (ie provide a valid biomarker for disease relapse in vivo) and also by limiting the numbers of biopsies required per examination with significant cost saving advantages to pathology services.

076 DOES CHANGES TOWARDS SAFER SEDATION PRACTICES REALLY IMPROVE ENDOSCOPIC OUTCOMES? A RE-AUDIT FOLLOWING IMPLEMENTATION OF GRS, BSG AND NCEPOD RECOMMENDATIONS

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Introduction: The NCEPOD report ''Scoping our practice'' (2004) emphasised sedation practice as a contributor to endoscopy related mortality. Following our audit of sedation practice in 2005[1] a number of

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GRS, BSG and NCEPOD recommendations were introduced. These included; feeding back personal practice, change in endoscopy reporting tool, introduction of pharmacy labelled/prepacked 5 mg syringes of midazolam (MD), adverse events recording of MD doses >5 mg and reversal agents use, better documentation/monitoring procedures of sedated patients and quarterly adverse events review.

Aims & Methods: Re-audit 12 months following the implementation of safer sedation practice to assess its impact on endoscopic outcomes. 7071 consecutive patients in a 6-month period in 2006 were identified using Unisoft database and compared with the audit data over the same period collected from the Endoscribe database in 2005 (7234 patients). ERCPs were not included in both data sets. Outcomes audited were MD doses, 30 day post procedure mortality (PPM), reversal agents use and immediate complications. PPM was correlated by identifying any death within 30 days of an endoscopic procedure using the hospital Medway IT system. Statistical analysis used were χ^2 (\chi>3.4 for $p<0.05$ significance) and Mann-Whitney (significance $p<0.05$) tests.

Results: Sedation was used in similar proportions of procedures in both years, ie 53% (n = 3816) in 2005 and 56% (n = 3916) in 2006. Sedation practice was improved: (1) overall mean MD dose (SD) was much lower at 2.9 (1.2) mg in 2006 *v* 4.9 (2.5) mg in 2005 ($p<0.0001$); (2) MD doses in patients aged >70 years were lower at 2.4 (1) mg in 2006 *v* 4.3 (2) mg in 2005 ($p<0.0001$); and (3) no endoscopist used mean MD doses >5 mg in 2006 compared to 18.75% (6/32) in 2005. However, the use of reversal agents (0.6% and 0.7% for 2005 and 2006 respectively; \chi = 0.1), overall PPM (0.7% v 0.8% for 2005 and 2006 respectively; \chi = 0.6) and sedated patients PPM (1.0% v 1.3% for 2005 and 2006 respectively; \chi = 1.4) were all similar. Furthermore, overall poor outcomes in sedated patients (ie either/or PPM/Reversal/Immediate Complications) were no different at 1.7% in 2005 and 2.0% in 2006 (\chi = 0.6). In PPM patients, the ages (74.5 (13) years *v* 74.3 (13) years; p = 0.8) and the MD doses used (2.3 (2) mg *v* 2.0 (1.3) mg in 2005 and 2006 respectively; p = 0.6) were similar.

Conclusion: With the implementation of safer sedation practice, there were substantial reductions in the doses of Midazolam used in 2006. However, this did not translate to improved hard end points in endoscopic outcomes, thus suggesting that the heavy emphasis placed by NCEPOD of the impact of sedation practice on mortality may be misleading.

1. *Gut* 2006;**55**(Suppl II):A57–217.

077 FIRST REPORTED CASE OF DIRECT JEJUNOSTOMY USING A DOUBLE BALLOON ENTEROSCOPE

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Introduction: This case report is supported by a five minute video of the endoscopic procedure described. A 48-year-old man was referred for consideration of long-term home parenteral nutrition. He was diagnosed with Type I diabetes mellitus at the age of 11 and glycaemic control had been poor. He developed peripheral neuropathy, diabetic retinopathy and was registered blind. For eight years prior to referral he had suffered progressive, intractable vomiting. His normal weight of 74 kg dropped to 53 kg (body mass index 25.6 to 18.3). Nuclear gastric emptying studies confirmed marked gastroparesis. Treatment with antiemetic and prokinetic drugs combined with nutritional supplementation failed. A percutaneous endoscopic gastrostomy (PEG) with a jejunal extension was inserted but he only tolerated 500 ml of feed daily. The jejunal tube was reinserted on three occasions in six months, after displacement by vomiting. Recurrent, prolonged admissions to hospital with dehydration and malnutrition prompted referral to our unit.

Aims & Methods: A double balloon enteroscopy (DBE) was performed, under general anaesthetic and radiographic control. The double-balloon enteroscope was inserted to 100 cm from the incisors, at which point a direct jejunostomy was performed (see accompanying video). Radiography and repeat enteroscopy confirmed correct placement of the feeding tube. The original PEG tube was retained to allow gastric venting.

Results: After an unremarkable recovery our patient was established on 1.5 l of *complete* feed daily, infused over 10 h. Despite intermittent hyperemesis there was no jejunal feed in the vomitus or the gastric contents drained through the PEG. His insulin regime was modified appropriately, he gained weight and was discharged. He remains at home and well to date.

Conclusion: Double balloon enteroscopy has been validated as safe and effective for examination of the small bowel and has been adopted by many major units. The therapeutic potential of DBE is an advantage over Video Capsule Endoscopy. There are several published studies reporting efficacy in the treatment of haemorrhagic lesions in the small bowel and case reports of use in endoscopic mucosal resection of small bowel lesions. In this case, DBE permitted insertion of a relatively distal feeding system in a patient where proximal enteral nutrition had failed. A PubMed search yielded no previous reports of this technique. This is therefore the first direct jejunostomy insertion using double-balloon enteroscopy reported in the world. In this case it has proven successful and has avoided the risk, technical difficulty and expense of home parenteral nutrition in a young blind patient.

078 THE FIRST UK CASE OF ENDOLUMINAL FUNDOPLICATION USING THE ESOPHYX DEVICE

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Introduction: We report the first UK case of endoscopic anti-reflux therapy using the EsophyX endoluminal fundoplication (ELF) device. GORD disease significantly reduces quality of life scores but treatment options are limited. Long-term PPI therapy is often unacceptable to patients while surgery is invasive and associated with significant side-effects. Endoscopic anti-reflux therapy has now emerged as a third option for patients with GORD. Unlike previous endoscopic techniques, the EsophyX device produces a full-thickness endoscopic fundoplication. Twelve month follow-up data reported from European centres are highly encouraging. St Mark's Hospital is the first UK centre to perform the EsophyX procedure as part of this registry based multi-centre study.

Aims & Methods: A 31-year-old man with PPI-responsive GORD had positive oesophageal pH studies and GERD-HRQL and REFLUX-QUAL scores consistent with symptomatic reflux. There was no evidence of an oesophageal dysmotility disorder. No hiatus hernia or Barrett's mucosa was seen at prior endoscopy. The referral for the EsophyX procedure was precipitated by his desire to avoid long-term anti-acid medication and to enjoy an unrestricted diet. The EsophyX ELF procedure is designed to recreate the normal anatomical and physiological conditions present at the gastro-oesophageal junction in healthy individuals. It has been shown that this junctional anatomy is critical in defining an individual's propensity to developing GORD.[1] The EsophyX device comprises of a valve moulding and full thickness fastener delivery device which fits around a conventional gastroscope. The device and scope are then inserted orally into the stomach under general anaesthesia. The procedure is reliant on two operators, one operating the device and the second maintaining clear visualisation with the retroflexed gastroscope. Multiple fasteners are then used to reconstruct the gastro-oesophageal valve to produce a 270 degree wrap.

Results: Other than a transient sore throat, the patient recovered well and fully from the procedure with no serious side effects. He was discharged home the following morning, having been admitted overnight as a precaution. He and other patients treated with the EsophyX device at this centre will continue to be followed-up for a further 2 years with respect to oesophageal physiology studies, medication usage and quality of life scores.

Conclusion: We are optimistic that the EsophyX ELF procedure will provide a safe and efficacious treatment option for patients with GORD who wish to consider an alternative to anti-acid medication or surgery.

1. **Oberg**, *et al. Surg Endosc* 1999.

Plenary session

079 CHROMOSCOPIC CONFOCAL LASER SCANNING IN VIVO BIOPSY FOR THE DETECTION AND CHARACTERISATION OF NEOPLASTIC LESIONS IN HIGH-RISK COLORECTAL CANCER COHORTS: ENTERING THE ERA OF HISTOENDOSCOPY IN THE UK

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Introduction: Confocal laser endomicroscopy (CLE) is now possible using the novel Pentax EC3870K. Development of histoendoscopy could potentially be the gold standard imaging modality in the colorectum.

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Aims & Methods: To prospectively assess the clinical applicability and predictive power of the EC3870K endomicroscope for the in vivo diagnosis of intraepithelial neoplasia (IN) during ongoing videoendoscopy. Patients assuming a high lifetime risk of colorectal neoplasia underwent colonoscopy using the EC3870K. Following ileal intubation, lesions were identified using conventional chromo-endoscopy (morphology class as per Paris guidelines) with CLE imaging graded according to Mainz criteria. 10% iv sodium fluorescein facilitated surface and deep imaging to the lamina propria. CLE imaging of both circumscribed lesions and 4 segmental normal colorectal quadrants was performed. Targeted biopsy specimens from the raster scanned colorectal segments were then compared with conventional histopathology.
Results: Forty patients completed protocol (22 male; median age 62 years (range 39–82)). The median ileal intubation and total procedure duration was 12 minutes (range 5–26) and 55 minutes (range 28–92) respectively. Ileal CLE revealed discrete goblet cells, stromal capillary loops, visible erythrocytes and mononuclear cells. Video chromoscopy revealed 162 lesions in 39 patients (73 (45%) Paris 0–II, 54 (33%) Paris Is, 35 (22%) Paris Ip)—median diameter 5 mm (range 1–22), 8 mm (range 2–34) and 10 mm (range 5–20 mm) respectively. CLE imaging was obtained on all 162 (100%) lesions. 5422 confocal images were then compared to 802 targeted biopsy specimens. Regarding primary end-points of IN prediction, when neoplastic endomicroscopic architecture was defined according to Mainz criteria for combined superficial and deep vascular net pattern and discrete crypt architecture (dilated vascular distortion with leakage elevation +/− tortousity and cryptic/goblet cellular attenuation with mucin depletion respectively), IN was predicted with an accuracy of (99.1%) (sensitivity 97.4%/specificity 99.3%)—MN $p>0.5$. The secondary end-point of image quality evaluation at re-review showed 76% of images were graded as satisfactory to good.
Conclusion: Endomicroscopy permits high quality cellular, subsurface vascular and stromal imaging in vivo enabling high accuracy prediction of neoplasia. Clinical practice may be radically changed in targeted cohorts where rapid high accuracy diagnosis of IN can be made with optimisation of on-table management decisions with an associated reduction in non-significant histopathological sampling—an important health economic requisite.

080 RISK OF CANCER IN INFLAMMATORY BOWEL DISEASE TREATED WITH AZATHIOPRINE: A UK POPULATION-BASED CASE-CONTROL STUDY

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Introduction: Azathioprine is an accepted part of the long term treatment of inflammatory bowel disease (IBD) but concerns exist regarding its carcinogenic potential. Studies in renal transplant and rheumatology patients have reported an increased risk of cancer where azathioprine is prescribed. In IBD, studies have suggested at most a small increased risk of lymphoma and protection against colorectal cancer but the overall risk of malignancy has not been established.
Aims & Methods: We conducted a case-control study using the General Practice Research Database. We examined the records of patients with IBD for azathioprine prescriptions and diagnoses of any cancer (excluding non-melanoma skin cancer) occurring after diagnosis. Prescriptions per year of follow-up were then grouped into tertiles for analysis. Azathioprine use was compared between cases (with a diagnosis of cancer) and controls (without). Subjects with less than one year of follow-up were excluded.
Results: 16 663 patients with IBD were identified of whom 15 771 had over 1 year of relevant follow-up data. Among these mean follow-up was 4.5 years. Of these subjects, 1976 (13%) had received at least one prescription for azathioprine and 431 patients were diagnosed with a cancer during the follow-up period. Univariate analysis of the occurrence of any cancer against azathioprine prescription showed a non-significant protective effect (OR = 0.88, 95% CI 0.76 to 1.02). Correction for the effect of age attenuated this effect, but no increase in risk was seen (OR 1.00, 95% CI 0.86 to 1.16). The association was not appreciably confounded by smoking, sex or BMI
Conclusion: We found no increased risk of cancer in people with IBD who have previously taken azathioprine. Indeed, in this the largest study of the effect of azathioprine upon malignancy yet undertaken frequency of prior azathioprine prescription was lower in the group of patients who developed cancer than in the control group, suggesting a potential protective effect. This was due to low rates of Azathioprine use in the elderly. After correction for this, there remained no significant increased risk of malignancy related to Azathioprine use in IBD and we can be fairly confident that the true risk is less than a 16% increase in malignancy risk.

081 THE PLACE OF MINIMAL ACCESS SURGERY AMONG PEOPLE WITH GASTRO-OESOPHAGEAL REFLUX DISEASE: THE REFLUX TRIAL

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Introduction: The two principal approaches routinely used in the NHS to treat patients with uncomplicated symptoms of confirmed gastro-oesophageal reflux disease (GORD) are medication and surgery. At present, it is uncertain which is the better, and for whom.
Aims & Methods: The REFLUX study, funded by the NHS HTA Programme, was a multicentre trial to evaluate the clinical effectiveness, cost effectiveness, and safety of a policy of relatively early laparoscopic surgery compared with continued medical management among people with GORD judged suitable for both policies. Patients with documented evidence of GORD (endoscopy and/or manometry/24 h pH monitoring) and with symptoms for longer than 12 months were identified, either retrospectively or prospectively, by participating clinicians in 21 UK hospitals. Of the 810 eligible patients who consented to participate, 357 were recruited to a randomised comparison: 178 allocated to surgical management and 179 to optimised medical management. The other 453 were recruited to parallel non-randomised preference groups: 261 choosing surgical management and 192 choosing optimised medical management. This presentation will concentrate on the randomised comparison. Outcome data were collected from self-completed postal questionnaire containing a disease-specific outcome-measure (The Reflux questionnaire), SF-36, and EQ-5D, all at participant-specific time intervals, equivalent to approximately 3 and 12 months after surgery. Primary analyses used the intention to treat (ITT) principle; secondary ''per protocol'' (PP) analyses were conducted amongst those who actually received their allocated management.
Results: The two randomised groups had similar baseline characteristics. Participants were on average 46 years old and 64% were men. 111 (62%) allocated surgery had fundoplication—either total or partial wrap—with a median length of stay of 2 days; complications were rare, with no re-operations within 12 months. At 3 months follow-up there were substantive differences across all measures, with the surgical group having the better scores. Differences persisted at 12 months although they were somewhat less marked in: Reflux questionnaire score 11.2 (95% CI 6.4 to 16.0; $p<0.001$); SF36 General Health 4.8 (95% CI 2.7 to 6.8; $p<0.001$); and EQ-5D 0.047 (95% CI −0.004 to 0.097; $p=0.07$). PP analyses, as expected, generated larger differences. 38% allocated surgery (PP 14%) compared with 90% (PP 93%) allocated medical management were taking some reflux related drug at 12 months.
Conclusion: Surgical management in patients requiring long-term medication to control their reflux symptoms significantly increases general and reflux-specific quality of life measures. Surgical complications in this study were rare.

Gastrointestinal physiology associates group

082 THE EFFECT OF PELVIC AFFERENT NERVE STIMULATION ON RECTAL COMPLIANCE

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Introduction: Constipation and faecal incontinence are common in spinal cord injury (SCI) patients. Electrical sacral nerve stimulators (SNS), implanted for bladder control, improve gut function through unknown mechanisms. Such devices are effective in nerve-intact patients. We hypothesised that sacral afferent stimulation, by altering aberrant sacral reflexes in SCI, may influence rectal compliance, and hence bowel function.
Aims & Methods: Four men with chronic SCI between C4-T5 were studied. Barostat rectal distension was performed in 50 ml steps with simultaneous compliance assessment. Measurements were repeated while stimulating the purely afferent dorsal penile nerve using surface electrodes connected to an impulse generator. Stimulation amplitude was set at twice the level required to stimulate the pudendo-anal reflex, and neuromodulation frequency altered at 0.2, 2 and 20Hz.
Results: Afferent neuromodulation significantly increased rectal compliance with increasing distension at 0.2 and 20Hz ($p<0.05$ and <0.01 resp). 2Hz stimulation did not achieve a significant increase in compliance compared to baseline ($p=0.1$) and there was no significant difference

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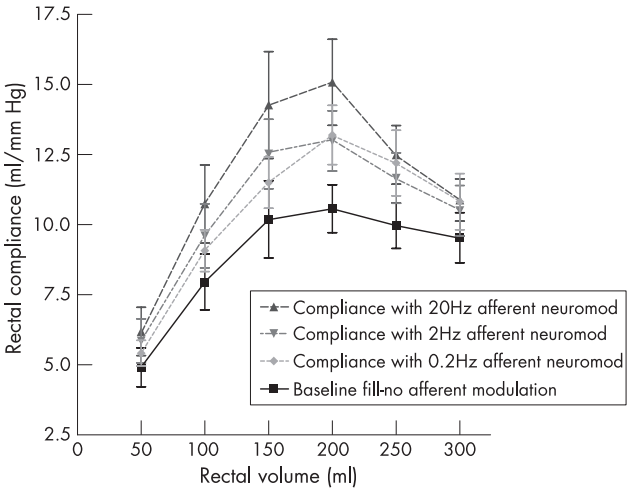

Abstract 082 Rectal compliance with distension, altered by pelvic afferent sacral nerve neuromodulation at different frequencies.

when comparing stimulation between 0.2 and 2Hz (p=0.6). The effect on rectal compliance was more marked at higher stimulation frequencies.
Conclusion: In SCI patients afferent sacral nerve stimulation alters rectal compliance in a stimulation frequency dependent manner. SNS may alter gut function through a sensory process. Such neuromodulation offers hope for therapy in SCI patients.

083 EVALUATION OF GASTRIC FUNCTION AND CONTROL OF MIGRATION OF OESOPHAGEAL REFLUX AFTER LAPAROSCOPIC NISSEN FUNDOPLICATION

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Introduction: Gastric emptying increases after Nissen fundoplication. The aim of this study was to document changes in gastric myoelectrical activity, if any, after surgery for GORD
Aims & Methods: The study group consisted of 27 symptomatic patients, with documented gastroesophageal reflux disease on 24 hour pH monitoring. Twelve patients had Barrett's oesophagus, 3 had previous endotherapy. All patients had detailed history, symptom questionnaire, manometry and pH and multi-channel electrogastrography (EGG) studies before surgery and at approximately 6 months postoperatively.
Results: Seventy four per cent of patients had some degree of preoperative gastric dysrhythmia. After surgery, 63% (17) of patients had normal percentages of basal electrical rhythm (>70% range 2–4 cycles per minute). Dominant frequency remained within the normal range but was significantly increased (p<0.01) from 2.3 to 3.0. Power ratio reduced from 2.1 to 1.8 (NS). There was also a significant reduction in post-prandial reflux, from 29.9 to 2.6% (p<0.001) which was associated with the improvement in normagastria after surgery. Laryngopharyngeal reflux (LPR) was identified in 18 patients (67%) preoperatively. This was significantly reduced (p<0.001) to 9 positive LPR postoperatively
Conclusion: Nissen fundoplication normalises gastric dysmotility in addition to increasing lower oesophageal sphincter tone. We conclude that surgical control of reflux with a floppy Nissen alters gastric motility which may have consequences for proximal migration of oesophageal reflux.

084 GUT SYMPTOMS IN DIABETES CORRELATE WITH AUTONOMIC ACTIVITY AND COMPONENTS OF THE RECTO-ANAL INHIBITORY REFLEX, NOT PUDENDAL NERVE LATENCIES

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Introduction: Anorectal dysfunction leading to faecal incontinence (FI) occurs in 20% of patients with diabetes mellitus (DM), and a number of motor and sensory abnormalities have been described. The problem occurs more often in patients with systemic autonomic neuropathy, but it remains unknown whether gut-specific autonomic dysfunction is associated. The recto-anal inhibitory reflex (RAIR) is an enteric reflex that reflects the integrity of the sampling mechanism in the physiology of faecal continence. We hypothesised that diabetic patients with FI have gut specific abnormalities—autonomic disturbance and abnormal RAIR parameters.
Aims & Methods: The following patients were studied: 31 type I DM (19 female, mean age 32; 19 FI and 12 constipation); 42 type II DM (26 female, mean age 38; 26 FI and 16 constipation); 21 controls (14 female, mean age 35). Patients underwent two systemic (cardiovagal autonomic tone (Mayo CAS score) and pudendal nerve terminal motor latency, PNTML (St Mark's electrode)) and two gut specific (autonomic tone (rectal mucosal blood flow-RMBF) and RAIR) neurological assessments. Three phases of the reflex were identified—the latency from stimulus to maximal sphincter relaxation; the duration of maximal relaxation; the time to recovery back to resting pressure. In addition, the amplitude of maximal reflex relaxation was compared between groups. All subjects completed symptom scores for FI (St Mark's) and constipation (Wexner).
Results: Systemic: CAS score in DM patients was not correlated with symptom severity for either FI ($r=-0.21$, p>0.10) or constipation ($r=0.14$, p>0.20). PNTMLs were not correlated with symptom scores (FI or constipation), RMBF or any component of the RAIR. Gut-specific: RMBF was lower in DM patients with constipation than controls (124 *v* 169, p<0.05) and correlated inversely with Wexner scores ($r=-0.79$, p=0.004). RMBF correlated with FI scores in DM patients ($r=0.65$, p=0.02). RAIR amplitude of relaxation was lower in constipated DM patients than controls (54 *v* 77%, p<0.03) and diabetics with FI (54 *v* 68%, p<0.05). RAIR recovery back to resting pressure was slower in diabetics with FI than constipation or controls (6.8 *v* 4.4 and 4.3 resp, p<0.01 both). This RAIR recovery time correlated with RMBF ($r=0.58$, p=0.04).
Conclusion: Symptoms in patients with DM correlate with gut specific features but not systemic ones. Specifically there were differences in the character of the RAIR, pointing towards a role for sphincter muscle dysfunction in diabetics with constipation and for sphincter neuropathy in diabetics with FI.

085 BILE ACID MALABSORPTION AND ILEAL HISTOLOGY IN DIARRHOEA-PREDOMINANT IRRITABLE BOWEL SYNDROME

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Introduction: Bile acid malabsorption (BAM) is characterised by watery diarrhoea and confirmed by subnormal (<10%) 7-day retention of 75-seleno-homo-taurocholic acid (SeHCAT). It occurs almost invariably after

Abstract 085

	D-IBD + BAM (n=31)	D-IBS no BAM (n=41)	p Value
Sex: M/F	15/16	18/23	
Age: mean (SD)	43 (12)	42 (17)	
SeHCAT: mean (SD) (%)	5.2 (2.5)	23.5 (11.1)	
Abnormal ileal histology	6/31 (19%)	2/41 (5%)	<0.05*
Villous atrophy	2	0	
Inflammation	4	2	
Av daily stool freq >2	25/31 (81%)	25/41 (61%)	0.12*

*Two-tailed Fisher exact test.

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ileal resection and frequently in severe ileal disease, for example, Crohn's. We observed BAM in one third of diarrhoea-predominant irritable bowel syndrome (D-IBS) patients (Smith MJ *et al. J R Coll Physicians London* 2000;**34**:448–51), an unexpected finding without obvious explanation. Terminal ileal (TI) villous atrophy in association with BAM has been reported.
Aims & Methods: To prospectively study the association of BAM and ileal histological changes in D-IBS. All patients with D-IBS (ROME II criteria) with or without BAM, seen over the last 24 months, were followed-up. Data on SeHCAT retention, TI histology (light microscopy H & E stain) and daily stool frequency were collected.
Results: See table. Seventy two patients with D-IBS were studied; 31 had BAM. TI histological changes occurred in one fifth of patients with BAM but only rarely in those without. Mild non-specific inflammation was the most common histological abnormality; ileal villous atrophy was rare (n = 2) and noted only with BAM. Stool frequency ⩾3 per day was slightly commoner in those with BAM.
Conclusion: Bile acid malabsorption in D-IBS is, in our experience, rarely associated with major ileal histological abnormalities. We therefore suggest that other mechanisms must be involved in causing BAM.

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086 GENDER DIFFERENCE IN GASTRIC CANCER IS UNRELATED TO GASTRIC ATROPHY

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Introduction: Most gastric cancers develop by progression from H pylori superficial gastritis to atrophic gastritis to cancer (as originally described by Correa). Male gender is a strong risk factor for gastric cancer with the age specific rise in the cancer occurring 10–20 earlier in males versus females. The mechanism of this gender effect and where it exerts its influence on the cancer pathway are unclear. We have investigated whether development of atrophic gastritis occurs at a younger age in males versus females.
Aims & Methods: Between 1995 and February 1997, 10234 subjects (male/female; 7021/3213, mean age; 49.0 (SD 8.9) in male, 49.4 (8.7) in female) participated in our Japanese endoscopic mass screening programme. Pepsinogen (PG) I and II levels were simultaneously assayed. We compared the age-specific percentage of atrophic gastritis (PG I/II <3.0) between males and females. We also studied the incidence of new gastric cancer development in the cohort of 6983 followed-up for 4.7 years. Multivariate analysis was conducted to assess the hazard ratios of gender and PG I/II.
Results: At the initial screening, 4909 subjects were seropositive for H pylori with the prevalence being similar between males and females (48.1% *v* 47.6%, p = 0.6). The prevalence of low PG I/II increased progressively with increasing age, and the rate and timing of increase was identical in males and females, being 11.7% *v* 14.4% in males *v* females for age 30–39, 21.6% *v* 25.1% for 40–49, 32.5% *v* 36.8% for 50–59, 46.5% *v* 45.6% for 60–69 and 50.0% *v* 45.6% in 70 and over. The annual gastric caner incidence rate was >3 times higher in males *v* females (0.17% *v* 0.05%, p<0.001). Male gender and low PG I/II were independent risk factors for the incidence of gastric cancer. Hazard ratio in males compared with females was 3.5 (95% CI 1.4 to 8.9, p<0.01) and hazard ratio for PG I/II<3.0 *v* ⩾3.0 was 5.1 (95% CI 2.5 to 10.3, p<0.0001).
Conclusion: This study indicates that the male predominance is not mediated via more rapid development of atrophic gastritis in males versus females.

087 INACTIVATION OF THE SECOND ALLELE IN PATIENTS WITH HEREDITARY DIFFUSE GASTRIC CANCER HARBOURING GERMLINE E-CADHERIN MUTATIONS

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Introduction: Approximately 10% of gastric cancers have a familial association. Hereditary diffuse gastric cancer (HDGC) is a cancer predisposition syndrome with autosomal dominant inheritance. Germline mutations of the E-cadherin tumour-suppressor gene (CDH1) are causative in 30–40% of HDGC cases and the penetrance of these mutations is 67–83%. Following Knudson's two-hit hypothesis both alleles of the E-cadherin gene must be inactivated for loss of function to occur.
Aims & Methods: The aim of the study was to determine how the second allele of the E-cadherin gene is inactivated in HDGC patients with germline CDH1 mutations. 13 patients from 7 HDGC families (mean age 49) provided formalin-fixed paraffin embedded tumour material for analysis. DNA extracted from the tumour material from each of these patients was used for PCR using exon-specific primers to amplify and sequence each of the 16 CDH1 exons. The putative effects of intronic mutations on splicing were investigated by in silico analysis using the LAGAN Alignment Toolkit to assess sequence conservation and Splicing Rainbow to identify splice factor binding sites. Loss of heterozygosity (LOH) analysis was carried out using the chromosome 16q microsatellite markers D16S3025, D16S496, D1623141 and D16S3067. Availability of corresponding normal DNA (from blood) only permitted analysis on five individuals.
Results: Seven potentially interesting intronic mutations were found and these were spread throughout the gene. These mutations had not previously been identified as polymorphisms. In silico analysis demonstrated that some of these mutations fall within conserved sequences and may affect the binding strength of positive and negative regulators of splicing. In addition many silent mutations and polymorphisms, which are not likely to effect protein expression, were also identified. In one patient loss of heterozygosity was identified at all of the interpretable loci analysed, indicating that this is the mechanism of inactivation of the second allele of the E-cadherin gene in this patient. FISH analysis is being conducted to determine the extent of the region of loss.
Conclusion: This is the first report that LOH can be the second hit in an individual with a germline CDH1 mutation. Intronic mutations have been identified in five individuals, however additional functional analysis will be required to determine their significance. Analysis of promoter methylation is being undertaken to determine if this is the mechanism of gene silencing in the remaining patients. In addition to genetic alterations, transcriptional regulation and post-translational modifications are other likely mechanisms of E-cadherin downregulation.

088 THE CLINICAL UTILITY AND DIAGNOSTIC YIELD OF ROUTINE GASTRIC BIOPSIES IN THE INVESTIGATION OF IRON DEFICIENCY ANAEMIA

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Introduction: Upper GI endoscopy and duodenal biopsy is standard practice in iron deficiency anaemia (IDA). Previous small studies suggest that gastric atrophy is common in patients with IDA. Despite this, gastric biopsy is frequently not performed in these patients despite having the opportunity to do so during endoscopy and the Royal College of Pathologists have suggested that gastric biopsy is of no clinical use in the macroscopically normal stomach.
Aims & Methods: This study aimed to determine the frequency of significant gastric pathology in patients with IDA which could potentially explain or contribute to the anaemia. Patients with upper GI cancer or ulceration were excluded. One hundred and sixty one patients were endoscoped for suspected IDA of whom 152 had gastric body biopsies. Gastric biopsies were evaluated by 1 pathologist and scored 0–3 for inflammation, atrophy and intestinal metaplasia. Patient notes were evaluated to determine final cause for anaemia, drug therapy and comorbidity. Two control groups were used. One group were 100 consecutive patients undergoing gastric biopsy without IDA and a second group of 63 patients without IDA or HP gastritis. Significant atrophy was defined as atrophy scored as 2–3 and this was compared in 2 groups using descriptive statistics using SPSS.
Results: 40/152 (26%) patients in IDA group showed body atrophy>1. In contrast 3/163 (1.8%%) in the control groups showed similar atrophy. This was highly significant (p<0.0001). Patients in IDA group were on average 10 years older (65 (18) *v* 55 (16)). In contrast, HP gastritis did not differ

Abstract 88

	Atrophy ⩽1	Atrophy 2–3
No anaemia (n = 163)	160 (98.1%)	3 (1.9%)
Anaemia (n = 152)	112 (73.6%)	40 (26.4%)

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significantly between the IDA group and the random control group (p = 0.233) Within the IDA group aspirin usage did not differ in patients with and without atrophy (p = 0.986). Coeliac disease was diagnosed in 6/156 IDA patients (3.8%) colorectal carcinoma in 4/161 (2.4%).
Conclusion: This study has shown a high level of significant gastric pathology in patients with anaemia. Moreover, there is a strong association between IDA and gastric atrophy suggesting that this might be an important and underrecognised cause of IDA. These patients may benefit from treatment of HP where applicable or in some cases a parenteral route of iron administration. These data suggest that routine gastric biopsy in patients with IDA is valuable and national guidelines should consider including this as part of the standard workup.

089 ADMINISTRATION OF DIMETHYLOXALYLGLYCINE AS A NOVEL GASTROINTESTINAL REPAIR STRATEGY

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Introduction: Hypoxia inducible factor-1 (HIF) is upregulated by low oxygen tension, increasing production of angiogenic peptides and growth factors. Its role in injury and repair is, however, unclear. Modulation of HIF levels may provide a novel approach to the prevention and/or treatment of gastrointestinal disease. We therefore examined the effect of dimethyloxalylglycine (DMOG), which increases intracellular HIF levels, in a variety of in vitro and in vivo models of gut injury and repair.
Aims & Methods: In vitro studies utilised promigratory (wounded monolayer) and proliferation ([^{3}H] thymidine incorporation) assays of human colonic HT29 epithelial cells. In vivo studies utilised a rat gastric (indomethacin, 20 mg/kg and 3 hour restraint) damage model.
Results: DMOG stimulated migration in a dose-dependent manner, causing an approximate twofold increase in migration when added at 25 μmol ($p<0.01$). Additive/synergistic effects were seen when DMOG was added to cells in hypoxic conditions. DMOG also stimulated thymidine uptake by about twofold when added at 50 μmol. In the in vivo indomethacin and restraint induced rat gastric damage model, both oral and subcutaneous administration of DMOG decreased gastric injury without influencing intragastric pH (50% reduction when 1 ml gavaged at 0.57 mM, $p<0.01$).
Conclusion: These initial studies suggest that non-peptide factors such as DMOG, that modulate HIF levels, may be useful to stabilise or repair gut mucosa. Further studies appear warranted.

090 IS MASTIC GUM EFFECTIVE IN THE TREATMENT OF FUNCTIONAL DYSPEPSIA? A RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL

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Introduction: Treatment of dyspepsia remains unsatisfactory. Mastic gum is a resinous exudates from the stem of Pistacia lentiscus varchia. It is a traditional natural remedy used throughout the eastern Mediterranean.
Aims & Methods: The aim of this study was to assess the efficacy of mastic gum in patients with functional dyspepsia. One hundred and eight patients were randomly assigned to receive either mastic gum 350 mg three times daily or placebo. After three weeks of treatment the change from baseline in the severity of symptoms of functional dyspepsia was assessed using the Hong Kong index of dyspepsia. Patients' global assessment of efficacy was also evaluated.
Results: 103 patients had outcome data. There was a marked improvement of symptoms in 41% of patients receiving placebo and in 75% of patients receiving mastic gum ($p<0.03$). The symptom score improved significantly overall in patients receiving mastic gum (-8.66 *v* -3.78 in the placebo group) ($p<0.05$). Individual symptoms that showed significant improvement with mastic gum were: stomach pain in general, stomach pain when anxious, dull ache in the upper abdomen and heartburn (<0.05 for all four symptoms).
Conclusion: Mastic gum significantly improves symptoms in patients with functional dyspepsia.

Pancreatic free papers

091 STEROIDS IN AUTOIMMUNE PANCREATITIS: DO THEY PRESERVE PANCREATIC ANATOMY AND FUNCTION?

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Introduction: A response to steroids has been used as a diagnostic criterion of autoimmune pancreatitis (AIP), with improvement in pancreatic masses/enlargement, biliary stricturing, and liver biochemistry usually seen within a few weeks. Historical experience suggests that, without steroids, progression to exocrine insufficiency may occur, but no placebo-controlled data exist. The aim of this study was to assess pancreatic anatomy and exocrine function in AIP patients undergoing steroid therapy.
Aims & Methods: All patients diagnosed with AIP in our unit from 2004–6, and commenced on steroid therapy, were included. Assessments of pancreatic volume and parenchyma (by CT/MRI), pancreaticobiliary ductal anatomy (by ERCP/MRCP), and exocrine function (Faecal Elastase 1 (FE1)) were made before and after commencing oral prednisolone.
Results: Eighteen patients (M:F, 16:2; mean age 56 years, range 29–77) were included. At presentation, pancreatic enlargement/diffuse swelling was shown in 15/18 (83%), of whom 2/18 had a discrete mass. Two patients had normal pancreatic size but poor contrast enhancement, and 1 patient had both normal size and enhancement (but other extrapancreatic features of AIP). Rescanning was performed a mean of 3.7 months after starting steroids. Reduction in pancreatic enlargement/swelling occurred in 16/18 (89%), but progression to pancreatic atrophy had occurred in 11/16 (69%) of these. In the 16 patients in whom pancreatic ductal anatomy could be defined, focal/diffuse pancreatic stricturing was documented in 12/16 (75%). In the 9 patients with diffuse irregular structuring, improvements were seen within 3 months of steroids in all, with near-normality in 2. No change was seen in 2 patients who had established calcific change (these presented >2 years prior to steroids). FE1 measurements were obtained in 12/18 (67%). Pre-steroid FE1 levels were available in 7 patients, of whom 6/7 (86%) had low levels (<200 μg/g of stool). On measurement of FE1 levels in 7 patients a mean of 7 months (range 4–13) after commencing steroids, low levels were demonstrated in 5 (71%).
Conclusion: Loss of pancreatic structure and function appears to be common in AIP, particularly in those with longstanding disease. Improvements in pancreatic ductal anatomy with steroids might suggest that early treatment could limit subsequent exocrine insufficiency, but this remains to be established.

092 VITAMIN D IN EXOCRINE PANCREATIC INSUFFICIENCY: A UK EXPERIENCE

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Introduction: Vitamin D deficiency is a recognised complication of fat malabsorption in EPI, a problem more likely in the UK, as periods of sunlight are less than in tropical climates and fortification of food products is not routinely practised.
Aims & Methods: To study the prevalence of Vitamin D deficiency in patients with EPI in a district general hospital in the UK. Prospective collection of data from patients seen with EPI (diagnosed by faecal elastase <200, pancreolauryl test ratio <30% or 13-C mixed triglyceride breath test <22%) over the last 5 years. Data collected include age and sex, cause of EPI, concurrent therapy with enzyme supplements (Creon) or antioxidants (Antox), history of bone pain or fractures, calcium profile, 25-OH Vitamin D3 levels and intact parathormone levels (iPTH). They were grouped into those with severe (<25 nmol/l), mild deficiency (25–50) and adequate (>50) levels of 25-OH Vitamin D3, in accordance with clinical practice.
Results: Cause of EPI: chronic pancreatitis, 20; No cause identified, 5 (see table).
Conclusion: Increased awareness of Vitamin D deficiency and access to its assay has led us to check 25-OH Vitamin D levels in all our EPI patients routinely. Vitamin D deficiency is common in EPI. When severe, it is associated with elevated PTH in some (7/12). Lack of musculoskeletal symptoms does not exclude Vitamin D deficiency. Serum calcium, phosphate and alkaline phosphatase are poor indicators of Vitamin D deficiency.

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Abstract 092

Parameter	Vitamin D3 levels		
	Severe def <25 nmol/l	Mid def 25–50 nmol/l	Adequate >50 nmol/l
Number of patients (n = 25)	12	9	4
Sex: M/F	5/7	7/2	2/2
Age (mean (SD))	53.8 (10.)	62.9 (13.0)	60.6 (13.2)
Musculoskeletal symptoms	8/12	7/9	3/4
On Creon or Antox at Vit D check	6/12	7/9	3/4
25OH Vit D3, median (range):nmol/l	7.75 (5–19)	37 (26–46)	67.85 (64.4–90)
Calcium, median (range):mmol/l	2.28 (2.06–2.51)	2.40 (2.33–2.57)	2.31 (2.22–2.41)
Phosphate, median (range):mmol/l	1.00 (0.61–1.18)	1.01 (0.85–1.31)	1.12 (0.74–1.39)
Alkaline phosphatase, median (range):IU/l	108 (72 = 416)	80 (40–146)	79.5 (68–116)
Intact PTH (iPTH), median (range):pg/ml	70.7 (8.4–317.2)*	27.6 (12.4–51.1)*	35.8 (19.5–52.5)

*Kruskal-Wallis non-parametric test: $p<0.05$.

Small bowel/nutrition free papers

093 WHAT ARE THE BEST IMMUNOLOGICAL TESTS FOR COELIAC DISEASE? A PROSPECTIVE ASSESSMENT OF 2000 BIOPSY VERIFIED RESULTS

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Introduction: The prevalence of coeliac disease (CD) in the UK population is 1%. With increasing case-finding strategies more patients are being tested. Currently a number of immunological tests may be used to diagnose CD, these include IgA/IgG gliadin antibody, IgA tissue transglutaminase (TTG) antibody and IgA endomysial antibody (EMA). Our aim was to validate these current immunological assays against the gold standard of duodenal biopsy.
Aims & Methods: Consecutive adult patients referred for gastroscopy were recruited by a single endoscopist over a 26-month period (January 2004 to April 2006). All patients had 4 biopsies taken from the second part of the duodenum. A blood sample was obtained from each patient and analysed for a total immunoglobulin A (IgA), IgA-Gliadin, IgG-gliadin, IgA-TTG and IgA-EMA. Patients were excluded if they had a known diagnosis of CD, a coagulopathy, active gastrointestinal bleed or a suspected carcinoma observed during the examination. Villous atrophy present on duodenal biopsy (Marsh grade 3) confirmed a diagnosis of CD. Total IgA was measured on a Behring BN2 nephelometer. IgA gliadin, IgG gliadin and human TTG antibodies were assayed on ELISA kits from Aesku. Serological samples with a titre of >15 U/ml were taken as positive. EMA were detected by immunofluorescence on primate oesophagus sections from Binding Site.
Results: 2000 patients were recruited: 1167 (58.3%) female, mean age 55.8, range 16–94. A total of 77 patients were diagnosed with new CD. The prevalence of coeliac disease in all patients attending for gastroscopy was 3.85% (77/2000). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the individual antibodies and combinations of TTG/EMA are shown in the table. Columns 6 and 7 describe how many biopsies result from using the different antibody strategies and how many cases of CD would be missed. The overall prevalence of IgA deficiency in our series was 0.7% (14/2000) 1 of which had CD. There were 7 patients with CD who were TTG negative; all 7 were IgA gliadin negative. One of the 7 CD patients (who presented with anaemia) had IgA deficiency and a negative IgG gliadin. One of the other TTG negative patients was EMA positive.
Conclusion: Based on these data we propose that a two-step (TTG first) testing model could be clinically applicable. This would substantially reduce the number of biopsies but at the expense of missing more patients (reduce sensitivity). IgA/IgG gliadin antibodies appear to be redundant when testing for CD.

Abstract 093 Accuracy of serological tests used to refer for biopsy

Serological test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Biopsies taken/ 2000	Missed CD/ 2000
Only TTG+	90.9	90.1	28.6	99.6	245	7
Only EMA+	87.0	98.0	64.4	99.4	104	10
If TTG+ and then EMA+	85.7	98.6	71.7	99.4	92	11
Either TTG or EMA+	92.2	91.1	29.3	99.7	242	6
IgG gliadin+	47.3	95.9	31.5	97.9	114	40
IgA gliadin+	49.4	89.6	16.0	97.8	238	39

+, positive.

094 WHAT IS THE OPTIMAL SITE AND NUMBER OF ENDOSCOPIC DUODENAL BIOPSIES REQUIRED TO DIAGNOSE COELIAC DISEASE?

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Introduction: There has been no formal study to attempt to identify the number of duodenal biopsies that are required in order to diagnose coeliac disease (CD). The current practice of quadrantic duodenal biopsy has evolved from historical data using the Crosby capsule and our recognition that villous atrophy may be patchy. Our aim was to assess different biopsy strategies, both in number and site, to find the optimal method for diagnosing CD.
Aims & Methods: Our aim was to assess different biopsy strategies, both in number and site, to find the optimal method for diagnosing CD. Patients were prospectively recruited if they had a positive endomysial (EMA) or tissue transglutaminase (TTG) antibody. 9 biopsies were taken from the duodenum. These were from set points and numbered 1–9 as follows: (1) duodenal bulb, (2–5) 4 quadrantic biopsies from the second part of the duodenum proximal to the ampulla and (6–9) 4 quadrantic biopsies distal to the ampulla. The quadrantic biopsies were taken with the ampulla positioned in the direct left view if possible and numbered respectively from upper-right, lower-right, lower-left and upper-left positions relative to the endoscope view. Each single biopsy was reported individually with H&E stain by one histopathologist. Histological features of CD were reported in concordance with the revised Marsh Grade (M) criteria. We assessed all 9 biopsies (per patient) for the presence and severity of villous atrophy.
Results: Fifty six patients were recruited: 33 (59%) female, mean age 47, range: 16–85. 53 had villous atrophy (M3a-c) present on at least one biopsy, in 2 patients the worst lesion seen was graded M2 and in 1 patient only M1 changes were seen. 3/56 patients had an identical degree of villous atrophy in all 9 biopsies (1×M1 and 2×M3b). 10 patients had biopsy specimens that varied between no-atrophy and atrophy. The table shows some of the biopsy regimes analysed and results for their sensitivities. For the minimal number of biopsies, the most sensitive biopsy regime for detecting villous atrophy was 3 duodenal biopsies (1 from the bulb, proximal and distal regions—regime A). If looking for the most severe

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Abstract 094 Sensitivity of different biopsy regimes to detect villous atrophy

Duodenal biopsy numbers	Villous atrophy detected if present sensitivity (%) (95% CI)	Was the most severe marsh grade detected sensitivity (%) (95% CI)
1,2,3 (regime A)	100 (93.2–100)	94.6 (85.3–98.2)
1,2,3,6 (regime B)	100 (93.2–100)	98.2 (90.6–99.7)
2.3	96.2 (87.2–99.0)	78.6 (66.2–87.2)
2.3.4.5	96.2 (87.2–99.0)	82.1 (70.2–90.0)
6.7.8.9	96.2 (87.2–99.0)	78.6 (66.2–87.2)

grade of villous atrophy 4 biopsies was most accurate (1 from the bulb, 2 from the proximal and 1 from the distal duodenum-regime B).
Conclusion: We would suggest that the optimal method for diagnosing CD is Regime B—this ensures recognition of all cases of CD, as well as detecting the most severe lesion. Our data suggest that we should no longer perform quadrantic duodenal biopsies but instead take a linear approach.

095 PROSPECTIVE STUDY OF THE PREVALENCE OF COELIAC DISEASE IN ADULTS WITH TYPE 1 DIABETES MELLITUS: EFFECT UPON GLYCAEMIC CONTROL AND QUALITY OF LIFE

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Introduction: The prevalence of coeliac disease (CD) in Type 1 diabetes mellitus ranges between 3% to 7% and the optimum screening profile is as yet undetermined. The effect of CD on metabolic control of diabetes is undetermined as is the effect on quality of life. The preliminary results are reported.
Aims & Methods: 1000 consecutive patients were recruited from the Sheffield Diabetes centre (mean age 42.3 years, 439 females). Antiendomyseal (EMA) and anti-tissue transglutaminase antibodies (tTG) and immunoglobulins were measured. Additionally Short Form-36 v2 was completed to measure quality of life. Patients with positive antibodies were offered duodenal biopsy.
Results: Twenty two patients had known CD prior to the study and were already established on GFD. 58 patients had previously undetected positive antibodies and 8 IgA deficiency. 19 were EMA/tTG positive and 39 tTG positive in isolation. 12 new cases of CD were found at biopsy (11/12 EMA positive) and all patients with IgA deficiency had a normal biopsy. Sensitivity and specificity for positive EMA/tTG was 91.7% and 99.3% respectively giving a PPV 0.83 and NPV 1. Median HbA1c levels in those with CD compared to age-sex matched controls were 8.5 and 7.3 respectively ($p<0.0001$). Quality of life scores were not significantly different. Stepwise multiple logistic regression from 13 clinical variables revealed only antibody positivity as being significant ($p<0.0001$).
Conclusion: The prevalence of coeliac disease in this cohort was 3.5%. Undetected coeliac disease has an adverse effect on metabolic control of diabetes but not quality of life scores. Combined EMA/tTG testing provides suitable sensitivity and specificity.

096 LONG-TERM FOLLOW-UP OF PATIENTS WITH MALIGNANT CARCINOID SYNDROME RECEIVING SANDOSTATIN LAR

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Introduction: Somatostatin analogues are used for symptomatic and therapeutic treatment of malignant carcinoid sydrome. Use of long-acting preparations has major implications in terms of convenience. There are few long-term data regarding the use of somatostatin analogues.
Aims & Methods: To assess the long-term effect of Sandostatin LAR on the management of patients with malignant carcinoid syndrome. Case notes of 60 consecutive patients (age range 30–78 years; 40 male and 20 female) treated with Sandostatin LAR attending a specialist neuroendocrine clinic were reviewed. 35 patients had primary tumour in the midgut, 12 in the foregut and 13 had unknown primary tumour sites. Patients had 3–6 monthly evaluation of symptoms, biochemical markers and CT imaging. 28 (47%) patients did not require any other therapy, however 32 (53%) patients required additional therapeutic modalities including chemotherapy, interferon and radionuclide targeted therapy.
Results: Fifty five of the 60 patients (92%) were commenced on a dose of 20 mg monthly, 5 (8%) on 30 mg. Of the 28 patients treated with Sandostatin LAR alone, median follow-up time is 25 months. 18 of these 28 (64%) improved and remained stable in terms of symptoms although 10 had deterioration of symptoms after an average of 12.4 months. Five of 28 patients (18%) had progressive disease on CT scans after an average time of 27 months. Increased symptoms or disease progression was an indication to increase the Sandostatin LAR dose. Of 32 patients requiring additional therapies, 21 were on Sandostatin LAR alone for an average of 18 months before beginning other treatments. 15 of the 32 patients (47%) had radiological progression; the remaining 17 were treated in view of biochemical progression or symptomatic deterioration. Side effects: of the total 60 patients, 6 (10%) were noted to have gallstones on CT imaging. 3 patients (5%) had abdominal pain after the injection, 6 (10%) had increased diarrhoea for up to 5 days following the injection.
Conclusion: Sandostatin LAR is a well tolerated long-term treatment. Somatostatin analogues are good at controlling malignant carcinoid syndrome. A significant proportion of patients maintained stable disease whilst on Sandostatin LAR. The anti-tumour/stabilisation effect of somatostatin analogues need to be assessed in randomised studies.

097 ANTI-TISSUE TRANSGLUTAMINASE ANTIBODY QUANTIFICATION IS USEFUL IN THE FOLLOW-UP OF COELIAC DISEASE PATIENTS

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Introduction: The optimal form of follow-up for coeliac disease patients is controversial. Traditionally follow-up has been largely clinical and dietetic, with blood tests used to identify deficiencies in folate, ferritin and vitamin B12.
Aims & Methods: This study aimed to assess the usefulness of serial quantitative tTG measurements in the outpatient follow-up of adult coeliac disease patients. 64 patients with known coeliac disease attending our coeliac disease review clinic had tTG, folate, vitamin B12 and ferritin measured at each clinic visit over a period of 2–5 years. tTG levels were measured using the Aeskulisa Ò tTG-A NEO ELISA kits. The patient's own assessment of their compliance to gluten free diet (GFD) was recorded.
Results: The tTG results divided the patients into 3 groups: 29 patients with repeatedly low tTG values, 16 patients with repeatedly high tTG values and 19 patients with changing tTG values. Of the 29 patients with low tTG 72% claimed to be strictly compliant and the remainder partially compliant. Of the 16 individuals with high tTG only 12% claimed to be strictly compliant, 44% partially compliant and 44% felt they were non-compliant. Low tTG was significantly associated with strict compliance ($p<0.001$). The high tTG group contained more abnormal laboratory results (ferritin, folate and vit B12 below the normal range) than the low tTG group (35% *v* 18%, $p<0.05$). The individuals with a changing tTG value enabled the time course of the fall in tTG to be defined, with patients strictly adherent to a GFD showing a reduction in tTG within the first 4–8 months. The quantitative nature of serial tTG was clearly superior to qualitative anti endomysial antibody (EMA) results in this group, as the early response to diet could be monitored before the EMA result became negative.
Conclusion: Serial quantitative tTG measurement in patients undergoing routine follow-up for coeliac disease may identify individuals with poor compliance with the GFD, who are at increased risk of nutritional deficiencies associated with their coeliac disease. tTG measurement may help targeting of limited dietetic resources to those patients who are most likely to benefit.

098 NEW INTRODUCER PEG-GASTROPEXY WITHOUT PROPHYLACTIC ANTIBIOTICS: A PROSPECTIVE RANDOMISED DOUBLE BLIND TRIAL

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Introduction: Peristomal infections are still the most common complications of PEG despite use of prophylactic antibiotics. A major problem associated with the administration of prophylactic antibiotics is the emergence of resistant microorganisms, especially the Methicillin resistant Staphylococcus aureus (MRSA) at the PEG site. In the introducer PEG technique, as the sojourn of PEG catheter through the oropharynx is avoided there are negligible chances of infectious complications. Introducer PEG, though known for 22 years, has not been popular because of risks

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Abstract 098

Grades of infection	Antibiotics	Placebo	p Value
0	16	17	
1	12	5	
2	2	8	0.585
3	1	1	
4	0	0	

and associated complications. However the new introducer PEG-gastropexy has been recently proved to be very safe.
Aims & Methods: We conducted a randomised double-blind placebo-controlled trial to determine the incidence of peristomal wound infections post PEG in patients undergoing this new introduce PEG-gastropexy with and without antibiotics. From October '03 till June '06, 63 patients underwent introducer PEG-gastropexy. Following randomisation they were assigned in to 2 groups. Group I comprised 32 patients in whom 30 minutes before the procedure an injection of Ceftriaxone antibiotic was given while 31 patients in group II underwent PEG-gastropexy with a placebo injection. PEG was done using the Freka (Pexact, Fresenius, Germany) under Propofol sedation. This is a new introducer PEG system in which anterior gastric wall is sutured non-surgically to anterior abdominal wall before catheter insertion under endoscopy. All the patients were followed-up by nutrition support team (NST) and the wound was inspected daily, the dressings changed and the peristomal wound assessment was done as per the point score system in which local redness, induration and exudation was recorded on a scale of 1–4 for first 7 days. In addition, the maximum combined score for each patient was also calculated and the wound reaction graded from 0–4.
Results: One patient died within 3 days of procedure due to myocardial infarction and so was excluded from analysis. Patient's age group ranged from 60 ± 15.0 years. Both the groups were well matched in terms of patient characteristics. There were 40 males and 22 females. There was no significant difference in the grades of infection in both the groups of patients undergoing PEG with or without antibiotics within 7 days (see table).
Conclusion: We conclude that this new introducer PEG-gastropexy can be performed safely without the need of any prophylactic antibiotics, which is a revolutionary finding. Thus all the scourges associated with antibiotic usage (like emergence of resistant microbiological strains, antibiotic associated diarrhoea and costs) can be potentially avoided in patients undergoing PEG feeding.

099 INCIDENCE OF REFEEDING SYNDROME IN GENERAL MEDICAL INPATIENTS ON ENTERAL FEEDING

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Introduction: BSG guidelines recommend daily monitoring of phosphate and electrolytes in all patients commenced on enteral feeding to identify electrolyte abnormalities pertaining to Refeeding syndrome (RS). The incidence of RS has been assessed in patients on intensive care, postoperative wards, with cancer and anorexia nervosa. There is little information on the incidence in a general medical inpatient population especially elderly patients who are likely to be at a higher risk when commenced on enteral feeding.
Aims & Methods: To determine the incidence of hypophosphatemia and other metabolic abnormalities predisposing to RS in general medical inpatients receiving enteral nutritional support. All hospitalised medical patients who were commenced on artificial enteral nutrition over a 6-month period January–June 2004 were studied. Post-surgical patients and patients on parentral nutritional support were excluded. All patients had full blood count, electrolytes including urea, phosphate, calcium, magnesium and glucose were measured before commencing feed followed by daily measurements for 1 week and then twice weekly for another week. Liver function tests were measured before and twice weekly for two weeks after feeding. Medical records of all the patients were reviewed for development of signs and symptoms of RS. Phosphate levels <0.50 mmol/l and 0.51–0.85 mmol/l were defined as treatable hypophosphatemia (TP) and moderate hypophasphatemia (MP) respectively.
Results: Forty patients received enteral feeding (26 NG; 1 NJ and 13 PEG). There were 17 males and 24 females. Median age was 78 years (range 23–94 years). 11 (28%) developed TP. 20 (50%) developed MP of which 4 went on to develop TP. Of the patients with TP, 2 had associated hypomagnesaemia, 4 had renal impairment and 3 had hypokalemia. 29% of patients over 65 years and 67% over 85 years developed TP compared to 20% in age below 65 years. 31% of PEG fed patients developed TP as opposed to 26% of NG and NJ fed patients. Patients with decreased oral intake for >10 days were at a higher risk of developing TP compared to those with low intake <10 days (56% *v* 17%). 71% of patients with low albumin developed TP and MP (43% TP). 81% of patients with raised white cell count (WCC) developed TP and MP (45% TP). At 2 weeks, 9 out of 11 patients with TP continued artificial feeding and 2 started oral feeding.
Conclusion: Over one quarter of medical inpatients commenced on enteral feeding developed electrolyte abnormalities which predispose to RS. Age over 85 years with decreased oral intake for >10 days, low albumin and raised WCC are high-risk predictors for developing RS. Our study reinforces the importance of regular monitoring for RS in this patient group when enteral feeding is commenced.

100 EFFECT OF MICROBIAL OVERGROWTH ON CYTOKINE EXPRESSION IN THE UPPER GASTROINTESTINAL TRACT OF PATIENTS RECEIVING ENTERAL NUTRITION

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Introduction: Enteral feeding via percutaneous endoscopic gastrostomy (PEG) tube is required for nutritional support in patients with dysphagia. Enteral tube feeding (ETF) bypasses innate defence mechanisms in the upper gastrointestinal tract resulting in microbial overgrowth, which can have a detrimental effect on the mucosal immune response.
Aims & Methods: The aims of this study were to characterise microbiotas colonising the upper gut in ETF and to assess the effects of enteral nutrition (EN) on proinflammatory cytokine expression in gastric and small intestinal mucosae. Seven patients undergoing PEG tube placement or replacement were studied to determine the types of microorganisms present in the upper gut in ETF. All patients had received nasogastric feeding prior to gastrostomy insertion. Gastric and small bowel aspirate and biopsy samples were obtained at endoscopy and the microbial populations investigated using quantitative real-time PCR. Tissue samples for cytokine analysis were collected from the seven ETF patients and compared with mucosal samples collected from 10 control subjects. Tissue cytokine expression was measured using real-time PCR.
Results: Patients receiving EN possess abnormal gastric and small intestinal microbiotas; the most commonly isolated organisms were enterobacteria and staphylococci. Expression of the proinflammatory cytokines IL1-α, IL6 and TNF-α was significantly higher in gastric and small intestinal mucosa from patients on normal diets in comparison with those on EN.
Conclusion: Enteral nutrition results in significant bacterial overgrowth in the upper gastrointestinal tract, this is associated with a significantly diminished proinflammatory cytokine response in gastric and small intestinal mucosae.

1. **O'May GA**, Reynolds N, Smith AR, *et al.* Effect of pH and antibiotics on microbial overgrowth in the stomachs and duodena of patients undergoing percutaneous endoscopic gastrostomy feeding. *JCM* 2005;**43**:3059–65.

101 SCREENING FOR MALNUTRITION IN OUTPATIENTS

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Introduction: The February 2006 NICE guidelines state that all outpatients should be screened for malnutrition at their first appointment and when there is concern. Malnutrition among inpatients is well known. But there is little information on the prevalence of malnutrition among outpatients.
Aims & Methods: To assess the nutritional status of outpatients in various clinics and determine proportion of patients at risk of malnutrition and thereby identify clinics where assessment may be of little value. The risk of malnutrition was also compared between different age groups. A validated questionnaire was used to assess the nutritional status of patients over age 18 attending various clinics at Royal Glamorgan Hospital in June 2006. Body mass index (BMI) was calculated. The answers were scored for malnutrition as low risk, possible risk and malnourished categories.
Results: 502 out patients underwent assessment and 3% (15 patients) were malnourished and 25% (125) were at possible risk of malnutrition. 66% of females were at no risk of malnutrition, while 30% were at possible risk and 4% malnourished. This compares to 78%, 20% and 3% in males

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Abstract 101 Distribution of malnutrition in various clinics

Clinic (no of patients)	Little/no risk (%)	Possible risk (%)	Malnourished (%)
Gastro (22)	55	41	4
Oncology (13)	62	15	23
COTE (25)	76	20	4
Cardiology (16)	88	12	0
Dermatology (38)	82	10	8
Endocrinology (5)	60	40	0
Fracture (12)	75	25	0
General medicine (5)	100	0	0
Haematology (88)	71	27	2
Obs & gynaec (10)	80	20	0
Ophthalmology (52)	75	25	0
Orthopaedics (86)	76	22	2
Surgery (66)	69	29	2
Podiatry (8)	88	0	12
Respiratory (6)	67	17	17
Rheumatology (36)	47	47	6

respectively. 60% of the possible risk group and 70% of malnourished group were over 65 years old. Possible risk of malnourishment and malnourishment were fairly consistent over age groups 18–84 years (20%–30% and 0%–4% respectively). In the group 85–100 years, 35% were at possible risk of malnutrition and 13% were malnourished. The prevalence of possible risk and malnourishment in various clinics are shown in the table. An inverse correlation existed between BMI and risk of malnutrition. 39% of the patients were overweight and 27% of our patients were obese.
Conclusion: Over a quarter of outpatients are malnourished or at risk. Elderly patients are more malnourished than non-elderly, and the clinics with the highest level of malnourishment are rheumatology, oncology and gastroenterology. General medicine, cardiology and podiatry clinics had lower proportion of patients at risk of malnutrition. This supports the NICE recommendation that all outpatients, especially high-risk clinic patients, must be screened for malnutrition.

102 TRAINING GASTROENTEROLOGISTS IN CLINICAL NUTRITION

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Introduction: The nutritional care of patients is now high on the agenda of both public and healthcare organisations. There are increasing expectations that gastroenterologists will lead on the delivery of nutritional care within NHS trusts, and therefore it is imperative that they receive appropriate training in clinical nutrition. They need the skills to lead a clinical service and to support the training of junior doctors to ensure they acquire the competency and skills set down in the foundation programme and the JCHMT gastroenterology curriculum.
Aims & Methods: This study sought to assess the extent of training opportunities and knowledge in clinical nutrition among gastroenterology SpRs. A questionnaire was distributed to those attending a regional training day and national course in clinical nutrition.
Results: Forty SpRs completed the questionnaire, 33% of whom were in the first two years of training. Although 68% of trainees were currently working in hospitals with a Nutrition Support Team, only 25% had attended nutrition ward rounds and 18% had received formal postgraduate training in clinical nutrition. 55% knew the prevalence of malnutrition in most UK hospitals and 78% identified serum albumin concentration as a poor measure of nutritional status. Knowledge of energy requirements was generally poor; 23% correctly identified the energy requirements of a catabolic patient and 33% knew appropriate protein requirements. 28% knew the energy content of one gram of protein, fat and carbohydrate, 23% knew how many grams of protein are equivalent to 1 gram of nitrogen and 43% identified the energy content of 1 litre of 5% dextrose. 68% correctly identified that 1 litre of 0.9% saline contains 154 mmol of sodium. 48% knew the recommended method for confirming the correct position of a fine bore nasogastric tube, while only 5% correctly answered a multistem question regarding contraindications to enteral tube feeding. 90% identified refeeding syndrome as a cause of electrolyte disturbance in a severely malnourished patient receiving parenteral nutrition.
Conclusion: These results demonstrate that understanding of basic concepts in clinical nutrition is poor among gastroenterology SpRs, despite a majority of trainees working in hospitals with a Nutrition Support Team. The provision of safe and effective nutritional care is a responsibility all doctors have to their patients, but achieving this will require improvements in the standards of education of training.

Case presentations

103 AN UNUSUAL CAUSE OF ACUTE LOWER GASTROINTESTINAL BLEEDING

V. Anumakonda[1], H. Bu-Hayee[1], G. Chung-Faye[1], S. Diaz-Cano[2]. [1]*Gastroenterology;* [2]*Histopathology, Kings College Hospital, London, UK*

Case Report: A 36-year-old presented with abdominal cramps, diarrhoea and several episodes of profuse rectal bleeding (1 week duration). No associated fever sweats or weight loss. He was haemodynamically stable. He had mild left iliac fossa tenderness, no organomegaly and bowel sounds were normal. Digital rectal examination revealed some fresh blood but no haemorrhoids and a normal prostrate. Other systems were unremarkable. Investigations: c-RP 10 mg/l, Hb 13.5 g/dl, WBC $8.34\times103/mm^3$, and platelets $162\times103/mm^3$. Multiple stool cultures were negative. A flexible sigmoidoscopy demonstrated blue lesions in the recto-sigmoid area, confluent inflammation of the descending and sigmoid colon, and relative rectal sparing, with ulceration. The histopathology specimens revealed ischaemic colitis with red cell extravasation, haemosiderin deposition and fibrosis. Mesalazine was discontinued. The patient had no further rectal bleeding and remained asymptomatic during his follow up over 6 months. This is first reported association of ischaemic colitis with Blue Rubber Bleb Nevus (BRBS) syndrome. BRBN are cavernous haemangioma lined by single layer of endothelium surrounded by thin connective tissue.[1] The fragility of thin wall may predispose to further bleeding into submucosa compromise the vascular supply. BRBNS is managed conservatively with iron replacement therapy and transfusions. Endoscopic laser photocoagulation, systemic treatment with corticosteroids, interferon and vincristine may also be effective.[2] Subcutaneous octreotide in the presence of active lesion proliferation or DIC has been used successfully.[3, 4] Skin lesions have been treated with the neodymium: YAG laser.[5]

1. **Nahm WK**, Moise S, Eichenfield LF, *et al.* Venous malformations in blue rubber bleb nevus syndrome: variable onset of presentation. *J Am Acad Dermatol* 2004;**50**(Suppl 5):S101–6.
2. **Apak H**, Celkan T, Ozkan A, *et al.* Blue rubber bleb nevus syndrome associated with consumption coagulopathy: treatment with interferon. *Dermatology* 2004;**208**:345–8.
3. **Nardone G**, Rocco A, Balzano T, *et al.* The efficacy of octreotide therapy in chronic bleeding due to vascular abnormalities of the gastrointestinal tract. *Aliment Pharmacol Ther* 1999;**13**:1429–36.
4. **Buonamico P**, Sabba C, Garcia-Tsao G, *et al.* Octreotide blunts postprandial splanchnic hyperaemia in cirrhotic patients: a double blind randomized echo-Doppler study. *Hepatology* 1995;**21**:134–9.
5. **Snijders S**, Oranje A P, De Leeuw J. Behandeling van cutane laesies van het blue rubber bleb naevus-syndrome met de neodymium: YAG-LASER 2006;**16**:33–34.

104 RELAPSING, REMITTING OBSTRUCTIVE LIVER FUNCTION TESTS

J. A. Jupp[1], S. Bridger[2], C. J. Hovell[2]. [1]*Gastroenterology, Poole General Hospital, Poole,* [2]*Gastroenterology, Dorset County Hospital, Dorchester, UK*

Case Report: A 65-year-old gentleman was referred by his GP with a 3 month history of anorexia, dry mouth and epigastric discomfort followed by jaundice with pale stools which slowly resolved. He had a past medical history of infectious hepatitis 35 years ago. He did not smoke or drink alcohol. Physical examination was unremarkable. Serum biochemistry revealed ALP 1465, ALT 495 and bilirubin 20 with normal INR and albumin. Hepatitis serology was negative. Abdominal ultrasound showed a bulky pancreas but normal liver and bile ducts hence an abdominal CT was performed. This demonstrated a diffusely enlarged ''sausage shaped'' pancreas but no focal lesion. The CBD was dilated to 12 mm and there were several small peri-pancreatic lymph nodes. Tumour markers were normal. ERCP showed a regular stricture at the distal end of the CBD of 2–3 cm length. There was also a 1–2 cm length irregular stricture of the pancreatic duct within the pancreatic head and irregular ductules. Biliary cytology was unremarkable. An endoscopic ultrasound revealed a pancreas of mixed echogenicity containing stranding lobulation but no

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mass lesion. The pancreatic duct was irregular and the CBD was thick walled. His symptoms resolved and LFTs returned to normal. However he subsequently became unwell again with deranged LFTs and facial swelling secondary to parotid and submandibular gland enlargement, which was confirmed by MRI. Schirmer's test was positive. Autoimmune profile, serum ACE and LDH were unremarkable. His ESR was 54. Parotid biopsy revealed a lymphohistiocytic infiltrate with evidence of chronic inflammation and gland atrophy. Serum IgG4 was elevated at 8.5 g/l (<1.3). Treatment with corticosteroids was commenced leading to a resolution of symptoms and return of biochemistry and imaging to normal. In this case we discuss the criteria for diagnosing a rare syndrome complex by means of history, laboratory data, imaging and histopathology.

105 WATERY DIARRHOEA: IS IT INFECTIVE, IATROGENIC OR IS THERE MORE TO IT?

M. Castelino, J. Gasem, D. Nazareth, B. Hamid, T. D. Wardle. *Gastroenterology, Countess of Chester Hospital, Beaumaris, UK*

Case Report: A 61-year-old white female was admitted to hospital with a history of shivering, fever, lethargy and intermittent watery diarrhoea for 8/52. Shortly prior to her presentation, she was treated with a course of antibiotics for a UTI and was also found to be hypothyroid, for which she was treated with thyroxine. The thyroxine, however, had to be stopped by her GP due to diarrhoea. She had no other significant past medical history. On examination she was drowsy and dehydrated. Her blood results confirmed neutrophilia (WBC 25.9 10×9/l), acute renal failure (urea 22.9 mmol/l, creatinine 327 μmol/l), metabolic acidosis (PH 7.32, HCO3 13.9, BE -10.6) and a raised CRP at 38 mg/l. Her stool was subsequently positive for clostridium difficile toxin (CDT). The patient was treated with IV fluids with potassium replacement, IV antibiotics and oral vancomycin. She made a good recovery with normalization of both her renal function and acidosis. She was discharged home to be followed up as an outpatient. However, she was readmitted 2 weeks later with an identical clinical and biochemical presentation, except for a raised serum calcium and a negative stool CDT. As part of the investigations of this patient's hypercalcaemia, a CT abdomen and chest was performed. CT chest showed evidence of pulmonary embolism and the CT abdomen showed some abnormalities. The histology of which revealed the underlying rare diagnosis. The patient was treated supportively along with the specific treatment. She made a good recovery and her diarrhoea stopped with no further recurrence of her renal failure.

106 FROM PHLEBOLITH TO SURGERY

G. W. Moran[1], T. Stone[2], A. Wolinski[2], R. Patel[3], B. J. M. Jones[1]. [1]*Department of Gastroenterology,* [2]*Department of Radiology,* [3]*Department of General Surgery, Dudley Group of Hospitals, Dudley, West Midlands, UK*

Introduction: This case describes a rare cause of rectal bleeding. It highlights an unusual clinical relevance of phleboliths seen on an abdominal radiograph in rectal bleeding.
Aims & Methods: A 52-year-old women was referred from her GP in 2005 with a history of chronic rectal bleeding, anaemia and constipation. In her twenties, she was dependent on iron injections and frequent blood transfusions at her local hospital. She had always been constipated and original investigations revealed external piles which were ligated. A barium enema was normal. There was no social or family history of note and routine physical examination revealed no abnormal findings. Proctoscopy showed only internal piles. Routine blood investigations revealed a haemoglobin count of 11.9 g/dl with a normal MCV, normal liver and kidney function, normal thyroid function test, B12/folate levels and coeliac serology. Colonoscopy revealed grossly abnormal sigmoid mucosa from 10 to 40 cm from the anal margin showing severe mucosal vascular malformations. Computer tomography (CT) angiography and magnetic resonance (MR) examinations were also performed.
Results: The diagnosis is colonic cavernous haemangiomatosis (CCH). Multiple submucosal and serosal calcified phleboliths are visible on CT angiography while a high signal is seen on the T2 weighted MR images in mucosal/submucosal areas.
Conclusion: Haemangiomas are rare benign vascular tumours that occur mostly in the rectosigmoid colon. Phleboliths are characteristically visible on plain abdominal films. CCH is commoner in younger males and it originates from embryologic sequestrations of the mesoderm. It can be focal, diffuse, localised or annular. Possible presentations include GI bleeding, obstruction, perforation, intussuseption or compression/invasion of adjacent structures. Other associations are Osler-Weber-Rendu disease, Blue Rubber Bleb Nevus syndrome, Klippel-Trénaunay-Weber syndrome, Maffucci's syndrome, diffuse neonatal hemangiomatosis, and Proteus syndrome. No medical treatment is available. Surgery should always be sphincter-saving. The commonest surgical technique is resection with coloanal sleeve anastomosis as in this case. This is the first case in the British literature.

1. **Dachman A**, *et al.* Colorectal haemagiomas: radiologic findings. *Radiology* 1988;**167**:31–4.
2. **Levy A**, *et al.* Gastrointestinal hemangiomas: imaging findings with pathologic correlation in pediatric and adult patients. *AJR* 2001;**177**:1073–81.
3. **Hervias D**. Diffuse cavernous hemangioma of the rectum: an atypical cause of rectal bleeding. *Rev Esp Enferm Dig* 2004;**96**:346–52.

107 AN UNUSUAL CAUSE OF GASTRIC OUTLET OBSTRUCTION

B. J. Sebastian[1], D. Mittapalli[1], M. Hussain[1], S. Afzal[1], V. Rudralingam[2], R. Hammonds[3], K. Akhtar[1]. [1]*Surgery, Rochdale Infirmary, Rochdale;* [2]*Radiology,* [3]*Gastroenterology, North Manchester General Hospital, Manchester, UK*

Introduction: Gall stones are a common surgical problem. We present an unusual presentation of this common problem.
Aims & Methods: A 72-year-old lady was referred to us with features of gastric outlet obstruction and weight loss. She was investigated with an upper GI endoscopy, barium meal and a CT scan, all of which showed gastric outlet obstruction with a mass lesion. The differential diagnosis was between a tumour and a foreign body. She underwent a laparoscopy which revealed an inflammatory mass involving duodenum, gall bladder and transverse colon. Another upper GI endoscopy on table suggested gall stones causing duodenal obstruction. A laparotomy, duodenotomy and removal of stones was performed. She made an uneventful recovery.
Results: Leon Bouveret first described gastric outlet obstruction by gall stones, a condition which came to be described as Bouveret's syndrome. It is considered as a type of gall stone ileus, associated with a bilio enteric fistula. The management is controversial and could be one stage operation with enterolithotomy, cholecystectomy and repair of the bilio enteric fistula, two stage where cholecystectomy and repair of fistula is done later or enterolithotomy alone.
Conclusion: Gallstone disease can present atypically leading to diagnostic and treatment dilemmas. Absence of previous biliary symptoms does not rule out the diagnosis of gallstone ileus. Investigations such as CT scan and MRI are helpful in diagnosis and treatment planning. The treatment of choice in patients with gallstone ileus would be to relieve the bowel obstruction, either endoscopically or surgically.

108 CARDIOLOGISTS: BEWARE OF ULCERS

J. Mannath, R. Polson. *Gastroenterology, Solihull Hospital, Birmingham, UK*

Case Report: A 78-year-old gentleman was admitted to the acute medical ward with history of general deterioration and worsening diarrhoea of 2 months duration. He was incontinent lately with perianal pain and noticed rectal bleeding on a few occasions. There was also history of significant weight loss and poor oral intake due to painful oral ulcers. He had history of ischaemic heart disease and underwent a coronary artery bypass grafting in January 2006, after he presented with a troponin positive cardiac event and pulmonary oedema. He was on a variety of cardiac medications including Aspirin, Simvastatin, Isosorbide Mononitrate, Bisoprolol, Nicorandil and Furosemide.
Aims & Methods: Clinical examination showed evidence of heart failure in the form of dependent oedema and bibasal crackles. Examination of oral cavity showed multiple ulcers and abdominal examination was unremarkable. On admission, his full blood count was normal and renal functions were deranged with urea of 21.3 mmol/l and creatinine of 150 μmol/l. His liver function tests were unremarkable apart from an elevated alkaline phosphatase of 358 iu/l.
Results: Rectal examination showed peri-anal ulcerations and sigmoidoscopy revealed a large rectal ulcer with normal mucosa in the rest of the visualised bowel. The biopsies showed non-specific chronic inflammation. The presence of oral ulcerations and non-specific rectal ulceration suggested Nicorandil as the offending agent and it was discontinued. The oral ulcerations improved in 2 weeks' time, however his heart failure worsened and in spite of optimal medical therapy he deteriorated and died.
Conclusion: There were recent reports about the occurrence of oral and peri-anal ulceration with the use of Nicorandil. It is important to identify this reversible cause of ulceration as this may lead to unnecessary surgical

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intervention. Most of the ulcers usually heal within 6 weeks of withdrawal of drug. The mechanism by which Nicorandil causes ulcerations is not clear, however it is likely to be mediated by a systemic mechanism rather than local irritation.

109 REFRACTORY PLEURAL EFFUSION FROM PANCREATO-PLEURAL FISTULA: A RARE COMPLICATION OF CHRONIC PANCREATITIS

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Introduction: Pleural effusion due to pancreatico-pleural fistula, a rare complication[1] results from the disruption of the pancreatic duct into the retroperitoneal space with resultant fistulous communication between the pancreas and the pleural cavity. Respiratory rather than abdominal signs and symptoms predominate needing a high index of suspicion, as presentation is often misleading and delay in diagnosis can lead to significant morbidity and mortality. Here we discuss one such case of pancreato-pleural fistula from chronic pancreatitis.
Aims & Methods: To highlight the misleading presentations from complication of chronic pancreatitis, particularly pancreato-pleural fistula.
Results: A 55-year-old man presented with increasing breathlessness and cough associated with abdominal pain. He had a background of chronic pancreatitis and alcoholism. Examination revealed massive right pleural effusion. His blood tests showed an elevated amylase, normal CRP, LFT and WCC. He was treated with therapeutic chest drainage, however this re-accumulated despite being drained on two separate occasions. Fourteen days after his admission the diagnosis of a pancreato-pleural fistula was suspected only after a pleural fluid analysis showed an amylase of 7751 iu/l. He was treated with TPN and Octreotide for a period of 2 weeks. His recovery was punctuated with repeated pleural effusions, which resolved gradually. At follow-up 6 months later he was well.
Conclusion: This case highlights the importance of identifying the proper aetiology, since repeated pleural drainage would neither have been a wise option, nor a long-term solution. Thoracic complications are seen most often in acute pancreatitis, commonly as pleural effusions in 3–17% of patients. Massive pleural effusions are seen in <1% of chronic pancreatitis. Amylase in the pleural fluid is an important test which is usually very high. MRCP or ERCP may help demonstrate a fistula.[2] Conservative management with TPN and Octreotide may close the fistula in up to 40% of the patients. Surgical treatment with excision of the pseudocyst is a further options[3] but can have up to 10% mortality.

1. **Rockey DC**, Cello JP. Pancreaticopleural fistula: reports of 7 patients and review of the literature. *Medicine* 1990;**69**:332–44.
2. **Dhebri AR**, Ferran N. Nonsurgical management of pancreaticopleural fistula. *JOP* 2005;**6**:152–61.
3. **Yin WY**. The role of surgery in pancreatic pseudocyst. *Hepatogastroenterology* 2005;**52**:1266–73.

110 AN UNCOMMON CASE OF ASCITES

D. Gupta, J. Mannath, J. Ostler, N. Shah. [1]*Gastroenterology, Birmingham Heartlands Hospital, Birmingham, UK*

Case Report: A 52-year-old builder presented with history of lethargy, weight loss of 2 stones, loss of appetite and abdominal distension of 6 weeks duration. He was a smoker and consumed 40 units of alcohol per week for the past 30 years. He probably had exposure to asbestos and had a family history of bowel cancer. On examination, he was alert and oriented, with stigmata of chronic liver disease but not jaundiced. He had ascites with a tender right hypochondrium and no organomegaly. His blood investigations showed neutrophilia, renal impairment with a creatinine of 146 μmol/l, deranged synthetic liver functions with an INR of 4.5 and albumin 27 g/l. The rest of the liver enzymes and serum amylase were normal. The initial diagnostic ascitic fluid showed an exudative ascites with a SAAG of 10 and a neutrophil count of 270/mm^3. This was compatible with spontaneous bacterial peritonitis for which he was commenced on appropriate intravenous antibiotics. However his clinical condition remained unchanged. CT scan of his abdomen showed a pancreatic pseudocyst at the head and body measuring 5 cm. Further fluid analysis showed no growth and it was negative for malignant cells. Interestingly the fluid amylase was markedly raised at 14856 IU/l. This confirmed pancreatic ascites and helped differentiate it from spontaneous bacterial peritonitis. An MRCP was arranged to delineate the pancreatic duct architecture. However he deteriorated rapidly and died in ITU due to renal failure and metabolic acidosis.
Conclusion: Pancreatic ascites, which is uncommon, can often be confused with complicated ascites with SBP. Ascitic fluid amylase should be done in all cases to exclude pancreatic ascites which has a significantly higher mortality. Pancreatic imaging to delineate duct anatomy is mandatory to plan further management. Management of these patients remain controversial. This includes conservative management like octreotide or Somatostatin infusions aiming at reducing the pancreatic exocrine secretions, pancreatic stenting or rarely pancreatic irradiation facilitating the closure of the fistula. Surgical options include pancreatectomy or a pancreatojejunostomy.

Plenary posters

111 LAMIN A/C STATUS IS A PROGNOSTIC INDICATOR IN COLORECTAL CANCER

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Introduction: Lamin A/C is a member of a group of proteins known as the A-type lamins. These proteins are expressed in most differentiated somatic cells where they are integral parts of the nuclear lamina—the complex meshwork underlying and supporting the nuclear membrane. Mutations in A-type lamins have been implicated in no less than 9 laminopathies (inherited diseases resulting in premature aging) and several epithelial-derived cancers, but to date, direct involvement in colorectal cancer has yet to be shown.
Aims & Methods: Patient information and tumour material was collected from 734 incident colorectal cancer cases participating in the Netherlands Cohort Study on Diet and Cancer. 4 micron sections were immunohistochemically stained for lamin A/C expression using the Jol2 mAb. A scoring system was devised for lamin A/C expression and slides were scored by two independent observers blinded to each others findings and patient data. Data analyses were based on 656 participants with available follow-up and lamin A/C expression data. Differences in patient, tumour and follow-up characteristics were analysed and subsequent hazard ratios (HR) for colorectal cancer related mortality according to lamin A/C status were estimated using Cox regression analysis.
Results: 463 specimens were scored as lamin A/C positive and 193 were scored as lamin A/C negative. During the follow-up period, from 1989 to 1997, 246 patients died, of which 161 died as a result of colorectal cancer. Patients with tumours expressing lamin A/C were observed to be slightly older, having substantially more colorectal cancer related deaths and a significantly decreased survival period. The lack of expression is associated with a decreased risk of mortality, HR 0.59 (95% CI 0.41 to 0.85, $p=0.006$) in the overall population as well as in the individual Dukes' A, B and C stages. Almost all Dukes D patients died within the follow-up period.
Conclusion: Our data show that the expression of lamin A/C in colorectal tumours is significantly linked to colorectal cancer associated mortality in patients. Regression analyses including lamin A/C expression and other factors associated with tumour initiation and progression indicate that lamin A/C expression is independently related to survival and is a strong candidate as a prognostic marker for colorectal cancer-related mortality.

112 INCREASED BIOMARKERS OF COLORECTAL CARCINOGENESIS ASSOCIATED WITH OBESITY AND ROUX-EN-Y GASTRIC BYPASS

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Introduction: The mechanistic basis of the link between obesity and increased colorectal cancer (CRC) risk is unclear. One hypothesis is that chronic inflammation associated with obesity drives colorectal carcinogenesis. It is as yet unproven whether weight loss reduces the risk of CRC. Therefore we studied the effect of weight loss on biomarkers of epithelial proliferation, as well as mucosal proinflammatory cytokines and systemic inflammatory markers.
Aims & Methods: Serum and rectal mucosa were obtained from 26 severely obese patients pre and 6 months post Roux en Y gastric bypass

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(RYGB) and 21 individuals with a normal BMI (18.5 to 25 kg/m^2). Patients with chronic inflammatory conditions were excluded. Crypt mitosis was determined in 40 microdissected Schiffs reagent stained crypts, in a blinded manner. Changes in mucosal mRNA transcripts of genes relating to inflammation, cell turnover and obesity were quantified by real-time PCR using the comparative \Delta\DeltaCt method. Serum CRP and IL6 were also measured.

Results: Obese patients (mean BMI (SEM) 54.8 (2.0) kg/m^2) had a higher number of crypt mitoses than individuals with a normal BMI (median 4.2 *v* 2.7; $p<0.001$). There was a mean weight loss of 23.4% following RYGB. However, there was a mean 2.1-fold increase in crypt mitosis count (95% CI 1.6 to 2.6) post-RYGB. Upwards expansion of the proliferative zone also occurred following RYGB, with an increase in the proportion of mitoses in crypt zones 4 and 5 (3.2 to 6.3%; $p=0.02$). Following RYGBP, the mean serum CRP fell from 8.6 to 3.8 mg/l ($p<0.001$) (cf to 0.8 mg/l in the normal BMI group) and serum IL6 fell from 5.2 to 3.2 pg/ml ($p<0.001$) (cf to 1.9 pg/ml in the normal BMI group). Increased mucosal mRNA transcription of COX1, COX2 and IL6 followed RYGB, although obesity-related genes (Adiponectin receptor1, IGF1) and cell turnover-related genes (MDM2, AKT3, BAX) were downregulated.

Conclusion: Crypt biomarkers of CRC risk were elevated in obese compared to normal BMI individuals, however these increased further post-RYGB. Systemic inflammatory markers were elevated in obese patients compared to individuals with a normal BMI, and fell post-RYGB. In contrast, the pattern of rectal mucosal gene expression was in keeping with a proinflammatory and tumorigenic state. This may reflect changes in the colorectal luminal micro-environment following RYGB. This is the first time that obesity has been shown to be associated with elevated mucosal biomarkers of carcinogenesis. These data also indicate that patients may be at increased risk of CRC following RYGB.

113 DIAGNOSTIC YIELD OF ENDOSCOPIC ULTRASOUND-GUIDED TRUCUT BIOPSY: EXPERIENCE FROM A TERTIARY REFERRAL CENTRE

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Introduction: A major advantage of linear endoscopic ultrasound (EUS) in clinical practice is the ability to get tissue diagnosis. Cytology can be obtained by fine needle aspiration (19 or 22G). Although EUS-guided fine needle aspiration (FNA) has a diagnostic accuracy of 80–90%, accuracy is lower without an on-site cytology facility. Additionally, there are certain lesions that visualisation and characterisation of tissue architecture is needed, in order to reach a diagnosis. To that end, a 19G trucut biopsy needle (TCB) has been designed. Core biopsy has clear advantages over cytology.

Aims & Methods: The aim of our study is to report the largest, single-centre experience of EUS-guided Trucut biopsy (TCB). Clinical details, EUS findings and performance characteristics of EUS-TCB were collected prospectively from 161 consecutive procedures (96 men) with median (range) age of 65 (22–86) years, between December 2002–September 2006.

Results: Lesions with a diameter of range (median) 0.5–9 (3) cm were sampled using 1–7 (3) passes to obtain tissue core of range (median) 0.1–1.9 (1) cm. Passes were made via oesophagus in 45, stomach in 104 and duodenum in 12. In 28 (17%) cases there were technical problems—equipment failure, 10 (6%); problematic penetrations and fragmentation, 18 (11%). In all passes, specificity and PPV were 100%. Two major post-procedure complications were bronchopneumonia (1) and cold abscess formation (1).

Conclusion: EUS-TCB yields diagnostic samples in 88%–90% of cases, the majority of which were accessible through the stomach and oesophagus. Future studies should compare the cost of EUS-TCB versus EUS-FNA with on-site cytology service.

114 ENDOSCOPIC BALLOON DILATATION AND SEQUENTIAL STENTING PROVIDES SAFE AND EFFECTIVE TREATMENT OF ANASTOMOTIC STRICTURES COMPLICATING ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: The biliary anastomosis has long been regarded as the Achilles heel of liver transplantation (OLTx) and anastomotic strictures (AS) complicate approximately 12% of primary grafts and 11% of re-grafts undertaken in Birmingham. If left untreated progressive stricturing at the site of the anastomosis will lead to biliary obstruction, graft damage and eventually fibrosis and cirrhosis. Traditional management of AS by surgical biliary reconstruction has begun to be replaced by endoscopic therapy in some centres. We present a prospective study of non-surgical management of AS complicating OLTx in the liver unit at QEH, Birmingham (UK).

Aims & Methods: Fifty three patients (21 male, 32 female; median age 48.5 years) were referred with biliary AS complicating OLTx between July 2000 and August 2006. 31 cases were late anastomotic strictures and the remainder presented in the first 3 months following transplantation. Cases were managed according to the Birmingham protocol and each case discussed with the multidisciplinary team. We present the short and long-term success of endoscopic treatment of AS.

Results: Biliary obstruction was relieved in 92.5% of patients and endoscopic therapy was technically successful in 81% of cases. 94% of patients who completed endoscopic therapy remained stent-free over the follow-up period (median 18 months stent-free follow-up). Two patients required stent re-insertion after developing biliary obstruction after completion of treatment. Patients required a median of 3 ERCPs, 2×24F balloon dilatations and maximal simultaneous insertion of two 10Fr Cotton Leung stents to successfully treat the stricture. Endoscopic therapy was well tolerated and associated with a low rate of complications; there were no severe or fatal complications. Eight patients did not respond to endoscopic therapy and were referred for surgical biliary reconstruction.

Conclusion: Endoscopic dilatation and sequential stent insertion provides good medium/long-term resolution of strictures at the biliary anastomosis and offers a safe and effective non-surgical means of managing early and late AS. 81% of patients with biliary AS referred to our service were successfully treated with endoscopic therapy. We believe that endoscopic dilatation and stenting should now be considered the treatment of first choice in patients with biliary anastomotic strictures complicating OLTx.

115 LAUREN SUBTYPING OF CARDIA CANCER PROVIDES FURTHER EVIDENCE OF TWO DISTINCT AETIOLOGIES

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Introduction: There are several reports of cardia cancer resembling oesophageal adenocarcinoma in being negatively associated with H pylori infection and positively associated with reflux symptoms. However, there are also reports of a positive association between cardia cancer and serological evidence of atrophy in H pylori-positive subjects, suggesting that some cardia cancers are aetiologically similar to non-cardia gastric cancers.

Aims & Methods: To determine whether cardia cancers in patients with gastric atrophy have a Lauren histological subtype resembling non-cardia

Abstract 113

	Overall (%)	Pancreas (%)	Non-pancreatic lesions (%)	Pancreas (TCB through the stomach) (%)
Sampling adequacy	89	88	90	91
Sensitivity	76	70	81	77
NPV	60	45	71	50
Accuracy	82	75	87	81

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gastric cancer whereas cardia cancers in subjects without atrophy are predominantly intestinal in histological subtype resembling oesophageal adenocarcinoma. We have studied the Lauren histological subtypes of 129 non-cardia cancers and 44 cardia cancers and related the histological findings to the serological presence of gastric atrophy (pepsinogen I/II <2.5). This was performed in a case-control study nested in Norwegian JANUS cohort.
Results: The non-cardia gastric cancers were 46% intestinal, 27% diffuse and 24% of mixed histological subtype. In these non-cardia cancers, gastric atrophy increased the risk of each histological subtype to a similar extent. In the 36 cardia cancers without serological evidence of gastric atrophy, the major histological subtype was intestinal (75%) with only 11% being diffuse and 11% mixed ($p<0.05$). The proportion of cancers with the intestinal histological subtype was significantly greater in these cardia cancers without atrophy compared to the non-cardia cancers. In the cardia cancers with evidence of gastric atrophy, the histological subtype resembled that of the non-cardia cancers being 38% intestinal, 25% diffuse and 37% mixed.
Conclusion: These findings provide further support for two distinct aetiologies of cardia cancer, one resembling oesophageal adenocarcinoma occurring in subjects without atrophy and being predominantly of intestinal histological subtype; the other being similar to non-cardia gastric cancer being associated with atrophy and with an equal proportion of intestinal and diffuse histological subtypes. Gastric atrophy and the histological subtype of cardia cancer may allow division of cardia cancers into those, which are gastric versus oesophageal in origin.

116 MYOFIBROBLAST WNT-5A FACILITATES INTESTINAL EPITHELIAL REPAIR THROUGH A NON-CANONICAL PATHWAY

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Introduction: Subepithelial myofibroblasts are closely involved in the initiation and coordination of intestinal epithelial repair in the inflamed gut, but the molecular signalling pathways are largely unknown. The cellular adaptations that occur during repair range from de-differentiation and migration to proliferation and re-differentiation, in a way that is strongly reminiscent of normal crypt-to-villus epithelial maturation. Because the Wnt/β-catenin signalling pathway has emerged as one of the key regulators of the self-renewing capacity of the intestine, we hypothesised that it has a similarly pivotal role in intestinal epithelial wound repair.
Aims & Methods: We used an established scratch wound method in Caco-2 cells to monitor the effects of colonic myofibroblasts (CCD-18co) on intestinal epithelial repair.
Results: Caco-2 wound closure over 24 hours was increased almost twofold by the presence of conditioned media from IL-1β stimulated, but not untreated, CCDs. In parallel, IL-1β-stimulated CCDs downregulated the differentiation markers sucrase-isomaltase and villin in the Caco-2 cells, while the proliferation marker c-myc was upregulated. Expression profiling identified Wnt-5A as the one Wnt-related gene that was differentially expressed between the IL-1β stimulated (up 27-fold) and untreated CCDs. Wnt-5A immunodepletion of the IL1β-CCD conditioned media completely abrogated its repair benefit. IL1β-CCD-mediated repair was not affected by the addition of the Wnt antagonist Dickkopf-1. Total and phosphorylated β-catenin protein levels in Caco-2 cells did not change after exposure to IL-1β-stimulated CCDs. Furthermore, IL1β-stimulated CCDs did not antagonise LiCl-induced canonical signalling.
Conclusion: These results identify an important role for myofibroblast-derived, non-canonical, Wnt-5A signalling in the de-differentiation and migration stages of epithelial wound repair in the gut.

117 DRUG DELIVERY SYSTEMS FOR TREATING INFLAMMATORY BOWEL DISEASES: THE EXTENT TO WHICH GASTROINTESTINAL PH INFLUENCES DRUG RELEASE FROM ENTERIC COATED PRODUCTS

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Introduction: A number of enteric coated preparations for targeting drugs to ileo-colonic regions of the gastrointestinal tract for the treatment of inflammatory bowel diseases are commercially available. Aim of this work was to investigate the extent to which luminal pH affects drug release from these delivery systems and any other physiological factors which may have an influence.
Aims & Methods: Placebo tablets coated with Eudragit S (dissolves at pH >7) to target the distal bowel were prepared. The coated tablets were radiolabelled with technetium-99m and administered in a two-way crossover study to 8 healthy male subjects. All volunteers were fasting on tablets administration and food was administered either after 30 minutes (pre-fed) or 4 h (fasted). The gastrointestinal transit and disintegration of the administered dosage forms was monitored by acquiring gamma scintigraphy images at 10 minute intervals for 12 h. A radiotelemetry capsule (Bravo pH system, Medtronic, USA) was radiolabelled with indium-111 and administered to the same subjects on both days of the study to measure the gastrointestinal lumenal pH.
Results: The mean gastric emptying times were 66 and 172 minutes for the fasted and pre-fed states respectively. Transit through the small intestine appeared to be quicker in the pre-fed state relative to the fasted states. Tablet disintegration occurred in 7 out of 8 subjects in the fasted state. However in the pre-fed state, disintegration occurred in only 5 out of 8 subjects. Rapid transit down the small intestine will mean that tablets may not have the opportunity to disintegrate until reaching the colon where the environment is unfavourable due to the very limited fluid volumes. A recent magnetic resonance imaging (MRI) study has shown that food consumption results in a significant reduction in water volume in the small intestine which may also contribute to explaining the failure of some of the tablets to disintegrate in the pre-fed state.[1] Disintegration occurred mainly in the ileo-caecal junction or ascending colon in the fasted state while the site of disintegration was more variable in the pre-fed state. The pH in the distal gut of all 8 subjects was greater than 7 on both days, thus suggesting that although gastrointestinal pH acts as a trigger for drug release it is not the only parameter.
Conclusion: The time and site of drug release from enteric coated tablets is influenced by the feed status and is more reproducible in the fasted state. Elevated pH in the distal gut is important in triggering drug release from enteric-coated dosage forms, however other gastrointestinal factors are likely to play a critical role.

1. **Schiller C**, *et al. Aliment Pharmacol Ther* 2005;**22**:971–9.

118 OUTCOMES OF CORTICOSTEROID AND THIOPURINE USE IN A POPULATION-BASED COHORT OF CROHN'S PATIENTS IN CARDIFF DIAGNOSED 1996–2005

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Introduction: Few data are available on the 1st use of corticosteroids (CS) and thiopurines (TP) in Crohn's disease from population-based cohorts in the UK. Population-based data are available from Denmark[1] and the USA[2] on CS use, but these were before TPs were widely used, and no population-based data give outcomes of TP use.
Aims & Methods: To report the rate and outcomes of first use of CSs and TPs, and rates of surgery in a cohort of 212 Crohn's patients resident in the City of Cardiff, diagnosed 1996–2005. For CS: 1 month(mo) outcomes were recorded as Complete response; Partial Response (symptom improvement but >3 bowel actions/day or persisting pain or blood); No Response (no improvement in symptoms, with persistent diarrhoea and/or abdominal pain and/or elevated inflammatory markers/weight loss). 1 year (yr) CS outcomes, and outcomes after 6 mo of TP treatment were recorded as Prolonged Remission [minor or no symptoms and off CS); Corticosteroid Dependent; or Treatment Failure (active disease despite drug treatment, or operation).
Results: 167 (79%) received CS (88% within 1 yr of diagnosis). 89% were given prednisolone, 11% budesonide. At 1 mo, 72 (43%), 74 (44%), 21 (13%) demonstrated complete, partial and no response, respectively. 150 of those patients had 1 yr follow-up and 76 (51%), 37 (25%), 39 (26%) showed prolonged response, corticosteroid dependence or treatment failure respectively. In 830 patient yrs follow-up, 40 patients were on CS for more than 1 yr with no more than 2 mo break at any time. 72 (43%) needed TP treatment, and 18 (12%) had surgery within 1 yr of CS. 112 (53%) received TP (97% azathioprine, median dose 125 mg, range 25–200), 3% 6-mercaptopurine (range 75–100 mg). They were started significantly earlier after diagnosis in the 2001–5 cohort, median 7 mo, *v* the 1996–2000 cohort, median 16 mo ($p<0.001$). 111 patients had at least 6 mo follow-up, and at 6 mo 42 (38%), 40 (36%), and 29 (26%) were in remission, CS-dependent and treatment failure respectively. 10% needed surgery within 6 mo. Lower total white cell count was significantly lower in the remission (median $6.2\times10\text{-}9$) *v* non-remission ($7.8\times10\text{-}9$) group ($p=0.005$). 2% had white cell count below $3.0\times10\text{-}9$ within 6 months and 13% experienced side-effects on TP.At end of follow-up however (median 26 mo) 11% required dose reduction or cessation due to leucopaenia, and 20% stopped TP because of side-effects.

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Conclusion: Rates of CS use are higher in this cohort than USA and Danish studies,[1, 2] but similar to other UK studies.[3] TPs are used earlier in the more recent quinquennium, but CS failures remain high. CS dependence remains common despite earlier use of TPs.

1. **Munkholm P**, *et al. Gut* 1994;**35**:360–2.
2. **Faubion WAJ**, *et al. Gastroenterology* 2001;**121**:255–60.
3. **Ho GT**, *et al. Aliment Pharmacol Ther* 2006;**24**:319–30.

119 THE LONG-TERM BURDEN OF INFLAMMATORY BOWEL DISEASE: A LARGE EPIDEMIOLOGICAL STUDY OF PATIENTS IN SCOTLAND

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Introduction: While the impact of exacerbation on the long-term health and quality of life of patients with inflammatory bowel disease (IBD) has been intensively studied, there is little information on the overall burden of IBD on healthcare systems in terms of clinical and financial resources. The Scottish National Health Service Record Linkage Database (~6.0 million population) holds one of the largest and most accurate patient-linked data sets available, allowing all hospital inpatient and day-case admissions in Scotland from 1981 to the present to be tracked.
Aims & Methods: A large epidemiological research project, guided by an independent steering panel, has been designed to interrogate this database to understand better the overall burden of illness associated with IBD. The results of initial analyses performed on the database for patients with IBD during the period 1981–2004 are presented. They include: the year-on-year prevalence of hospital admissions; the cumulative number of individual episodes treated per year; and the length of stay (LOS) when hospitalised. The possible impact of ulcerative colitis (UC) on mortality was also assessed by review of an incident cohort of 438 patients hospitalised for the first time for UC in 1986 (without prior cancer or cardiovascular disease) and followed over 19 years.
Results: The number of admissions per year for IBD increased from 1981 to 2004 (table). The total number of bed days per year increased by approximately 20% during the same period; however, the mean LOS per episode decreased from 15.4 days (1981) to 4.2 days (2004). In the incidence cohort of patients with UC, 278 were below and 160 were at least 50 years of age in 1986. After 19 years, 119 patients had died (mortality rates of 7.9% and 60.3% in each age group, respectively). Six (5%) deaths were related to colorectal cancer.
Conclusion: The number of hospital admissions, individual episodes and total bed days for patients with IBD has steadily increased over the last 19 years. The reasons are likely to be multifactorial, possibly including an increase in surgical procedures and routine endoscopic screening.

120 BONE MARROW TRANSPLANTATION INDUCES REMISSION IN CROHN'S DISEASE: WHERE DO THE CELLS GO?

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Introduction: Recent studies show that bone marrow (BM) transplantation induces remission in Crohn's disease. We used a mouse model of Crohn's disease to elucidate the mechanism of action of BM transplantation.
Aims & Methods: Female mice were lethally irradiated and rescued by a BM transplant from male donors. After 6 weeks experimental colitis was induced by an injection of trinitrobenzene sulphonic acid (TNBS), and colons analysed 1–14 days later. In situ hybrydisation for Y chromosome was combined with immunohistochemistry for α-SMA, ICAM-1, EphB4, ephrinB2 and other specific antigens to determine their phenotype. A novel triple staining method combined in situ hybridisation, immunohistochemistry and autoradiography to show cell activity.
Results: Cells derived from BM (Y chromosome expressing) contributed significantly to myofibroblasts and to endothelial cells, pericytes and vascular smooth muscle lining cells in blood vessels. BM contributed to both angiogenesis and neovasculogenesis, confirmed by vessels composed entirely of BM-derived cells. BM-derived myofibroblasts are active shown by their expression of collagen mRNA.
Conclusion: This is the first observation of BM-mediated neovasculogenesis in colitis. We provide an insight into the regenerative function of BM by highlighting the capacity of BM to engraft within inflamed colons and form multiple, functional lineages.

121 HAEMOPHAGOCYTIC SYNDROME COMPLICATING LIVER TRANSPLANT CARRIES A POOR PROGNOSIS

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Introduction: Haemophagocytic syndrome (HPS) is a life threatening disorder characterised by TH1 cytokine secretion and resulting in accumulation of activated macrophages. HPS have recently been reported as a common finding in patients with multi-organ failure. The literature of HPS in association with liver transplantation (LTx) however, is limited to case reports only.
Aims & Methods: Review our clinical experience of the presentation; management and outcome of HPS in association with LTx. All bone marrow examinations performed at King's College between 1993 and 2004 were reviewed. 186 patients with acute or chronic liver disease (CLD) had undergone bone marrow for unexplained thrombocytopenia (median 32×109/l, 1–84×109/l) in association with the sepsis syndrome. Within this cohort 43 patients had received a LTx; 31 patients received a first transplant (12 for acute liver failure (ALF) and 19 for chronic liver disease) and a further 12 were retransplanted.
Results: Presentation was invariably during first ITU admission for those with ALF, but for routine CLD transplants or re-transplantation there were early and late peaks corresponding to the immediate post transplant period or representation at the time of further surgery. Serial organ failure scores (SOFA) were high (median 10, range 4–19). Positive CMV serology was noted in 20/43 cases, with a further 3 having histopathological evidence of CMV, which is significantly higher than in the transplant population as a whole (53% *v* 5%, Fischer exact test $p<0.005$). Bone marrow examination revealed variable cellularity (9 hypercellular, 17 normocellular, 9 hypocellular) and differing degrees of macrophage infiltration (8 normal, 7 increased, 21 markedly increased). Specific treatments aimed at the precipitant of the HPS included: human immunoglobulin (HIg) alone 8 cases, HIg and antiviral 23, antiviral alone 6 and in 3 HIg and systemic chemotherapy. Despite aggressive supportive and specific therapies overall ITU mortality was 41% with a median survival of 42 days. Those with previous CLD had the worst prognosis with an 88% ITU mortality. Univariate analysis of laboratory and physiological variables at diagnosis revealed that only the degree of macrophage infiltration predicted outcome ($p<0.04$) and this remained significant with logistic regression ($p<0.03$). A strong correlation existed between time from LTx to development of HPS

Abstract 119 Summary data for selected years, total per year for IBD (UC, Crohn's disease)

	1981	1988	1996	2004
Patient admissions IBD	1628	2263	4293	5700
(UC, CD)	(743, 900)	(1016, 1280)	(2204, 2165)	(2830, 3010)
Number of episodes IBD	2587	3552	7112	11389
(UC, CD)	(1066, 1528)	(1401, 2163)	(3255, 3888)	(4911, 6548)
Total bed days IBD	39933	39053	40485	47721
(UC, CD)	(17093, 22893)	(14176, 24995)	(15244, 25512)	(18636, 29383)

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and time from LTx to positive CMV serology (Pearson $p<0.05$). CMV positivity, however, was not a predictor of outcome.
Conclusion: HPS carries a very poor prognosis and is common post liver transplant, although frequently undiagnosed. The degree of bone marrow macrophage infiltration is the best prognostic marker.

122 LYMPHOCYTE STEROID SENSITIVITY IN SEVERE ALCOHOLIC HEPATITIS

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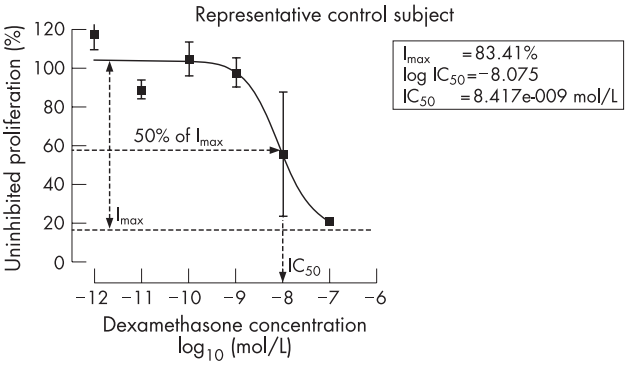
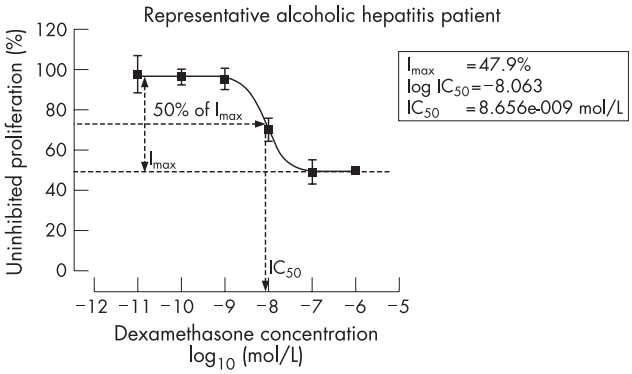
Introduction: Corticosteroids are an established therapeutic option in acute alcoholic hepatitis (AAH), but response to therapy is variable and mortality with steroid treatment remains around 16%.[1] Measurement of ex vivo lymphocyte steroid sensitivity has been used to predict response to steroids in ulcerative colitis.[2] The present study adapts this technique to assess steroid resistance in AAH and evaluate other treatments.
Aims & Methods: Peripheral blood mononuclear cells were isolated from patients with severe AAH (DF>32) and matched controls. Proliferation was stimulated with phytohaemagglutinin, inhibited with concentrations of Dexamethasone from 10^{-6} to 10^{-11}M, and measured by incorporation of ^{3}H-thymidine. Results were expressed as percentage of uninhibited proliferation and plotted against Dexamethasone concentration. Maximal inhibition (I_{max}) and IC_{50} were calculated.
Results: Compared to control subjects, the majority of patients with AAH had reduced lymphocyte steroid sensitivity, evident in lower values of I_{max}. Representative data are illustrated.
Conclusion: These results demonstrate that lymphocyte steroid sensitivity, like clinical response to corticosteroids in AAH, is variable and often reduced. Investigation is required to clarify whether this is an intrinsic property of the individuals affected or a result of the disease process. Further studies will investigate the correlation between steroid sensitivity and outcome. Intriguingly, the addition of low-dose Theophylline to the reaction appeared to restore steroid sensitivity in a number of samples, identifying a potential adjunctive therapy to improve clinical response.

1. **Mathurin P**, *et al. J Hep* 2002;**36**:480–7.
2. **Hearing SD**, *et al. Gut* 1999;**45**:382–8.





Abstract 122

123 CHANGES IN PORTAL BLOOD FLOW AND LIVER OXYGENATION FOLLOWING INTRAPORTAL INJECTION OF PANCREATIC ISLET-SIZED DEXTRAN BEADS

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Introduction: The physiological events which immediately follow the clinical practice of pancreatic islet transplantation, via the portal vein, are poorly understood. This stage of the procedure is estimated to result in a 60% graft loss of islets between their injection and engraftment into the liver. Rises in portal pressure can limit islet graft volume infusions and multiple intraportal grafts are associated with permanent rises in portal pressure. We have studied the effect of portal embolisation on portal vein haemodynamics and liver tissue oxygenation using inert beads in an intraportal rodent transplantation model. Beads were used to distinguish between islet and liver related factors.
Aims & Methods: Male Sprague-Dawley rats (6 week old) were injected intraportally with 500 dextran beads (75–150 μm diameter). Subjects (n=26) were divided into 6 groups as per the day following intraportal bead injection for the measurement of physiological parameters into days 1, 3, 5, 7, 14 and 28. A control group (day 0 or baseline) did not receive any intraportal beads. The following parameters were measured under isofluorane anaesthesia: portal vein pressure, systemic blood pressure (A.D. Instruments pressure transducer), portal blood flow (Transonic doppler flow probe), and liver parenchyma oxygenation (Unisense 25 μm oxygen-sensing needle probe inserted into at least 3 points in each liver).
Results: Portal vein flow rates began to fall from baseline (controls) 13.8 ml/min (1.2) immediately by day 1 to 10.7 ml/min (1.4) in the day 7 group ($p<0.05$) before rising to 15.2 ml/min (0.9) similar to controls by day 28 ($p<0.01$). In the control group the portal pressure was 8.6 mm Hg (0.95) which began to rise by day 1 to a peak of 13.1 mm Hg (0.8) in the day 7 group ($p<0.05$) and falling back to baseline value of 8.4 mm Hg (0.35) by day 28 ($p<0.05$). Partial pressures of oxygen did not vary significantly between control values and any point after bead infusions, being around 5.0 to 6.6 kPa. Mean arterial pressures were on average above 80 mmHg.
Conclusion: These findings document a peak change around day 7, when the highest portal pressure and lowest portal flow is observed, before returning to baseline levels by 28 days. Other studies describing the release of growth factors such as VEGF and HGF demonstrate a peak level at this time point post-transplant. The rat liver has an abundant hepatic arterial supply and we postulate a greater degree of shunting may be occurring from this circulation to compensate for reduced portal blood flow, thus maintaining liver oxygenation. This may have implications for the relatively ''oxygen-hungry'' islets in the immediate post transplant period.

124 REPRODUCIBILITY OF VISCERO-VISCERAL AND VISCEROSOMATIC SENSITISATION INDUCED BY INTRADUODENAL CAPSAICIN INFUSION

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Introduction: Capsaicin activates TRPV-1 receptors on spinal and vagal afferents and its infusion into the duodenum evokes burning and cramping sensation and sensitises the duodenum to experimental stimuli. Whether duodenal capsaicin infusion reproducibly sensitises other visceral and somatic structures with convergent spinal innervation is not known.
Aims & Methods: To determine whether duodenal capsaicin infusion reproducibly induces viscero-visceral (oesophagus) and viscero-somatic (abdominal wall) sensitisation. Eight subjects were recruited (7 female). A catheter was positioned in the proximal duodenum with a second in the distal oesophagus. Pain thresholds (PT) to electrical stimulation (ES) were assessed in the oesophagus, area of somatic referral (AOR) on the abdominal wall and control region (foot). Capsaicin was then infused into the duodenum (2 ml/min for 30 minutes). The concentration of capsaicin used was 400 μg/ml with a saline control. Subjects were studied on 3 occasions (2×400 μg/ml, 1×saline) in a randomised order and both operator and subject were blinded. PT in all regions were recorded at 15 and 45-minutes post infusion. Visual analogue scales (VAS) for pain, unpleasantness, nausea and anxiety were recorded at 5-minute intervals during the infusion and a short McGill pain questionnaire was used to describe the discomfort.

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Results: Significant and reproducible reductions in oesophageal PT were seen on both occasions at 400 μg/ml (−12.76 mA and −15.25 mA, p=0.033, p=0.007) when compared to saline. Significant reductions in AOR PT were seen on both occasions at 400 μg/ml (−9.09 mA and −9.44 mA, p=0.027, p=0.026) when compared to saline. No differences were seen in foot PT. VAS scores for pain were higher that for the other psychophysical measures. The most common verbal descriptors used to describe the capsaicin infusion were cramping, hot-burning and aching. Tolerance of the infusion falls broadly into 2 groups; those who tolerate the full 30 min, and those who only tolerate a very short infusion (<6 min). There was a correlation between the lengths of infusion tolerated within an individual between the two visits (ICC=0.729).
Conclusion: Capsaicin infusion into the proximal duodenum induces sensitisation in visceral and somatic regions known to have convergent afferent input at the spinal cord level. These data provide further evidence that central sensitisation plays an important role in the development of visceral hypersensitivity.

125 THE FERMENTABLE FIBRE SUBSTRATE PECTIN CAN ENHANCE TUMOUR YIELD IN THE APCMIN/+ MOUSE MODEL OF INTESTINAL CANCER

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Introduction: There is some controversy regarding the relationship between dietary fibre intake and colorectal cancer, and it has been suggested that rapidly fermentable fibres may enhance carcinogenesis by stimulating cell proliferation in the colon.[1, 2] Such effects may be influenced by the diet used, as semisynthetic (SS) diets may be hypoproliferative.[3] This was investigated in a mouse model of intestinal cancer, namely the multiple intestinal neoplasia, ApcMin/+ mouse.
Aims & Methods: ApcMin/+ mice were fed a standard chow or SS diet with or without 10% apple pectin. After 8 weeks they were killed, and the intestines fixed for polyp scoring and for the determination of cell proliferation. Two-way analysis of variance was used to look for effects of diet and pectin and any interaction between these.
Results: The caecum and colon were lighter in the SS fed mice and pectin significantly increased the weight of these tissues and the small intestine in both groups. Pectin increased polyp number in the small intestine in both groups, but the effects appeared to be greater in the SS fed mice. Pectin was also associated with a small but significant increase in polyp diameter and thus burden. Few polyps were seen in the colon, but there were significantly less in the mice fed the SS diet and no effect of pectin was detectable.
Conclusion: The trophic actions of pectin and its enhancement of polyp number were not significantly altered by the use of semisynthetic diets showing that the trophic effect of such colonic substrates and increased tumour yield are not an artefact of the basal diet. The increased tumour yield observed indicates that such fermentable substrates[4] should not be used to boost fibre intake.

1. **Wasan HS**, Goodlad RA. Fibre-supplemented foods may damage your health. *Lancet* 1996;**348**:319–20.
2. **Goodlad RA**. Dietary fibre and the risk of colorectal cancer. *Gut* 2001;**48**:587–9.
3. **Mathers JC**. Nutrient regulation of intestinal proliferation and apoptosis. Proceedings of the Nutrition Society, 1998;**57**:219–23.
4. **Goodlad RA**, Englyst HN. Redefining dietary fibre: potentially a recipe for disaster. *Lancet* 2001;**358**:1833–4.

126 ESOMEPRAZOLE FOR TREATMENT OF UNEXPLAINED CHEST PAIN IN PRIMARY CARE: A PROSPECTIVE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED MULTICENTRE STUDY

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Introduction: Chest pain is one of the most common reasons for patients to present to primary care physicians or hospital emergency departments, and is often non-cardiac in origin. In many patients, underlying gastrooesophageal reflux disease is the source of the pain and a trial of proton pump inhibitor therapy is often used to identify chest pain with reflux-based aetiology.
Aims & Methods: This study compared esomeprazole with placebo for the relief of unexplained chest pain or discomfort. Primary care patients with ⩾2 weeks of pain or discomfort in the chest (of moderate severity on ⩾2 of the last 7 days) and of unidentifiable cause were included. Patients with identifiable non-cardiac causes of chest pain (eg musculoskeletal disorders, gastrooesophageal reflux disease) were excluded, as were patients with known cardiac disorders, abnormal ECG, troponin or exercise test results at baseline. Patients were randomised to esomeprazole 40 mg twice daily (bid) or placebo for 4 weeks, and stratified according to frequency of heartburn or acid regurgitation as follows: <2 d/week (stratum 1); or ⩾2 d/week (stratum 2). The primary variable was relief of chest pain or discomfort (measured by daily dairy on a 7-grade Likert scale), analysed by stratum. Relief was defined as ⩽1 d with minimal symptoms during the last 7 d of treatment.
Results: A total of 599 patients were included in the intention-to-treat population (316 males, mean age 46.9 years); 297 patients received esomeprazole 40 mg bid (stratum 1, n=153 and stratum 2, n=144) and 302 received placebo (stratum 1, n=161 and stratum 2, n=141). Esomeprazole was significantly more effective than placebo for the relief of chest pain in stratum 1 (38.7% *v* 25.5%, p=0.018). However, the difference was not significant in stratum 2 (27.2% *v* 24.2%). Esomeprazole was significantly more effective than placebo when the two strata were combined in a post hoc analysis (33.1% *v* 24.9%; p=0.035). Esomeprazole was well tolerated. One patient (placebo group) developed a non-fatal myocardial infarction during the study. Discontinuations due to adverse events were similar between the esomeprazole and placebo groups (3.3% and 2.9%, respectively).
Conclusion: Esomeprazole is more effective than placebo for relief of unexplained chest pain in primary care patients when patients with identifiable non-cardiac causes of chest pain or known cardiac disorders, abnormal ECG, troponin or exercise test results have been excluded. This treatment regimen is generally well tolerated in these patients.

127 THE NEW RADIOLABELLED SOMATOSTATIN ANALOGUE 90YTTRIUM-DOTA-OCTREOTATE FOR THE TREATMENT OF METASTATIC NEUROENDOCRINE TUMORS: INITIAL RESULTS AND TOLERABILITY IN A SERIES OF 47 PATIENTS

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Introduction: Radiolabelled somatostatin analogues are used not only for tumour visualisation, but also for treatment of metastatic neuroendocrine tumours. Previous studies have assessed radiolabelled octreotide, but recent evidence suggests that radiolabelled octreotate has even higher binding to type II SSTR.
Aims & Methods: To estimate efficacy and tolerability of a new radiolabelled somatostatin analogue, 90Yttrium-Tyr3-DOTA-octreotate (90Y-DOTA-octreotate), in patients with metastatic neuroendocrine tumours which progressed, despite the administration of other treatments. Forty seven patients (mean age was 60.4 years, range: 34–85 years) with metastatic neuroendocrine tumours were studied. In most patients the tumours were either low or intermediate-grade, while 11 patients had high-grade tumours. The latter had received chemotherapy in the past. All patients received 1–3 cycles of the 90Y-DOTA-octreotate every 2–3 months, either intravenously (19/47,40.4%) or intra-arterialy (28/47,59.6%). In 8 patients of the latter group the intrarterial administration was combined with particle embolisation of hepatic metastases. Intravenous amino acids were also administered for protection of renal function. Clinical and/or radiological response to treatment was defined as the improvement of symptoms and/or either stabilisation or reduction of tumour growth, respectively. Mean follow-up period was 10.1 months (range 2–21 months).
Results: In all patients the post treatment scintigraphic scan demonstrated uptake and localisation by the tumour. Clinical improvement was noted in 28/47 (59.5% patients) after 1–3 treatments. Stabilisation of tumour growth was achieved in 11/17 (64.7%) patients, who had completed the 3 cycles of treatment, and in 7/13 (53.8%) in those who had 2 cycles so far. Radiological response, even lower (4/11, 36.3%), was noted also, in the high-grade group of patients who had progressed despite chemotherapy. Bone marrow toxicity (WHO grade II) was noted in 6/47 (12.7%), persisting at 3 months in two patients with significant bone metastases.

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One of them who had chemotherapy in the past, developed also irreversible mild renal failure (WHO grade II), despite prophylactic amino acids.
Conclusion: 90Y-DOTA-octreotate seems to be a well tolerated and safe treatment for patients with progressive neuroendocrine tumours, despite a risk for bone marrow toxicity in patients with large-volume bone metastases. Early results regarding efficacy are promising. Longer follow-up and more patients are required for better evaluation of tumour response.

128 IS RESEARCH WITHIN THE BRITISH SOCIETY OF GASTROENTEROLOGY IN DECLINE?

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Introduction: Abstract presentations at scientific meetings allow rapid dissemination of novel research and opportunity for peer review before submission for publication. The percentage of published abstracts from other medical speciality meetings ranges from 11%–78%. We previously demonstrated that almost 70% of abstracts presented at the BSG spring meeting of 1994 were published as a full paper. However we have also reported that the number of publications achieved by gastroenterology trainees prior to starting consultant posts has fallen over the last decade. We therefore sought to assess the outcome of abstracts presented at the BSG over the period 1994–2002.
Aims & Methods: All abstracts presented at the BSG between 1994 and 2002 were assessed. MEDLINE and EMBASE databases were reviewed using cross-referencing of first and senior author and at least one key word from the abstract title. Abstracts and possible full publications were then examined in tandem to ensure they represented the same study. Publication rates were compared between meetings and study type, design, category, sample size, journal of publication, impact factor and lag time to publication also analysed.
Results: The number of abstracts presented ranged from 578–330 but did not vary significantly between years. However the number of abstracts presented that went on to full publication fell (323 to 142; $r=-0.687$; $p=0.04$) with the percentage in 1994 (spring and autumn combined) of 57.63% falling to 30.67 by 2004 ($r=-0.761$; $p=0.02$ Pearson's correlation). While the number of publications being published in high impact (>4) journals did not differ over the years analysed the mean impact factor increased significantly (2.96–4.22; $r=0.90$; $p=0.001$), while the time to publication fell (mean (months) 23 (SD 15.04) to 19.9 (SD 12.56); $p=0.001$; Student's *t* test). There was no significant difference with regard to study type, design, category, sample size or journal of publication.
Conclusion: The number of presentations at the BSG going on to achieve full publication has fallen significantly. Possible explanations could be related to a shift in trainees expectations and targets, with acceptance of work at the BSG being seen as sufficient reward, without progression on to full publication. Another alternative is that the SPR training grade no longer necessitates a period of research to ensure career progression. Our observations may explain the documented fall in number of full publications achieved by gastroenterology trainees at the time of entry to consultant level.

1. **Sanders DS**, Carter MJ, Hurlstone DP, *et al.* Research outcomes in British gastroenterology: an audit of the subsequent full publication of abstracts presented at the British Society of Gastroenterology. *Gut* 2001;**49**:154–5.
2. **Hopper AD**, Atkinson R, Prtak L, *et al.* Research trends in British gastroenterology: publication rates in newly appointed NHS consultants over a nine year period. *Gut* 2004;**53**:913.

Abstract 128 Abstract publication rates: 1994–2002

Year	Abstracts presented (n)	Abstracts published (n)	Abstracts published (%)
1994	574	323	57.63
1995	485	223	45.98
1996	463	203	43.84
1997	330	115	34.74
1998	399	120	30
1999	578	179	30.91
2000	390	161	41.28
2001	414	146	35.34
2002	463	142	30.67

129 MAKING A MOLE HILL OUT OF A MOUNTAIN: USE OF BSG GUIDELINES AND GRS PRINCIPLES TO REGAIN WAITING LIST CONTROL IN ENDOSCOPY

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Introduction: The Queens Medical Centre in Nottingham played a major role in research work in the field of colorectal cancer screening in the 1990s. This left the department with a huge screening follow-up population. Principles of service improvement were applied to deal with a major endoscopy waiting list backlog at the Queens Medical Centre in November 2004.
Aims & Methods: The aim of this exercise was to validate all patients on the endoscopy waiting list, through applying BSG guidelines to the follow-up population, and agreed colonoscopy referral guidelines for all first diagnostic examinations. We also aimed to apply service improvement principles to all aspects of endoscopy unit work. Patient records were systematically pulled and clinical details reviewed against the principles of BSG guidelines. Other changes included introduction of partial booking, employment of an endoscopy business manager, pooling of lists, recruitment of an endoscopy fellow, and monitoring of capacity and demand data, as well as setting up waiting list initiatives at weekends for 6 months.
Results: In November 2004 we had 1431 patients awaiting first diagnostic lower GI examinations, and 965 on the follow-up or planned list. Waiting times for urgent examinations was 3 months, and for routines up to 3 years. Follow examinations were many years overdue. Of 1431 patients on the first diagnostic list, 16% were no longer appropriate, 20% diverted to Barium enemas, 10% did not respond to validation or declined the test. The remainder 54% underwent colonoscopy. Of the 965 patients on the planned waiting list 33% did not fit BSG guidelines and were removed from waiting list. 5% had their date delayed. 62% were invited to have colonoscopy, of whom 8% did not respond or declined the test. 480 colonoscopies were performed at waiting list initiatives and the remainder accommodated into unit capacity. Partial booking was introduced, and DNA rates fell from 12% to 4%. 85% of all lists previously cancelled due to annual leave or other commitments were used through cross cover.
Conclusion: Application of BSG colonoscopy guidelines and service redevelopment principles allowed reduction of waiting times for routine colonoscopy from 3 years to 6 weeks, and for planned examinations from several years overdue to being up to date.

130 MONOCLONAL ANTIBODIES TO THE COELIAC IMMUNODOMINANT GLIADIN PEPTIDE

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Introduction: The immunodominant gliadin epitope for coeliac diseae has been identified as alpha-2-gliadin 57–75. This stimulates DQ2 restricted gluten sensitive T cells in vitro and causes coeliac toxicity in vivo.
Aims & Methods: We wished to raise monoclonal antibodies to this peptide for use in assays for gluten detection. Peptide alpha-gli-57–75 was made by solid phase synthesis. Following conjugation to PPD, this was used as an immunogen in mice. Monoclonal antibodies were generated and characterised by ELISA and dot-blot assay. A competitive ELISA was used to determine the gliadin content of malt-based samples including beers.
Results: Antibody CDC-6 was found to recognise 16/16 samples of bread wheat tested, including Spelt wheat. The antibody cross-reacted with rye, barley and, to a lesser extent, oats ethanolic extracts, but not maize. Preliminary competition ELISAs revealed the presence of between 672 and 1024 ppm gliadin in three beers available in the UK. Malt and malted breakfast cereals were heavily laden with the gliadin epitope.
Conclusion: The epitope recognised by our antibody is widely distributed in bread wheat varieties, including Spelt or ancient wheat. Oats appears to have some copies of this epitope. Malting enzymes do not destroy the epitope, thus malted products are likely to be toxic for coeliac patients.

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Colorectal/anorectal posters

131 MOLECULAR ANALYSIS OF BACTERIAL DIVERSITY IN HEALTHY AND CANCEROUS COLONIC MUCOSAE

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Introduction: Several epidemiological studies have shown differences in intestinal microbiotas between various human population groups in relation to colorectal cancer risk and colorectal adenoma formation. However, mucosa associated bacterial diversity in healthy and cancerous mucosae has not been investigated.
Aims & Methods: This study investigated bacterial diversity in the healthy and cancerous mucosae using molecular analysis. Mucosal biopsies were taken from 25 patients undergoing emergency or elective surgery requiring colonic resection. None had any bowel preparation before surgery and all patients were found to have primary colonic cancer. Eight had right-side colonic tumours, while 14 had left-sided tumours, and three had lesions in the transverse colon. Fourteen patients were males (range 59–81 years) and 11 were females (range 61–76 years). Mucosal sections were taken from cancerous mucosae, and at the point furthest away from the diseased tissue (healthy mucosa). Qualitative analysis of bacterial populations was done using denaturing gradient gel electrophoresis (DGGE) and quantitative measurements by real-time PCR. Mucosal bacteria were also visualised in situ using confocal laser scanning microscopy (CLSM). Wilcoxon matched paired test were used for statistical analysis.
Results: DGGE banding profiles were found to vary between individuals, and in healthy and cancer mucosa gels in the same individual. Real-time PCR showed that mucosal cell population densities were significantly higher in healthy colonic mucosa compared with cancerous tissue, and that they were not dependent on location of the lesion. Lactic-acid producing bacteria such as species belonging to the genera Bifidobacterium and Lactobacillus were significantly higher on the healthy mucosa ($p<0.005$), while counts of E coli, other enterobacteria and bacteroides were significantly higher at tumour sites ($p<0.005$).
Conclusion: Mucosal-associated bacterial diversity and distribution on healthy and cancerous mucosae were host dependent, in that considerable interindividual variation was observed. Specific patterns of bacterial colonisation at colonic cancer sites may be a contributory factor in the aetiology of CRC, while other bacteria may have protective functions.

132 REFERRAL LETTERS FOR TWO WEEK WAIT FOR SUSPECTED COLORECTAL CANCER DO NOT ALLOW A STRAIGHT-TO-TEST PATHWAY

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Introduction: Some clinicians have argued that 2 week wait rule for suspected colorectal cancer patients can go ''straight to test'' to facilitate time to diagnosis and treatment. However, others have felt that referral letters are not reliable enough to allow this pathway.
Aims & Methods: We have studied the letters referring patients under the 2 week wait rule for suspected colorectal cancer prospectively over a 6 month period. The examining consultant was asked to outline the tests he would perform having read the letter, and then again after a consultation with the patient. The outcome of these tests was tracked.
Results: Between April 2006 to September 2006, we studied 217 patients with a median age of 73 (range 24–94), referred under the 2 week wait rule for suspected colorectal cancer. Having only read the referral letter the most frequently requested test was colonoscopy (55%) then barium enema (21%), colonoscopy with CT (18%), followed by flexible sigmoidoscopy or CT scan alone (7%, 5% respectively). After consultation with the patient, tests requested based on the GP letter were changed in 90 patients (41%), 47% were booked for colonoscopy, 19% for colonoscopy with CT scan, 16% for barium enema, 11% for flexible sigmoidoscopy, 7% for CT scan, and flexible sigmoidoscopy with barium enema in 1 patient. The referral indication which had tests changed most often was definite palpable rectal mass (75%), while patients referred with definite palpable right-sided abdominal mass had their tests least often changed (11%). A total of 22 patients were found to have colorectal cancers (10%), 30 patients were diagnosed with polyps (14%). Only 19 out of 143 colonoscopies (13.2%) showed pathology beyond the sigmoid colon (4 cancers and 15 polyps), and of those who had a flexible sigmoidoscopy initially, only 3 subsequently went on to have colonoscopy.
Conclusion: A significant number of patients had tests changed after a clinical consultation. However only a small number required further investigations having had a consultation prior to their initial investigations. We conclude that 2 week wait patients for suspected colorectal cancer should be seen in the clinic and should not proceed straight to test.

133 PREOPERATIVE CARDIAC ASSESSMENT FOR ELECTIVE PELVIC COLORECTAL CANCER SURGERY: DO WE NEED GUIDELINES?

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Introduction: The fundamental role of preoperative assessment in elective surgery is to identify patients who present with specific risk factors that potentially increase the risk of surgical complications or death from the planned surgery. In particular, patients awaiting colorectal surgery are regarded to be at an increased risk simply because of the very nature of this type of surgery which is defined as intermediate to high risk.
Aims & Methods: Our aim was to assess the availability and application of guidelines for the process of cardiac risk assessment of patients undergoing elective pelvic colorectal cancer surgery. We circulated a questionnaire to 400 colorectal surgeons in the UK who are members of the ACPGBI who agreed for their details to be circulated for answering research questionnaires investigating whether departmental/unit protocols existed for the routine preoperative cardiac assessment of patients undergoing colorectal pelvic cancer surgery. We also proposed 3 clinical scenarios and asked respondents to indicate the most appropriate tests for each. Finally we asked respondents to indicate if they thought there is a role for formal guidelines for the cardiological preoperative workup for ALL elective pelvic colorectal cancer cases.
Results: Of the 400 questionnaires sent, 200 replies were completed (50%). Some 149 (74.5%) indicated that they do not have a departmental/unit protocol for the routine preoperative cardiac assessment of patients undergoing colorectal pelvic cancer surgery. Of the 45 (22.5%) who did have such a protocol, 17 (9%) used guidelines based on local research, 12 (6%) used the American College of Cardiology/American Heart Association guidelines and 19 (10%) indicated that they used guidelines obtained from nationally published data. There was wide variation in the answers to choosing the investigations most appropriate in the 3 hypothetical clinical scenarios. Only 80 (40%) thought there is a role for cardiology guidelines in the preoperative workup for all elective pelvic colorectal cancer cases.
Conclusion: In patients undergoing elective pelvic colorectal cancer surgery (surgery with the highest morbidity and mortality rate of all elective colorectal cancer cases) there are no uniform national guidelines and wide variation in local guidelines among colorectal surgeons. Similar patients may be undergoing widely differing preoperative investigations in different centres and it would seem there is a clear need for standardisation in this area in this high risk group.

134 A NOVEL FINDING—GLOBAL DNA HYPOMETHYLATION IN DIVERTICULAR DISEASE: A PILOT STUDY (THE BORICC STUDY)

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Introduction: Structural changes within the colonic wall result in the formation of colonic outpouchings seen in diverticular disease (DD). Consequently, there is some evidence to suggest that changes in gut microbiota with resultant decreased immune response drives a low grade mucosal inflammatory response.[1] We hypothesise that this inflammatory response may have effects on the colonocyte genome, specifically, epigenetic changes such as DNA methylation. There is no data to date on genomic DNA methylation status in DD.
Aims & Methods: To determine the DNA methylation status in a cohort with macroscopically non-inflammed DD. 29 subjects were recruited (10 DD patients and 19 age and sex-matched normal controls). Colorectal mucosal biopsies were obtained and DNA extracted. Genomic DNA methylation was measured using the tritium-labelled cytosine extension assay (3[H] dCTP) as described by Pogribny *et al.*[2] In this assay, the extent of 3[H] dCTP

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Abstract 134

Subject group	Age (SD)	hs CRP (mg/dl)	Genomic DNA methylation (DPM × 10^3/μg DNA)
Normals (n = 19) M:F = 1:1	58 (11)	1.3 (1.4–3.1)	12.3 (8.2–15.8)
DD (n = 10) M:F = 1:1	58 (11)	3.3* (1.8–5.8)	28.3* (15.3–50)

*Statistically significant. Figures in brackets indicate 95% confidence interval.

incorporation into DNA is inversely proportional to the global DNA methylation status. Blood was collected for measurement of serum high sensitivity C-reactive protein (hs CRP).
Results: DD subjects had significantly higher level of methylation ($p<0.03$) than control subjects. Folate status was similar in both groups. After controlling for smoking, DD subjects had a higher hs CRP value compared to controls which was statistically significant ($p<0.04$) (hs CRP was measured in 9 controls).
Conclusion: In this pilot study, we have shown evidence of global DNA hypomethylation in patients with diverticular disease possibly as a consequence of low grade mucosal inflammation. There is evidence of systemic subclinical inflammation as determined by elevated hs CRP levels in DD subjects compared to controls. Further studies to correlate inflammatory markers within faeces with methylation status is underway.

This study is funded by the Food Standards Agency (N12015)

1. **Foch M**, *et al. J Clin Gastroenterol* 2004;**38**(Suppl 5):S2–7.
2. **Pogribny I**, *et al. Biochem Biophys Res Commun* 1999;**262**:624–8.

135 NOVEL PRELIMINARY FINDINGS OF MITOCHONDRIAL DNA MUTATIONS IN COLONIC CRYPTS OF PATIENTS WITH DIVERTICULAR DISEASE (THE BORICC STUDY)

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Introduction: We have previously shown that mitochondrial DNA (mtDNA) mutations may act as a putative biomarker for DNA damage.[1] Oxidative damage which can occur as a result of chronic inflammation, may cause mtDNA mutations which unlike nuclear DNA, is not as well protected. MtDNA mutations have been shown to occur within colonic crypt stem cells which clearly result in respiratory chain deficiency.[2]
Aims & Methods: To characterise the presence of cytochrome c oxidase (COX) deficient crypts and the accumulation of mtDNA mutations in colonic crypts of patients with Diverticular disease (DD). Fresh frozen colorectal tissue from 35 patients; 25 age and sex-matched patients with macroscopically normal colons as well as tissue from 10 patients with DD were analysed histologically and histochemically. COX deficiency is the pathological hallmark of mtDNA mutations. The percentage of COX deficient crypts were calculated from transverse sections counted; only crypts that had more than 50% COX deficient cells were defined as COX deficient.
Results: Percentage COX deficient crypts were significantly higher in those with DD ($p=0.04$). High sensitivity C Reactive Protein (hs CRP), was also higher in the DD group but this did not reach statistical significance (hs CRP was measured in 13 controls).
Conclusion: This novel preliminary finding of higher COX deficiency within colonic crypts in DD compared to controls suggests a further role of COX in characterising mt DNA mutations. Further studies to correlate dietary intake with these mutations are underway.

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1. **Arasaradnam RP**, *et al. Gut* 2006;**55**:11 A24.
2. **Greaves LC**, *et al. Proc Natl Acad Sci U S A* 2006;**103**:714–19.

136 PERCUTANEOUS ENDOSCOPIC COLOSTOMY WITHIN A TERTIARY REFERRAL COLORECTAL PRACTICE: EVIDENCE TO SUPPORT CURRENT NICE GUIDELINES?

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Introduction: Percutaneous endoscopic colostomy (PEC) is an alternative to surgery in patients with recurrent sigmoid volvulus, recurrent pseudo-obstruction and severe slow transit constipation. A percutaneous tube, placed under direct endoscopic visualisation in the colon, acts as an irrigation or decompressant channel or, via direct traction and secondary fibrosis, provides colonic ''fixation'' to the anterior abdominal wall. NICE has recently published official guidance on PEC use in the UK but recommendations are restricted because of the paucity of published experience. We report our prospectively obtained experience particularly concerning the safety and efficacy of PEC insertion at a single tertiary referral centre.
Aims & Methods: Thirty three patients with recurrent sigmoid volvulus, acute or chronic pseudo-obstruction and idiopathic slow transit constipation were selected to undergo the procedure. Using a technique similar to percutaneous endoscopic gastrostomy insertion, PEC tubes were placed in the appropriate colonic sites. Patients with recurrent sigmoid volvulus and constipation had their tubes left in indefinitely whereas patients with pseudo-obstruction had their tubes left in for a variable period of time depending on their symptoms.
Results: Thirty five procedures were performed on 33 patients who were followed up for a median period of 35 months (range 21–89). 19/33 (58%) patients underwent PEC for recurrent sigmoid volvulus. 10/33 (30%) patients underwent PEC for idiopathic slow transit constipation and 4/33 (12%) for recurrent pseudo-obstruction. Three patients (9%) developed peritonitis. Two were fit for operation, 1 having a laparotomy and washout and the other, a sigmoid colectomy. Two patients who had PEC insertion for constipation required subtotal colectomy; one because of faecal urgency and the other because of site pain. There were other minor complications (bleeding, site infection, ''buried bumper syndrome'' and pain) in 8 patients with PEC resiting required in 2 cases. There was one recurrence of sigmoid volvulus because of the removal of one of 2 PECS due to infection. Subsequent resiting of a PEC was successful in this patient. There was no recurrence of symptoms in any other patients with a PEC in situ. Eventual symptom resolution occurred in 29 patients (88%).
Conclusion: This is the largest prospective study to date addressing the safety and efficacy of PEC. It adds to the minimal existing data on the procedure and confirms the addition of the PEC procedure to the therapeutic armamentarium for the treatment of recurrent sigmoid volvulus and colonic motility disorders, particularly in the high surgical risk patient.

137 FLEXIBLE SIGMOIDOSCOPY AND BIOPSY FOR INVESTIGATION OF DIARRHOEA: HIGH RATE OF MICROSCOPIC ABNORMALITY IN MACROSCOPICALLY NORMAL MUCOSA

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Introduction: Flexible sigmoidoscopy (FS) is frequently used to investigate both acute onset diarrhoea that fails to resolve and chronic diarrhoea. Routine biopsy is recommended to avoid missing diagnoses that may not

Abstract 135

Subject group	Age (SD)	hs CRP (mg/dl)	% COX deficiency
DD (n = 10) M:F = 1:1	58 (11)	3.3 (1.8–5.8)	7.7* (3.8–12.2)
Control (n = 25) M:F = 1:1	59 (11)	1.9 (1.8–3.8)	3.2 (1.6–5.3)

*Statistically significant. Figures in brackets indicate 95% confidence intervals.

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Abstract 137 Histological findings

	Macroscopically normal	Macroscopically abnormal	Macroscopic appearance unknown	Total
Procedures	162	110	19	291
Biopsied	81	78	8	167
Histology				
Normal	63	19	3	85
Polyp/dysplasia	2	12	0	14
Ulcerative colitis	0	10	0	10
Crohn's colitis	1	3	0	4
Indeterminate colitis	2	12	0	14
Pseudomembranous Colitis	0	2	0	2
Infectious colitis	7	5	2	14
Microsopic colitis	1	0	1	2
Melanosis coli	1	1	0	2
Non-specific inflammation	3	5	1	9
Other	1	5	1	7
Adenocarcinoma	0	4	0	4

be apparent on macroscopic appearance such as microscopic and collagenous colitis.

Aims & Methods: We conducted a retrospective study to assess biopsy rate and looked at macroscopic findings and histological findings arising from 1 year's worth of FS preformed for investigation of diarrhoea. Details of all FS performed between March 2005 and March 2006 were obtained using the Endoscribe database search facility, where the indication field contained the word ''diarrhoea''. These records were exported to a Microsoft Access database and matched with the corresponding histological records from the hospital central datastore. We then determined what proportion of procedures had had biopsies, and what diagnoses made, both macroscopically and with histology. We assessed the correlation between endoscopic diagnosis and histological.

Results: The macroscopic diagnosis was ''normal'' in 162 cases, ''abnormal'' in 110 cases and ''unstated'' in 19 cases (see table). In the macroscopically normal group, biopsy was carried out in 81 (50%) of cases. 18 of these biopsies (22%) demonstrated significant abnormalities (see table).

Conclusion: Performing biopsies, even with macroscopically normal mucosa, results in a high diagnostic yield. We recommend that routine biopsies should be performed in all new cases of diarrhoea requiring investigation by flexible sigmoidoscopy. Failure to do so could result in missed diagnosis in as many as 22%.

138 THE ASSOCIATION OF PROXIMAL COLORECTAL NEOPLASIA AND DISTAL POLYPS IN A LARGE DISTRICT GENERAL HOSPITAL

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Introduction: It has been suggested that flexible sigmoidoscopy is an effective screening tool for colorectal carcinoma because a high proportion of cancers are within reach of the flexible sigmoidoscope and as many as 50% of proximal cancers will have distal polyps leading to colonoscopic examination. We report our experience of colorectal cancer over a 26 month period and identify how many proximal advanced colorectal neoplasias would be discovered if flexible sigmoidoscopy was the initial investigation and further examination depended on the presence of distal polyps.

Aims & Methods: Endoscopic records were analysed to identify all patients diagnosed with colorectal cancer by colonoscopy or flexible sigmoidoscopy from 11/05/06 to 26/07/06. The histology results were reviewed to confirm the diagnosis. Only adenocarcinomas were included. The presence and position of polyps found on the examination finding a cancer or any previous examinations within the time period were recorded. Cancers were considered either proximal (caecum to splenic flexure) or distal (descending colon to rectum.)

Results: 239 patients were identified as having a tumour by the endoscopist in 2594 colonoscopies and 3682 flexible sigmoidoscopies. 223 patients had an adenocarcinoma confirmed on histology. 49 (22%) of 223 colorectal adenocarcinomas were proximal to hepatic flexure. Of these 49 tumours only 5 (10%) were associated with distal polyps. The 5 patients with proximal cancer and distal polyps, had polyps in sigmoid (4) or descending colon (1). 1 hyperplastic, 1 not biopsied, 3 tubulvillous adenoma with severe dysplasia.

Conclusion: The distribution of colorectal cancer is similar to that reported previously with 22% of colorectal cancers being found proximal to the splenic flexure. These results suggest that the presence of distal polyps may be a less reliable trigger for full colonoscopic examination than previously reported. A proposed method of screening for colorectal cancer using a flexible sigmoidoscopy followed be a colonoscopy if distal polyps were identified would miss 44 of 49 (90%) of proximal cancers in this population. However 80% of cancers would still be identified. The finding of a hyperplastic polyp in one patient would not prompt further examination based on previously used criteria (size >1 cm, villous histology, multiple polyps, severe dysplasia or malignancy) therefore 45 of 49 (92%) of proximal cancers would be missed. Previous studies have suggested that 48–54% of proximal colorectal cancers are associated with distal polyps, much higher than our findings. Flexible sigmoidoscopy is safer, cheaper, and more convenient for patients than colonoscopy but its efficacy for detecting proximal cancer in a screening programme may be much lower than previously suggested.

139 FUNCTIONAL SYMPTOMS AND THEIR PSYCHOLOGICAL CORRELATES IN PATIENTS WITH A RECTOCOELE AND EVACUATION DIFFICULTIES

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Introduction: Evacuation difficulties associated with a rectocoele often have a coexistent functional component. Ignoring problems such as pelvic incoordination, digitation and straining is associated with poor outcome from surgery. Biofeedback treats abnormal function and addresses concomitant psychological features. Whether psychological or anatomical factors are associated with specific functional symptoms is unknown. The aim of this study was to identify the interplay of functional, psychological and anatomical factors in patients with evacuation disorder. This has potential implications for choice of treatment.

Aims & Methods: Seventy three women with evacuation difficulties attributed to a symptomatic rectocele underwent standard anorectal physiology (manometry and sensitivity) and barium proctography. Psychological assessment was by questionnaire: Hospital Anxiety and Depression Scale to assess anxiety (HAD-A) and depression (HAD-D); psychometric functioning using the SCL-90, focusing on somatisation (SOM) and obsessive compulsive traits (OC). The SCL-90 questionnaire generates a global severity index subscale (GSI), estimating overall burden of psychological morbidity.

Results: Patients who vaginally digitated (22/73, 30%), compared to those who did not, had lower levels of anxiety (8 *v* 5.7, $p=0.04$) somatisation (SCL-SOM 50.3 *v* 55.8, $p=0.01$) and psychological morbidity (SCL-GSI 50.3 *v* 53.5, $p=0.02$). Comparing those who digitated anally (20/73, 27%) to non-digitators there were hypersensitive to rectal distension (urge volume 95 *v* 74 ml, $p=0.03$). This was associated with greater anxiety (HAD-A 9.1 *v* 6.6, $p<0.03$) and higher scores of SCL-SOM (59.9 *v* 51.9, $p=0.0003$), SCL-OC (55.7 *v* 51.3, $p=0.01$) and SCL-GSI (56.6 *v* 51.1, $p=0.002$). For those that strained to evacuate (46/73, 63%) compared to

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those who didn't there was tendency to depression (HAD–D 8.3 *v* 6.0, p=0.04), SCL-OC (53.8 *v* 50.2, p=0.02) and SCl–GSI (53.6 *v* 50.8, p=0.03). There was an inverse correlation between distension threshold and anxiety (urge volume $r=-0.3$, p=0.01) and somatisation (urge volume $r=-0.62$, $p<0.01$). There were no correlations between rectocoele size and psychological or anorectal physiology variables.
Conclusion: We have shown that specific anorectal symptoms correlate with specific psychological profiles—vaginal digitators have low anxiety and somatisation scores, anal digitators high anxiety, somatisation and obsessive traits. The relation between anxiety or somatisation and rectal distension sensitivity highlights the close relation that exists between psychological state and gut function. This study demonstrates the importance of addressing psychological influences in patients with evacuation difficulties, even if associated with a large trapping rectocoele, a common independent indication for surgery.

140 COMPONENTS OF THE RECTO-ANAL INHIBITORY REFLEX CORRELATE WITH GUT SYMPTOMS IN FUNCTIONAL AND NEUROPATHIC CONDITIONS

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Introduction: The recto-anal inhibitory reflex (RAIR) describes the transient relaxation of the anal sphincter in response to rectal distension. It is a measurable reflex that reflects the integrity of an important aspect of the mechanism maintaining faecal continence, namely the sampling mechanism. The anatomic substrate of the reflex is at enteric nerve plexus level, being absent in Hirschsprung's disease and after low anterior resections, but being preserved in spinal cord injury (SCI). The aim of this study was to analyse whether distinct components of this reflex can be differentiated in healthy volunteers (HV), patients with idiopathic faecal incontinence (FI), constipation, multiple sclerosis (MS) and SCI.
Aims & Methods: As part of standard anorectal physiology, the following subjects had assessment of their RAIR: 21 HVs (14 female, mean age 35), 78 FI (63 female, mean age 45; urge FI in 44, passive FI in 34); 74 constipation (59 female, mean age 32; slow transit (STC 47), evacuation dysfunction 27); 49 MS (31 female, mean age 40; 35 with FI, 14 constipation); 71 SCI (32 female, mean age 37; 46 supra-conal, 25 cauda equina). The reflex was elicited by rapid inflation of 50 ml of air into a latex balloon seated at the top of the anal canal, while recording maximal resting pressure with an 8 channel water-perfused manometry system.
Results: Three phases of the reflex were identified—the latency from stimulus to maximal sphincter relaxation; the duration of maximal relaxation; the time to recovery of resting pressure. FI patients: neither urge nor passive FI was associated with any significant difference in RAIR phases compared to controls. Compared with controls, patients with post-defecation soiling had longer maximal relaxation (0.5 *v* 1.2 s, $p<0.03$) and longer recovery time (4.3 *v* 6.3 s, $p<0.05$). Constipation: neither STC nor evacuation dysfunction was associated with any changes in reflex phases compared to controls. MS: MS patients with FI, not constipation, had longer latency (2.7 *v* 1.8 s, $p<0.03$) and longer maximal relaxation (1.2 *v* 0.7 s, $p<0.05$). SCI: Compared to controls, both supra-conal and cauda equina patients had longer latencies (1.6 *v* 2.6 *v* 2.0 s, $p<0.05$ both), and cauda equina patients only had longer recovery (6.6 *v* 4.3 s, $p<0.02$).
Conclusion: Analysing components of the RAIR provides reproducible and potentially helpful information in understanding the pathophysiology of gut symptoms in functional and neuropathic conditions. In functional FI, post-defecation soiling is associated with an abnormally prolonged RAIR, suggesting that delayed recovery of internal sphincter tone is responsible for this symptom. In neuropathic conditions similar abnormal phases of the RAIR in MS and SCI may explain the faecal incontinence seen in some of these patients.

141 WHAT DOES MR PROCTOGRAPHY ADD IN COMPARISON TO FLUOROSCOPIC PROCTOGRAPHY IN PATIENTS WITH EVACUATION DIFFICULTY?

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Introduction: In investigating the functional abnormalities that occur in patients with evacuation difficulties, erect fluoroscopic barium proctography (FP), the current gold standard, imparts a small but significant dose of ionising radiation. Furthermore, impaired evacuation is often a symptom of more global pelvic floor dysfunction, and accurate assessment of the anterior and middle pelvic compartments may help optimise therapeutic strategy. Supine MR proctography (MRP) allows assessment of the whole pelvis, although its role in assessing rectal evacuation dynamics has not been validated. Finally, the putative clinical value of MRP over FP has not been evaluated.
Aims & Methods: Thirty women with evacuation difficulty underwent both FP and MRP according to standard protocols. MRP was reported by a GI radiologist, blinded to the result of FP. A consensus committee (gastroenterologist, 2 colorectal surgeons, 2 urogynaecologists, 2 GI radiologists) undertook live reporting of FP, knowledgeable of the clinical findings. Each patient's MRP was then reviewed by the committee, and additional findings not identified by FP were noted to create a consensus reference standard. Note was then made as to whether FP and MRP agreed, under- or overestimated abnormalities compared to this standard. The impact of each imaging modality on (1) diagnostic confidence and (2) management was assessed by the clinician in charge (visual analogue scale, VAS).
Results: Both tests agreed with the consensus diagnosis in 11/30 (37%), MRP alone in 9/30 (30%) and FP alone in 10/30 (33%). MRP failed to identify: anismus (5/13, 38%), intussusception (8/18, 44%), trapping within a rectocoele (1/11, 9%) and pelvic floor descent on straining (8/29, 28%), compared to 1/13, 8%; 5/18, 28%; 3/11, 28% and 3/29, 10% respectively for FP. MRP overestimated rectocoele size in 9/30 (30%) but revealed peritoneocoeles in 8 patients, cystocoeles in 26 and gynaecological prolapse in 25, none of which were identified by FP. Referring clinicians found the combination of both tests helpful in influencing management over either test individually in 12/30 (40%), particularly when abnormalities of anterior or middle compartments were identified. MRP was deemed unhelpful in influencing management in 10/30 (30%), (of whom 6 (60%) had underlying anismus), and FP in 6/30 (20%).
Conclusion: MRP identifies abnormalities in anterior and middle pelvic compartments. However, MRP underestimates prevalence of functional rectal evacuation difficulties and intussusception, possibly due to patient positioning and reduced viscosity of contrast gel compared to barium. Fluoroscopic and MR proctography are complementary, and particularly where patients have combined functional and anatomical abnormalities.

142 MUCOSAL BACTERIAL ISOLATES FROM HUMAN COLON CANCER INDUCE NUCLEAR LOCALISATION OF BETA CATENIN IN HUMAN COLON CANCER EPITHELIAL CELLS

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Introduction: Dysregulation of Wnt/β-catenin signaling followed by nuclear translocation of β-catenin is an early event in oncogenesis. Mucosa-associated E coli are found in increased numbers in colonic mucosa in patients with colon cancer.[1] We hypothesise that mucosa-associated E coli may play a role in colon cancer pathogenesis by interacting with epithelial cells and inducing nuclear translocation of β-catenin.
Aims & Methods: The effect of E coli isolated from human colon cancers on localisation of β-catenin in colon epithelial cells was studied. DLD-1 cells, a colon carcinoma cell line with biallelic inactivation of adenomatous polyposis coli gene, were cultured with eight E coli mucosal isolates from patients with colon cancer and K-12, a laboratory E coli strain. Cells were incubated with bacteria for 4 hours (at a bacterium to cell ratio of 100:1) and then incubated in cell culture medium containing gentamicin (500 mg/l) for 16 hours. Serum-starved cells were incubated with Prostaglandin-E2 as a positive control.[2] Cellular localisation of β-catenin was assessed by immunofluorescence microscopy. Images were analysed using AQM Advance 6 software (Kinetic Imaging, UK) and nuclear localization of β-catenin was quantified and expressed as a ratio of the intensity of nuclear to whole cell fluorescence.
Results: The ratio of the intensity of nuclear to whole cell β-catenin (N:WC) was greater in DLD-1 cells incubated with mucosal E coli isolates (n=8; mean N:WC ratio=1.047; SD 0.427) compared to the negative control (no bacteria; mean ratio N:WC=0.906; SD 0.250, $p<0.0001$). Incubation with E coli K12, however, had no significant effect on β-catenin nuclear localisation (p=0.385). When the effect of each of the E coli isolates was analysed separately, no significant difference in the ratio of nuclear to whole cell fluorescence was observed in DLD-1 cells incubated with the E coli isolate HM44 (ratio N:WC 0.940; SD 0.341) compared to the negative control (p=0.354). Incubation with each of the other seven isolates produced a significantly increased ratio ($p<0.05$). Bacterial supernatant from colon cancer E coli isolate HM329 also caused increased

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nuclear translocation of β-catenin (ratio N:WC 1.064; SD 0.406; p=0.085).
Conclusion: Mucosal E coli isolates from colon cancer induce nuclear localisation of β-catenin in human colon cancer epithelial cells. This supports the hypothesis that mucosa-associated bacteria may promote development of human colon cancer through regulation of β-catenin signalling.

1. **Martin**, *et al.* Enhanced E. coli adherence and invasion in Crohn's disease and colon cancer. *Gastroenterology* 2004;**127**:80–93.
2. **Castellone**, *et al.* Prostaglandin E2 promotes colon cancer cell growth through a Gs-axin-beta-catenin signaling axis. *Science* 2005;**310**:1504–10.

143 WHAT IS THE BEST METHOD FOR ASSESSING SEVERITY IN FUNCTIONAL CONSTIPATION—EVALUATION OF SYMPTOMS BY THE CLINICIAN, PERFORMING INVASIVE INVESTIGATION OR SELF-ASSESSMENT OF QOL BY THE PATIENT?

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Introduction: Functional constipation (FC) is assessed by describing symptoms deemed by clinicians to be markers of severity (eg stool frequency, consistency). Results of invasive investigation (eg transit study, proctography) can also be used. However, symptom assessment by clinician is not always precise and the assumption that investigation results correlate with severity is not validated. Evaluating the impact that FC has on quality of life (QOL) may be more representative of severity.
Aims & Methods: To determine whether symptom evaluation by clinician, results of investigations or patient measurement of constipation specific QOL gives the best assessment of severity by correlating with a validated measure of overall QOL. Symptoms in consecutive FC patients (Rome II criteria) assessed by a single clinician using a Likert scale. Cumulative constipation score (CC-score) also calculated. Radio-opaque marker studies (total and segmental transit time) and radio-isotope defecating proctography[1] performed (% evacuation, evacuation rate, evacuation time, pelvic floor descent). Patient Assessment of Constipation (PAC-QOL)[2] to assess constipation specific QOL (high score = poor QOL). SF-36 to assess overall QOL (high score = good QOL). SF-36 includes Physical Component Summary (PCS) and Mental Component Summary (MCS). Normal population reference values are available.[3] Analysis by Pearson correlation.
Results: 122 patients: 97% female. Mean age: 43 years. Complete data for all. Mean PCS 43, mean MCS 36 (normal reference 50). No correlation between overall QOL (PCS and MCS) and clinician evaluation of symptoms or CC-score. No correlation between PCS or MCS and colonic transit (either total or segmental). No correlation between overall QOL and proctographic parameters. There was correlation between constipation specific QOL and overall QOL: PAC-QOL *v* MCS ($r=-0.5$, $p<0.01$); PAC-QOL *v* PCS of SF-36 ($r=-0.3$, $p<0.01$). PAC-QOL did not correlate with transit, proctographic parameters, CC score or individual symptoms.
Conclusion: Overall QOL is reduced in FC compared to the normal population. Patient self-assessment of QOL is the method of choice for measuring severity in FC rather than symptom evaluation by clinician or the results of invasive investigations. These latter approaches still have a role to play in diagnosis and management. Assessing overall and constipation specific QOL provides information about severity relevant to everyday practice and research.

1. **Papachrysostomou M**. Obstructive defecation and slow transit constipation: Proctographic parameters. *Int J Colorectal Dis* 1994; **9**:115–20.
2. Mapi Research Trust.
3. QualityMetric inc.

144 CAN ENTEROCUTANEOUS FISTULA BE EFFECTIVELY MANAGED IN A REGIONAL UNIT?

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Introduction: The management of enterocutaneous fistula following surgery involves a multidisciplinary approach. It has been suggested that complex cases should only be managed in selected national centres.
Aims & Methods: This was a prospective study of 51 patients with established enterocutaneous fistula referred to a regional unit over a 16 month period. Six were internal referrals, 45 from institutions elsewhere. 42 were small bowel, 9 large bowel, with 18/51 (35%) associated with inflammatory bowel disease. Mean age was 51, with the median number of previous operations 3. The establishment of nutritional support, eradication of sepsis, appropriate wound management and restoration of normal physiology was attempted in all cases. Definitive surgical management was deferred for at least 6 months after the last abdominal surgical intervention. 11 (22%) were dependent on parenteral nutrition. All patients were followed up for a minimum of 6 months.
Results: The overall mortality was 4 (8%), in all cases before definitive surgery; three from overwhelming sepsis, the other from mesenteric infarction. 18/48 (38%) fistula healed spontaneously. 30 (62%) underwent definitive surgical management with a re-fistula rate of 4 (14%). Only one of these required further surgery, 3 healing spontaneously. There were no postoperative deaths. No patients were left dependent on parenteral nutrition.
Conclusion: The results compare favourably with those obtained in designated national centres for the management of enterocutaneous fistula (overall mortality 9.5–10.8%, operative mortality 3–3.5%)[1, 2] and suggest that these patients can be effectively managed in regional units. In addition, more local treatment may improve patients' psychological ability to deal with a condition that involves prolonged in patient care.

1. **Lynch AC**, Delaney CP, Senagore AJ, *et al.* Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery. *Ann Surg* 2004;**240**:825–31.
2. **Hollington P**, Mawdsley J, Lim W, *et al.* An 11-year experience of enterocutaneous fistula. *Br J Surg* 2004;**91**:1646–51.

145 RECTAL ADMINISTRATION OF HIGH DOSE VANCOMYCIN IS SUCCESSFUL IN INDUCING REMISSION OF CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA WHICH HAS FAILED TO RESPOND TO STANDARD THERAPY

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Introduction: Clostridium difficile is a common cause of nosocomial infection in the UK. It is associated with marked morbidity and caries a mortality of up to 2–4%. Failure to respond to medical therapy occur in 7–20% of patients often resulting in total colectomy. Vancomycin resistance is rare. The authors describe an alternative method of antibiotic administration, which promises to reduce the need for surgical intervention.
Aims & Methods: Three patients with CDAD on SHEA criteria were identified who demonstrated failure to induce clinical remission following standard therapy with oral metronidazole, oral vancomycin, Brewer's yeast and intravenous immunoglobulin. All patients received rectal vancomycin 500 mg in 250 ml of 0.9% saline qds. All patients had plasma vancomycin levels monitored on alternate days throughout therapy.
Results: Remission was induced in all patients within six days following which they were converted to oral vancomycin and discharged on a tapering 6-week regime. Despite the theoretical risk of absorption of vancomycin through denuded mucosa in severe colitis, plasma vancomycin levels were undetectable throughout the treatment period. No significant side effects were identified in any patients undergoing rectal therapy.
Conclusion: In patients who have failed to respond to standard medical therapy for proven CDAD, rectal vancomycin appears to offer a promising alternative to colectomy. These encouraging early results will need to be confirmed by a suitably powered randomised controlled trial. However in patients unsuitable or unwilling to undergo colectomy following standard medical management, this approach may offer an attractive alternative.

1. **Gerding DN**, *et al. Infection Control Hospital Epidemiology* 1995;**16**:459–77.

146 FAILED COLONOSCOPY: THE RADIOLOGICAL SOLUTION FOR ACHIEVING COLORECTAL CANCER TARGETS

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Introduction: Introduction of the 31 and 62 day targets in colorectal surgery has increased pressure on colonoscopic resources.[1 2] Even in expert hands, incomplete colonoscopy occurs in approximately 10% of

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cases.[1 3] This introduces delay and the need for further investigations while the ''clock is ticking''.

Aims & Methods: To achieve a system that would allow complete radiological imaging for at least 80% of patients undergoing incomplete colonoscopy. This imaging should be provided on the original bowel preparation and therefore within a suitable time period. All patients undergoing colonoscopy over a three-month period were observed. Those having failed colonoscopy were assigned to further bowel imaging (either barium enema or CT colonoscopy (CTC), according to protocol). CTC was indicated if a stricture prevented colonoscopic completion. Patients intolerant to endoscopy underwent barium enema.

Results: Out of 470 attempted colonoscopies, 34 failed (5M, 29F), mean age 61 years (range 22–86). Hence a completion rate of 93%. 14(41%) of the failures were due to poor bowel preparation, making them inappropriate to undergo another bowel study on the protocol. 20 (59%) were appropriate to have a further study and 12 (60%) underwent a further test. Two had a CTC and 10 had barium enemas (7 same day, 2 following day, 1 after weekend). Two of the barium enema reports stated poor coating of the bowel. Eight (40%) did not follow the study's protocol for individual reasons. In 3 patients colonoscopy revealed a tumour and CT staging was required. One patient refused further investigation, and imaging for another was not arranged. Two had a looping/fixed sigmoid and 1 had a sigmoid stricture with no lesion discovered on water soluble study.

Conclusion: The incomplete colonoscopy rate of 7% resulted on a practical ability to provide a service for same day preparation imaging. Colonoscopic preparation did not leave the colon ''too wet'' therefore CTC and barium enema gained reliable results. 13 out of 20 (65%) either had or were offered a further study, therefore, saving diagnostic time and preventing repetitive bowel preparations without risk of swamping an already ''full'' imaging service. With continuing use of this protocol, complete bowel imaging could be achieved in close to 100% patients.

1. **Scott MA**, Knight A, Brown K, *et al.* A single common urgent pathway for all colorectal referrals reduces time to diagnosis and treatment. *Colorectal Dis* 2006;**8**:766–71.
2. **Thorne K**, Hutchings HA, Elwyn G. The effects of the Two-Week Rule on colorectal cancer diagnostic services: a systematic literature review. *BMC Health Serv Res* 2006;**3**:43.
3. **Glancy DG**, *et al.* Fast-track barium enema: meeting the two-week wait rule for patients with suspected colorectal cancer. *Colorectal Dis* 2005;**7**:241.

147 CLOSTRIDIUM DIFFICILE: EXPERIENCE OF THE HIGHLY-VIRULENT EPIDEMIC STRAIN 027

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Introduction: Outbreaks of C difficile-associated diarrhoea (CDAD) due to the strain O27 have occurred since 2001 and are associated with increased complications and mortality. In an 83 case outbreak of CDAD in our hospital, O27 was the predominant strain.

Aims & Methods: We studied patient notes and drug charts and compared previous antibiotic exposure to total antibiotic usage in the hospital (expressed as number of days of use or patient-days) during the outbreak to determine the risk of a particular antibiotic being associated with CDAD.

Results: We obtained full data for 69 patients, mean age 84.1. Early in the outbreak 12 out of 14 stool isolates were O27. 59 patients received antibiotics in hospital before the onset of diarrhoea. Cefuroxime was the antibiotic most closely associated with CDAD. A significantly weaker association was found for several other antibiotics (see table). In 10 cases cefuroxime was given as a single prophylactic dose at the time of surgery and in 5 this was the sole hospital antibiotic exposure. 53 patients were treated initially with oral metronidazole (Met); 6 died before day 10; 17 (32%) responded within 10 days (30-day mortality 0%); 30 did not respond by day 10 (30-day mortality 20%). 6 patients unable to take oral therapy received IV Met with no responders. The remaining 10 patients received no specific treatment. 23 cases who did not respond to oral Met received oral vancomycin (Vanc) with 11 responders. Relapse occurred in 16 of 42 patients (38%). 10 responded to oral Met or Vanc. IV immunoglobulin was used in 6 cases after failure of oral Met or Vanc. Two of these responded rapidly, 5 survived, but relapse after immunoglobulin occurred in 2. Flexible sigmoidoscopy was done in 8 patients for non-response to treatment and showed an alternative diagnosis (of ulcerative colitis) in 1 patient. The outbreak was controlled by use of an isolation ward and strict infection control measures. Total 30-day mortality was 17 (24.6%).

Conclusion: In common with other reports of O27 outbreaks, this series showed poor treatment response and increased mortality compared to studies of non-O27 CDAD. Antibiotics have differing propensity to cause CDAD and a single dose of cefuroxime is sufficient. Failure to respond to initial treatment was associated with a poor prognosis. The relapse rate was similar to published series, and oral Met or Vanc were usually effective. IV immunoglobulin as a third line agent was only partially effective.

Abstract 147

	Use per case of CDAD (patient-days)	Comparison with cefuroxime
Cefuroxime	47.8	
Gentamicin	51.0	NS
Co-amoxiclav	52.9	NS
Ciprofloxacin	68.0	NS
Amoxicillin	73.5	NS
Clarithromycin	104	NS
Erythromycin	136	p=0.003
Flucloxacillin	251	p<0.001
Tazocin	350	p=0.021
Teicoplanin	367	p=0.018
Benzylpenicillin	398	p=0.012
Penicillin V	0 cases	p<0.001
Vancomycin IV	0 cases	p=0.031

148 DERIVATION OF A SCORE FOR IDENTIFYING COLORECTAL CANCER IN PRIMARY CARE

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Introduction: Selection of patients for investigation for possible colorectal cancer is difficult.[1] Some symptoms, such as severe anaemia, have a high enough risk to justify urgent referral on their own. Many authorities would include new onset rectal bleeding in this group. However, most colorectal cancers present to primary care with ''softer'' symptoms such as diarrhoea, constipation, loss of weight or abdominal pain.[2] These symptoms do not lead to an urgent referral, and are associated with the longest diagnostic delays and worse staging and survival. This study sought to establish a scoring system to help GPs identify which of these patients would benefit from urgent investigation.

Aims & Methods: This study was nested within a larger case-control study of all 349 colorectal cancers in patients over the age of 40, and 1744 age, sex and practice matched controls.[3] All symptoms reported in the two years before the cancer was diagnosed were identified. For this study, we examined only those patients who had reported at least one of abdominal

Abstract 148 Frequency of symptoms and score

Variable	In cases (n=117)	In controls (n=433)	Log OR	Caper score
Constipation	46 (39)	125 (29)	0.98	25
Loss of weight	44 (38)	81 (19)	0.93	20
Abdominal pain	75 (64)	139 (32)	0.62	15
Diarrhoea	55 (47)	146 (34)	0.41	10
Haemoglobin 12–12.9	11 (9)	18 (40	0.92	20
Haemoglobin 10–11.9	21 (18)	46 (11)	1.34	30

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pain, loss of weight, diarrhoea or constipation to their GP, but who had not reported severe anaemia (Hb <10.0 g/dl) or rectal bleeding, nor had findings suggestive of colorectal cancer (an abnormal rectal examination or positive faecal occult blood). A multivariable logistic regression analysis of the symptoms reported by these patients was performed. The logarithmic odds ratio was multiplied by a convenient number (24) and rounded to produce an additive scoring system (the CAPER score). The performance of the CAPER score was tested against the whole dataset.

Results: 550 patients fulfilled the entry criteria (117 cases, 433 controls). The frequency of the symptoms and the logistic regression results and CAPER score are shown in the table. The area below a receiver operating characteristic curve using the CAPER score only in patients with a soft symptom was 0.78. A threshold of 35 points or more on the CAPER score had a sensitivity of 69% and a specificity of 77%. This score equated to a risk of colorectal cancer of around 2% if used in the whole primary care population with a soft symptom.

Conclusion: The CAPER score is the first scoring system aimed at selecting which patients with a soft symptom of colorectal cancer would most benefit from urgent referral. A feasibility study has shown GPs will use it, and that cancers with a positive CAPER score, but who do not fulfil the NICE criteria for urgent referral, do indeed exist.

1. **Hamilton W**, Sharp D. Diagnosis of colorectal cancer in primary care: the evidence base for guidelines. *Fam Pract* 2004;**21**:99–106.
2. **Barrett J**, Jiwa M, Rose P, *et al*. Pathways to the diagnosis of colorectal cancer: an observational study in three UK cities. *Fam Pract* 2006;**23**:15–19.
3. **Hamilton W**, Round A, Sharp D, *et al*. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *Br J Cancer* 2005;**93**:399–405.

149 RESULTS OF SURGICAL EXCISION OF RECURRENT RECTAL CANCER

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Introduction: Surgery for recurrent rectal cancer is often not undertaken because of the risk of intraoperative technical difficulties and the doubtful benefits. The aim of our study was to assess the outcome of series of patients who underwent resection of locally recurrent rectal cancer with curative intent.

Aims & Methods: Twenty four patients (13 female; medium age 52 years, range 33–85) underwent: extended low anterior resection (ELAR), 7 (29%); low anterior resection (LAR), 10 (42%); abdomino perineal resection (APR), 2 (8%); subtotal colectomy (STC), 2 (8%); restorative proctocolectomy, 1 (4%); and transanal excision, 2 (8%) as the primary surgery for an index cancer in the midrectum (7–29%) and lower rectum (17–71%).

Results: Median (range) time from primary surgery to recurrence was 12.5 (3–54) months. The majority underwent APR as the second surgical procedure (16), pelvic excentration (1), STC (1), ELAR (1) and local resection (2). Three patients refused surgery. Perioperative mortality was 2 (9%), and 5 (23%) had major postoperative morbidities (neurogenic bladder/bladder injuries, 3; anastomotic leaks, 1; anastomotic strictures, 1). So far 8 (38%) have died of cancer while 14 (62%) have survival between 6 to 60 months since the cancer was first diagnosed.

Conclusion: If it is possible to undertake curative surgery for recurrent rectal cancer surgery, it offers worth while survival benefit. Most recurrent rectal cancers were found to be originally lower third.

150 USING SOMATIC APC MUTATIONS AS CLONAL MARKERS IN COLONIC POLYPS

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Introduction: Conventional wisdom suggests that human tumours are clonal in origin as cancer is a disease of stem cells. However earlier work in both humans[1] and mice[2] suggests that up to 79% of adenomas are polyclonal. We sought to investigate this definitively using somatic APC markers as clonal markers.

Aims & Methods: We sought to investigate polyp polyclonality definitively using somatic APC markers as clonal markers. Paraffin embedded polyp tissue was obtained from patients with classical familial adenomatous polyposis, attenuated FAP and sporadic lesions. Individual crypts were dissected from across the polyps using laser capture microdissection. Somatic mutations in whole polyp lysate were identified using SSCP analysis of the mutation cluster region of the APC gene. Individual crypt lysate DNA were then amplified by nested PCR and sequenced using an ABI 3100 sequencer.

Results: All 5 classical FAP polyps analysed, including a microadenoma just 5 crypts in size were polyclonal with some dysplastic crypts possessing identified somatic mutations but with other crypts in the same polyp wild-type. Five attenuated FAP polyps, however were clonal with the same mutation identified in all dissected crypts, including one polyp demonstrating clonal second and third hits. Three sporadic polyps were also clonal for their identified mutations, however one sporadic polyp was heterogeneic for a somatic mutation suggesting polyclonality. Top down growth was also demonstrated in this lesion with mixed crypts demonstrating a somatic mutation at the top of the crypt but not at the bottom.

Conclusion: These results raise several questions. (1) Are the earliest lesions, the microadenomas, in FAP polyclonal from the outset? (2) As lesions grow, do they revert to monoclonality as one clone outgrows the rest, possibly via a top-down mechanism in larger polyps? (3) Can these results be explained on the basis of very early collision of crypts with a second APC mutation? If the latter then the proportion involved would indicate non-random collision, possibly through epithelio-mesenchymal interactions, and this early cooperativity between early neoplastic crypts warrants closer study.

1. **Novelli MR**, *et al. Science* 1996;**272**:1187.
2. **Merritt S**, *et al. PNAS* 1997;**94**:1392.

151 LAPAROSCOPIC ANTERIOR RECTOPEXY IMPROVES BOTH OBSTRUCTED DEFECATION AND FAECAL INCONTINENCE IN PATIENTS WITH RECTAL INTUSSUSCEPTION

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Introduction: Classical posterior rectopexy for obstructed defecation due to rectal intussusception is controversial, 50% complain of similar or worse constipation afterwards. Laparoscopic anterior rectopexy (LAR) involves limited anterior rectal mobilisation, avoids ''denervation inertia'', and improves obstructed defecation in 80% in rectal prolapse.

Aims & Methods: We aimed to review our functional results in rectal intussusception and compare them to those in rectal prolapse. Carefully selected patients (grade 3 and 4 rectoanal intussusception with normal transit failing conservative treatment, no history of abuse) operated for rectal intussusception were prospectively analysed. Endpoints were changes in preoperative constipation (Cleveland) and incontinence (FISI) scores at 3 months, complications and length of stay (LOS).

Results: Thirty patients underwent LAR. Complications were seen in 13% and median LOS was 2 days. Constipation was improved in 25/30 (83%) patients (median Cleveland score from 13 to 4, $p<0.0001$). Incontinence was improved in 22/24 (92%) patients (median FISI score from 33 to 8, $p<0.0001$). No patients experienced deterioration in function. Improvements in rectal intussusception were similar to those seen in rectal prolapse (constipation improved in 78%, Cleveland 8 to 4, $p<0.0001$; incontinence improved in 90%, FISI 40 to 8, $p<0.0001$).

Conclusion: LAR improves obstructed defecation similarly in both rectal prolapse and rectal intussusception. LAR avoids worsening constipation by avoiding posterior rectal mobilisation and probably rectal denervation inertia. The defecatory disorder in each is similar and predominantly mechanical.

152 SIDE POPULATION CHARACTERISTICS AND ROLE OF β1 INTEGRIN IN ADHESION OF ISOLATED HUMAN COLONIC CRYPT EPITHELIAL CELLS

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Introduction: Intestinal epithelial stem cells are located at the base of crypts and their isolation and characterisation will facilitate investigation of factors regulating their function. The very small population of stem cells from bone marrow (and also other tissues) can be identified by the ''side-population'' (SP) phenotype. SP cells' differential ability to efflux Hoechst dye is sensitive to verapamil and fumitremorgin C. Adherence to extracellular matrix (secreted by adjacent cells such as myofibroblasts) is likely to be an

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important property of intestinal stem cells. Previous studies have shown high level of β1 integrin expression by human colonic crypt epithelial cells.
Aims & Methods: Determine in isolated crypt epithelial cells, (1) the presence of SP cells and (2) role of β1 integrin in adhesion.
Methods: Crypt epithelial cells were isolated and disaggregated from normal human colonic mucosal samples using ethylenediaminetetraacetic acid and pancreatin. SP cells were studied by flow cytometry after staining with Hoechst 33342, in the presence or absence of fumitremorgin C or verapamil. Adherence of epithelial cells to collagen I and intestinal myofibroblasts was studied in the presence or absence of anti-β1 integrin antibody. Intestinal myofibroblasts were isolated from colonic mucosal samples denuded of epithelial cells. Expression of collagen 1 transcripts was studied by RT-PCR. Data are expressed as mean (SEM).
Results: Cells able to efflux Hoechst dye (SP cells) represented 0.18 (0.04)% of the total viable colonic crypt cell population (n = 10). Cells with SP characteristics decreased by 73.1 (5.5)% and 87.8 (8.0)% in the presence of verapamil (n = 6) and fumitremorgin C (n = 4) respectively. Anti-β1 integrin antibody significantly reduced adherence of colonic crypt epithelial cells to collagen I (cells/cm^2: 196.3 (58.7) *v* 33.2 (10.4), n = 6; $p<0.03$) but did not affect adherence to monolayers of intestinal myofibroblasts (cells/cm^2: 2329 (923.5) *v* 3147.5 (543.4), n = 6; $p>0.05$). Expression of collagen I transcripts by myofibroblasts was confirmed by RT-PCR (n = 3). Adhesion to myofibroblasts did not enrich for colonic crypt epithelial cells expressing high levels of β1 integrin (assessed by flow cytometry).
Conclusion: 1. Isolated human colonic crypt epithelial cells contain a very small population of cells with SP phenotype, similar to that described for stem cells in the bone marrow. 2. Anti-β1 integrin antibody inhibited adherence of isolated colonic crypt epithelial cells to collagen I but not to monolayers of collagen I-expressing intestinal myofibroblasts.

153 ASSESSMENT OF MACROPHAGE FUNCTION WITHIN THE STROMA OF SPORADIC COLORECTAL POLYPS

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Introduction: We have previously reported an increased population of macrophages in the stroma of colonic adenomatous polyps but the functional nature of these cells remains unclear. The balance of activated proinflammatory macrophages to regulatory ones determines the overall direction of the inflammatory process and each type of cell has different metabolic activities. Classically activated macrophages express inducible nitric oxide synthase (iNOS) to increase intracellular nitric oxide and reactive oxygen species while regulatory macrophages express arginase I in order to reduce intracellular NO.
Aims & Methods: The aim of this study was to investigate the phenotype of macrophage infiltration within sporadic colonic adenomas compared to those found within adjacent normal mucosa. Macrophage phenotype was assessed using an immunohistochemical double staining technique based on sequential staining of 2 discrete cell markers in 15 colonic polyps and 12 normal mucosal biopsies from 12 patients attending for colonoscopy as part of the colorectal cancer screening program. Macrophages were identified by expression of CD68, a macrophage cell surface glycoprotein, using alkaline phosphatase as enzyme tracer with liquid red as chromogen. Classically and alternatively activated macrophages were identified by expression of either iNOS or arginase I, respectively, by immunostaining incorporating a peroxidase enzyme tracer with DAB as chromogen. The number of CD68 positive cells was counted to represent macrophage stromal population. In addition, each tissue was stained for both iNOS and arginase I and the predominant macrophage type was identified within that specimen.
Results: In adenomas, there was a statistically significant increase in the number of iNOS positive macrophages compared to adjacent normal mucosa ($p = 0.001$). 91% of the CD68 positive cells expressed iNOS within the polyps, compared to 20% within normal mucosa ($p = 0.001$). There was also a statistically significant increase in the number of arginase I positive macrophages in the adenomas compared to normal mucosa ($p = 0.014$), although these only represented up to 20% of the macrophages within the polyps.
Conclusion: Our data have shown that macrophages within the stroma of adenomatous colonic polyps predominantly express iNOS, suggesting classical activation with proinflammatory function. Stromal-epithelial interaction in the presence of this macrophage population is likely to induce a pro-oxidant microenvironment, rich in mutagenic reactive oxygen species and subsequently exert genotoxic pressure with direct and indirect influences on early carcinogenesis. These findings are likely to be relevant to the pathogenesis of sporadic colorectal cancer.

154 ASSESSMENT OF INFLAMMATORY CELL PHENOTYPE IN SPORADIC HYPERPLASTIC POLYPS

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Introduction: The natural history of hyperplastic polyps is not fully understood but they are not thought to hold malignant potential. However, several case reports suggest that malignant change may occur within hyperplastic lesions and molecular studies suggest that they are genetically heterogeneous with some associated to microsatellite instability and K-ras mutations. While hyperplastic polyps are usually small in size (less than 1 cm), they still represent raised lesions exposed to some degree of physical, chemical and microbial stress. We previously reported increased inflammatory cell infiltrate in sporadic colorectal adenomas and hypothesise that this inflammatory activity is key to cell transformation towards malignancy.
Aims & Methods: The aim of this study was to assess the inflammatory cell phenotype of sporadic hyperplastic polyps. Neutrophil, macrophage, activated T cell and T helper cell infiltrate was assessed in 40 sporadic hyperplastic polyps identified from a pathology diagnostic database and retrieved from archival tissue stores. Inflammatory cell phenotype was studied using immunohistochemical techniques and compared to inflammatory cell activity in a cohort of 35 normal colonic mucosal biopsies. Monoclonal antibodies against neutrophil elastase, CD68, CD25 and CD4 were used to assess the presence of neutrophils, macrophage, and T cells of activated and helper subsets, respectively.
Results: There was no difference in activated T cell, T helper cell and neutrophil infiltrate in hyperplastic polyps compared to normal colonic mucosa, $p = 0.468$, $p = 0.233$, and $p = 0.309$, respectively. There was however a statistically significant increase in stromal macrophage infiltrate seen in the hyperplastic polyps, $p = 0.001$
Conclusion: This study has shown evidence of increased macrophage infiltration within the stroma of sporadic hyperplastic polyps compared to normal colonic mucosa. The significance of this in relation to the natural history of these lesions is unclear. It may be that the activity of these stromal macrophages exert genotoxic pressure and contribute to the genetic heterogeneity of these lesions.

155 SURVEILLANCE COLONOSCOPY FOR ADENOMATOUS POLYPS: ARE WE COMPROMISING THE PATIENT CARE?

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Introduction: British Society of Gastroenterology (BSG) has published guidelines for follow-up of colonic adenomatous polyps. The study aimed to survey the practice of surveillance of adenomatous polyps in comparison with BSG guidelines.
Aims & Methods: A questionnaire based on BSG guidelines was sent to 242 clinicians in the North West region of England. The clinicians not performing colonoscopy were excluded and the data analysed according to three stratification groups (low, intermediate and high risk groups).
Results: Response rates were 53.72% (130 of 242) of which 75 (63.08%) were performing colonoscopy (gastroenterologists (GE)-25, general surgeons (GS) - 23, colorectal surgeons (CRS) – 27). In low risk group, the follow-up practice matched with the guidelines in 57.14% of responses (GE, 64%; GS, 43.48%; CRS, 70.37%) and the rest were doing more frequently. In the intermediate group, the practices of 45.33% (GE, 56%; GS, 30.43%; CRS, 48.15%) were in accordance with the guidelines. In high-risk group, only 46.67% (GE, 68%; GS, 45.45%; CRS, 30.43%) of responses were in accordance with the guidelines and surprisingly, more than one third of responses revealed less frequent follow-up in contrast to the other groups, where roughly 40% did more frequent follow-up. For the large sessile adenomatous polyps, two third responses revealed less frequent follow-up.
Conclusion: Overall, surveillance practices of only half of the consultants were in accordance with the BSG guidelines with the low/intermediate group being followed-up more frequently exposing patients to unnecessary risks and increasing work load on the unit and the high-risk group followed less frequently with risk of delayed diagnosis. Adherence to the guidelines may decrease the workload on the endoscopy unit without compromising patient care.

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156 COLORECTAL SCREENING: WHAT WOULD YOU CHOOSE?

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Introduction: The field of colorectal cancer screening has dramatically changed in the past two decades. The growing evidence base behind screening has prompted the introduction of national screening programmes in several countries. The exact form of screening is still under debate and this was the basis of our survey.
Aims & Methods: Our aim was to ask what BSG members would opt for if they were the patient offered screening. A questionnaire-based survey was sent in Jan 2006 to 150 BSG members selected randomly from the BSG members register. Recipients were asked which screening method they would choose and what they would then do if this test was positive.
Results: Fifty nine questionnaires were returned (40%). For routine screening at age 50 only 17 (28%) opted for FOB testing, 21 (35%) for colonoscopy every 10 years, 11 (18%) for virtual colonoscopy every 10 years, 2 (3%) for flex sig every 10 years, 7 (11%) for no screening. If FOB testing chosen (17/59) then 14 (82%) would follow-up with colonoscopy if positive. One recipient (5%) would repeat FOBs, 1 opted for flex. sig. with 1 for barium enema. If 1 first degree relative had been affected by bowel cancer below age 50 then 48 (81%) opted for colonoscopy, 7 (11%) for virtual colonoscopy, 1 (1.5%) for FOBs, 1 for flex. sig. with 1 for barium enema. The colonoscopy group (48) were asked how often for screening. 35 (73%) opted for 5 yearly, 6 (13%) for 10 yearly, 3 (6.5%) for 2 yearly. 6 (85%) in the virtual group opted for 5 yearly. If the first degree relative had been aged 51–70, 37 (63%) would still opt for colonoscopy with 8 (13.5%) for FOBs, 8 (13.5%) for virtual colonoscopy, 4 (7%) for no screening. Again groups were asked how often. In the colonoscopy group 21 (57%) opted for 5 yearly, 15 (41%) for 10 yearly. At the end of the survey the recipients were asked which screening method they thought was most cost effective. 24 (40%) said colonoscopy, 22 (37%) FOBs, 5 (8%) flex sig, 4 (7%) virtual colonoscopy with 2 for flex sig and barium enema.
Conclusion: Our results highlight the differences in the approach to screening. It is interesting that most BSG members would opt for colonoscopy above FOBs, particularly given the introduction of the national screening programme. Is this based around growing evidence for screening colonoscopy or by putting the gastroenterologist in the position of the patient? Another interesting aspect raised was the growing acceptance of virtual imaging. This is not widely used as a screening tool in the UK but is perhaps a method that will be increasingly useful as technology advances. It will be interesting to see how colorectal screening progresses with time and the emergence of more evidence and technology.

1. **National Institute for Clinical Excellence**. Colorectal cancer service guidance. 2004.
2. **Ransohoff DF**. Colon cancer screening in 2005: status and challenges. *Gastroenterology* 2005;**128**:1685–95.

157 COLONIC ANATOMICAL VARIATIONS AS SEEN BY VIRTUAL COLONOSCOPY SCOUT IMAGES: WHY COLONOSCOPY IS TECHNICALLY CHALLENGING

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Introduction: There is considerable variability of colon anatomy as indicated by the diversity encountered during colonoscopy. V3D virtual colonoscopy (Viatronix) recreates a 3D endoscopic view of the large bowel from multiplanar CT images. Following rectal air insufflations, a scout image is obtained which provides a 3D rotatable image of the colon. This image provides a picture of the native lie of the colon and provides the opportunity to study colon anatomy in vivo.
Aims & Methods: 100 patients underwent same day V3D and optical colonoscopy (OC) by experienced endosopists. The supine V3D scout images were reviewed independently by two advanced gastroenterology trainees. The lie of the ascending and descending colon is constant as they are in the retroperitoneal space. The variable segments (sigmoid, splenic flexure, transverse colon and hepatic flexure) of the colon were classified according to their complexity. A convoluted colon was defined as three intermediate or complex segments. A difficult sigmoid was classified where the sigmoid was of intermediate or highly complex configuration, with the remainder of the colon uncomplicated. Other permutations included the transverse dip where both splenic and hepatic flexures were of intermediate or high complexity and the straight colon where none of the segments revealed complexity. The type of colon lie was then related to colonoscopy times and completion rates.
Results: See table and example of a convoluted colon.

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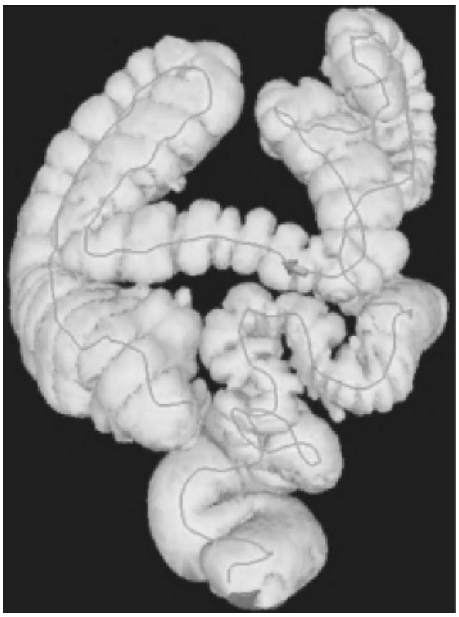
Anatomical pattern	Number (%)	Time OC (mins)	Completion rate (%)
Convoluted colon	30	36.7	93
Straight colon	18	21.6	100
Difficult sigmoid	13	26.3	85
Difficult sigmoid and splenic	19	24.4	94
Transverse dip	20	25.7	80



Abstract 157

Conclusion: Scout images derived from virtual colonoscopy identified five variations of colonic anatomy. The straight colon occurs in around one in five patients, and when present, was always successfully negotiated. There is a suggestion that patients with a transverse dip are most difficult to colonoscope, reflecting the combination of a complex splenic and hepatic flexure.

158 POTASSIUM CHANNEL BLOCKADE PREVENTS INCREASED COLONIC PERMEABILITY DURING ISCHAEMIA: A NOVEL THERAPEUTIC STRATEGY TO REDUCE SEPSIS ASSOCIATED WITH LIVER SURGERY

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Introduction: Gut ischaemia during major liver surgery increases intestinal permeability and bacterial translocation, increasing the risk of systemic sepsis. Cell hypoxia activates potassium (K^+) channels in a variety of tissues, and the ability of mastoparan (a G protein agonist) to enhance paracellular permeability in T84 colonic cell monolayers is linked to an increase in basolateral membrane K^+ conductance.
Aims & Methods: We evaluated the effect of acute metabolic stress on basolateral K^+ channels in human colonic crypts, and the effect of K^+ channel blockade on ischaemia-induced changes in colonic paracellular conductance. Crypts were isolated from human colonic biopsies (Bowley *et al. Gut* 2003;**52**:854–60). Crypts were exposed to metabolic inhibitors 100 μM dinitrophenol (DNP) + 5 mM deoxyglucose (DG), and sheets of resected human sigmoid colon mounted in Ussing chambers were exposed to 100 μM DNP without oxygenation. Whole cell K^+ currents in intact crypts were measured using the perforated patch-clamp technique (0.24 mg/ml amphotericin in pipette). Paracellular conductance in colonic

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sheets was estimated from changes in electrical parameters following apical membrane permeabilisation by nystatin, under control oxygenated conditions, and during addition of 100 μM DNP without oxygenation, in the absence or the presence of the intermediate conductance K^+ (IK) channel blocker clotrimazole (CLT).
Results: Within 5 minutes, DNP + DG activated whole-cell K^+ currents, increased whole-cell conductance from 0.9 (0.2) nS to 2.7 (0.5) nS ($p<0.0.02$; n = 7), and hyperpolarised crypt cells from −55 (6) mV to −74 (3) mV ($p<0.015$). 10 μM CLT completely inhibited this increase in whole-cell conductance ($p<0.015$). In colonic sheets, exposure to DNP without oxygenation increased paracellular conductance from 5.7 (1.1) $mS.cm^{-2}$ to 12.8 (1.7) $mS.cm^{-2}$ ($p<0.01$, n = 6), this effect being completely inhibited by 20 μM CLT (n = 4).
Conclusion: Metabolic stress associated with acute cell hypoxia causes a profound increase in colonic paracellular conductance (permeability), which is dependent on the activation of basolateral IK channels. Intraoperative use of drugs that block/inhibit IK channels may minimise the risk of sepsis associated with ischaemic injury to the gut.

159 STREPTOCOCCUS BOVIS BACTERAEMIA: A MARKER FOR COLONIC AND LIVER DISEASE

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Introduction: Streptococcus bovis is non-enterococcal group D streptococcus which is a normal inhabitant of gastrointestinal tract in humans. Streptococcus bovis bacteraemia/endocarditis is known to be associated with colonic pathology mainly cancer and hepatic dysfunction has been suggested to predispose patients to systemic bacteraemia in previous studies.
Aims & Methods: We conducted a 10-year retrospective study to evaluate the incidence of streptococcus bovis bacteraemia and its associated disease conditions in a district general hospital. This was a retrospective study conducted over 10 years between January 1996 and January 2006. All patients diagnosed with streptococcus bovis bacteraemia during this period were included. The data were collected through the microbiology department. Seven patients were identified in total and all their case notes were analysed.
Results: Of the seven patients, five were male. The age range was 56–90 years (median 83 years). Two patients were diagnosed to have infective endocarditis associated with the bacteraemia. Four out of the seven patients had colorectal cancer associated with bacteraemia. Two patients who were already known to have colorectal cancer and underwent elective colorectal cancer surgery developed S bovis bacteraemia in the post-operative period. Two patients who had bacteraemia associated with infective endocarditis were diagnosed with colorectal cancer, two weeks and one month respectively, after the episode of bacteraemia by colonoscopies. Both patients did not have any significant bowel symptoms. Three out of the seven did not have any formal bowel investigations due to advanced age and coexistent medical problems. All seven patients had liver function tests done and six had ultrasound of the abdomen done. One patient was noted to have deranged liver function tests (Bili74 μmol/l, Alk Phos 459 IU/l, ALT 327 IU/l and AST 603 IU/l) and the ultrasound of the same patient showed diffuse parenchymal liver disease. All the other patients had normal liver function tests and ultrasound.
Conclusion: Our study illustrates that the incidence of S bovis bacteraemia is very low. It also confirms its association with colorectal cancer and hepatic dysfunction. So, all patients with documented Streptococcus bovis bacteraemia/endocarditis should have colonic investigations and baseline liver function tests done, with further ultrasound/CT of liver if they are abnormal.

160 COMPARISON OF HIGH RESOLUTION MAGNIFICATION ENDOSCOPY, NARROW BAND IMAGING WITH MAGNIFICATION AND CHROMOENDOSCOPY WITH MAGNIFICATION IN THE ASSESSMENT OF NEOPLASTIC AND NON-NEOPLASTIC COLORECTAL LESIONS

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Introduction: The distinction of non-neoplastic from neoplastic colorectal polyps can increase the efficiency of treatment by eliminating the time and cost of unnecessary biopsies or polypectomy. Though chromoendoscopy has long been propagated as a technique to improve mucosal visualisation, it has not been widely practised in the West. Narrow band imaging (NBI) with magnification is a novel endoscopic imaging technique that enhances the visualisation of surface microstructure and microvasculature without the need for dye spray. We evaluated the diagnostic accuracy of high resolution magnification endoscopy (HRME), NBI with magnification and chromoendoscopy with magnification to assess various colorectal lesions.
Aims & Methods: A total of 31 colorectal lesions in 24 patients (15 men, mean age 68.2 years) were assessed during routine colonoscopy using the Olympus prototype NBI video endoscopy system. Each lesion was evaluated using three modalities: first by HRME then by NBI with magnification and finally by chromoendoscopy with magnification using 0.4% indigo carmine spray. Polyps were classified based on the Kudo's pit pattern (KPP). Additionally, in the assessment of these lesions with NBI and magnification, the meshbrown capillary network (MBCN) of each polyp was also described (Type I—absent pattern, Type II—regular capillary network, Type III—irregular capillary network). The KPP and MBCN description of each polyp was recorded during the procedure. The accuracy of differentiating neoplastic (Types III, IV and V- KPP, Type II and III -MBCN) from non-neoplastic lesions was then compared with reference to the final pathological diagnosis.
Results: The lesions were located in the caecum (2), ascending colon (5), transverse colon (4), descending colon (2), sigmoid colon (9) and rectum (9). According to the Paris Classification, morphologically, 9 were classified as type Is, 7 type Ip, 1 type Isp, 13 type IIa and 1 type IIa-c. The sensitivity, specificity, positive and negative predictive values for HRME for differentiating neoplastic from non-neoplastic lesions was 75%, 33%, 91% and 13% respectively; NBI with magnification (without MBCN) 85%, 50%, 92% and 33% respectively, NBI with magnification (with MBCN) 96%, 50%, 93% and 67% respectively and chromoendoscopy 96%, 50%, 93% and 67% respectively.
Conclusion: With the addition of the MBCN classification, NBI with magnification is as effective as chromoendoscopy in predicting neoplastic from non-neoplastic polyps in real-time colonoscopy.

161 ADENOMATOUS POLYPS ARE UNCOMMON IN PATIENTS WITH ULCERATIVE COLITIS BUT INCREASE THE RISK OF DEVELOPING COLORECTAL CANCER

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Introduction: Risk of cancer in patients with ulcerative colitis (UC) is higher than the general population. The importance of adenomatous polyps in contributing to this increased cancer risk is unclear. Recent evidence suggests that the prevalence of adenomatous polyps is less common in this patient population. We aimed to ascertain the prevalence of adenomatous polyps in patients with ulcerative colitis and compare it with a control population and assess the risk of developing colon cancer in patients with adenomatous polyps.
Aims & Methods: We performed a retrospective audit of endoscopic and histological records of patients with a confirmed diagnosis of UC from 1991–2004. Patients undergoing colonoscopy for altered bowel habit or abdominal pain were used as a control group. Data were obtained from the electronic patient data records of St George's hospital.
Results: Twenty three (5.8%) of patients with UC had adenomatous lesions in the colon of which 16 (4%) were thought to be sporadic adenomas and the rest dysplasia associated lesion or masses (DALMs). In contrast 77 (9.3%) of 828 controls had at least one adenomatous polyp. Adenoma's were significantly less common in patients with UC ($p = 0.04$). Risk of developing adenocarcinoma was 4.4/1000 patient years duration (pyd) for UC patients without detectable adenomas or DALMs and 16.4/1000 pyd for patients with sporadic adenomas detected and 36.4/1000 pyd for patients with DALMs detected.
Conclusion: Adenomatous polyps, occur less frequently in patients with UC compared to controls but cause a fourfold increase in the risk of developing a colorectal cancer in this patient population.

162 IRON DEFICIENCY ANAEMIA AND THROMBOCYTOSIS: PREDICTORS OF MORTALITY IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the second most common cause of cancer related deaths in the UK. In 2002 approximately 35 000 new cases of CRC were diagnosed in the UK.[1] Beale *et al* suggested that three fifths of patients with CRC are iron deficient at presentation, of which two thirds are

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anaemic.[2] This loss of iron is thought to be secondary to chronic gastrointestinal haemorrhage and is related to the site and size of the tumour.[3] Consequently one would expect individuals with CRC and a coexisting IDA to be more likely to have an advanced disease process and thus suffer a reduced survival rate. Yet there is a paucity of evidence to support this theory.

Aims & Methods: Demographic and pathologic data were gathered retrospectively in all individuals diagnosed with CRC in 2004 at a single centre, Hereford County Hospital. Subjects were divided into anaemic and non-anaemic groups. A haemoglobin (Hb) level below 11 g/dl defined the anaemic population. Iron deficiency status was determined by a mean corpuscular volume (MCV) <76 fl and/or mean cell haemoglobin (MCH) below 27 pg and/or hypoferritinaemia(<15 μg/l). Criteria studied included mortality at 18 months, tumour site and Dukes stage, haemoglobin level, markers of iron status and thrombocytosis.

Results: The study population included 106 subjects, with 45 anaemic and 61 non-anaemic individuals. Demographic variables were similar between the two groups. Iron deficiency was present in 31 out of 45, and 0 out of 61 of the anaemic and non-anaemic patients respectively. Anaemic patients compared to non-anaemic patients had a significantly higher mortality at 18 months ($p=0.008$, Fisher's exact test), more advanced Dukes stage ($p=0.04$), right sided in site ($p=0.002$) and a higher prevalence of thrombocytosis ($p=0.001$). No significant difference in mortality was found when comparing those with a normal iron status in the anaemic and non-anaemic populations ($p=0.3$), and those with a normal or low iron status in the anaemic group ($p=0.5$). Non-anaemic subjects more commonly presented with rectal cancer (46% *v* 16%, $p=0.002$). Thrombocytosis was significantly associated with mean cell haemoglobin ($p<0.001$) and mortality ($p=0.001$).

Conclusion: Anaemia is a marker of increased mortality in CRC but has been little studied. Thrombocytosis and a low MCH are particular risk factors. Both of these are thought to be representative of significant gastrointestinal blood loss. We propose increased blood loss from advanced tumours is the cause and urgent evaluation of the entire colon is essential in such patients.

1. **Office for National Statistics**. *Cancer statistics registrations 2005.* London: National Statistics).
2. **Beale A**, *et al. Colorectal Disease* 2005;**7**:398–402.
3. **Li F**, *et al. J Gastroenterology* 1999;**34**:195–9.

163 COLORECTAL CANCER: MAPPING EXPRESSION STUDIES: FROM MURINE MODELS ONTO HUMAN DISEASE

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Introduction: Inactivation of the adenomatosis polyposis coli (APC) gene is recognised as one of the first important genetic lesions in the pathogenesis of colorectal cancer. Inactivation of APC stabilises α-catenin, which translocates into the nucleus activating TCF/LEF with subsequent transactivation of many target genes through the Wnt signalling pathway. A Cre-Lox mouse model has been previously developed, wherein an inducible Cre transgene deletes APC within the intestinal epithelium, showing that loss of APC causes immediate activation of the Wnt signalling pathway, failure in cell migration and cell differentiation, perturbation of the normal crypt/villus homeostasis, induction of cell death, and induction cell proliferation. A microarray gene analysis of this unique mouse model has identified a cohort of Wnt regulated gene alterations for which there has been little previous association with neoplasia.

Aims & Methods: To determine if genes that are dysregulated following deletion of APC in mice, as identified by our previous microarray analysis, are also dysregulated in human colorectal cancers. Total RNA samples were extracted from colorectal cancer tissues with matched neighbouring ''normal'' mucosa from the random patients. The selection of candidate genes was based on the previous work from the Cre-Lox mouse model. mRNA expression levels for the homologous human candidate genes were determined by performing taqman, real-time PCR assay on paired tumour and normal samples of patients. Candidate gene expression levels in tumour tissues were presented as the fold changes relative to the normal tissues for each patient.

Results: 12 homologous human candidate genes have been tested on the first random paired patient samples. mRNA expressions of 4 (out of 12) genes showed dramatically elevated levels as the fold change median values: AXIN2 (7.6-fold); Fn14 (5.5-fold); CITED1 (6.4-fold); CD44 (5.2-fold), respectively.

Conclusion: Data from taqman real-time PCR analysis demonstrate how transferable the candidate genes identified in the mouse model are to the study of human colon cancer. Elevated AXIN2 gene and CD44 gene expressions and corresponding gene encoded protein functions have been well studied, which again validates the process. The upregulations of Fn14 (TNFRSF12A) gene and CITED1 gene as Wnt pathway targets have not previously been detected in human colon cancer and therefore are novel candidates for future investigation.

Gastroduodenal posters

164 MUCOSAL ASSOCIATED BACTERIAL DIVERSITY IN THE STOMACH AND DUODENUM

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Introduction: Little is known about mucosa-associated gastric and duodenal microbiotas, their diversity, the distribution of microorganisms in different regions of the upper gut, or the influence of Helicobacter pylori on bacterial colonisation.

Aims & Methods: The aim of this study therefore was to compare mucosal populations in different parts of stomach and duodenum, and to investigate the effects of H pylori on bacterial densities on the mucosal surface. Polymerase chain reaction in combination with denaturing gradient gel electrophoresis) was used for quantative analysis and real-time PCR and fluorescent in situ hybridisation for quantification and visualisation of bacterial communities. Samples were taken from 15 patients undergoing upper GI endoscopy for non-specific upper gastrointestinal symptoms. Seven were male, mean age 41 years and 8 were female, mean age 43. Samples were taken from the antrum and pylorus of the stomach, and the first and second part of the duodenum. All endoscopic and histopathological examinations were reported as normal. Test for H pylori were negative in all samples. Wilcoxon matched paired test was used for statistical analysis.

Results: DGGE analysis of the gastric antrum and pylorus showed band profiles that were similar in some patients, but different in others. Similar observations were made for duodenal DGGE gel patterns, suggesting a large degree of host dependency. Sequences analysis positively identified H. pylori in five gastric samples and four duodenal samples despite their being considered negative using traditional methods. The main sequences obtained from DGGE gels from the stomach and duodenum were species from the genera Lactobacillus, Bifidobacterium, Streptococcus, Candida, together with Staphylococcus aureus, H pylori and Peptostreptococcus anaerobius. Quantitative analysis showed total mean bacterial densities were ca. 3.9 and 4.1 (log10 per mg mucosal biopsy sample) in the gastric antrum and pylorus, respectively ($p>0.5$). Similarly, in the duodenum, mean bacterial densities were ca. 4.1 and 3.8 (log10 per mg mucosal biopsy sample) in the first and second part of the upper small gut ($p>0.5$). H pylori, Lactobacillus, Candida and Staphylococcus aureus were the most abundant organisms in the stomach, as determined by real-time PCR, with only a few bifidobacteria being found, while H pylori, bifidobacteria and candidas formed the bulk of bacterial communities in the duodenum. Helicobacter positive patients had higher bacterial colonisation in the stomach and duodenum, but carriage of this pathogen did not affect the overall species composition of mucosal communities.

Conclusion: Mucosal bacterial communities in the stomach and duodenum are considerably more complex than was previously thought, with differences in the diversity and distribution.

165 HELICOBACTER PYLORI dupA IS NOT ASSOCIATED WITH DUODENAL ULCERS IN POPULATIONS FROM SOUTH AFRICA, SCOTLAND, CHINA AND USA

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Introduction: A novel *H pylori* gene (*dupA*) has recently been shown to be significantly associated with duodenal ulceration (DU) and protective against gastric cancer (GC), in populations from South Korea, Japan, and Colombia. Strains that possessed *dupA* also induced more IL-8 secretion from gastric epithelial cells (Lu *et al. Gastroenterology* 2005;**128**:833). We therefore looked at the presence of this gene in *H pylori* isolates from four other countries, and determined disease associations.

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Aims & Methods: Forty five South African strains (13 DU, 18 GC, 15 gastritis), 51 Scottish strains (7 DU, 18 GC, 26 gastritis), 31 Chinese strains (12 DU, 4 GU, 2 DU/GU, 1 GC, 12 gastritis), and 45 American strains (21 DU, 2 GU, 2 DU/GU, 20 gastritis) were used for *dupA* typing by PCR using a set of novel primers. Strains that were negative for *dupA* for the first two reactions, which amplifies the 3′ and 5′ regions, were repeated with six further reactions, and were then considered as positive for *dupA* if they had at least five positive PCR products. The *vacA* and *cag* pathogenicity island (PaI) status of all strains had been previously determined. IL-8 secretion from AGS cells co-cultured with *H pylori* strains for 6 h was determined by ELISA.
Results: 84.4% South African strains (92% DU), 41.2% Scottish strains (14.3% DU), 32.3% Chinese strains (16.7% DU), and 44.4% American strains (47.6% DU) were positive for *dupA*. There was no significant association between *dupA* and disease status in any population, but when the data were combined, although there was no association with DU, GU, PUD, or gastritis, there was a significant positive association with GC ($p = 0.003$). The presence of *dupA* was also significantly associated with s1/m1 *vacA* types ($p = 0.002$), and the *cag* PaI ($p = 0.01$). *H pylori* strains (either possessing of lacking the *cag* PaI) that were *dupA* positive did not induce significantly more IL-8 secretion from AGS cells than strains that were *dupA* negative.
Conclusion: Although the numbers of strains used in each population in this study are small, there was clearly no association between *dupA* and DU, in individual populations, or overall (47.2% DU *v* 47.4% gastritis *dupA*+). The association with GC (72.3% *dupA*+ overall) is intriguing. Large differences in *H pylori dupA* status between countries and in particular the high occurrence of *dupA* in a South African population might imply that *dupA* is associated with ethnicity.

166 COMH: ISOLATION, PURIFICATION AND CHARACTERISATION OF A UNIQUE H PYLORI PROTEIN

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Introduction: Many organisms, including *H pylori*, share the property of DNA uptake from their environment (competence) which is used as an energy source and occasionally for genetic transformation. This is enabled by a complex network of ComB proteins, located close to and within the bacterial cell membrane. *H pylori* alone possesses the *comH* gene and when deleted, the organism loses competence.[1] We were able to express the ComH protein in our earlier work.[2] Here we report on its purification and partial characterisation.
Aims & Methods: To determine if ComH protein is a nuclease and to identify its location within the cell. The *H pylori* laboratory strain 26695 was cultured and its DNA isolated. The *comH* gene was amplified by PCR, and cloned and expressed in various expression vectors. Antibodies against ComH were raised in rabbits and the antisera used to detect the location of the protein in vivo.
Results: (1) As reported earlier, the optimum conditions for expression were achieved with the pGEX-KG system. High levels of GST-ComH fusion protein were obtained but proved insoluble. (2) The *comH* gene was cloned in a pET21-histidine (his), an expression vector. The his-tagged ComH protein expressed was purified using affinity and anion exchange chromatography. (3) ComH was tested for nuclease activity in liquid assays, and under various conditions. No nuclease activity was detected. (4) Nevertheless, ComH was able to bind single-stranded (ss) DNA in electrophoretic mobility assays, with a binding constant (K_d) of 36 nM at pH 7. (5) Antibody against GST-Com H protein was raised in rabbits and then purified. Western blotting and FACS showed that the purified antibody adhered to the cells, indicating that the ComH against which it is directed is located in the outer membrane and that its surface is exposed.
Conclusion: This is the first time the ComH protein, the product of the unique *H pylori* competence gene *comH*, has been expressed, purified and partially characterised. Against expectation, it is not a nuclease but it is able to bind ssDNA with high efficiency. Its function remains unknown but we presume is in some way essential in making *H pylori* competent.

Konstantinos Kostidis is a Research Fellow of the Bardhan Research and Education Trust (Registered Charity No 328452)

1. **Smeets**, *et al. comH*, a novel gene essential for natural transformation of *Helicobacter pylori*. *J Bacteriol* 2000;**182**:3948–54.
2. **Kostidis**, *et al.* comH: purification of a unique *H pylori* protein. *Gut* 2005;**54**(Suppl 2):A86.

167 HOW ROBUST IS DATA COLLECTION IN UPPER GASTROINTESTINAL CANCER REFERRALS AT LOCAL AND NATIONAL LEVELS?

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Introduction: The Department of Health (DOH) has highlighted cancer waiting times (CWT) as an important cancer quality measure. Among CWT measures, the two week wait (2WW) is one benchmarked measure in the overall objective of improving the overall outcomes in patients suspected of having cancer. Nevertheless it has recently been reported that 95% of 21 abstracts to the British Society of Gastroenterology (BSG) (2001–3) suggested that implementation of the 2WW had a negative or mixed impact on service delivery. Moreover it is currently believed that poor specificity of the DOH guidelines is contributing to the low cancer yield from this referral pathway. Notwithstanding the above concerns, little is known about the robustness of data collection at loco-regional and national levels.
Aims & Methods: To assess the robustness of data collected on suspected upper gastrointestinal (UGI) cancer referrals to Newham University Hospital NHS Trust (NUHT) and to compare reported numbers on the local and national databases. Every suspected UGI cancer referral received by the NUHT was manually counted for 24 months (January 2004–December 2005) (Local Count) and this number compared with the local Trust database, the National Cancer Waiting times data collection system database (Open Exeter), and the DOH Cancer Waiting Times Statistics website. Summary data were created.
Results: The number of patients counted is shown in the table. The degree of underreporting was consistent over the 24-month period when the monthly variation in the suspected UGI cancer referrals for the Local Count and Open Exeter was examined. In addition, analysis of the quarterly referrals for suspected UGI cancer referrals demonstrated both local underporting on the Trust database and central underreporting by both Open Exeter and DOH. Indeed the mean number of referrals by the central databases (Open Exeter and DOH) represented only 71% of all referrals.
Conclusion: There is underreporting of cancer referral data at both a local and central level. That only a 6% attrition rate exists at a local level of data collection and a 29% attrition rate exists at the national level suggests a more significant problem exists with the robustness of national data. In the current circumstances of NHS deficits, such underreporting of activity in national databases may adversely effect appropriate funding of acute hospital Trusts in the future.

Abstract 167 Cumulative suspected upper gastrointestinal cancer referrals 2004–5

Local count	Trust database	Open Exeter	DOH count
287	271	195	215

168 GASTRIC PHENOTYPE AND GORD SYMPTOMS INDICATE TWO DISTINCT AETIOLOGIES OF CARDIA CANCER

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Introduction: The gastric cardia is a common site of malignancy but the aetiology of these tumours and their relationship to non-cardia gastric cancer and oesophageal adenocarcinoma remain unclear. Non-cardia cancer is strongly associated with atrophic gastritis while oesophageal adenocarcinoma occurs in subjects without atrophy. We have investigated the relationship between atrophy and cardia cancer comparing it with non-cardia cancer and oesophageal adenocarcinoma.
Aims & Methods: 138 patients, including 66 gastric non-cardia cancer, 53 gastric cardia cancer and 19 oesophageal adenocarcinoma and similar number of age and sex-matched controls with normal endoscopy have been studied. Serum pepsinogen I/II was use as a serologic marker of atrophic gastritis and categorised to five quintiles. History of gastro-esophageal symptoms was incorporated in logistic regression analysis.
Results: The risk of gastric non-cardia cancer progressively increased with decreasing PG I/II quintiles indicating positive association with atrophy. There was a trend for reduced risk of oesophageal adenocarcinoma with decreasing PG I/II quintiles suggesting an inverse relationship of the cancer

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Abstract 168

	Gastric non-cardia OR (95% CI)	Gastric cardia OR (95% CI)	Oesophageal adenocarcinoma OR (95% CI)
PG I/II quintiles			
5th	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
4th	3.88 (0.47–31.96)	0.99 (0.42–2.33)	1.20 (0.12–11.56)
3rd	7.84 (0.92–66.63)	0.60 (0.21–1.69)	1.77 (0.18–17.78)
2nd	11.13 (1.32–93.90)	0.44 (0.15–1.27)	0.29 (0.02–3.91)
1st	25.44 (3.35–193.02)	4.18 (1.93–9.06)	0.59 (0.04–8.53)
GORD symptoms			
None	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
1–2/week	0.29 (0.11–0.79)	1.09 (0.40–3.01)	5.12 (0.73–35.93)
⩾3/week	0.76 (0.16–3.63)	5.84 (1.64–20.75)	12.59 (1.34–118.39)

with atrophy. The association of cardia cancer with atrophy was quadratic in form with the lowest PG I/II quintile (1st) being associated with significantly increase cancer risk, but a progressive falling risk associated with quintiles 5 to 2. GORD symptoms showed a significant inverse relationship with non-cardia cancer, and a potent direct association with oesophageal adenocarcinoma. There was a direct relationship between severe form of GORD symptoms and cardia cancer.
Conclusion: The positive association of severe atrophy with cardia cancer indicates some cases being similar to non-cardia gastric cancer. The relationship with severe GORD indicates other cardia cancers are similar to oesophageal adenocarcinoma.

169 EVALUATION OF RISK STRATIFICATION IN THE CO-PRESCRIPTION OF GASTROPROTECTANTS IN PATIENTS ADMITTED TO HOSPITAL

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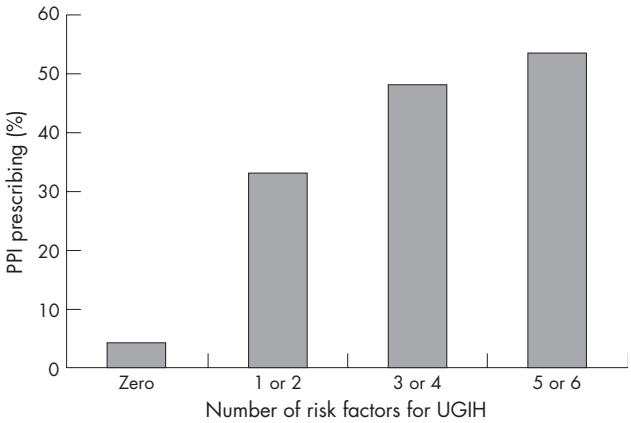
Introduction: Proton pump inhibitors (PPI) have shown efficacy in reducing the risk of upper gastrointestinal haemorrhage (UGIH) associated with the use of drugs such as non steroidal anti-inflammatory drugs (NSAIDs) and aspirin. We examined whether PPI co-prescribing is based on a rational assessment of risk.
Aims & Methods: The admission records of 160 unselected hospital inpatients were reviewed. PPI use at the time of admission was recorded. The relative risk of significant UGIH was estimated based on a number of factors: age>70, history of cardiovascular disease, history of PUD or UGIH, use of aspirin, other anti-platelet agents, anticoagulants, NSAIDs, corticosteroids, Hb<11 g/dl on admission to hospital.
Results: The median age of the study population was 74 years (IQR 63–82 years). 61/160 (38%) of patients were taking a regular PPI on admission to hospital. 10% had a documented history of PUD. 61/160 (38%) of patients were receiving regular aspirin and 18/160 (11%) were taking clopidogrel. 14/160 (8.8%) patients were receiving NSAIDs (in two cases coxibs). The proportion of patients prescribed a PPI was greater in aspirin users than non-users (51% *v* 30%, p=0.01, Fisher Exact Test). PPI use increased with number of risk factors for UGIH: 0 risk factors, 5% PPI use; 1 or 2, 33%; 3 or 4, 48%; 5 or 6, 53%. Half of all patients with multiple risk factors (>3) for UGIH were not co-prescribed a PPI.
Conclusion: PPI co-prescribing as a gastroprotection strategy is widespread but currently does appear to consistently take account of relative risk of UGIH.



Abstract 169

170 TO BIOPSY OR NOT TO BIOPSY? IS COELIAC SEROLOGY THE ANSWER—THE GUIDELINES SAY SO

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Introduction: The British Society of Gastroenterology (BSG) guidelines for iron deficiency anaemia (IDA)[1] state that all patients should be initially screened for coeliac disease (CD) with serological markers, and if negative negating the need for small bowel biopsy at oesophago-gastro-duodeno-scopy (OGD).
Aims & Methods: Data were collected retrospectively on all patients who underwent an OGD from May 2005 to August 2006 for IDA to assess whether screening for CD had been undertaken either serologically, in accordance with the guidelines, or histologically.
Results: 285 patients underwent investigation for IDA, during the study period. 63.4% were female with a median age of 63.4 years (range 17–93). All patients were screened for CD. 120 patients (42%) were screened serologically for CD prior to OGD. Of these, 10 patients had positive CD serology. 269 patients (94.5%) had a small bowel biopsy, 12 of whom had CD. All patients with positive CD serology had subsequent biopsy and consistent histology. No patients with normal CD serology had abnormal small bowel histology.
Conclusion: These results support the guidelines; serology is a robust screening method for CD as a cause of IDA. However, the majority of patients with IDA are still having a small bowel biopsy despite normal serology. The guidelines, if followed, should alter the way that CD is screened for in IDA and consequently reduce the number of small bowel biopsies taken. Although controversial, the guidelines have significant implications for in both time and financial terms.

1. **British Society of Gastroenterology**. *Guidelines for the management of iron deficiency anaemia* (http://www.bsg.org.uk/pdf_word_docs/iron_def.pdf).

171 A CROSS-SECTIONAL SURVEY TO ASSESS THE USEFULNESS OF THE ROME III DYSPEPSIA SYMPTOM SUBGROUPS IN A LARGE COMMUNITY SAMPLE

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Introduction: The Rome III classification of functional gastroduodenal disorders were published earlier this year and recommended the subdivision of functional dyspepsia into two distinct symptom subgroups:

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epigastric pain syndrome and postprandial distress syndrome. As yet this classification has not been validated in a community sample of individuals with dyspepsia.

Aims & Methods: The authors examined dyspepsia symptom subgroups in a large number of individuals originally randomly selected from the general population who were invited to participate in a community screening programme for Helicobacter pylori. All individuals completed a validated 15-item dyspepsia questionnaire (the Leeds dyspepsia questionnaire (LDQ)) at study entry, and the presence or absence of dyspepsia was assigned using these data. Those reporting heartburn or regurgitation at a frequency of once a week or more were classified as suffering from gastro-oesophageal reflux disease, and excluded from further analysis. Symptom subgroups were created using individual symptom items from the LDQ (epigastric pain, early satiety, and nausea or vomiting). The degree of overlap between these different subgroups was then examined.

Results: 8407 individuals were originally recruited of whom 3177 (38%) had dyspepsia according to the LDQ. However, 1290 described heartburn or regurgitation at a frequency of once a week or more and were therefore excluded, leaving 1887 (22%) individuals with Rome III dyspepsia with a mean age of 45 years, 1008 (53%) of whom were female. 1269 (67%) reported epigastric pain, of whom 730 (57.5%) described it as their predominant symptom. 684 (36%) reported nausea and/or vomiting, of whom 126 (18%) described either as their predominant symptom. 609 (32%) reported early satiety, of whom 88 (14.5%) described it as their predominant symptom. Furthermore 337 (18%) individuals were not classifiable into any of these three symptom subgroups. Of the 1550 individuals who described symptoms compatible with one of the three subgroups, 781 (50%) were in at least two subgroups, and 234 (15%) were in all three.

Conclusion: The new symptom subgroups recommended by the Rome III process still led to considerable overlap of classification in this large population-based sample. In addition, a significant minority of individuals with dyspepsia remained unclassifiable using these criteria. Data are required from other population-based studies examining this issue to assess the usefulness of these subgroups in clinical practice.

172 OUTPATIENT MANAGEMENT OF MINOR UPPER GASTROINTESTINAL HAEMORRHAGE

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Introduction: There are two validated scoring systems which predict outcome in patients with upper GI haemorrhage (UGIH): the Rockall Score (RS) and the Glasgow Blatchford Score (GBS). We have previously shown that GBS is a significantly more sensitive pre-endoscopy predictor of death and the need for endoscopic therapy, blood transfusion or surgery than RS in patients presenting with UGIH.[1] In this study, patients with a GBS $\leqslant 2$ and age <70 years required no intervention and none of them died. The aim of the current study was to apply these findings to clinical practice and to study outcomes and patient preference.

Aims & Methods: From June 2006 all patients presenting with UGIH have had a pre-endoscopy GBS calculated. If the GBS is $\leqslant 2$ and the patient <70 years they are allowed home and have an outpatient endoscopy on the next working day. However, such patients are not sent home (and thus have an inpatient endoscopy) if they have active comorbidities, a history of varices, are anticoagulated, or are unaccompanied at home or have no transport or telephone. Data were prospectively recorded regarding outcome (death, endoscopic intervention, transfusion and surgery), length of hospital stay, and patient preference.

Results: Over a 4-month period, 125 patients presented with UGIH. 29/125 (23.2%) fell within the above criteria for outpatient endoscopy. 12/29 (41.4%) were discharged, 11/12 had an outpatient endoscopy, 1/12 declined further investigation. 0/11 required endoscopic intervention. 7/11 perceived outpatient management as preferable, 2/11 would have preferred inpatient management, 2/11 were undecided. 17/29 patients fell within discharge criteria but were treated as inpatients as they had other factors that prevented their discharge, including alcohol excess/withdrawal (8), patient choice (2), significant pain or nausea (2), admission in the middle of the night (3) and reasons unknown (2). 16/17 did not require any form of intervention, 1/17 patients received endoscopic intervention for a Mallory–Weiss tear and none died.

Conclusion: These preliminary data suggest that outpatient management of minor UGIH may be safe in patients <70 years and with a GBS $\leqslant 2$. This cohort comprises of 23.2% of admissions for UGIH, 41.4% of whom were managed safely in the outpatient setting. Most patients with minor UGIH prefer outpatient management, which on average saves 2.5 bed days per patient.

1. **Warshow U**, Hare NC, Sanyal A, *et al.* Pre-endoscopy discharge of upper gastrointestinal haemorrhage: is it safe? BSG 2006. *Gut* 2006;**55**(Suppl II):A61.

173 A COMPARISON BETWEEN IRAQI AND IRANIAN HELICOBACTER PYLORI STRAINS

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Introduction: *Helicobacter pylori* causes peptic ulceration and gastric cancer. Virulence factors include (1) the *cag* pathogenicity island (*cag*+ strains are associated with gastric ulceration and cancer and strains with more CagA EPIYA motifs are associated with cancer), (2) VacA (s1, i1, and m1 types are associated with gastric cancer) and (3) *dupA* (*dupA*+ strains are associated with duodenal ulcer). Although pangastritis is common in Iraq, gastric atrophy is rare. Additionally, the incidence of gastric cancer in Iraq appears lower than that of Iran.

Aims & Methods: In this project, virulence determinants of both Iraqi and Iranian strains were studied and compared. 49 and 60 strains from patients with different clinical outcomes were collected from Iraq and Iran, respectively (DU Iraq 15, Iran 8; GU 5, 9; non-ulcer 29, 43). We specifically excluded strains from cancer patients, and we have reported those separately. PCR was performed to determine the presence of *cagA* and its EPIYA motif number, the status of *dupA* genotype, and allelic variation of *vacA*.

Results: The rate of *cagA* positivity was similar among strains from Iraq and Iran (35/49 (71%) and 46/60 (77%), respectively) and its presence was significantly associated with PUD in Iraq ($p<0.005$) but not Iran. The presence of *cagA* alleles with >3 EPIYA motifs was significantly higher among Iranian strains than those from Iraq ($p<0.01$). There was no association between *vacA* signal and mid region and PUD in either population. In Iraq, there was a significant association between i1 genotype and GU ($p<0.01$) (4/5 (80%) of GU compared with 7/35 (20%) of non-GU patients), but not in Iran. Finally, 16/49 (33%) and 23/60 (38%) of Iraqi and Iranian strains respectively typed positive for *dupA*. While a significant association between infection with *dupA*-positive strains and DU was observed for Iraqi patients ($p<0.01$), there was no association for Iranian subjects.

Conclusion: Virulence factors present in both Iraqi and Iranian *H pylori* strains are similar to those in Western strains. The presence of *cagA* with more EPIYA motifs in Iran may help explain the high cancer incidence rate. A novel association was found between i1 genotype and GU in Iraqi strains. Despite the similarity of virulence factors between Western countries and Iraq, the cancer rate in Iraq is still low which may indicate the presence of an enigma in the region.

174 INVESTIGATION AND MANAGEMENT OF PATIENTS REFERRED WITH NON-RESPONSIVE COELIAC DISEASE: RESULTS OF 110 CASES

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Introduction: Coeliac disease (CD) affects 1% of European and North American populations. It is treated with a gluten-free diet (GFD). Unfortunately 30% of patients diagnosed with CD fail to improve with a GFD or later relapse.[1] A small number have refractory coeliac disease, defined by persistent enteropathy on a strict GFD with other causes excluded (at 6 months).

Aims & Methods: To report our experience of the investigation and management of 110 patients referred to a tertiary centre over a 2-year period with non-responsive CD (NRCD). Notes of all patients with NRCD referred over 2 years were reviewed; those with abnormal duodenal histology and no other cause identified were assumed to have RCD.

Results: 110 patients (33 males) were identified as having NRCD. 12 were incorrectly diagnosed. 45 patients were not adhering to a strict GFD; of these 24 were inadvertently ingesting gluten and 21 admitted non-compliance. In those with NRCD, more than 1 cause for symptoms was found during investigation of most patients. The most common causes are shown in the table. Of 9 patients thought to have RCD 2 had ulcerative jejunitis, and 3 had developed small intestinal lymphoma. 27 other diagnoses were made.

Conclusion: The management of NRCD requires establishing a clear cause that can be found in 90% of cases. Continued gluten ingestion is the main reason for NRCD. Microscopic colitis and bacterial overgrowth are common treatable causes of continued symptoms. Overall 9.2% of

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Abstract 174

Cause	n
Refractory coeliac	9
Dietary non-compliance	21
Inadvertent gluten	24
Microscopic colitis	10
Bacterial overgrowth	9
IBD	7
Functional	12
Lactose intolerance	6
Anorexia nervosa	2
Lactose intolerance	2
Pancreatic insufficiency	2
Drug induced	2
Colorectal cancer	1
HIV	1

non-responders were diagnosed with RCD. Such individuals should be considered for treatment with immunosuppressive therapy and undergo frequent review to monitor for the potential development of lymphoma.

1. **Pink IJ**, Creamer B. Response to a gluten-free diet of patients with the coeliac syndrome. *Lancet* 1967;**1**:300–4.

175 INVESTIGATING THE RELATION OF SOCIAL DEPRIVATION AND RATES OF HELICOBACTER PYLORI INFECTION USING STOOL ANTIGEN TESTING: ANALYSIS OF 2368 CASES

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Introduction: Helicobacter pylori is the most common chronic bacterial infection in humans. It is thought to be more common in areas of social deprivation and with increasing age. Testing for the presence of H pylori is an integral part of investigating dyspepsia without alarm symptoms in UK patients. The H pylori stool antigen test (HPSA) is currently utilised for this purpose in both primary and secondary health care in Gateshead, England. Our results have been collected in a central database which was used to perform the analysis.
Aims & Methods: We analysed the database to determine rates of H pylori in our community and then correlated this with age, sex and social deprivation (based on postcode). Patient demographics were and HPSA results were taken from the database. Postcodes were converted to local ward codes and these were allocated a deprivation score. Ward level scores based on 1991 census data were obtained. The deprivation score used was the Carstairs index (combines local measures of unemployment, car ownership, overcrowding and social class—higher scores = greater deprivation). Each ward was also given a quintile score based on the degree of deprivation when compared to the nation as a whole (1 being least deprived and 5 the greatest) to allow for subgroup analysis of positive results when compared to national deprivation averages.
Results: There were 2994 tests between 01/03/05 and 03/04/06. Cases were excluded where no postcode was available or if the test was a repeat of a previously positive result. This left 2368 cases for analysis. male:female ratio 1052:1316. 353 were <30 years old, 1446 were 30–60 years old and 569 were >60 years old. 739 patients tested positive (31.2% of all tests). The mean deprivation score for this group was 3.71 (range −4.2 to 9.029) and 3.2 (range−5.53 to 9.029) ($p<0.001$, Mann–Whitney U test) for patients testing negative. In patients from less deprived groups (1 and 2 quintile scale) there were 74 +ve tests from 293 samples (25.26% positive). This compares to 469+ve tests from 1411 samples (33.24% positive) in the lowest social group (5) ($p=0.004$, Fisher's exact test). The relative risk of testing positive for H pylori in more deprived areas was 1.31 The % of males testing +ve was 31.65% (n = 333). In females it was 30.85% (n = 406). In the <30 age group, 25.77% (n = 91) tested +ve, rising to 29.8% (n = 431) and 38.13% (n = 217) in the 30–60 and over 60 age groups respectively. The p values for the differences between groups were <0.001 except when comparing risk of positivity in the <30 and 30–60 group ($p=0.076$).
Conclusion: H pylori infection is common in patients with presenting with dyspepsia in our region. The risk of infection increases with age and greater deprivation as determined by the Carstairs index. Analysis of central databases may allow for targeted health education and promotion in areas of highest risk.

176 DISCREPANCIES BETWEEN SEROLOGY AND HISTOLOGY FOR THE DIAGNOSIS OF COELIAC DISEASE IN A DISTRICT GENERAL HOSPITAL. IS THIS AN UNRECOGNISED YET COMMON PROBLEM IN HOSPITALS THROUGHOUT THE UK?

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Introduction: Published data on the sensitivity and specificity of serological testing for coeliac disease indicate that serology can be relied upon to diagnose or exclude disease without the need for a gastroscopy and duodenal biopsies. Most hospitals around the UK rely on such serology with confidence and often combine more than one test to improve the sensitivity and specificity of the test to near 100%. At Medway hospital we noticed a growing number of patients with histological positive biopsies but negative serology.
Aims & Methods: We collected all serology done for coeliac disease for the three years from 2003–5 (3056), and the total number of positive duodenal biopsies which had a serology done as well (26). We then correlated the serology with the histology results.
Results: A total of 42 patients had positive biopsies; 16 patients proceeded directly to biopsy because there was such a strong clinical suspicion of coeliac disease. Of the 26 patients with positive D2 biopsies and serology, 12 (46%) had negative tissue transglutaminase (tTG), 17 (65.4%) had negative IgA antigliadin and 15 (57.7%) had negative IgG antigliadin. When combining tTG with IgG and IgA antigliadin to improve the sensitivity, 5 patients (19.2%) had completely negative serology results and 6 (23%) had equivocal serology. Therefore 11 patients (42%) had non-predictive serology.
Conclusion: Gastroenterologists have grown to rely on serology for the diagnosis and more importantly, for the exclusion of coeliac disease. These results show a significant discrepancy between serology and histology results at Medway Hospital. The laboratory techniques used at this hospital are standardised and probably similar those used in most hospitals in the country. Even if this discrepancy were to be mirrored in a small number of hospitals, how many patients with coeliac disease are being missed every year across the UK?

177 UPPER GASTROINTESTINAL BLEEDING AND THE CHANGING USE OF COX-2 SPECIFIC NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

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Introduction: With the concerns over the vascular side-effects of COX-2 specific non-steroidal anti-inflammatory drugs (NSAIDs), rofecoxib was withdrawn, a study of celecoxib was halted, and alternative therapies were recommended by the regulatory authorities.
Aims & Methods: Given the relative gastrointestinal safety of COX-2 NSAIDs and the greater ulcerogenic potential of alternative conventional NSAIDs, we aimed to assess the incidence of upper gastrointestinal bleeding in light of the changing use of these compounds. We examined the numbers and clinical characteristics of patients developing haematemesis and/or melaena in the South West of Scotland (population of 290 000). Comparisons were made between data collected over one calendar year BEFORE and the year AFTER rofecoxib was withdrawn. Drug intake and prescriptions were documented including those for NSAIDs, low-dose aspirin (75-mg) and other antithrombotic drugs (clopidogrel, dipyridamole, and warfarin). Other clinical details, smoking and excess alcohol intake (>20 units/week) were also noted.
Results: The table shows the incidence of upper gastrointestinal bleeding (numbers per 100 000 of the population) in one calendar year BEFORE as compared with the year AFTER rofecoxib was withdrawn in all patients and in relation to peptic ulcer risk factors. The withdrawal of rofecoxib was associated with a drop in the use of celecoxib, a rise in the use of other relatively mild NSAIDs (meloxicam, etodolac, and etoricoxib), and continued rise in the use of low-dose aspirin and other antithrombotic drugs.
Conclusion: The rise in the incidence of upper gastrointestinal bleeding is not related to the changing use of NSAIDs. Instead, it reflects the increasing use of low-dose aspirin and other antithrombotic drugs, and the rise in alcohol-related bleeding.

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Abstract 177

	Before	After	χ^2	p Value
All patients	98.7	143.4	21.126	p<0.001
NSAIDs	13.3	16.1	0.658	p=0.42
Low-dose aspirin	26.6	38.4	5.442	p=0.02
Other antithrombotic drugs	12.1	30.2	19.626	p<0.001
Aspirin plus other antithrombotics	4.7	11.8	7.726	p=0.005
Excess alcohol	23.5	36.4	7.140	p=0.008

178 CHANGING EPIDEMIOLOGY OF PEPTIC ULCER BLEEDING: A PROSPECTIVE 10-YEAR WHOLE COMMUNITY STUDY

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Introduction: Peptic ulcer (PU) is still the most common cause of upper GI bleeding. Our gastrointestinal bleeding unit (GIBU) has accepted all admissions from a stable population of 485 600 since 1991. Patients are managed according to an agreed protocol defining transfusion requirements and surgical referral which has been reviewed and undergone modification over the years, and has seen the established relevance of H pylori infection and usage of proton pump inhibitors.
Aims & Methods: This dedicated unit provides an ideal opportunity to assess the natural history and epidemiology of peptic ulcer bleeding. Analyses were performed on the prospectively collected data from all admissions to GIBU with bleeding from a peptic ulcer from October 1991 to 2001.
Results: Of 1978 admissions, 737 had a bleeding gastric ulcer (GU) and 1241 bled from a duodenal ulcer (DU). The total number of bleeding ulcers has fallen ($p<0.01$), principally among the male patients with DU, but there has been a slight increase in bleeding GU. The median age for all peptic ulcer bleeders has increased from 67 in year 1 to 70 in year 10 ($p=0.02$) and has been accompanied by a rise in the comorbid disease. Aspirin ingestion has almost doubled 24% in year 1 to 44% in year 10 ($p<0.001$), as have those taking warfarin therapy from 3.8% to 7.2% ($p=0.002$). The percentage taking NSAID (24%) and acid suppression (22%) has remained unchanged. Despite a population decrease in smoking, the percentage of peptic ulcer bleeding patients who smoke has increased from 31% in year 1 to 36% in year 8 before falling to 27% in year 10. The number of significant bleeds has remained unchanged at 64%, although the number requiring a blood transfusion has decreased ($p=0.002$). In the first 2 years, as part of the management protocol, only a few (8%) had endoscopic therapy, by year 10 this number had increased to 28%. During the same period the surgical referral rate has progressively fallen from 46% in year 1, to 19% in year 3 and 8% in year 10 ($p<0.0001$). On the other hand, the rebleeding rate has been stable at 16% and the 30 day all cause mortality rate for PU bleeding has remained stable at around 7%.
Conclusion: The natural history of peptic ulcer bleeding is changing. The decreasing incidence of DU is likely to be as a result of decreased rates of H pylori infection. Despite an ageing population with more comorbid disease, aspirin and anticoagulation use, alongside use of endoscopic therapy, a decrease in blood usage and need for surgical intervention, the mortality rate has remained stable.

Gastrointestinal pathology posters

179 THE PUTATIVE STEM CELL MARKER CD24 IS PRESENT AS VARIABLY GLYCOSYLATED ISOFORMS IN COLORECTAL CANCER

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Introduction: CD24 is a heavily glycosylated cell surface protein that is bound to the cell membrane via a glycosylphosphatidylinositol anchor. The antigen is normally expressed on human neutrophils, pre B-lymphocytes, T-cells, ganglion cells but is thought to be a stem cell marker in the human intestine. Upregulation of CD24 has been reported in a variety of solid tumours, and in colorectal cancer strong cytoplasmic CD24 staining has been shown to be significantly associated with tumour progression and shortened patient survival times.
Aims & Methods: The aim of the study was to investigate CD24 expression in human colorectal cancers and cell lines. mRNA levels of CD24 were tested in 17 colorectal cancer cell lines by quantitative real-time PCR using locked nucleic acid technology in the form of the UniversalProbe Library (Roche). Western blot analysis was used to examine protein levels in these cell lines with a mouse monoclonal anti-CD24 antibody (Labvision Corp). In order to study the expression of CD24 in tumours, a tissue microarray (TMA) panel derived from 462 colorectal cancers together with whole tissue sections from a smaller number of colorectal cancers ($n=10$) underwent immunohistochemical (IHC) staining using same antibody.
Results: CD24 mRNA was found to be expressed in every single cell line tested. There was however a large variation in the levels of CD24 message expression with nearly a 1000-fold difference between the highest and lowest expressors (VACO10MS and RKO respectively). This correlated with the level of protein expression as evaluated by Western Blots. CD24 is glycosylated and, unexpectedly, different glycosylation patterns are present in different cell lines with some cell lines expressing up to three different isoforms. Immunohistochemical analysis showed that CD24 was not expressed in normal colonic mucosa but could be detected in stromal lymphocytes. In the TMA, 351/462 (76%) tumours showed fairly homogeneous cytoplasmic CD24 expression.
Conclusion: CD24 is not expressed in normal colonic mucosa but shows intense expression in a most colorectal tumours. The level of expression varies up to 1000-fold between tumours and there are differentially glycosylated protein isoforms. The specific roles of these isoforms as well as secondary messengers remain to be elucidated.

180 NOVEL AND CONCOMITANT MUTATIONS OF KRAS AND BRAF IN COLORECTAL CANCER CELL LINES

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Introduction: KRAS and BRAF encode small proteins which form part of the RAS/RAF/MAP kinase cascade. This is an important pathway that mediates a variety of functions such as cell growth, differentiation and apoptosis. Gain-of-function KRAS and BRAF mutations occur in a variety of different cancer types. Mutations of both genes are found in colorectal cancers and, since both activate the same signalling pathway, have been thought to be mutually exclusive. Recent reports, however, suggest that mutations of the KRAS and BRAF genes may occur in the same tumour.
Aims & Methods: We aimed to ascertain whether KRAS and BRAF mutations occurred as true concomitant events or whether previous reports are due to tumour heterogeneity. We investigated 26 well known colorectal cancer cell lines (ie homogeneous tumour cell populations) for KRAS/BRAF mutations and correlated these with other genetic features. The GTP binding domain of KRAS and the kinase domain of BRAF were examined in their entirety. Initially expressed mutations were sought through mRNA extraction followed by RT-PCR and bidirectional sequencing. Mutations found in mRNA were further validated by analysis of genomic DNA (encompassing exons 2–4 of KRAS and exons 11–15 of BRAF). Identification of novel mutations was followed by evolutionary analysis by comparing paralogs and orthologs using Clustal X.
Results: In total, 21/26 (80%) cell lines had a mutation in either KRAS or BRAF. Mutations of KRAS were found in 14/26 (53%) cell lines and there was no association with mismatch repair (MMR) or CIMP status. Ten of these mutations were heterozygous whilst unexpectedly, in 4 cell lines, the KRAS mutations were homozygous. Mutations occurred mainly in codons 12, 13, 61 and 146. However, we also provide the first ever report of a codon 117 mutation. This is an evolutionarily conserved residue in the GTP binding domain of KRAS. Mutations of BRAF were found in 9/26 (34%) cell lines and there was no association with MMR or CIMP status. All mutations

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were heterozygous and most were the commonly described V600E. However, we also provide the first ever reports of mutations in codon 529 and 581—both are evolutionarily conserved residues in the kinase domain. Concomitant KRAS and BRAF mutations were found in 2/26 (7%) cell lines confirming that these mutations can occur together.
Conclusion: Activation of the RAF/RAF pathway occurs frequently in colorectal cancers and mutations occur at a wider range of residues than previously reported. The occurrence of homozygous KRAS mutations and concomitant KRAS/BRAF mutations shows that this pathway may be gene dosage dependent.

181 INVESTIGATING EPIGENETIC PATHWAYS IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) develops due to sequential somatic gene mutation. It is also apparent that this is accompanied by gene silencing through methylation of CpG islands located within gene promoter regions (epigenetic change). Some tumours appear to have a propensity for widespread promoter methylation—the so-called CpG Island Methylator Phenotype (CIMP) and CRCs can be subdivided into CIMP+ and CIMP− categories using a panel of genes that can discriminate between the tumour types. However, the impact of the CIMP+ phenotype on tumour biology is uncertain since (1) many genes undergo age-related methylation, (2) frequently only one allele at a locus is methylated (partial methylation) causing uncertain changes in gene dosage, and (3) the relationship of the CIMP and genetic pathways is unclear.
Aims & Methods: The aim of this study was to investigate epigenetic changes in a series of 26 colorectal cancer cell lines and correlate these with genetic changes. DNA and RNA was extracted from all cell lines. DNA underwent bisulphite modification followed by methylation specific PCR to evaluate promoter methylation of the 5 genes comprising the CIMP panel (NEUROG1, SOCS1, IGF2, RUNX3, CACNA1G). This identified the CIMP status of the cell lines and was followed by further analysis of 5 different tumour suppressor genes (CDH1, APC, p14, p16, MLH1) and 2 genes of biological interest (CDX1, MGMT). Finally, all cell lines were tested for levels of MGMT expression using real-time PCR.
Results: The CIMP panel was successfully completed in 22/26 cell lines. CIMP+ was defined as promoter methylation at $\geqslant 3$ loci and, by this criterion, 11 cell lines fell into each category. 83% of cell lines with microsatellite instability (MSI) were CIMP+ and whilst not statistically significant (due to small numbers) it does reflect the association between MSI and CIMP+ described in primary tumours. There was no association with BRAF or KRAS mutation. CIMP+ status was associated with MLH1 methylation ($p<0.03$) and there was an association with p16 methylation and, interestingly, a negative association with APC methylation. Partial methylation was seen at many loci and quantitative PCR of MGMT showed no significant difference between cell lines showing partial and non-methylation. There was complete abrogation of expression when both MGMT alleles were methylated.
Conclusion: Our data show that CRC cell lines are a good model of CRC. There were interesting associations between CIMP+ status and methylation of certain promoters which need further investigation. Partial methylation at a locus does not appear to significantly alter gene expression and is therefore of uncertain biological relevance.

182 IRON INDUCED UPPER GI EROSIONS: A COMMON PATHOLOGICAL FINDING

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Introduction: Although iron induced gastrointestinal injury has been long known about, it is not generally recognised as a cause of upper GI pathology by gastroenterologists or pathologists and until very recently there has been little in the literature.
Aims & Methods: This study aimed to document cases of iron related upper GI pathology and relate this to clinical parameters and iron treatment. The pathology database was searched for cases of iron deposition in oesophageal, gastric and duodenal biopsies between 1999 and 2006. In addition, cases were collected prospectively from November 2005 to July 2006 as part of an audit of endoscopy in iron deficiency anaemia. Cases were examined to determine the site and pattern of iron deposition (luminal/surface, lamina propria, macrophages, epithelial, vascular) and associated pathology. Patient notes were examined for indication for endoscopy, details of iron and other treatment, haematology and underlying diseases.
Results: Fifty nine patients were identified, 44 from past records and 15 prospectively. 64 episodes of iron deposition were identified: 7 oesophageal, 28 body, 18 antrum and 10 duodenal. There was a steep increase in annual frequency in diagnosis from retrospective series (1999:2, 2006:13) while 9.3% of patients endoscoped for iron deficiency anaemia (15/161) showed detectable iron on routine H&E staining. In the oesophagus, iron deposition was frequently accompanied by ulceration (6/7) while in the stomach, 39/46 showed reactive or erosive gastritis with 29/46 showing erosion or ulceration. Here, iron was typically deposited superficially in strips of crystalline material and/or in lamina propria. Duodenal deposition was usually in villous tips in macrophages without ulceration. The notes of 47 patients were reviewed. All 47 had a history of prior iron treatment (43 ferrous sulphate, 1 ferrous fumarate, 3 unknown) which varied from 1 day to 3 years (median 2 months) with cumulative dose from 0.4–324 g (median 30 g). 25 patients were on aspirin and/or NSAIDs. No patient had haemosiderosis or haemochromatosis.
Conclusion: This is the largest reported series of iron induced upper GI pathology. Iron deposition in the upper GI tract is commonly seen in patients on oral iron and it is frequently associated with erosions in oesophagus and stomach. It likely represents the pathological manifestation of the frequent clinical complaint of GI intolerance to oral iron, and in such patients an alternative iron preparation or route should be considered. Pathologists and gastroenterologists should be aware of this common pathological finding.

183 A BLINDED COMPARISON OF CAPSULE ENDOSCOPY AND HISTOLOGY IN THE EVALUATION OF NON-RESPONSIVE COELIAC DISEASE

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Introduction: Non-responsive CD may be due to failure to adhere to a gluten-free diet (GFD), an additional diagnosis, incorrect initial diagnosis, assessment too soon after commencing a GFD or refractory CD. Complications of refractory CD include ulcerative jejunitis and lymphoma. This study aimed to evaluate capsule endoscopy (CE) in identifying patients with histological evidence of refractory CD and excluding those who did not, as well as detecting complications.
Aims & Methods: Patients with non-responsive CD (on a GFD for at least 12 months with continuing symptoms) underwent a CE. All had a repeat endoscopy with distal duodenal biopsies, at most, 3 months earlier. The videos were analysed by an experienced observer (LM). CE changes consistent with CD (eg villous atrophy, scalloping of folds) were classified as mild or moderate to severe. The observer was blinded to the results of the histology. Concordance between CE and histology (Marsh 1–2 or 3–4) was then calculated using the Kappa statistic.
Results: Nineteen patients (14 female; mean age 57 years, range 18 to 82) underwent a CE. In 3 studies the video ended in the terminal ileum (passage of the capsule subsequently confirmed by patients). CE reported 10 (53%) videos as normal (2 had incidental angiodysplasia), 3 (16%) had mild changes and 6 (31%) had moderate–severe changes. Two (11%) had acute ulcers along the jejunum and ileum, consistent with ulcerative jejunitis. No small bowel tumours were seen. Histology was available in 18 of the 19 patients. CE demonstrated concordance with histological changes in 14 of the 18 patients (78% concordance). Twelve had histological features of CD on a GFD. Of those 12 CE identified endoscopic features of CD in 8 (67%). CE was normal in those 6 patients with no histological changes (ie sensitivity of 67%, specificity of 100%, positive predictive value of 100% and negative predictive value of 60%). The kappa statistic was 0.65.
Conclusion: The kappa statistic suggests a substantial degree of concordance between histology and CE findings. Ulcerative jejunitis is frequently missed on biopsy and in this study it was detected in only 1 of the 2 cases diagnosed by CE. The negative predictive value of CE in this study suggests up to 40% of patients with a normal CE may have refractory CD. Endoscopy with distal duodenal biopsies is superior to CE in detecting refractory, proximal small bowel CD but since its complications are often out of reach of the biopsy the strength of CE lies in its ability to visualise the entire small bowel. CE has a complementary role to histology in detecting refractory CD and is helpful in investigating its complications as well as other causes of non-responsive CD.

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184 NATURAL POLYMORPHISM IN THE HELICOBACTER PYLORI VACUOLATING CYTOTOXIN SIGNAL SEQUENCE AFFECTS TOXIN PRODUCTION

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Introduction: The *H pylori* vacuolating cytotoxin gene, *vacA*, is naturally polymorphic, one of the most diverse regions being the signal region (type s1 or s2). Signal type determines vacuolating activity: type s1 strains are vacuolating; and type s2 strains are non-vacuolating. Heterogeneity in VacA levels between strains also exists, and analysis of type s1 and s2 signal sequences has shown that they differ in the cleavage recognition site at positions -3 and -6. In type s1 the more favourable serine and proline residues are at positions -3 and -6 respectively, whereas type s2 strains have leucine present at -3 and glycine at -6.
Aims & Methods: We aimed to characterise the effect of polymorphic differences in the *vacA* signal cleavage site on VacA production. Isogenic *H pylori* mutant strains of 60190 (type s1; tox+) encoding *vacA* alleles, in which serine at position -3 was replaced by leucine, and proline at -6 was replaced by glycine were prepared. Mutant strains of Tx30a (type s2; tox-) encoding *vacA* alleles, in which leucine at position -3 was replaced by serine, and glycine at position -6 was replaced by proline were also prepared. Duplicate 24-h broth cultures of duplicate transformants of each isogenic mutant were prepared, and separated. Supernatant and cell pellet samples were corrected for bacterial density and analysed by western blotting and ELISA with anti-VacA antibody. The positions of the signal cleavage site were determined using N-terminal protein sequencing.
Results: For strain 60190, replacing serine with leucine at position -3 did not significantly reduce VacA production compared to the control. However replacing proline with glycine at the -6 position significantly reduced VacA production compared to the control (28% reduction ($p<0.05$)). Substitutions at both the -6 and -3 positions also significantly reduced VacA production compared to the control (23% reduction ($p<0.05$)). For Tx30a, replacing leucine with serine at postion -3 significantly reduced VacA production compared to the control (54% reduction ($p<0.005$)). Replacing glycine with proline at position -6 significantly reduced VacA production compared to the control (51% reduction ($p<0.005$)). Substitutions at both the -6 and -3 positions also significantly reduced VacA production compared to the control (77% reduction ($p<0.005$)).
Conclusion: These results indicate that differences in the VacA signal sequence affect VacA production. We speculate that these naturally-occurring differences affect signal sequence processing efficiency. The reduction seen in VacA production for the Tx30a isogenic mutants was surprising and may reflect differences in signal peptidase specificity.

185 VITAMIN D CONTROLS CDX-1 AND 2 TUMOUR SUPPRESSOR FUNCTION IN COLORECTAL CANCER

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Introduction: CDX-1 and CDX-2 transcription factors regulate embryonic tissue differentiation,[1] and have also been identified as tumour suppressor genes.[2] Currently the factors which regulate the tumour suppressor function of CDX-1/2 are unknown.
Aims & Methods: The aim of this study was to identify the factors which regulate CDX-1/2 tumour suppressor function. Paired samples of colorectal adenocarcinoma and adjacent normal colon from 6 patients, were harvested and then cultured for 24 hours with sodium butyrate, vitamin D or control medium only. mRNA was extracted by standard techniques, and quality assessed using newly developed 3′:5′ and inhibition assays, prior to quantification by real-time reverse transcription polymerase chain reaction (RT-qPCR).
Results: For individual patients, Vitamin D decreased CDX-2 mRNA expression levels in adenocarcinoma cells (median 4.5-fold difference, $p<0.005$), compared to butyrate or medium only cultures. No clear pattern of CDX-1 regulation could be identified. In contrast, culturing adjacent normal colonic epithelial cells with butyrate or vitamin D showed no change in CDX-1,2 mRNA expression levels, when compared to medium only cultures.
Conclusion: This work indicates for the first time that the tumour suppressor function of CDX-2 may be regulated by vitamin D. Further investigation of CDX-1/2 tumour suppressor function may provide a basis for future novel therapies for colorectal cancer.

1. **Beck F**. *Gut* 2004;**53**:1394–6.
2. **Bonhomme C**, *et al. Gut* 2003;**52**:1465–71.

186 HOX GENE GRADIENTS WHICH PATTERN THE EMBRYONIC GUT ARE ALSO PRESENT IN THE ADULT HUMAN GUT

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Introduction: In the embryo differentiation of the gut occurs in response to segmental HOX gene transcription, with contrasting relative mRNA expression patterns in small and large bowel. In the adult human it has been hypothesised that maintenance of gut morphology occurs by continued HOX gene expression both postnatally and throughout adulthood.[1] Transcription factors which regulate HOX genes have been linked with pathological transformation of bowel morphology (eg Barrett's oesophagus,[2] intestinal metaplasia of the gallbladder,[3] colorectal adenocarcinoma[4]), but the involvement of individual HOX genes in such conditions cannot be assessed due to inadequate data describing expression in normal gut tissue.
Aims & Methods: The aim of this study was to identify and quantitate the expression pattern of HOX genes in normal adult human small and large bowel. Paired samples of ileum and ascending colon from 3 patients were harvested with four unmatched rectal samples. mRNA was extracted using standard techniques, and RNA was quality assessed using 3′:5′ and inhibition assays. Quantification of a representative selection of HOX genes was performed by real-time reverse transcription polymerase chain reaction (RT-qPCR).
Results: Clear differences in relative HOX factor mRNA expression were found in ileal samples, as compared to ascending colon/rectum. Relative mRNA expression pattern in terminal ileum was: CDX2>B6>A3>C10>C6>CDX1. In contrast relative mRNA expression levels in both large bowel and rectal tissue were: CDX2>B6>C10>C6>A3>CDX1.
Conclusion: Relative HOX mRNA expression levels differ between adult human small and large bowel, in a similar fashion to embryonic gut. These findings provide evidence for the previously hypothesised role of HOX genes in the maintenance of tissue morphology in the adult human gut. In addition, further investigation of HOX function in normal tissue may subsequently allow a meaningful examination of their role in changes of gut morphology caused by pathological processes.

1. **Deschamps J**, *et al. Int J Dev Biol* 1999;**43**:635–50.
2. **Vallbohmer D**, *et al.* 2006;**19**:260–6.
3. **Osawa H**, *et al. Am J Surg Pathol* 2003;**27**:1442–7.
4. **Bonhomme C**, *et al. Gut* 2003;**52**:1465–71.

Neurogastroenterology/motility posters

187 ABDOMINAL DISTENSION IS RELATED TO DELAYED GASTROINTESTINAL TRANSIT IN IRRITABLE BOWEL SYNDROME WITH CONSTIPATION

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Introduction: Patients with irritable bowel syndrome with constipation (IBS-C) often have slow gastrointestinal (GI) transit[1] and exhibit a diurnal increase in abdominal girth (ie abdominal distension) that is related to a feeling of worsening bloating.[2]
Aims & Methods: The aim of this study was to investigate whether IBS-C patients with delayed GI transit exhibit greater abdominal distension and more severe bloating than do patients with normal transit. Abdominal girth was recorded for 24 hours using the validated technique of Ambulatory Abdominal Inductance Plethysmography[3] in 27 IBS-C (Rome II) patients, aged 18–68 years (3 male) and 24 healthy volunteers (HV), aged 21–58 years (3 male). Within 2 weeks of this recording, both small (SBT) and large (LBT) bowel transit were assessed. SBT was determined from the rise in breath hydrogen after a standard meal,[4] and LBT from the number of 3 differently shaped radio-opaque markers (24 of each ingested on 3 consecutive days) identified on plain abdominal *x* ray 72 hours after ingestion.[5] The severity of abdominal bloating was also assessed on a scale of 0–3, where 3 = severe.
Results: As anticipated, IBS-C patients reported more severe abdominal bloating (IBS: 2.00 (1.73 to 2.26), mean (95% CI) *v* HV: 0.33 (0.07 to 0.59); $p<0.001$), and exhibited greater abdominal distension (change in girth from the beginning to end of day: 3.8 cm (2.2 to 5.5) cm *v* 0.46 cm (−1.1 to 2.0) cm; $p=0.007$) and slower LBT (52 hours (45 to 58) hours *v* 35 hours (28 to 42) hours; $p=0.003$) but not SBT (330 min (291 to 368)

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min *v* 293 min (262 to 325) min; p = 0.35) compared with HV. Using the 97.5 percentile for LBT in HVs (ie >59 hours), 48% of IBS-C patients had delayed LBT and these patients exhibited greater abdominal distension (5.3 cm (3.7 to 6.9) cm) than those with normal LBT (2.4 cm (−0.1 to 5.0) cm; p = 0.03). Furthermore, there was a direct relationship between LBT and the degree of abdominal distension in IBS-C patients (r = 0.51, p = 0.006). There was no difference in bloating severity between patients with (2.00 (1.60 to 2.39) and without (2.00 (1.61 to 2.38): p = 0.63) delayed LBT.
Conclusion: IBS-C patients with delayed large bowel transit have greater abdominal distension than those with normal transit. Drugs that accelerate transit may therefore be expected to alleviate this often troublesome problem.

1. *Gut* 1983;**24**:404–11.
2. *Gut* 2004;**53**(Suppl III):A114.
3. *Gut* 2001;**48**:216–20.
4. *N Engl J Med* 1969;**28**:122–7.
5. *Gastroenterol* 1987;**92**:40–7.

188 IS VISCERAL HYPOSENSITIVITY ASSOCIATED WITH ABDOMINAL DISTENSION IN IRRITABLE BOWEL SYNDROME?

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Introduction: Irritable bowel syndrome (IBS) patients with a history of bloating can be divided into those who distend (ie exhibit an increase in abdominal girth) and those who do not.[1] Those who bloat alone have been shown to be more viscerally sensitive than those who bloat and distend.[2]
Aims & Methods: The aim of this study was to examine whether abdominal distension differs between IBS patients who are hypo-, normo-, or hypersensitive to balloon distension. Abdominal girth was recorded for 24 h using the validated objective technique of Ambulatory Inductance Plethysmography[1] in 70 IBS patients (Rome II) with a history of bloating, aged 18–73 years (39 IBS-C, 26 IBS-D, 5 IBS-alt, 62 female) and 44 healthy volunteers, aged 18-67 years (42 female). Within 7 days of this recording, rectal sensitivity was assessed using a barostat technique, in which pain thresholds were determined using the ascending method of limits followed by tracking.
Results: Compared with our departmental 95% normal reference range for the sensory threshold for pain of 24–38 mmHg;[3] 22 (32%) were found to be normo-sensitive, 31 (44%) hypersensitive and 17 (24%) hyposensitive to distension. Hyposensitive patients distended significantly more (change in girth from beginning to end of day +7.8 cm (6.2 to 9.4) cm; mean (95% CI)) than both normo-sensitive (+4.0 (2.1 to 6.0); p<0.001) and hypersensitive (3.1 cm (1.7 to 4.5); p<0.001) patients. In addition, significantly more of the hyposensitive patients, (14/17) distended beyond the normal reference range of >6.9 cm than either normo- (9/22, p<0.01) or hypersensitive (5/31, p<0.01) patients. Although there was no significant difference in diurnal change in girth between hyper- and normo-sensitive patients (p = 0.42), fewer of the hypersensitive patients exhibited changes in girth beyond the normal reference range than those who were normo-sensitive (p = 0.06).
Conclusion: These results show for the first time that IBS patients who are viscerally hyposensitive are more likely to exhibit the greatest changes in abdominal girth (ie distend). Furthermore they confirm our previous preliminary observations that hyper-sensitivity is more likely to be associated with the symptom of bloating alone.[2]

1. **Houghton**, *et al. Gastroenterology* 2006:1003–10.
2. **Lea**, *et al. Gastroenterology* 2003:A–398.
3. **Lea**, *et al. Aliment Pharmacol Ther* 2003;**17**:635.

189 IRRITABLE BOWEL SYNDROME IN THE ELDERLY: AN OVERLOOKED PROBLEM?

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Introduction: It is well known that irritable bowel syndrome (IBS) patients commonly consult about their problem between the ages of 30 and 50, although in a large proportion of these individuals, symptoms have been present for many years.[1] It is also known that in secondary care IBS is commonly associated with multiple non-colonic symptoms including lethargy, backache, urinary symptoms and chest pain which result in referral to different specialities and the condition remaining unrecognised.[2] However, there is very little information on whether the condition persists into old age, and no data on how it manifests itself in the elderly or its prevalence in elderly care clinics.
Aims & Methods: Using the previously validated Elderly Bowel Symptom Questionnaire (EBSQ),[3] this study aimed to assess the extent of this problem in consecutive outpatients attending elderly care clinics relating the results to the presenting complaint, non-colonic symptomatology and final diagnosis. Of the 230 consecutive patients who attended the Elderly clinics in Wythenshawe Hospital, 211 completed the questionnaire and were included in the study.
Results: Fifty six (26%) of 211 patients had symptoms compatible with a diagnosis of IBS irrespective of their presenting complaint. However despite the exclusion of abdominal pathology a diagnosis of IBS was only documented in one patient. 69.6% of patients had suffered from their IBS symptoms for over 5 years. Not surprisingly abdominal pain, bloating and bowel dysfunction including urgency were more common in IBS patients (p<0.001). However other symptoms significantly more common in the IBS compared to non-IBS patients were backache (76.7% *v* 52.9%, p<0.001), constant lethargy (73.2% *v* 49.7%, p = 0.002), chest pain (62.5% *v* 44.5%, p = 0.02), headaches (55.3% *v* 26.4%, p<0.001) and urinary frequency (37.5% *v* 23.2%, p = 0.04). Independent predictors of IBS on logistic regression have been listed in the table.

Abstract 189 Significant independent predictors of IBS derived from logistic regression

	Odds ratio	95% CI
Bloating	17.61 (p<0.001)	5.20 to 59.62
Stool urgency	3.64 (p<0.001)	1.77 to 7.45
Headache	3.44 (p<0.001)	1.82 to 6.51
Backache	2.47 (p<0.05)	1.01 to 5.99

Conclusion: IBS appears to be seriously underrecognised in elderly care clinics even after negative investigation. Making the diagnosis, despite the presence of coexistent disease, could reduce the overall burden of suffering, improve quality of life, prevent repetitive investigations and have significant economic advantages.

1. **Lea R**, Whorwell PJ. *Gut* 2002;**51**:305–6.
2. **Whorwell PJ**, McCallum M, Creed FH, *et al. Gut* 1986;**27**:37–40.
3. **Talley NJ**, O'Keefe EA, Zinsmeister AR, *et al. Gastroenterology* 1992;**102**:895–901.

190 WHAT IS THE OPTIMAL DURATION OF OESOPHAGEAL PH MEASUREMENT AND SYMPTOM ASSESSMENT? A PROSPECTIVE STUDY USING 96 H BRAVO RECORDINGS

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Introduction: The day-to-day variability of oesophageal acid exposure in patients with suspected gastro-oesophageal reflux disease (GORD) is high and 20–30% of patients receive a different diagnosis on repeated 24 h catheter based pH testing. Preliminary reports by the authors and others suggested that 48 h pH testing by the catheter-free Bravo system increase measurement reliability and diagnostic accuracy; however these reports were retrospective and underpowered to determine the optimal duration of reflux investigation.
Aims & Methods: Prospective study of 40 consecutive patients with typical reflux symptoms (18M:22F; 46 (21–70) years). Endoscopy and trans-oral delivery of the Bravo capsule 6 cm above the Z-line were performed. Patients returned after 48 and 96 h to download data. The day-to-day variability of pH measurements was calculated. Patients were classified by acid exposure (abnormal: >4.2% time pH<4) and symptom index (positive SI: >50% association of reflux events and any symptom) during each 24 h and 48 h test period. The reliability of 24 h *v* 48 h pH testing was assessed with 96 h results as the reference standard.
Results: Complete four-day recordings were available for 32/40 (80%) patients (n = 4 detachment <96 h, n = 4 consent withdrawn due to symptoms off treatment). There was no difference in pH measurement or SI over time (p>0.1). Oesophageal acid exposure: Within patient variability was higher for 24 h (±30%) than 48 h (±22%) test periods relative to the 96 h reference standard (p<0.01). Pathological acid exposure was present in 18–19 patients on any test day and 13 patients on every test day. Different diagnoses were reported in 11/32 (34%) and 3/32 (9%) patients on 24 h and 48 h pH testing respectively (p<0.01). Diagnostic reproducibility of pH testing was improved by prolonged studies (kappa score, 24 h = 0.32 (poor) *v* 48 h = 0.81 (very good)). Results were similar for the DeMeester score and alternative pH ''diagnostic cut-offs'' for GORD. Symptom assessment: different results were reported in 21/32 (76%) and 12/32 (37%) patients on 24 h and 48 h SI assessment respectively (p = 0.07). A positive 96 h SI was found in 2/15 (13%) and 13/17 (77%)

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patients in whom <2/4 days and ⩽2/4 days had a significant association between reflux events and symptoms respectively (p<0.01).
Conclusion: Increasing the duration of pH testing from 24 h to 48 h improves the reliability of pH testing and symptom assessment (compared to a 96 h ''reference standard''). Prolonging pH testing beyond 48 h provides little improvement in diagnostic yield but may be justified in borderline cases and to confirm the association between reflux events and symptoms in patients with inconsistent results on the first two test days.

191 IS TARGETING LOCUS OF CONTROL A DESIRABLE OUTCOME OF BIOFEEDBACK IN FUNCTIONAL CONSTIPATION?

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Introduction: Behavioural therapy, biofeedback, is an effective treatment for functional constipation, whether related to slow or normal transit. The treatment is better tolerated and more effective than long-term laxative use. Biofeedback is a complex operant conditioning based treatment, incorporating aspects of habit training and enhancing coordination of pelvic floor and abdominal musculature. The prognostic factors that determine outcome remain unknown. We hypothesised that patients who viewed themselves as potentially having control of their condition (''internal'' locus of control) would be more likely to improve symptoms than those who believed someone other than themselves had control over their situation (''external'').
Aims & Methods: 146 consenting patients with functional constipation (Rome II) referred to two tertiary referral centres were enrolled. Patients completed the following questionnaires: Locus of Control of Behaviour (LCB, low scores reflecting internal and high scores external control), BSI (reflecting psychological traits, including a somatisation subscale where score >63 implies a somatisation trait) and HAD (anxiety and depression). 99 patients completed a course of biofeedback (median 4 sessions) and returned the same questionnaires as pre-treatment. 56 had slow transit and 43 normal transit.
Results: At the end of treatment 88/146 patients (60%) were symptomatically improved, and of the 99 with completed questionnaires 61 had improved (62%). Outcome was not related to transit – 33/56 (59%) slow transit and 26/43 (65%) normal transit patients responded. Locus of control: Patients had high LCB scores (30.9+11.7) which fell (11.9+9.8, p<0.04) in those successfully treated, but was unchanged in those who did not (28.8+10.2). Initial LCB scores did not predict outcome. BSI: somatisation scores >63 were observed in 15/98 (15%) patients. High scores were seen in 10/61 (16%) patients who had improved and 5/37 (14%) who had not. HAD scores: at baseline were within population norms for anxiety (mean = 9.4+3.8) and depression (mean = 5.8+3.6). Anxiety was improved by successful treatment (mean 5.7+3.8, p<0.05) but depression was not 4.2+3.5. Improvement in anxiety was independent of altered locus of control.
Conclusion: A beneficial response to biofeedback is associated with the development of an internal locus of control. This was not related to transit and not dependent on altering anxiety or mood. Improvement was also not related to a tendency to somatisation. The aim of enhancing a patient's sense of being in control of their symptoms is therefore an achievable and desirable aim of biofeedback therapy in functional constipation.

192 USING THE GUT RESPONSE TO ACUTE STRESS TO STUDY THE PATHOPHYSIOLOGY OF IRRITABLE BOWEL SYNDROME

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Introduction: Evolving knowledge of the stress response has offered insights into the aetiology of irritable bowel syndrome (IBS). We have previously shown that acute physical (cold pressor-CP) and psychological (dichotomous listening-DL) stress alters gut specific autonomic tone and gut sensitivity in patients with IBS (Murray *et al. Gastroenterology* 2004;**127**:1695). This model provides both the opportunity to study putative novel IBS drugs, and the opportunity to study aspects of visceral physiology. Firstly, does convergence of afferent input at spinal level occur (by comparing effect of upper limb *v* lower limb CP); secondly, does tolerance to stressful stimuli occur with repeat exposure, and can it be avoided.
Aims & Methods: The stress model described previously was performed under three experimental paradigms. Experiment 1—does lumbosacral spinal convergence occur?: 15 patients with c-IBS (12 female, mean age 31) and 11 control subjects (7f, mean age 35) underwent two CP studies, one of upper and one lower limb >1 week apart. Experiment 2—does adaptation develop to DL?: 16 patients with c-IBS (13f, mean age 32) and 9 control subjects (6f, mean age 37) underwent 3 DL studies, each >1 week apart. Experiment 3—can this adaptation be avoided?: 14 patients with c-IBS (11f, mean age 32) and 11 control subjects (7f, mean age 37) underwent 3 DL studies supplemented by mental arithmetic, each >1 week apart. Endpoints for all experiments were subjective stress perception (VAS), autonomic function (rectal mucosal blood flow, RMBF) and visceral sensitivity (rectal electrosensation, RES).
Results: Experiment 1: lower limb CP induced identical stress physiological response as upper limb. As in previous studies, c-IBS patients had a stress-induced reduction in RMBF and RES pain threshold, while controls only showed the RMBF reduction. Experiment 2: in c-IBS, stress-induced reduction in RMBF was 34% *v* 24% (1st test *v* 3rd, p<0.05) and RES threshold (23% *v* 19%, p = NS). Controls showed no significant differences between 1st and 3rd tests (RMBF 26% *v* 28% resp; RES 1% *v* −1% resp). Experiment 3: there was no significant difference in stress induced reduction in RMBF or RES threshold between 1st and 3rd tests in c-IBS or controls.
Conclusion: The physical stress model suggests that convergence of visceral and somatic input at the spinal cord is not an important mechanism in man, with lower limb CP responses being similar to upper limb. For psychological stress, repeated DL testing may induce tolerance in IBS patients—especially in terms of autonomic response. Supplementing DL testing with mental arithmetic prevents this adaptation. Finally, the validity and reproducibility of the gut response to physical and psychological stress has been demonstrated.

193 POOR QUALITY OF LIFE PREDICTS THE NEW ONSET OF IRRITABLE BOWEL SYNDROME. A LONGITUDINAL 10-YEAR FOLLOW-UP STUDY

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Introduction: Studies have indicated that irritable bowel syndrome (IBS) is associated with poor quality of life, but it is unclear whether IBS causes poor quality of life, or whether those with poor quality of life are more likely to develop IBS. This is the first study to address this issue.
Aims & Methods: The authors performed a longitudinal 10-year follow-up study of individuals previously recruited into a community screening programme for Helicobacter pylori. All surviving, traceable participants were contacted via postal questionnaire that utilised the Manning criteria to diagnose IBS. Baseline demographic data (including: age; gender; social class; tobacco, alcohol, and coffee consumption; and ethnicity), quality of life (assessed via the psychological and general well-being index and split into tertiles), IBS symptom data, and dyspepsia symptom data (captured via validated questionnaire) were already on file. Written informed consent was sought to examine primary care records, and data on use of non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin over the 10-year period were extracted from these. The associations between these data and new onset of IBS at 10 years in those asymptomatic at baseline were explored using univariate analysis. Independent risk factors were determined by performing multivariate logistic regression to control for all these demographic data and lifestyle factors.
Results: Of 8407 individuals originally involved, 4003 (48%) responded to the questionnaire. Mean age of responders was 55 years, and 2247 (56%) were female. 220 (5.6%) of 3948 individuals providing data at baseline had IBS, compared to 696 (18%) of 3925 individuals providing data at 10-year follow-up, when dichotomised according to questionnaire data. Of 3728 individuals without IBS at baseline, 542 (14.5%) developed new onset IBS at 10 years. Female gender (odds ratio (OR) 2.15; 99% confidence interval (CI) 1.66 to 2.79), dyspepsia at baseline (OR 2.23; 99% CI 1.71 to 2.92), lower social class (IV and V versus I and II: OR 1.99; 99% CI 1.35 to 2.93), NSAID use (OR 1.78; 99% CI 1.35 to 2.36), and low quality of life (bottom *v* top tertile: OR 4.60; 99% CI 3.26 to 6.48) all significantly increased likelihood of new onset IBS at 10 years, while consumption of alcohol reduced the likelihood (OR 0.57; 99% CI 0.39 to 0.84). Following multivariate logistic regression female gender, dyspepsia at baseline, NSAID use, and lower quality of life remained significant risk factors for new onset IBS.
Conclusion: New onset IBS developed at a rate of almost 1.5% per year. Low quality of life at baseline exerted a strong effect on development of IBS at 10 years in our model.

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194 WHO CONSULTS WITH IRRITABLE BOWEL SYNDROME? A LONGITUDINAL 10-YEAR FOLLOW-UP STUDY

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Introduction: Irritable bowel syndrome (IBS) is a chronic relapsing, remitting disorder, the natural history of which has been studied extensively. However, few studies have examined factors that influence the likelihood of consulting a general practitioner (GP) with symptoms in those who are symptomatic, particularly over a long time period.
Aims & Methods: The authors performed a longitudinal 10-year follow-up study of individuals previously recruited into a community screening and treatment programme for Helicobacter pylori (H pylori). All surviving, traceable participants were contacted by a postal questionnaire that utilised the Manning criteria to diagnose IBS. Baseline demographic data (including: age; gender; social class; tobacco, alcohol, and coffee consumption; and ethnicity), quality of life (assessed via the psychological and general well-being index), and dyspepsia symptom status (captured via a validated questionnaire) were already on file. Written informed consent was sought to examine primary care records, and data on the use of non-steroidal anti-inflammatory drugs (NSAIDs) and aspirin, and the number of IBS and dyspepsia-related consultations over the ten-year period were extracted from these by two individuals. The associations between these data and any IBS-related consultation were explored using univariate analysis. Independent risk factors were determined by performing multivariate logistic regression to control for all these demographic data and lifestyle factors.
Results: Of 8407 individuals originally involved, 4003 (48%) responded, and 3266 (39%) gave consent to examination of primary care records. The mean age of included individuals was 55 years, and 1799 (55%) were female. 651 (20%) had IBS at either baseline or 10-year follow-up, when dichotomised according to questionnaire data. Of these, 113 (17%) consulted their GP with symptoms. Age, dyspepsia symptom status at baseline, tobacco, alcohol and coffee consumption, ethnicity, social class, and quality of life had no effect on IBS-related consultation behaviour following univariate analysis, but female gender (odds ratio (OR) 2.04; 99% confidence interval (CI) 1.02 to 4.07), H pylori infection (OR 2.02; 99% CI 1.17 to 3.48), any dyspepsia-related consultation during the 10-year study period (OR 2.43; 99% CI 1.40 to 4.20), and NSAID use (OR 2.34; 99% CI 1.19 to 4.60) all significantly increased the likelihood of consultation. These associations remained significant following multivariate logistic regression.
Conclusion: Reasons for consulting a GP with IBS are probably multifactorial, but there was a strong link to consultation behaviour with, but not symptoms of, dyspepsia in our model.

195 GROUP 1 VOLTAGE-GATED POTASSIUM CHANNELS IN THE GASTROINTESTINAL TRACT: DISTRIBUTION AND POTENTIAL MEDIATORS OF MOTILITY DYSFUNCTION

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Introduction: The expression of combinations of voltage-gated K+ (Kv) channels regulates the activities of many excitable and non-excitable cells. We have previously reported autoantibodies to ion channel epitopes in dysmotility disorders.[1] Kv1 channel distribution in the central nervous system and cardiovascular system is well characterised, but very little is known of Kv1 channel distribution and function in the gastrointestinal tract.
Aims & Methods: In the present study we have investigated the distribution of six major Kv1 channel subunits in mouse gastrointestinal tract, and human stomach, jejunum, ileum and colon. Indirect immunohistochemistry was performed on formalin-fixed, paraffin embedded sections of murine stomach, small bowel and colon using the avidin-biotin peroxidase complex (ABC) method. Polyclonal anti-Kv1.1, Kv1.2, Kv1.3, Kv1.4, Kv1.5 and Kv1.6 were used as primary antibodies. Sections were examined under light microscopy and staining scored by two investigators after reaching consensus and independently by an experienced third investigator.
Results: Significant variation was seen in the distribution of subunits in different parts of the bowel wall ($p<0.05$). The greatest concentration of Kv1 subunits was found in the intestinal surface epithelial cells, gastric chief cells and enteric ganglia. Kv1.1, 1.2, 1.3, 1.4 and 1.5 immunoreactivities were similar in small bowel surface epithelium whereas Kv1.6 was detected at a lower intensity. Colonic surface enterocytes were intensely stained with anti-Kv1.2, Kv1.3 and Kv1.4 antibodies. In the stomach, Kv1.1, Kv1.2 and Kv1.3 immunoreactivities were prominent in chief cells. Gastric myenteric ganglia also showed strong immunoreactivity for Kv1.3. The submucosal ganglia of the small bowel were strongly immunopositive for all six Kv1 subunits. Myenteric ganglia showed the same levels of immunoreactivity, although as seen in the surface epithelium, Kv1.6 staining was moderate. Colonic ganglia were at least moderately positive for all six subunits. Gastrointestinal smooth muscle, including vascular smooth muscle was negatively or weakly positive for Kv1 subunit expression.
Conclusion: This is the first comprehensive description of the distribution of voltage-gated K channels throughout the gastrointestinal tract. The high density of Kv1 subunits in surface epithelial cells and enteric ganglia was unexpected. The demonstration of a common antigenic profile provides a potential mechanism whereby damage to enterocytes could produce an immune response with enteric neuron cross reactivity leading to impaired motility, for example in post-infective irritable bowel syndrome.

1. **Knowles CH**, Lang B, Clover L, *et al.* A role for autoantibodies in some cases of acquired non-paraneoplastic gut dysmotility. *Scand J Gastroenterol* 2002;**37**:166–70.

196 GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH MARFAN SYNDROME

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Introduction: Fibrillin-1, an essential component of elastin, is deficient in Marfan syndrome (MS). We postulate that this may be associated with abnormal gastrointestinal (GI) function. However, the frequency of gastrointestinal symptoms in MS has not previously been studied.
Aims & Methods: To assess the prevalence of GI symptoms in patients with MS. All patients aged 18 or over, included in the database of a specialist MS clinic were invited to take part in this postal study, to complete a previously validated Rome II questionnaire and the hospital anxiety and depression score. Sex and age matched ($\pm$7 years) outpatients attending a hospital hypertension clinic were also invited to complete the same questionnaire as well as the anxiety and depression score. They were compared with age- and sex-matched community controls
Results: Of 203 MS patients contacted, 118 (58%) returned the questionnaire. MS patients experience frequent more frequent abdominal discomfort and IBS compared to community controls. They also experience

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	Marfan patients	Patients from hypertension clinic	Community controls
Male:Female	56:62	17:26	56:62
Age in years (mean, range)	50, 18–82	47, 23–81	51, 22–80
Abdominal discomfort	47 (40%)	6 (14%)*	18 (15%)**
IBS	31 (26%)	6 (14%)	12 (10%)*
Diarrhoea predominant IBS	9 (8%)	2 (5%)	2 (2%)
Constipation predominant IBS	12 (10%)	0 (0%)	3 (3%)
Constipation	22 (19%)	2 (5%)	17 (14%)

IBS, irritable bowel syndrome.
*$p<0.01$; **$p<0.0001$.

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more abdominal discomfort than hypertensive controls. The latter difference is unaffected by the presence or absence of anxiety and depression.
Conclusion: There is a higher prevalence of frequent abdominal discomfort and IBS among MS patients compared to controls. Further studies are required to elucidate the pathophysiological basis of these symptoms, and to determine their impact on the quality of life of patients with MS.

197 THE RELATION BETWEEN EXOCRINE PANCREATIC HYPOFUNCTION AND PATIENTS FULFILLING THE ROME II CRITERIA FOR IRRITABLE BOWEL SYNDROME (DIARRHOEA PREDOMINANT): A PREVALENCE STUDY WITH CONTROLS AND THERAPEUTIC OUTCOMES

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Introduction: Patients who meet the Rome II criteria for IBS may have other underlying pathologies. A historical study suggested that 20% of patients with IBS had an abnormal triolein breath test. Recent data describe a higher prevalence for chronic pancreatitis within the general population than previously reported. For these reasons, we wished to determine the prevalence of exocrine pancreatic insufficiency in patients with diarrhoea predominant irritable bowel syndrome (D-IBS) and investigate the role of pancreatic enzyme supplementation.
Aims & Methods: 403 consecutive patients were referred to our unit over an 18-month period who met the Rome II criteria for D-IBS. Those willing to participate had baseline stool frequency and stool consistency recorded along with demographics and weight. Patients were then investigated as per British Society of Gastroenterology IBS guidelines (2000). A stool sample was provided and faecal elastase-1 (Fel-1) was determined. Those patients with a Fel-1 level of less than 100 μg/g of stool were offered pancreatic enzyme supplementation in the form of Creon 40 000 units tds. Concurrently, age and sex matched D-IBS (therapeutic controls) with a Fel-1 greater than 100 were also offered the same pancreatic enzyme supplementation. Pancreatic imaging was performed using ultrasound or CT. Patients were reassessed at six weeks. We also assessed Fel-1 in 50 individuals without IBS (prevalence controls).
Results: 314/403 patients with D-IBS (77.9%) provided a suitable sample for Fel-1 estimation (mean age 46.3 years, 95 males). 19/314 (6.1%) had a Fel-1 <100 whereas 0/50 prevalence controls had an abnormal Fel-1 ($p=0.08$). Pancreatic enzyme supplementation reduced median stool frequency from 6/day to 1.5/day in 18/19 (94.7%) D-IBS with a Fel-1 <100 ($p<0.0001$). By comparison median stool frequency was reduced in 1/15 (6.7%) with Fel-1 >100. In 4 patients with a Fel-1 <100 there were abnormalities on pancreatic imaging (3 chronic pancreatitis and 1 atrophic pancreas).
Conclusion: This is the first study to assess the relationship between exocrine pancreatic hypofunction and D-IBS. Reduced faecal elastase-1 appears to be common in patients with D-IBS. In addition, patients' symptoms are responsive to pancreatic enzyme supplementation. These data suggest that patients with D-IBS should be investigated for exocrine pancreatic hypofunction.

198 RECTAL ENDOCRINE CELLS: NO POST-INFLAMMATORY HYPERPLASIA IN COLITIS

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Introduction: Gut endocrine cells (EEC) produce regulatory peptides to co-ordinate gut function, and may be implicated in the response to injury. EEC decline in active colitis,[1] yet in post-infectious irritable bowel syndrome (PI-IBS) and murine gut infection EEC numbers increase,[2, 3] a process possibly connected to symptoms. It is unknown what happens to EEC in quiescent colitis, or whether a PI-IBS equivalent exists.
Aims & Methods: To serially quantify mucosal EEC in colitis and correlate EEC changes with non-colitic symptoms. Rectal biopsies were taken in active ulcerative colitis ($n=9$ subjects), and repeated after 4 months normal treatment. A bowel symptom questionnaire was completed. Matched healthy controls were also biopsied ($n=5$). Inflammation and EEC (chromogranin A, 5-HT, PYY, enteroglucagon) were blindly scored. Analysis used Mann–Whitney.
Results: (a) Baseline biopsy: all colitic samples had significantly fewer EEC than controls per $\times 200$ high power field (hpf) (mean absolute EEC count 37.5+16.7 *v* 134.0+20.9, $p<0.01$), and also fewer EEC per crypt (mean relative EEC count 3.4%+1.3 *v* 8.6%+1.1, $p<0.01$). The relative percentage of EEC type was observed to differ between colitics and controls: 5-HT 32 *v* 44%; PYY 50 *v* 39%; EGG 18 *v* 17%. (b) Second biopsy: inflammation improved in 4 subjects. EEC increased in each, but remained significantly fewer than control values (mean change +18+9/hpf). In two subjects the inflammation had entirely resolved histologically, but EEC numbers remained low (9 and 33 *v* 134 in controls). In 5 subjects inflammation showed no improvement, with no recovery in EEC numbers (mean change -13+17/hpf). The ratio of EEC types was unchanged: 5-HT 29%; PYY 55%; EGG 16%. (c) Symptoms: despite improved inflammation the symptom score of two patients deteriorated, with IBS-like features. These two had the lowest proportion of 5-HT cells in the first (4% and 20% respectively *v* 32% group) but not second biopsy (22% and 28% respectively *v* 29%).
Conclusion: The data confirm the prior report that EEC numbers decrease in colitis, adding that EEC counts remain suppressed even with histological resolution. Inflammatory mediators may remain active despite histological resolution. The data also suggest a switch in lineage commitment toward PYY-secreting cells with a reduction in 5-HT cells. In particular, a post-inflammatory increase in 5-HT cells, as observed in PI-IBS[2] was not supported, even in the small group of patients with prominent functional symptoms. Further studies are required to address the molecular mechanisms controlling EEC differentiation in IBD.

1. *Gastroenterology* 2004;**126**:1657–64.
2. *Gastroenterology* 2003;**125**:1651–9.
3. *Gut* 2006;**55**:492–7.

199 ABNORMALITIES OF SMALL BOWEL AND COLONIC WATER CONTENT IN DIARRHOEA-PREDOMINANT IRRITABLE BOWEL SYNDROME: NOVEL INSIGHTS FROM MAGNETIC RESONANCE IMAGING

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Introduction: Diarrhoea-predominant irritable bowel syndrome (IBS-D) symptoms are often exacerbated by bran but the underlying mechanisms are poorly understood. We have previously shown that bran accelerates scintigraphic small bowel transit[1] and increases small bowel secretions in healthy controls.[2] Recent developments in magnetic resonance imaging (MRI) allow non-invasive, patient-acceptable monitoring of small bowel water content (SBWC), small bowel transit time (SBTT) and ascending colon water content (ACWC) under physiological conditions. An intestinal flow index (IFI) can then be calculated from AUC 0-240 minutes/SBTT.
Aims & Methods: To assess small intestinal secretion, transit and colonic response to a bran-containing meal in diarrhoea-predominant IBS (IBS-D) patients. Nine IBS-D patients (5 male, 4 female), meeting Rome III criteria for IBS-D in whom microscopic colitis and coeliac disease had been excluded and 16 healthy controls (8 male, 8 female) attended at the MRI unit having fasted overnight. After fasting scans they ate a standard 331 kcal rice pudding with 15 g of coarse wheat bran. Serial MRI imaging was then performed at 45 min intervals for 4.5 hours. The volume of fluid in the bowel at each time point was calculated by integrating all image pixels containing water signal above a given threshold.
Results: Shown as mean (SEM). Fasting SBWC in IBS-D patients at 80 (16) ml was significantly reduced versus controls 138 (17) ml, $p<0.05$. Fasting ACWC in IBS-D was 16 (5) ml, significantly greater than control values 2 (1) ml ($p<0.003$). SBTT of the meal was significantly faster in IBS-D, 145 (15) min versus control 239 (15) min, values very similar to previous scintigraphic estimates of transit time for the same meal (260 (25) min).[2] IBS-D patients showed a greater increase in postprandial SBWC and in IFI which was 162 (46) versus 143 (16). In 4 out of the 9 patients this was associated with postprandial mass movements of the colonic contents whilst no controls showed such mass movements.
Conclusion: IBS-D patients show accelerated transit, increased proximal colon water content which when combined with increased postprandial colonic contractions are likely to contribute to the postprandial urgency and loose stools characteristic of such patients. MRI is a patient acceptable way of documenting these changes and is an ideal biomarker to objectively evaluate efficacy of new treatments.

1. **Hebden JM**, *et al. Am J Gastroenterol* 2002;**97**:2315–20.
2. **McIntyre A**, *et al. Gut* 1997;**40**:223–7.

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200 FACTORS DETERMINING THE PERCEPTION OF THE REFLUX EVENTS IN GORD PATIENTS

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Introduction: Only a minority of the reflux episodes detected by intraluminal ambulatory monitoring are perceived by patients. We investigated the determinants of perception of gastro-oesophageal reflux events in patients who presented with typical reflux symptoms.
Aims & Methods: In 36 patients with symptoms suggestive of gastro-oesophageal reflux, 24-h ambulatory Combined Multichannel intraluminal impedance-pH, monitoring was performed after cessation of acid suppressive therapy. In the 21 patients who had at least one symptomatic reflux episode, characteristics of symptomatic and asymptomatic reflux episodes were compared.
Results: 1501 reflux episodes were detected in these 36 patients; they reported 292 symptoms, of those 141 symptoms correlated to reflux events. Symptoms, which correlated with reflux episodes, were predominantly Heartburn and regurgitation, chest pain correlated with reflux episodes only on seven occasions. Compared with asymptomatic episodes, symptomatic episodes were associated with a larger pH drop ($p<0.001$), lower nadir pH ($p<0.05$), and higher proximal extent ($p<0.001$). Symptomatic reflux episodes had a relatively longer volume and acid clearance time ($p<0.05$ and $p<0.002$). Symptomatic episodes were preceded by a higher oesophageal cumulative acid exposure time ($p<0.05$). The proximal extent of episodes preceding regurgitation was larger than those preceding heartburn; Only 3.7% of the symptomatic reflux episodes were weakly acidic. Postprandial period (60 min) had higher proportion of symptomatic episodes compared with other periods (41 out of 481 *v* 100 out of 1027). Purely gas reflux episodes were symptomatic only in minority of cases, half of them had a recoded drop in pH by <0.5 units.
Conclusion: Heartburn and regurgitation are more likely to be experienced by the patients when the pH drop is large, proximal migration of the refluxate is high, and bolus and acid clearance from the oesophagus is delayed. It appears that sensitisation of the oesophagus by prior repeated exposure of the mucosal lining could be responsible for increased perception of acid reflux. Pure gas reflux associated with a pH drop can be perceived as heartburn and regurgitation.

1. **Sifrim D**, *et al.* Gastro-oesophageal reflux monitoring: review and consensus report. *Gut* 2004;**53**:1024–31.
2. **Shay S**, *et al.* Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers. *Am J Gastroenterol* 2004;**99**:1037–43.

201 EXPLORING PSYCHOPHYSIOLOGICAL PHENOTYPES FOR VISCERAL PAIN

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Introduction: Neonatal pain reactivity and temperament correspond with differences in autonomic regulation. The relevance of these psychophysiological phenotypes for adult visceral pain responses is unknown.
Aims & Methods: To determine if similar psychophysiological phenotypes exist for visceral pain in a healthy adult population. 19 volunteers (8 male, ages 20–55) had 10 painful oesophageal balloon distensions delivered by a swallowed catheter. Autonomic regulation (cardiac vagal control (CVC), cardiac sympathetic index (CSI), heart rate (HR)) was measured pre-intubation (baseline) and during pain. Personality traits were determined separately.
Results: Baseline CVC correlated negatively with neuroticism ($r=-0.6$; $p=0.007$), baseline HR ($r=-0.4$; $p=0.07$), CSI ($r=-0.5$; $p=0.02$) and with CVC in pain ($r=-0.5$; $p=0.028$) but positively with HR in pain ($r=0.6$; $p=0.01$). HR in pain correlated positively with extroversion ($r=0.64$; $p=0.003$) but negatively with neuroticism ($r=-0.5$; $p=0.03$). Hierarchical and K-wise cluster analyses confirmed impressions from correlation analysis of 2 psychophysiological profiles for visceral pain: one group (group 1, $n=11$) with lower baseline CVC ($p=0.0001$) but higher baseline HR ($p=0.02$) and CSI ($p=0.015$) an increase in CVC during pain ($p=0.1$) but an attenuated HR response in pain ($p=0.016$) higher neuroticism ($p=0.0004$) and lower extroversion ($p=0.016$). The other group (group 2, $n=8$) had a converse profile. In other words group 1 had a paucity of parasympathetic (PNS) regulation at rest but a PNS predominant defence response whereas group 2 had high resting PNS regulation but a predominantly sympathetic defence response with PNS withdrawal. These results are similar to ANS profile differences between high (group 1) and low (group 2) anxiety animals at rest and in pain and may reflect different passive (freeze/tonic immobility—group 1) and active (fight/flight—group 2) coping/defence repertoires.
Conclusion: Two psychophysiological phenotypes for visceral pain were found which could represent a psychobiological basis for active and passive coping repertoires. The prevalence and relevance of these for clinical visceral pain warrants further assessment.

202 BLOOD PRESSURE RESPONSES TO DISTAL OESOPHAGEAL ACIDIFICATION AND THEIR RELATION TO SENSITISATION IN A HUMAN MODEL OF VISCERAL PAIN HYPERSENSITIVITY

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Introduction: Visceral pain hypersensitivity (VPH) is a common feature of functional gastrointestinal disorders (FGD). Life stress has been associated with both the onset and exacerbation of FGD. How it modulates visceral sensory perception is unknown, but may be mediated in part by the autonomic nervous system (ANS). We have shown previously that distal oesophageal acidification induces sensitisation of spinal dorsal horn neurones leading to the development of VPH in the non-acid exposed proximal oesophagus (PO).[1] Variability exists in the degree to which individuals sensitise but whether differential ANS responses between individuals explain this is unknown.
Aims & Methods: To determine whether differences in autonomic reactivity, as measured by continuous real time BP monitoring, predict the degree of VPH to oesophageal acidification. In nine healthy volunteers, pain thresholds (PT) to electrical stimulation (in milliamperes, mA) were determined in the PO and foot (somatic control) pre- and post a randomised double-blind 30-minute distal oesophageal infusion of either 0.15M HCl or saline. All subjects had BP monitoring before and during the infusion via a non-invasive Portapress system.
Results: All subjects bar one sensitised to acid infusion with a fall in PT of ⩾6 mA. Acid infusion resulted in a significant fall in PT in the PO compared to saline (mean change in PT averaged over all time points −5 mA (4.5 mA SD) Vs +1.4 mA (2.9 mA SD) $p<0.01$). Average maximum change in PT was −9.5 mA (8.7 mA SD) for acid *v* 4.4 mA (5.6 mA SD) for saline. There were no significant differences in mean arterial pressure (MAP) averaged over 5 minutes at baseline (81.0 mm Hg (14.4 mm Hg SD) acid visit *v* 81.3 mm Hg (16.9 mm Hg SD) saline, $p=0.82$) and during the first 5 minutes of the infusion (94.1 mm Hg (14.4 mm Hg SD) acid visit *v* 94.2 mm Hg (18.2 mm Hg SD) saline, $p=0.73$). However acid infusion caused a greater rise in MAP compared to saline (99.3 mm Hg (17.7 mm Hg SD) *v* 94.6 mm Hg (17.9 mm Hg SD), $p=0.05$), an effect more pronounced on the exclusion of the one non-sensitiser ($p=0.03$). With simple linear regression the degree of sensitisation (maximum fall in PT from baseline) inversely correlated with MAP at the end of the acid infusion in those 7 individuals that sensitised >6 mA ($p=0.0002$), suggesting that those individuals that were able to raise their BP most to acid infusion sensitised the least.
Conclusion: Oesophageal acidification raises MAP, an effect that is greater in those that develop VPH. In turn those that mount the greatest BP response to this stressor sensitise the least. Further work in larger numbers incorporating other autonomic measures is now warranted.

1. **Sarkar**, *et al. Lancet* 2000;**356**:1154–9.

203 FUNCTIONAL HEARTBURN PATIENTS WITH SOMATISATION TRAIT DEMONSTRATE GENERALISED VISCERAL HYPERSENSITIVITY

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Introduction: Visceral hypersensitivity (VH)—heightened perception to experimental visceral stimuli—is a commonly observed phenomenon in patients with functional gastrointestinal disorders (FGIDs). It is often associated with somatic hypersensitivity. One proposed mechanism of VH is augmented afferent input at spinal cord level (''central sensitisation''). With overlap of afferent input from different regions of the GI tract, central sensitisation may explain symptom overlap between different FGIDs. Functional heartburn (FH) is a FGID characterised by heartburn with normal oesophageal mucosal appearances and normal acid exposure. We hypothesised that FH patients without symptoms of irritable bowel

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syndrome (IBS) have a tendency to visceral and somatic hypersensitivity, which may be related to personality traits.
Aims & Methods: Eighteen consecutive patients with FH (7 male, mean age 40) and no symptoms of IBS (Rome II) were compared with 16 patients with erosive reflux disease (ERD, 9 male, mean age 42) and 16 naïve controls (8 male, mean age 42). All subjects underwent (in random order) either infusion of pH1 HCl or saline >1 week apart. At baseline and 30 minutes they underwent a rectal barostat study (perception and pain), anal electrosensation (pain) and VAS assessment of abdominal pain.. All patients completed the BSI questionnaire, particularly to assess somatisation (BSI-som score >61 suggests significant somatisation tendency).
Results: With saline, FH patients had lower barostat thresholds than ERD and controls (perception 22.9 *v* 29.2 *v* 28 mmHg resp, $p<0.03$ for both; pain 36.9 *v* 43.9 *v* 43.4 mmHg resp, $p<0.01$ for both). Anal pain threshold was lower in FH (11.1 mA) than ERD (13.6 mA, $p<0.05$) but not controls (11.6 mA, p=NS). Acid infusion reduced (1) barostat thresholds in FH, not ERD or controls (perception 19.7 *v* 30 *v* 25.6 mmHg resp, $p<0.01$ for both; pain 27.8 *v* 41.1 *v* 36.1 mmHg resp, $p<0.05$ for both) (2) VAS pain intensity (3.2 *v* 1.8 *v* 1.1 resp, $p<0.01$ for both) and (3) anal pain threshold (10.1 *v* 14.7 *v* 12.3 mA resp, $p<0.03$ for both). Compared to saline, acid infusion reduced thresholds for barostat volumes and anal pain, and increased abdominal pain in FH patients only. This VH was seen in 13 of 18 (72%) patients, all of whom had BSI-som >61. Of 5 patients not showing VH, 1 had BSI-som >61.
Conclusion: Patients with FH—and not ERD or controls—demonstrate central sensitisation to oesophageal acid infusion. This development of sensitivity occurs in FH patients who do not have symptoms of IBS, suggesting an underlying tendency that is present in a significant proportion of these patients, particularly those with somatisation trait.

Oesophagus posters

204 THE EFFECTS OF OBESITY ON OESOPHAGEAL FUNCTION AND ACID EXPOSURE IN PATIENTS WITH REFLUX SYMPTOMS

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Introduction: The increasing prevalence of obesity and gastro-oesophageal reflux disease (GORD) suggests an association between these two conditions. The link remains controversial although a recent study using high resolution manometry demonstrated that obese subjects have raised intra-gastric pressure, gastro-oesophageal pressure gradient, and are more likely to have disruption of the oesophago-gastric junction leading to hiatus hernia or reflux to occur.
Aims & Methods: This study aimed to establish whether these demographic and manometric changes are associated with increased oesophageal acid exposure in clinical practice. A prospective study of 574 patients referred for oesophageal investigation. Height, weight and waist circumference (WC) were measured. Reflux symptoms were assessed by a validated questionnaire. Manometry assessed lower oesophageal sphincter (LOS) pressure, total and abdominal LOS length and peristalsis for 10 water swallows in the seated position. 24-h ambulatory pH studies were performed. Multivariate regression identified associations of oesophageal acid exposure (%time pH<4/24 h) with demographic and manometric measurements.
Results: Patients referred for reasons other than reflux symptoms or patients who failed intubation or to attend were excluded (n=167). Complete manometry and pH data were available for 407/484 (84%); M:F 45%:55%. The prevalence of obesity was similar in both sexes; obesity tended to increase with age. Oesophageal acid exposure was positively associated with reflux symptoms ($p<0.001$). Increasing body mass index (BMI kg/m^2) and WC were associated with more severe oesophageal acid exposure (both $p<0.002$) but not reflux symptoms ($p\sim0.1$). Increasing oesophageal acid exposure was associated with shorter abdominal LOS length ($p<0.001$), lower LOS pressure ($p<0.002$), and peristaltic contractile pressures ($p<0.04$). Increasing WC was also associated with shorter abdominal LOS length ($p<0.001$), lower LOS pressure ($p<0.004$), and peristaltic contractile pressures ($p<0.05$). None of these associations were present when a correction for height was included in the regression analysis (ie BMI). The magnitude of the effect on LOS and contractile pressure across the observed range was similar to that expected from increasing intragastric pressure with central obesity (~5 mmHg).
Conclusion: In patients referred for investigation of reflux symptoms obesity is associated with increasing oesophageal acid exposure. Analysis of the demographic and manometric data suggests that this is due to a rise in intragastric pressure and gastro-oesophageal pressure gradient related to central adiposity. Longitudinal studies are needed to confirm whether variation in intra-abdominal pressure due to weight change has effects on oesophageal function and acid exposure in GORD.

205 INFLAMMATION AND BARRETT'S METAPLASIA; THE ROLE OF TNFα IN CLONAL EXPANSION

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Introduction: Evidence thus far would indicate that the inflammatory response plays a role in the early stages of Barrett's metaplasia. However much less is known about the influence of inflammatory signalling in the clonal expansion of the Barrett's lesion, leading to increased malignancy.
Aims & Methods: We have used in vitro and ex vivo cell models to investigate the effect of TNFα signalling, as a surrogate for inflammation, on a number of biological endpoints important to clonal expansion, including cell growth, cell cycle, apoptosis, anchorage-independent growth, and migration.
Results: Using Western blotting and immunohistochemistry, both in vitro and ex vivo cell models were found to express a protein consistent with the TNF receptor 1 (TNFR1). In two squamous carcinoma cell lines OE21, and TE10; and two adenocarcinoma cell lines OE33, SEG1, TNFα at concentrations between 5 and 25 ng/ml, was found to induce a significant decrease in cell number ($p<0.05$) over 72 hours, as measured microscopically. This decrease in cell numbers may be in part due to TNFα-induced blockade of the cell cycle but more significantly due to a TNFα-induced increase in cellular apoptosis (60–70%). Addition of the TNFR1 antagonist Infliximab blocked the growth arrest induced by TNFα treatment ($p<0.05$). All cell lines were able to form colonies in an agarose colony forming assay, indicating autonomy to anchorage-dependent growth. TNFα reduced the ability of cells to form large colonies in an agarose medium, indicating an increase in the ability of cells to grow in an anchorage-independent mechanism. Treatment with TNFα; did not affect cellular migration as measured using a migration scratch assay.
Conclusion: In conclusion, this data shows that TNFα can affect epithelial cell biology including changes in cellular endpoints important to clonal expansion and thus neoplastic progression. Furthermore, it was clear that addition of the anti-TNFα treatment Infliximab blocked some of the TNFα-induced endpoints, importantly at a physiological concentration, and thus may provide an alternative therapeutic modality to Barrett's metaplasia, but not later on the disease stage such as adenocarcinoma.

206 A ROLE FOR NITRIC OXIDE IN THE INVASIVE PROCESS IN OESOPHAGEAL ADENOCARCINOMA

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Introduction: Oesophageal adenocarcinoma (AC) generally arises within areas of metaplasia known as Barrett's oesophagus (BO). Increasingly it is recognised that reflux components are important in promoting progression of BO to AC. Work to date has principally focussed on acid and bile salts as the drivers of progression. Recently, high concentrations of nitric oxide (NO) in the lumen have been demonstrated in patients during reflux. Luminal NO is produced as a consequence of a reaction between salivary nitrite and low pH in the presence of vitamin C. Importantly, NO has been shown to play a role in a number of cancer related processes including DNA damage, angiogenesis, apoptosis, tumour migration and invasion.
Aims & Methods: To investigate the ability of physiological levels of NO to modulate invasive activity of oesophageal cell lines in an in vitro model. The following oesophageal cell lines were used in this study: FLO (AC, gift of Dr Beer), GihTERT (high-grade dysplasia) and QhTERT (BO, both gifts of Dr Rabinovitch). The NO donor MAHMA NONOate (Axxora) was used to deliver NO to cells in culture. Long-term survival following NO was assessed by clonogenic assay. For the in vitro invasion assay, cells were added to Matrigel (BD) coated trans-well inserts (BD), treated with 25–100 μM NO and incubated for 24 h. NO-induced changes in gene expression were examined by SYBR-green real-time PCR.
Results: Oesophageal cell lines tolerated physiological levels of NO without any loss of clonogenic survival. All of the cell lines showed some level of invasion in vitro in the absence of NO with FLO cells showing the highest level of invasion, consistent with the stage of disease from which the cell lines were derived. The addition of NO enhanced the ability of GihTERT

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and FLO cells but not QhTERT cells to invade through Matrigel ($p>0.05$ for 25 μM NO and above). NO-induced invasive behaviour correlated with the induction of matrix metalloproteinases (MMPs) 1 and 9 and tissue inhibitor of MMP 1 (TIMP1), all of which have previously been implicated in invasion. Maximum gene expression was observed 1–3 h after the addition of NO ($p>0.05$) and had returned to basal levels after 22 h ($p>0.05$). Osteopontin, an important regulator of cell adhesion, displayed a biphasic response with decreased expression 1 h after the addition of NO followed by increased expression after 3 h. A number of other genes (MMP2, MMP3, MMP7, MMP10 and TIMP2) did not show statistically different changes ($p>0.05$).
Conclusion: Concentrations of NO known to be generated in the lumen of the oesophagus in vivo are insufficient to induce cell death of oesophageal cell lines in vitro. NO may promote disease progression in the later stages of carcinogenesis by increasing invasive potential through the regulation of genes known to be involved in invasion.

207 RISK OF MORTALITY AND CANCER INCIDENCE IN BARRETT'S OESOPHAGUS

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Introduction: There are very few prospective follow-up studies of Barrett's oesophagus (BO) cohorts assessing the risk of extra-oesophageal cancer incidence or mortality. Such studies are necessary in order to understand the overall risks of cancer and death experienced by BO patients.
Aims & Methods: This analysis set-out to assess the risk of such outcomes in a cohort of 597 BO patients recruited at Leeds General Infirmary.[1] Patients were excluded from the analysis if they had a cancer diagnosis (excluding non-melanoma skin cancer) prior to or within 6 months of their BO diagnosis or if they were aged less than 18 years at BO diagnosis. Mortality and cancer incidence information were provided by the Office of National Statistics. Using the general population of West Yorkshire for calculation of expected numbers of events, standardised mortality ratios (SMRs) and standardised incidence ratios (SIRs) were calculated using indirect standardisation and STATA 8.2.
Results: After exclusions, 502 BO patients remained for analysis, of which 431 had a BO diagnosis of specialised intestinal metaplasia (SIM) and 71 had a diagnosis of columnar-lined oesophagus. Each analysis was conducted for all BO patients and the SIM group alone, results of which did not differ. Therefore the results of the full BO cohort are discussed. All-cause mortality was found to be elevated in BO patients (SMR = 1.21; 95% CI 1.06 to 1.37; $p<0.01$) and remained so after oesophageal cancers were excluded (SMR = 1.16; 95% CI 1.01 to 1.32; $p<0.05$). Increased risks were also found for malignant neoplasm of the oesophagus (SMR = 7.26; 95% CI 3.87 to 12.42; $p<0.001$) and diseases of the digestive system (SMR = 2.03; 95% CI 1.11 to 3.40; $p<0.05$). No altered risks were seen for all other mortality analyses including colorectal cancer, cerebrovascular diseases and circulatory diseases, although for the SIM group alone mortality from circulatory disease was borderline statistically significant (SMR = 1.24; 95% CI 1.00 to 1.52). In the cancer incidence analysis oesophageal malignancy (SIR = 8.66; 95% CI 4.73 to 14.53; $p<0.001$) and OA (SIR = 14.29; 95% CI 7.13 to 22.56; $p<0.001$) were found to be increased in BO. There was a statistically significant increased SIR found for malignant neoplasm of digestive organs, but this disappeared once oesophageal malignancies were excluded. No altered risk was seen for other analyses including that of colorectal cancer.
Conclusion: Although this analysis provides anticipated increased risk estimates for oesophageal cancer incidence and mortality in BO, it finds no evidence for increased risks of other forms of cancer or causes of death as have been occasionally proposed.

1. **Bani-Hani K**, Sue-Ling H, Johnston D, *et al.* Barrett's oesophagus: results from a 13-year surveillance programme. *Eur J Gastroenterol Hepatol* 2000;**12**:649–54.

208 OESOPHAGEAL CARCINOMA IN THE WEST MIDLANDS: CHANGING INCIDENCE AND THE INFLUENCE OF SOCIOECONOMIC STATUS AND ETHNICITY

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Introduction: The incidence of oesophageal cancer, especially oesophageal adenocarcinoma (OA), has risen in the developed world in the last 30 years. In the US, oesophageal squamous cell carcinoma (OSCC) is associated with deprivation and black ethnicity and oesophageal adenocarcinoma (OA) with affluence and white ethnicity. The influence of social deprivation and ethnicity on oesophageal cancer has not been studied in the UK.
Aims & Methods: West Midlands Cancer Intelligence Unit (WMCIU) data were used to study the incidence of OSCC and OA and to examine the influence of age, gender, socioeconomic status (Townsend Quintiles by postcode) and ethnicity (Hospital Episode Statistics). The WMCIU covers 10% of the population of England. Validation of coding of cancer morphology and site was performed in 28% (n = 4252) of cancers by examination of patient records.
Results: From 1977–2004, 15 138 oesophageal cancers were identified within the unchanging borders of the registry. Oesophageal cancer incidence increased—five year rolling directly age standardised incidence rates per 100 000 (95% CI): 1977–81 men 8.57 (8.03–9.1), women 5.04 (4.69–5.39); 2000–4 men 13.73 (13.13–14.32), women 6.28 (5.92–6.64). OSCC incidence has not significantly altered, but OA incidence is rapidly rising, particularly in men: 1977–81 men 2.14 (1.87–2.4), women 0.52 (0.41–0.64); 2000–4 men 8.53 (8.06–9.0), women 1.72 (1.53–1.9). The median age of diagnosis of OA (IQR) has risen: 1977–81: men 65 (58–71.8), women 72.5 (63.3–78); 2000–4 men 70 (61–77), women 78 (69–83). OSCC was strongly associated with the most socially deprived quintile (5) (1977–81: men quintile 5–6.19 (5.05–7.33) versus quintile 1–1.85 (1.31–2.4); women quintile 5–3.67 (2.88–4.45) versus quintile 1–2.03 (1.52–2.54)). This association persisted until 1999–2003 when the rising incidence in the most affluent quintile converges with the most deprived quintile. OA was not associated with differences in social deprivation or affluence. OA was significantly more common in white men 7.30 (6.92–7.68) and women 1.49 (1.34–1.64) compared with black and Asian populations. OSCC was not associated with any particular ethnic group.
Conclusion: Within the West Midlands, the incidence of OA is rapidly rising, particularly in men. The incidence of OSCC has not significantly altered in the last three decades. OSCC has been strongly associated with deprivation, but this association has recently been lost. OA is not associated with differing socioeconomic status. OA is associated with white ethnicity.

209 CHRONIC ATROPHIC GASTRITIS IS A MAJOR RISK FACTOR FOR OESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Introduction: H pylori induced atrophic gastritis is a well established predisposing factor for non-cardia gastric cancer. In contrast the lesion is negatively associated with oesophageal adenocarcinoma.. However, recently one study from Sweden and one from Japan have suggested a positive association between atrophic gastritis and oesophageal squamous cell carcinoma (OSCC). We have examined the relationship in a high risk population for OSCC.
Aims & Methods: This was a case-control study based on Ardabil, Northwest Iran. A total of 45 patients (24 male and 21 female, mean ages

Abstract 209 Relation between risk of OSCC and gastric atrophy expressed by serum PG I/II

PG I/II quintile	Univariate OR (95% CI)	p Value	Multivariate* OR (95% CI)	p Value
5th: 5.66–8.63	1.00 (Ref)		1.00 (Ref)	
4th: 4.31–5.54	1.91 (0.29–12.46)	0.501	4.99 (0.38–64.99)	0.220
3rd: 2.95–4.25	5.53 (1.07–28.59)	0.041	15.90 (1.68–150.35)	0.016
2nd: 2.14–2.86	5.99 (1.17–30.60)	0.032	13.28 (1.42–124.06)	0.023
1st: 0.16–2.14	8.70 (1.78–42.65)	0.008	32.97 (3.34–325.53)	0.003

*Note: ORs in multivariate analysis are adjusted for smoking and GORD symptoms.

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62) with OSCC were studied with 45 age and sex-matched controls. Serum pepsinogen I/II was use as a serologic marker of atrophic gastritis. History of smoking and gastroesophageal symptoms were included in multivariate logistic regression analysis.
Results: A statistically significant direct relationship was apparent between gastric atrophy (low PG I/II) and risk of oesophageal squamous cell carcinoma in both univariate and multivariate analysis (table). Current and past (ever) smokers had significantly higher risk of cancer compared to non smokers with OR (95% CI) of 5.76 (1.70 to 19.45). GORD symptoms did not show significant relationship with this cancer in any level.
Conclusion: Atrophic gastritis is an independent risk factor for oesophageal squamous cell carcinoma. The mechanism of the association is unclear and requires investigation.

210 ACID-RELATED OESOPHAGEAL SENSITIVITY, NOT DYSMOTILITY, DIFFERENTIATES SUBGROUPS OF PATIENTS WITH NON-EROSIVE REFLUX DISEASE

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Introduction: Patients with non-erosive reflux disease (NERD) account for 50–70% of patients with gastro-oesophageal reflux disease. They experience reflux symptoms in the absence of any endoscopic mucosal breaks and often experience symptoms with a similar frequency and severity as those with erosive reflux (ERD). Patients with NERD can be stratified by whether there is a relationship between symptoms and acid exposure (NERD:acid+), or not (NERD:acid−). Differences in the intraoesophageal distribution and the perception of acid reflux have been demonstrated between NERD and ERD patients, which may relate to differences in oesophageal motility and sensitivity between the two groups. The aim of this study was to investigate the effect of oesophageal infusion of hydrochloric acid (HCl) on oesophageal motility and sensitivity in patients with NERD.
Aims & Methods: Thirty nine consecutive patients with reflux disease (11 NERD:acid+ (oesophageal acid exposure >4%), 14 NERD:acid− and 14 ERD demographically-matched groups) attending for oesophageal function studies were studied, along with 12 healthy controls. HCl pH1 or saline were infused at 400 ml/h in random order into distal (5 cm above lower oesophageal sphincter (LOS)), then proximal (20 cm above LOS) sites in the oesophagus. The following observations were made at baseline and after 30 minutes of each infusion: oesophageal contraction amplitude, duration and waveform, LOS pressure, pain intensity by VAS.
Results: NERD patients had significantly higher pain sensitivity to acid compared to ERD and controls (proximal VAS 6.6 *v* 3.9 *v* 2.8 resp, $p<0.03$ both; distal 4.8 *v* 3.2 *v* 2 resp, $p<0.04$ both). ERD patients differed from controls ($p<0.05$ for both proximal and distal acid). Proximal acid infusion caused greater pain than distal only in NERD patients ($p<0.05$), not ERD or controls. When comparing NERD:acid− with NERD:acid+ patients the acid and saline sensitivity were more pronounced in the former (proximal acid 7.2 *v* 5.8 resp, $p<0.03$; distal acid 5.5 *v* 3.9 resp, $p<0.01$; proximal saline 4 *v* 3.1 resp, $p<0.05$). There were no significant differences in oesophageal contraction or LOS pressure between the groups in any of the motility parameters.
Conclusion: NERD patients, and to a lesser extent ERD patients, are sensitive to acid in the oesophagus, being more sensitive proximally than distally. Hypersensitivity is most marked with NERD patients who have a normal pH profile. The relationship of these changes to symptom index and psychological state remains to be determined. This sensitivity is independent of significant motility change.

211 COX-2 AND INOS GENE POLYMORPHISMS IN THE REFLUX OESOPHAGITIS–BARRETT'S OESOPHAGUS–OESOPHAGEAL ADENOCARCINOMA SEQUENCE

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Introduction: Chronic inflammation is implicated in carcinogenesis, as it can result in tissue damage due to production of free radicals. These cause activation of ''pro-survival'' genes including cyclo-oxygenase 2 (COX-2) and inducible nitric oxide synthase (iNOS), which can lead to carcinogenesis through DNA damage, angiogenesis and immunosupression. There is extensive evidence that expression of both COX-2 and iNOS is increased in oesophageal adenocarcinoma (OAC), its precursor Barrett's oesophagus (BO) and in reflux oesophagitis (RO).
Aims & Methods: The aim of this study was to investigate possible associations between variations in the COX-2 and iNOS genes and these increasingly common oesophageal conditions. In a case-control study, patients with OAC (n= 210), BO (n=212), RO (n=230) and population controls (n=248) were recruited from throughout Ireland. Using genomic DNA extracted from blood samples, single nucleotide polymorphisms in the COX-2 3′ untranslated region (8473 T>C) and iNOS codon 608 (Ser>Leu) were genotyped using a TaqMan 5′ nuclease assay. Allele and genotype frequencies were compared between cases and controls using the Chi-square test. Logistic regression analysis was used to test for association between genotype and disease whilst adjusting for potential confounding factors including age, sex, body mass index, smoking and alcohol intake.
Results: A significantly higher COX-2 8473 C allele frequency was observed in OAC cases than controls ($p=0.02$). The COX-2 8473 TC genotype was associated with an increased risk of OAC (OR=1.54, 95% CI 0.99 to 2.39), and this risk was higher in association with the COX-2 8473 CC genotype (OR=1.75, 95% CI 0.89 to 3.43). No significant differences were observed in the distribution of iNOS Ser608Leu alleles or genotype between the different disease groups and controls.
Conclusion: The variant COX-2 8473 C allele was associated with an increased risk of OAC compared to the wild type allele. To our knowledge this is the first study to date investigating these genetic variations in association with oesophageal disease. Further larger studies are required to assess whether the variant COX-2 8473 C allele may be a useful potential genetic marker for susceptibility to OAC.

212 POLYMORPHISMS IN DNA REPAIR GENES AND THEIR ASSOCIATIONS WITH RISK OF REFLUX OESOPHAGITIS, BARRETT'S OESOPHAGUS AND OESOPHAGEAL ADENOCARCINOMA

H. R. Ferguson[1], H. R. Ferguson[1], L. J. Murray[1], B. T. Johnston[1], L. A. Anderson[1], S. J. Murphy[1], P. Watson[2], J. McGuigan[3], J. V. Reynolds[4], H. Comber[5], C. P. Wild[6], L. J. Hardie[6]. [1]*Centre for Clinical and Population Sciences, Queen's University Belfast;* [2]*Department of Gastroenterology;* [3]*Department of Surgery, Royal Victoria Hospital, Belfast, UK;* [4]*Department of Surgery, St James's Hospital, Dublin;* [5]*National Cancer Registry, Ireland, Cork, Ireland;* [6]*Molecular Epidemiology Unit, University of Leeds, Leeds, UK*

Introduction: Oxidative stress is a major cause of DNA damage in cells and the base excision repair (BER) pathway repairs such damage. The BER pathway involves various enzymes, but two of the most important are hOGG1 and XRCC1. The hOGG1 enzyme repairs the lesion 8-oxoGuanine, levels of which have been shown to be increased in Barrett's oesophagus (BO) and oesophageal adenocarcinoma (OAC). XRCC1 acts as an important scaffold protein in DNA repair. Cigarette smoking has been implicated in the pathogenesis of OAC, BO and reflux oesophagitis (RO). XPD enzyme, as part of the nucleotide excision repair pathway, helps to repair smoking related DNA damage.
Aims & Methods: The aim of this study was to investigate possible associations between polymorphisms in the hOGG1, XRCC1 and XPD genes and RO, BO and OAC. Patients with RO (n=230), BO (n=212), OAC (n=210) and population controls (n=248) were recruited in an all Ireland case-control study. Using extracted genomic DNA, single nucleotide polymorphisms in hOGG1 codon 326 (Ser>Cys), XRCC1 codon 399 (Arg>Gln) and XPD codon 751 (Lys>Gln) were genotyped. Allele and genotype frequencies were compared between cases and controls using the χ^2 test. Logistic regression analysis was used to test for association between genotype and disease whilst adjusting for potential confounding factors including age, sex, body mass index, smoking and alcohol intake.
Results: A significantly lower hOGG1 326Cys allele frequency was observed in OAC cases than controls ($p=0.03$). The hOGG1 Ser326Cys and Cys326Cys genotypes were associated with a reduced risk of OAC (OR=0.73, 95% CI 0.47 to 1.12; OR 0.33, 95% CI 0.10 to 1.14). No significant differences were observed in the distribution of XRCC1 Arg399Gln and XPD Lys751Gln alleles or genotype, between the different disease groups and controls.
Conclusion: The variant hOGG1 326Cys allele was associated with a reduced risk of OAC compared to the wild type allele. There is a need for future studies to establish the functional impact of this polymorphism, as well as larger epidemiological studies assessing its association with these increasingly common oesophageal pathologies.

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213 ORNITHINE DECARBOXYLASE AS A MARKER OF DYSPLASIA IN BARRETT'S OESOPHAGUS

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Introduction: Barrett's oesophagus (BO) is a pre-malignant condition and current practice is to perform periodic surveillance endoscopy to detect dysplastic change. A reliable biomarker of malignant progression would allow more effective surveillance targeted at high risk patients. Ornithine decarboxylase (ODC) is a rate limiting enzyme in the biosynthesis of polyamines, which have a vital role in cell proliferation and differentiation. Levels of ODC are elevated in various malignancies including colorectal cancer.[1]
Aims & Methods: We hypothesise that ODC levels are higher in BO than in non-metaplastic gastric mucosa, and higher in dysplastic compared to non-dysplastic BO. From each patient, endoscopic biopsies were taken from the Barrett's segment and the upper stomach, immediately frozen in liquid nitrogen, and subsequently incubated with a radiolabelled substrate. The amount of $^{14}CO2$ released is proportional to the amount of ODC in the original tissue sample. Results are expressed as pmoles of ODC per hour per mg of tissue (pmol/h/mg). Groups were compared using non-paired *t* test.
Results: Twenty three patients with non-dysplastic BO and 11 with dysplastic BO were studied. 10 patients had low grade dysplasia, 1 high grade. Baseline demographics were similar in the two groups. The mean ODC level was 40.28 pmol/h/mg in gastric mucosa, 126.98 pmol/h/mg in non-dysplastic Barrett's mucosa, and 369.0 pmol/h/mg in dysplastic BO (gastric *v* non-dysplastic BO, $p<0.01$: non-dysplastic *v* dysplastic BO, $p=0.03$).
Conclusion: ODC levels are higher in Barrett's mucosa than in gastric mucosa. Levels are significantly higher in dysplastic BO than in non-dysplastic BO. ODC warrants further study as a potential marker of dysplastic change and subsequent malignant progression in BO. Inhibitors of ODC may have a role to play in the chemoprevention of adenocarcinoma related to Barrett's oesophagus.

1. **Weiss TS**, Bernhardt G, Buschauer A, *et al*. Polyamine levels of human colorectal adenocarcinomas are correlated with tumor stage and grade. *Int J Colorectal Dis* 2002;**17**:381–7.

214 THE RELEVANCE OF LOW-GRADE DYSPLASIA IN COLUMNAR-LINED OESOPHAGUS

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Introduction: The incidence of adenocarcinoma (AC) in columnar-lined oesophagus (CLO) with low-grade dysplasia (LGD) has been variously reported as around between 0% and 12% per annum (pa) in small series. The fate of non-progressive LGD is also controversial.
Aims & Methods: The aim of this study was to examine the population with LGD in CLO, the rate of development of high-grade dysplasia (HGD) and AC and also examine those patients who remained with LGD or reverted to non-dysplastic CLO (ndCLO) in a large cohort from UK National Barrett's Oesophagus Registry (UKBOR). Medical records of 283 patients with LGD in CLO from 7 UK centres registering with UKBOR were examined and data extracted on histological follow-up. Incidence data were modelled using an exact Poisson distribution.
Results: 144 patients had 290 biopsies prior to LGD diagnosis (median time from CLO diagnosis to LGD 2.77 years, maximum 17.36 years). Of these, 141 patients (97.9%) had ndCLO at diagnosis (including 18 (12.5%) with indefinite changes for dysplasia (INDEF)), 2 had HGD and 1 had AC (with LGD being biopsied at an urgent follow-up OGD); 3 patients had findings of HGD between initial diagnosis of ndCLO and LGD and 38 (26.4%) had findings of INDEF.

217 had 535 biopsies after initial LGD diagnosis. 17 (11.8%) patients had biopsies of AC following LGD (including the patient with AC prior to LGD) and 12 developed HGD. 75 (34.6%) had persistent LGD for at least one further set of biopsies and 45 (20.7%) had LGD at their most recent set of biopsies, with the remaining patients having reverted to INDEF (37 patients, 17.1%) or ndCLO (111 patients, 51.2%) at their most recent set of biopsies. The annual incidence of AC in LGD was 17/633.7 patient-years of follow-up (2.7% pa 95% CI 1.6 to 4.3% pa). A further 12 patients developed HGD during follow-up, yielding a combined annual incidence of HGD and AC of 29/633.7 (4.6% pa 95% CI 3.1 to 6.6% pa).
Conclusion: 148 patients (68.2%) had reverted to ndCLO/INDEF at final follow-up. Patients found to have LGD are at a significant risk of developing HGD and AC compared to those without dysplasia and should be followed-up closely to enable early detection of HGD/AC.

215 EFFECTIVENESS OF TWO WEEK RULE REFERRAL SYSTEM FOR PATIENTS WITH SYMPTOMS OF DYSPHAGIA

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Introduction: The Department of Health (DOH) in July 2000 introduced guidelines on referral of patients suspected to have upper gastrointestinal cancer. Purpose of guidelines is to help general practitioners (GPs) identify those patients who are more likely to have cancer and would require urgent assessment and upper GI endoscopy within two weeks that is under the two week rule (TWR) referral system. DOH has predicted that 1 out of 15 of upper GI endoscopy referrals under the TWR guidelines would have cancer.
Aims & Methods: To assess effectiveness of TWR referral system in picking up cancer in patients with symptoms of Dysphagia and to assess appropriateness of referrals by GPs. It was a retrospective study carried at West Cumberland Hospital (District General Hospital). Data were collected from the computer software Endoscribe and patients' notes were consulted as required. All patients referred with complaints of Dysphagia during the year 2004 were included in the study. Patients were categorised as being under the TWR or the routine or non-two week rule (NTWR) referral system.
Results: The study included 206 patients (female: 106; male: 100) referred with dysphagia. Their mean age was 64 (TWR 66 years : NTWR 62 years). There were 108 patients referred under TWR and 98 under NTWR. Cancers were detected in 9% (n=18) patients. Out of these 12% (n=13) were under TWR and 5% (n=5) under NTWR. Thus overall 1 out of 11 of all the patients of dysphagia had cancer. Benign oesophageal strictures were detected in 14% (n=29) patients (TWR:15% and NTWR:13%) and reflux disease was detected in 41% (n=85) patients (TWR: 42% and NTWR:40%).
Conclusion: Cancer pick up rate in the category of dysphagia was 1:11. This was more than the overall cancer detection rate predicted by the DOH under the TWR for upper gastrointestinal cancers. Thus to improve early cancer detection rate, it is recommended that dysphagia should be appropriately assessed as a serious symptom with a view to refer under the TWR system. This will not only improve the early cancer detection rate, but will also be helpful in early management.

216 NON-ENDOSCOPIC IMMUNOCYTOLOGICAL SCREENING TEST FOR BARRETT'S OESOPHAGUS

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Introduction: The incidence of oesophageal adenocarcinoma (AC) is increasing rapidly with a 5-year survival of less than 20%. AC generally occurs on the background of the metaplastic condition Barrett's oesophagus (BO), which affords the opportunity for early detection and intervention. However, the majority of patients with BO remain undiagnosed. Population screening for BO by endoscopy is impractical and expensive although it has been recommended by the American College of Gastroenterology for male patients over 50 years with reflux symptoms.
Aims & Methods: The aim of this study was to develop a non-endoscopic screening test for BO suitable for primary care. A non-endoscopic sampling device, a capsule-sponge attached to a string, was used to obtain oesophageal specimens from 43 BO patients (confirmed on endoscopy and biopsy) and 53 healthy volunteers. Liquid based cytology was used to create a cell-monolayer. Since cytology alone lacks sensitivity and specificity we developed an immunocytological test based on the abnormal proliferation characteristics of the surface of the Barrett's mucosa. The immunomarker used was minichromosome maintenance protein 2 (Mcm2). Samples were considered positive if columnar cells had nuclear staining. Three individuals unaware of the clinical diagnosis assessed the slides. To determine the acceptability of the test, the patients used a linear rating tool (10 enjoyable, 5 neither unpleasant nor pleasant, 0 very unpleasant).

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Results: The acceptability of the capsule was rated as 4.4 (0.3). Adequate specimens were retrieved from 91/96 (94.8%) patients. The mean number of slides made from 1 specimen was 11.9 (0.7). 27/41 (66%) BO specimens had positive Mcm2 positive staining compared with 17/52 (33%) specimens from healthy volunteers giving a sensitivity and specificity of 67%. The negative (NPV) and positive predictive values (PPV) of the test are 72.9% and 61.3% respectively. One of the limitations of the study is that healthy volunteers were not endoscoped. Hence, in a subgroup analysis comprising control patients without a history of heartburn (41 subjects) the specificity increased to 80%. The corresponding NPV and PPV were 71.1% and 77.1%.
Conclusion: The sampling device is generally acceptable to patients and it gives a large yield of cells amenable to RT-PCR, FACS or immunocytologial analysis. The preparation and the analysis of the resultant immunocytological specimen could be automated thus reducing the cost. However, although the sensitivity and specificity of the test compares well to other screening test in current clinical practice, other markers may perform better and should be investigated.

217 ELASTIC SCATTERING SPECTROSCOPY FOR THE DETECTION OF ANEUPLOIDY IN BARRETT'S OESOPHAGUS

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Introduction: Aneuploidy (altered DNA copy number) is an independent marker of future cancer risk in patients with Barrett's oesophagus without high grade dysplasia (HGD). Such a patient has a five year adenocarcinoma risk of 38% if they have aneuploidy compared to 0% in the absence of aneuploidy in a cohort study of 322 patients. Elastic Scattering Spectroscopy (ESS) is a real-time in vivo technique which detects changes in the physical properties of cells. We have already demonstrated a sensitivity for detecting HGD in Barrett's oesophagus of 92%. The measurement of aneuploidy by either image or flow cytometry is labour intensive and therefore at present is not deliverable in routine clinical practice. If a fast, reliable, in vivo method such as ESS could detect aneuploidy during routine surveillance endoscopy, biopsies could be targeted to high-risk patients.
Aims & Methods: Can ESS detect aneuploidy in vivo in Barrett's Oesophagus in the absence of HGD? Matched optical and conventional biopsies were taken from patients with Barrett's oesophagus. Biopsies demonstrating HGD were excluded. The biopsies were then processed for aneuploidy using image cytometry analysis. Paraffin was removed from a 40 μm section, and nuclei were liberated with protease. The nuclei were spun onto a slide and stained with Feulgen for automated image analysis and histogram generation.
Results: 976 spectra from 258 sites were collected from 60 patients with Barrett's oesophagus. Histograms were blindly analysed by two observers and consensus was reached in all cases. 205 sites were classified as diploid and 53 sites were classified as having image abnormalities. No sites contained HGD. We constructed a new statistical algorithm using both jacknife and bootstrap training techniques to discriminate between aneuploid and diploid sites without HGD. The results were almost identical using both statistical techniques. ESS correctly identifying aneuploid sites using both statistical methods with a sensitivity of 83% and specificity of 78% and the area under the ROC curve was 0.86 displaying ''good'' discrimination.
Conclusion: ESS can detect aneuploidy in Barrett's oesophagus in vivo in the absence of HGD. Over 85% of patients undergoing surveillance do not have aneuploidy in their Barrett's oesophagus so if ESS could successfully exclude aneuploidy, these patients would not require a further endoscopy for at least five years. Resources could then be focused on the surveillance or even treatment of patients with aneuploidy. This ESS algorithm for the detection of aneuploidy requires prospective testing.

218 THE PRESENCE OF ANEUPLOIDY FOLLOWING PHOTODYNAMIC THERAPY PREDICTS LATE RELAPSE TO HIGH-GRADE DYSPLASIA OR ADENOCARCINOMA

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Introduction: Aneuploidy (altered DNA copy number) has been shown to independently predict future cancer risk in patients with Barrett's Oesophagus but without high-grade dysplasia (HGD). Photodynamic therapy (PDT) has been shown to be effective for the treatment of HGD in Barrett's oesophagus but in a randomised controlled trial, 14% of patients still developed cancer. One suggested reason for this is that residual Barrett's left after PDT may harbour genetic abnormalities.
Aims & Methods: The aim of this case control study was to assess whether residual aneuploidy in one or more biopsies after PDT predicted future relapse to HGD or cancer after apparent clearance of these abnormalities. In a series of 106 patients undergoing PDT, one patient in whom PDT initially cleared HGD later developed recurrent HGD and 4 others developed invasive cancer. These patients had undergone at least 3 endoscopies with biopsies that were clear of HGD after treatment. Ten controls were selected. They had a similar length of Barrett's and HGD but did not develop recurrent disease during a follow up period in excess of 2 years. In all 15 of these patients, the Barrett's oesophagus was assessed for aneuploidy before and 3–6 months after PDT using image cytometry. Two samples were processed from each 2cm of Barrett's (one biopsy from the posterior wall and one from pooling the other biopsies taken at the same level) A 40 μm section was cut, the paraffin removed with xylene and the nuclei liberated using protease. They were stained with Feulgen and a histogram of DNA content calculated using an automated image cytometry machine (Fairfield Imaging).
Results: The patients who developed cancer or recurrent HGD did so after a median of 14 months (10–38 months). The ten controls were clear of HGD or cancer during follow-up (median 37 months, range 26–60 months). There was no difference in the presence of aneuploidy between the groups before PDT. Four out of the five cases and 8/10 controls had aneuploidy prior to therapy. All five of the cases (5/5, 100%) and only one of the controls (1/10, 10%) had aneuploidy in at least one of the specimens processed 3–6 months after treatment (Fisher's exact test, $p=0.002$).
Conclusion: Late relapses to HGD and cancer are a concern following PDT and appear to occur in 14% of patients in the published literature. Early identification of these patients would permit further treatment prior to relapse or more intensive surveillance. Additionally, since the future cancer risk is very low in patients without residual aneuploidy, these patients could avoid intensive surveillance endoscopy following therapy which would improve the patient acceptability and cost effectiveness of PDT. These results need to be confirmed in a larger cohort of patients.

219 PROSPECTIVE TRIAL OF LAPAROSCOPIC NISSEN FUNDOPLICATION VERSUS PROTON PUMP INHIBITOR THERAPY FOR GASTRO-OESOPHAGEAL REFLUX DISEASE: SEVEN-YEAR FOLLOW-UP

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Introduction: Laparoscopic Nissen fundoplication and proton pump inhibitor (PPI) therapy are both established treatments for gastro-oesophageal reflux disease (GORD). We have performed a prospective randomised study comparing these two treatments (*Br J Surg* 2005;**92**:695–9) and now have long-term follow-up data.
Aims & Methods: Between July 1997 and August 2001, 217 patients took part in a randomised controlled trial comparing laparoscopic Nissen fundoplication and PPI therapy for the treatment of GORD. After a median of 6.9 years (range 4.3–8.3) patients from Norwich (84% of the cohort) were followed up and asked to complete a reflux symptom questionnaire.
Results: There were 91 patients in the surgery arm (Group 1) and 92 patients in the PPI arm. 54 patients randomised to PPI went on to have anti-reflux surgery after 12 months (Group 2a); the remaining 38 did not (Group 2b). 75% of patients responded to the postal questionnaire. Mean Demeester symptom scores (range 0–9) are shown in the table. In all 3 groups there was a significant improvement in symptom score by 12 months ($p<0.01$ Mann–Whitney). However, patients in Group 2a

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	Description	n	Start	12 months	Median of 6.9 years
Group 1	Surgery	91	3.5	0.9	1.1
Group 2a	PPI then surgery	54	3.3	2.3	0.7
Group 2b	PPI alone	38	2.4	1.1	0.9

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experienced a further improvement following subsequent surgery ($p<0.01$) despite having had optimal PPI treatment beforehand.
Conclusion: Both optimal PPI therapy and laparoscopic Nissen fundoplication are effective and durable treatments for GORD. However, surgery offers additional benefit for those who have only partial symptomatic relief whilst on PPIs.

220 THE EFFECTS OF ORAL SUPPLEMENTATION WITH N-3 FATTY ACIDS ON BARRETT'S EPITHELIUM IN HUMANS

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Introduction: Evidence from animal and in vitro studies indicates that n-3 fatty acids may inhibit carcinogenesis, and epidemiological studies suggest a reduced risk of oesophageal cancer in populations with high consumption of fish. One of the possible mechanisms for this chemopreventive effect is by suppression of eicosanoid production through inhibition of the enzyme cyclo-oxygenase (COX)-2. In this study we have determined the effects of dietary supplementation with the n-3 fatty acid eicosapentaenoic acid (EPA) on tissue eicosanoid levels (PGE2 and LTB4) and cyclo-oxygenase-2 (COX-2) activity in Barrett's oesophagus.
Aims & Methods: Fifty participants with known Barrett's oesophagus agreed to take part in this study. Endoscopic biopsies were taken at a recorded level from the area of Barrett's, and then 30 randomly assigned patients consumed EPA capsules (1.5 g/day) for 6 months, the other 20 acted as controls. At the end of this period patients were re-endoscoped and biopsies taken at the same level. Tissue samples were analysed for mucosal lipid profile, PGE2, LTB4 and COX-2 protein and RNA levels. Levels of cellular proliferation were also measured by Ki-67 immunohistochemistry.
Results: There was a significant increase in mucosal EPA content after dietary supplementation (6 months *v* baseline: 2.4% *v* 0.8% of total lipid content; $p<0.001$). EPA supplementation significantly reduced levels of COX-2 protein in Barrett's biopsies as measured by immunoblotting and ELISA ($p<0.05$) but had no influence on COX-2 RNA levels. Levels of PGE2 and LTB4 were concordant between biopsies ($r=0.6$ $p<0.01$) but supplementation had no influence on these levels or on Ki-67 as measured by immunohistochemistry.
Conclusion: In this study supplementation with 1.5 g/day EPA significantly altered levels of n-3 fatty acids and reduced COX-2 levels in Barrett's tissue. However, total eicosanoid levels, and moreover proliferative activity, remained unchanged—we hypothesise that any chemopreventive effect of fish oils is independent of these mechanisms.

221 OESOPHAGEAL METAL STENTS: NOT EXACTLY ''FIRE AND FORGET''

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Introduction: Metal stents are commonly used in the palliative treatment of oesophageal cancer. However, stent insertion is often followed by problems which lead to a substantial hospital workload.
Aims & Methods: A prospective audit was undertaken between Nov 2004 and Oct 2006 of patients treated by the insertion of self-expanding metal stents. Data were recorded at diagnosis and when a stent was placed. Subsequent contacts were logged by the nurses running the upper GI cancer MDT.
Results: During the audit, 64 patients were diagnosed with oesophageal malignancy. Of these 49 were treated by metallic stenting at some time during their clinical course. Forty two patients were men and 7 women; ages ranged from 51 to 92 years (mean 74). Most tumours (47) involved the lower oesophagus; 24 extended into the stomach. There were 37 adenocarcinomas, 11 squamous cancers and 1 was a bronchogenic cancer with oesophageal invasion. In 47 patients an Ultraflex stent was placed. In the other two—where the procedure was used as a holding measure before surgery—a removable Niti-S stent was inserted. Nine patients were alive at the time of analysis and 39 had died, with one patient lost to follow-up. Survival in the patients who had died ranged from 2–452 days (median 150); the patients alive at the end of the study had a median survival to date of 131 days. Minor complications (chest pain, reflux) were almost universal immediately after stenting. The patient with the lung primary had a severe bleed during insertion and died. Two patients were found to have minor perforations which resolved on conservative treatment. In one man the first stent was incorrectly positioned and a second had to be placed. Thirty one of the patients discharged after stenting used the telephone support line; the number of calls for advice ranged between 1 to 17 with a median of 3. Most surviving patients spent further time in hospital (37 out of 48), the number of admissions ranging from 1 to 9 with total hospital stays between 1 and 45 days. On average, those who later died spent 20.6% of their remaining lives in hospital. Thirty four follow-up endoscopies were needed in 21 patients. In 10 subjects with possible obstruction the stent was patent and the problem was regurgitation. Seven patients developed bolus obstruction. A possible benign stricture proximal to a stent was dilated 5 times in 1 patient before a recurrent tumour was confirmed. Ten cases of tumour ingrowth occurred; 3 of these were treated by argon plasma coagulation and 4 by implantation of a second stent. The other 2 endoscopies were to remove stents inserted as a temporary measure before surgery.
Conclusion: Metal stents are useful in the palliation of oesophageal cancer. However, placement is associated with considerable later problems both for the patient and for the GI team managing this difficult condition.

222 HB-EGF AND TGF-α MEDIATE LEPTIN-INDUCED EPIDERMAL GROWTH FACTOR TRANSACTIVATION AND PROLIFERATION IN OESOPHAGEAL ADENOCARCINOMA CELLS

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Introduction: Obesity is a risk factor for oesophageal adenocarcinoma (OAC). Hyperleptinaemia is a feature of obesity. Expression of the epidermal growth factor receptor (EGFR) has been demonstrated in OAC and it has been shown to correlate with severity of disease. We recently showed that leptin may promote oesophageal adenocarcinogenesis by stimulating proliferation and inhibiting apoptosis of OAC cells in an EGFR-dependent manner.[1] The details of this leptin-induced intracellular signalling mechanism in OAC are, however, yet to be fully elucidated.
Aims & Methods: The aim of this study was to examine the role of the EGFR and its ligands in leptin-induced EGFR transactivation and proliferation in OAC. Leptin receptor (Ob-R) expression in OE33, OE19, BIC-1 and FLO-1 OAC cell lines was examined with reverse transcriptase-polymerase chain reaction (RT-PCR) and immunoblotting. The effects of leptin on gene expression of the EGFR and the EGFR-ligands, amphiregulin (AR), transforming growth factor alpha (TGF-α) and heparin binding-EGF (HB-EGF) were assessed using real-time quantitative RT-PCR. The effect of leptin on secretion of AR, TGF-α and HB-EGF by OAC cells was determined by ELISA. The role of AR, TGF-α and HB-EGF in leptin-induced OAC cell proliferation was determined using neutralizing antibodies. Proliferation was assessed by the thiazoyl blue (MTT) assay and apoptosis by ELISA of intracellular nucleosomes.
Results: OE33, OE19, BIC-1 and FLO-1 OAC cells all expressd both long and short forms of the leptin receptor (Ob-R) mRNA and protein. Leptin treatment for 4–24 hours did not significantly affect EGFR mRNA expression, but significantly increased mRNA expression of HB-EGF by 287%, TGF-α by 60% and AR expression by 56%: however leptin only increased the secretion of HB-EGF and TGF-α. Leptin stimulated proliferation of OAC cells and this was abolished by two distinct EGFR kinase inhibitors (AG1478 and PD153035). EGFR inhibition also abolished the anti-apoptotic effects of leptin. Pretreatment of OE33, OE19, BIC-1 and FLO-1 OAC cells with neutralising antibodies to HB-EGF and TGF-α but not to AR abolished the proliferative effects of leptin. Leptin stimulated a significant increase in tyrosine-phosphorylation of the EGFR.
Conclusion: Leptin driven OAC cell proliferation requires transactivation of the EGFR. Leptin stimulates OAC cell proliferation via upregulation and increased release of HB-EGF and TGF-α but not AR, which are responsible for the EGFR transactivation. Consequently, the EGFR is a potential therapeutic target in OAC and the pathways linking the leptin receptor with EGF-ligand expression are potential chemopreventative targets in Barrett's oesophagus.

1. **Ogunwobi O**, Mutungi G, Beales IL. *Endocrinology* 2006; **147**:4505–16.

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223 GLOBULAR ADIPONECTIN INHIBITS LEPTIN-INDUCED PROLIFERATION OF OESOPHAGEAL ADENOCARCINOMA CELLS VIA ACTIVATION OF ADIPONECTIN RECEPTOR-1

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Introduction: Obesity is a potent risk factor for oesophageal adenocarcinoma (OAC). Adipose tissue secretes the peptide hormones leptin and adiponectin, these are reciprocally regulated. Obesity is characterised by hyperleptinaemia and hypoadiponectinaemia and we have recently shown that leptin stimulates proliferation and inhibits apoptosis of OAC cells by stimulating a cascade of intracellular signalling mechanisms, including several key phosphorylation steps. Consequently, we hypothesised that leptin and adiponectin may interact to regulate oesophageal epithelial cell proliferation.
Aims & Methods: The aim of this study was to investigate the interaction between leptin and adiponectin on oesophageal epithelial cells and the underlying cellular mechanisms. Expression of adiponectin receptors on OE33, OE19, BIC-1 and FLO-1 human oesophageal adenocarcinoma cells, ChTRT high grade dysplastic Barrett's cells and non-tumorigenic IEC-18 rat intestinal epithelial cells was determined by RT-PCR and western blotting. The effects of leptin and adiponectin on proliferation were assessed using the MTT assay. The role of adiponectin receptors was assessed with RNA interference and the serine-phosphatase inhibitor okadaic acid was used to examine apsects of intracellular signalling.
Results: OE33, OE19, BIC-1, FLO-1 and ChTRT cells all expressed both isoforms (AdipoR1 and AdipoR2) of the adiponectin receptor. IEC-18 cells expressed only AdipoR1. Leptin induced a dose-dependent increase in cell number of oesophageal and IEC-18 cells. Full length adiponectin (fAd) did not affect basal or leptin-induced proliferation in OAC cells. However when added to unstimulated cells, globular adiponectin (gAd) caused a dose-dependent decrease in oesophageal cancer cell numbers. Similarly gAd caused a decrease in IEC-18 cell numbers compared to control treatment. In co-treatment experiments gAd dose-dependently reduced the proliferative responses of oesophageal adenocarcinoma and IEC-18 cells to leptin. Transfection of a specific AdipoR1 siRNA reversed the anti-proliferative effect of gAd, but okadaic acid had no effect.
Conclusion: Increasing concentrations of leptin stimulate proliferation of oesophageal adenocarcinoma cells, but increasing concentrations of gAd cause a decrease in cell numbers. Concentrations of globular adiponectin seen in lean people attenuate the proliferative effects of leptin. This effect is dependent on AdipoR1, but not on serine-threonine-phosphatase activity. The combination of hyperleptinaemia and hypoadiponectinaemia may promote hyperproliferation in Barrett's oesophagus and promote carcinogenesis. Activation of AdipoR1 may have therapeutic uses in oesophageal adenocarcinoma.

224 AUDIT ON BARRETT'S COLUMNAR-LINED OESOPHAGUS SURVEILLANCE IN A DISTRICT GENERAL HOSPITAL: THE IMPLICATIONS OF BSG GUIDELINES

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Introduction: The aim of Barrett's surveillance is to detect early oesophageal carcinoma (OAC) arising in dysplastic columnar-lined oesophagus (CLO). The British Society of Gastroenterology (BSG) has issued guidelines for the management of CLO,[1] but is limited by the lack of evidence of the natural history of the disease.
Aims & Methods: To evaluate our current practice in the management of patients with CLO and the implications of BSG guidelines. A retrospective analysis of all patients with the diagnosis of CLO from January 2001 to December 2005, identified from endoscopy and pathology database.
Results: From 1/1/2001 to 31/12/2005, there were 508 patients diagnosed with CLO, 366 males and 142 females; median age range 60–69. There were 261 patients with a new diagnosed of CLO and 248 patients were undergoing surveillance endoscopy. 10 patients in the former group developed OAC in the background of CLO. In the surveillance group, 5 had developed OAC. This gives a prevalence rate of 2.0%. Surveillance intervals were based on the degree of dysplasia. Nearly half of CLO patients with evidence of indefinite dysplasia or atypia were re-scoped within 1 year. 50% of CLO patients with low grade dysplasia were surveyed within 1 year. Those with high-grade dysplasia were surveyed between 1–3 monthly intervals; 40% within the group developed OAC. Our current practice on the management of CLO estimates a cost of £25,000 per year. An estimate of an extra £5,000 per year is required to adhere to the recent BSG guidelines.
Conclusion: Our current surveillance practice in the management of patients with CLO is not done in a consistent manner. Only 1/3 of patients with CLO associated OAC were identified in the surveillance group. There are financial implications of implementing BSG guidelines in the management of patients with CLO.

1. **British Society of Gastroenterology**. *Guidelines for the diagnosis and management of Barrett's columnar-lined oesophagus.* BSG, 2005.

225 INTERVENTIONS FOR CHRONIC COUGH ASSOCIATED WITH GASTRO-OESOPHAGEAL REFLUX: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

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Introduction: Gastro-oesophageal reflux is a condition where the lower oesophageal sphincter is abnormally relaxed and allows the stomach's acidic contents to flow back or ''reflux'' into the gullet (oesophagus). It can also cause heartburn. Gastro-oesophageal reflux is a common condition and the most frequent cause of indigestion in the UK. The aim of this paper is to investigate the efficacy of treatment for gastro-oesophageal reflux disease (GORD) on chronic cough in children and adults without an underlying respiratory disease.
Aims & Methods: Systematic review and meta-analysis was conducted searching Cochrane, Medline, and Embase databases (from September 1966 to October 2006), and references from relevant review articles. Included in the review were Randomised controlled trials on GORD treatment for cough in children and adults without primary lung disease. Two reviewers independently selected studies and extracted paediatric and adult data on primary (clinical failure) and secondary outcomes.
Results: Seventeen studies were selected. Meta-analysis was limited to eight studies in adults that compared proton pump inhibitors with placebo. All outcomes favoured proton pump inhibitors: the odds ratio for clinical failure (primary outcome) was 0.25 (95% CI 0.05 to 1.29); numbers needed to treat (NNT) was 6 (harm 51 to ∞ to benefit 2.6). For secondary outcomes, the standardised mean difference between proton pump inhibitors and placebo was -0.52 (-1.03 to 0.02) for mean cough score at the end of the trial and -0.30 (-0.64 to 0.05) for change in cough score at the end of the trial. Subgroup analysis with generic inverse variance analysis showed a significant mean change in cough (-0.43 SD units, -0.76 to -0.08).
Conclusion: The results show that the use of a proton pump inhibitor to treat cough associated with GORD has some effects in some adults. The effect, however, is less universal than suggested in consensus guidelines on chronic cough and its magnitude of effect is uncertain.

226 NOVEL GENOMIC ABERRATIONS IN OESOPHAGOGASTRIC CANCER

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Introduction: Oesophageal junctional adenocarcinoma is increasing in incidence and has a poor outcome. It is envisaged that molecular tumour characteristics will ultimately aid prognostication and lead to targeted therapies. Previously chromosomal analysis of oesophageal and junctional tumours has identified gains in chromosomes (chr)7, 8, 17 and 20 and losses in chr 3–6 and 17–20. A whole genome analysis of a large oesophagogastric sample set has not been undertaken. Thus, we performed whole genome chromosomal analysis of snap frozen

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oesophagogastric tumours to identify both novel and frequent chromosomal aberrations.
Aims & Methods: 167 Oesophageal, gastric and junctional tumours were prospectively collected from 1993–1998. Histological diagnoses were confirmed and DNA extracted using ProteinaseK/RNaseA. ArrayCGH analysis was performed using a 30K, 60-mer oligomicroarray slide, which provided a mean resolution of 350 kb. Data were analysed using the snapCGH package of the R (Bioconductor) statistical system and Microsoft Excel, amplifications were identified using the common regions of amplification algorithm, while deletion were identified, and amplifications confirmed, by direct inspection of chromosome plots.
Results: Systematic analysis revealed frequent genomic aberrations on chr 7 and 11 while chr 19 showed a smaller number of low level amplifications and minimal deletions. 24% of samples showed chromosomal aberrations on chr7 and 19% of samples showed aberrations on Chromosome 11. Detailed analysis of chr 7 showed high level amplifications at a number of loci including 7q21.13 with increased copy number of claudin 12,7q21.2 with increased copy number of CDK6 and also 7p11.2 with increased copy number of receptor tyrosine-protein kinase ErbB-1. Chromosome 11p15.4 revealed a common deletion resulting in loss of copy number of homo sapiens matrix metalloproteinase 26 (MMP26).
Conclusion: A whole genome approach to arrayCGH analysis has successfully identified common regions of gain and loss. It confirms common genomic amplifications such as ErbB-1 and more interestingly identifies novel genomic aberrations affecting genes involved in cell cycle control (CDK6), adhesion (Claudin12) and matrix proteolysis (MMP26), thus identifying potential novel therapeutic targets that require further investigation.

227 THE UTILITY OF ENDOSCOPIC TRI-MODAL IMAGING FOR THE DETECTION OF DYSPLASTIC LESIONS IN BARRETT'S OESOPHAGUS

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Introduction: The Endoscopic Trimodal Imaging system (ETMI) incorporates high-resolution endoscopy (HRE), autofluorescence imaging (AFI) and narrow band imaging (NBI) with magnification in a single device. AFI takes advantage of tissue autofluorescence to image suspicious lesions which appear pink in a green (normal) background. NBI with magnification on the other hand allows visualisation of mucosal surface architecture and microvasculature. It would therefore seem logical to use AFI as a red flag technique to detect suspicious lesions in the overview mode and then evaluate these lesions in even greater detail with NBI and magnification before targeting them for biopsies. The aim of this study was to investigate the diagnostic potential of ETMI and the relative contribution of each modality for the detection of high grade dysplasia (HGD) and early cancer (EC) in Barrett's oesophagus (BO).
Aims & Methods: Forty one patients, referred for endoscopically inconspicuous early neoplasia (n=15) or participating in a regular surveillance program (n=26) were examined with the ETMI system (Olympus prototype). The oesophagus was first inspected with HRE followed by AFI for the detection of additional suspicious lesions. All suspicious lesions detected with HRE/AFI were revaluated with the corresponding modality (AFI/HRE) before inspection with NBI and magnification to evaluate the presence of abnormal mucosal and vascular patterns. This was followed by targeted biopsies. Random four quadrant biopsies were then performed and all biopsies subsequently sent for blinded histopathological assessment.
Results: Per patient analysis of biopsies revealed 13 of the 41 patients having HGD/EC. In 7 patients, HRE detected 9 lesions out of which 8 were also positive with AFI. In 5 patients, no abnormalities were seen on inspection with HRE and HGD/EC was solely diagnosed with AFI (8 lesions). In 1 patient HGD was diagnosed only with random biopsies. In the per biopsy analysis of the 82 lesions which were detected, (27 with HRE and 55 with AFI), 33% of the lesions detected with HRE contained HGD/EC (89% of which were also visualised with AFI). Of the 55 suspicious lesions which were identified with AFI alone and not seen with HRE, 8 contained HGD/EC (false positive rate of 85%). Evaluation with NBI and magnification after AFI reduced the false positive rate to 20%.
Conclusion: AFI may lead to the detection of additional dysplastic lesions in BO after HRE. Though it is associated with a high false-positive rate, this may be reduced by the addition of NBI with magnification. Randomised cross-over studies are needed to assess its full potential in BO surveillance.

228 RISK FACTORS FOR BARRETT'S OESOPHAGUS AMONG MIDDLE-AGED MEN WITH REFLUX DISEASE: A CASE-CONTROL STUDY

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Introduction: In a minority of reflux patients, mucosal inflammation (reflux oesophagitis, RO) is associated with the development of Barrett's metaplasia (BM). Each year, about 0.5% of people with BM develop adenocarcinoma (AdC). The factors that determine why a patient with RO develops BM are incompletely understood.
Aims & Methods: The present case-control study aimed to explore risk factors associated with the presence of BM in middle-aged men with reflux disease. A consecutive series of male, caucasian, middle-aged patients (born 1945–65) were identified from endoscopy records. Cases of BM included those with at least 3 cm of columnar mucosa (confirmed histologically) and the control group included those with RO (LA Grade A-B), identified in a ratio of 1:2 (BM n=203; RO, n=401). Each individual was sent a locally-piloted postal questionnaire, incorporating a validated reflux score, lifestyle questions and items regarding present and past weight (at age 20), waist measurement and height.
Results: The response rate was 39.4% (BO, n=90; RO, n=148), with respondents closely age-matched (mean (SD) years: BO 51.2 (6.1); RO 50.7 (5.9)). Compared to controls, BM patients reported: (1) longer duration of heartburn symptoms (>12 years, p=0.003; >20 years, p=0.005); (2) a higher body mass index (BMI) at age 20 years (23 *v* 22, p=0.047); but (3) A lower frequency of eating within an hour of bedtime (9% *v* 18.5%, p=0.047). No significant differences in frequency of nocturnal symptoms, current BMI, aspirin or NSAID use, smoking, alcohol, frequency of exercise or ''fast food'' consumption.
Conclusion: Among middle-aged, white males with reflux disease, the presence of BM was associated with a longer history of reflux symptoms and a higher reported BMI in early adult life. Overweight young adults with reflux may be at particular risk of developing BM. This is consistent with epidemiological data suggesting that reflux symptoms and obesity are independent risk factors for AdC. The mechanisms whereby obesity might enhance the risk of malignant progression remain unclear.

229 DEVELOPMENT OF A NEW SCORING SYSTEM TO PREDICT ENDOSCOPIC DIAGNOSIS IN PATIENTS WITH DYSPHAGIA

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Introduction: Dysphagia is an alarm symptom that requires urgent investigation. However, patients with dysphagia may have a variety of underlying pathologies. Identifying patients most likely to have malignancy is usually a matter of clinical judgement. There has been no validated symptoms-scoring system to assist selection of such patients in order to offer them a higher priority endoscopy.
Aims & Methods: The aim of this study was to correlate symptoms recorded in a specifically designed Central Dysphagia Service (CDS) referral form with diagnosis in order to establish a model to prioritise endoscopy within the group of dysphagia referrals. Data from 435 patients with dysphagia referred through the CDS were retrospectively analysed. A number of variables including age, gender, specific symptoms as recorded on the checklist were correlated with endoscopic findings. Univariate analysis (χ^2 and *t* test) was used to identify the independent variables that significantly correlated with oesophageal cancer. These variables were entered to a binary logistic regression analysis to create a model, which by using a desirable combination of variables can stratify dysphagia patients into different groups according to the risk of having oesophageal malignancy.
Results: From our cohort of 435 patients (200/235 M/F, mean age 61.8 (14.3) years), 10.7% were diagnosed with malignancy, 6.1% had a benign stricture, 8.9% had a dysmotility disorder, and 4.1% had a benign ENT pathology. The remaining patients had either a normal endoscopy (29.5%) or a variety of benign endoscopic diagnoses such as oesophagitis or hiatus hernia. Male gender, age, dysphagia for liquids, localisation of dysphagia (neck/chest), progressive symptoms, weight loss >3 kg, duration of symptoms<6 months, acid reflux were independently associated with malignancy. The binary logistic regression analysis identified a two-step approach to classify patients; on the basis of age and constant identified 19.7% of patients, none of whom had sinister pathology. Thereafter on the basis of equation taking into account six variables (sex, age, weight loss,

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localisation of dysphagia, acid reflux and duration of symptoms) identified a group of patients (48.6% of total referrals) with 20% diagnosis of cancer. In this latter group, all but one cases of diagnosed cancer were included.
Conclusion: In this study we were able to identify two subgroups of patients; a very low risk for cancer, that endoscopy can be done in a more elective basis and a high risk one that would require urgent endoscopy. This approach can help in the prioritisation of endoscopy in busy endoscopy units by reducing the number of ''unnecessary'' urgent endoscopies, in favour of those patients who may need them most.

Pancreas posters

230 EVALUATION OF THE USE OF CA 19-9 IN THE SETTING OF A DISTRICT GENERAL HOSPITAL

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Introduction: The suitability of tumour markers in the context of screening, diagnosis, prognosis and monitoring is influenced by their specificity and sensitivity. Carbohydrate antigen 19-9 (CA 19-9) is a sialylated glycoprotein detected by the monoclonal antibody 1116 NS 19-9. It was first discovered in human colorectal carcinoma cell lines and is associated with cell adhesion. Specificity for pancreatic and biliary malignancy make it useful in determining diagnosis and recurrence of pancreatic cancer and cholangiocarcinoma.[1–3]
Aims & Methods: The aim of this study is to assess the use of the tumour marker CA 19-9 in the setting of a District General Hospital. The medical records of patients for whom a request for CA 19-9 had been made over an 8-month period at QMH were identified. Information including patients' age, sex, consultant speciality, concomitant illnesses, indication for request, further investigations, diagnosis, treatment and follow-up was analysed.
Results: Ninety nine patients were identified for whom CA 19-9 was requested and further data were available. The indication for requests for CA 19-9 were divided in 5 main categories: diagnosis of pancreatic or biliary cancer (13/99 = 13.1%), diagnosis of colorectal cancer (30/99 = 30.3%), follow-up of colorectal cancer (19/99 = 19.2%), screening for other gastrointestinal cancers (32/99 = 32.3%) and unspecified cancer screening (5/99 = 5.1%). Levels of CA 19-9 were higher than 1000 U/ml (normal range 0–37) in 3/99 (3%) patients (including one pancreatic adenocarcinoma, one cholangiocarcinoma and one colon cancer). CA 19-9 levels were between 120 U/ml and 1000 U/ml in 7/99 (7.1%) patients (including one cholangiocarcinoma, two breast cancers, one tubulovillous adenoma and three normal findings). In 14/99 (14.1%) patients levels of CA 19-9 were between 37 U/ml and 120 U/ml. 8/14 (57.1%) patients had further investigations (CT scan or barium enema). No malignancy was found in these patients. In 6/14 (42.9%) no further test were arranged to investigate the elevated CA 19-9 levels. 75/99 (75.8%) patients had normal CA 19-9 levels (less than 37 U/ml). In 5/75 of these (6.7%) malignancy was found (4 colon cancer, one renal cell carcinoma).
Conclusion: CA 19-9 is frequently requested in a DGH. Its use is not limited to the diagnosis and follow-up of pancreatic and biliary carcinoma. The indication for the majority of requests was for the diagnosis and follow-up of colon cancer for which CA 19-9 has a low sensitivity and specificity. This leads to false positive results leading to unnecessary investigations and stress for patients. False negative results may lead to delayed cancer diagnosis although this was not detected in this study.

1. **Pancreatic section of the British Society of Gastroenterology**. Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinoma. *Gut* 2005;**54**:1–16.
2. **Duffy MJ**, van Dalen A, Haglund C. Clinical utility of biochemical markers in colorectal cancer: European Group on Tumour Markers (EGTM) guidelines. *Eur J Cancer* 2003;**39**:718–27.
3. **Jiang XT**, Tao HQ, Zou SC. Detection of serum tumor markers in the diagnosis and treatment of patients with pancreatic cancer. *Hepatobiliary Pancreat Dis Int* 2004;**3**:464–8.

231 VASCULAR ENDOTHELIAL GROWTH FACTOR AND CALPROTECTIN IN BLOOD AND BILE FOR DIAGNOSIS OF PANCREATOBILIARY CARCINOMA: A PILOT STUDY

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Introduction: Pancreatobiliary carcinomas are difficult to diagnose even with advanced imaging, endoscopic and histopathological techniques. Serum tumour markers, in particular CA 19.9, can help in guiding difficult surgical and oncological decisions where other investigation is equivocal. Calprotectin has been proposed as a tumour marker for colorectal cancer in both serum and stool as well as for ovarian cancers. Vascular endothelial growth factor (VEGF) is expressed by cholangiocarcinoma cells in vitro and is thought to have a major role in tumour angiogenesis.
Aims & Methods: We aimed to test whether calprotectin in plasma and/or VEGF levels in serum, and calprotectin and/or VEGF levels in bile could distinguish between patients presenting for ERCP with pancreatobiliary carcinomas or non-malignant causes. We validated commercially available ELISA kits for calprotectin (PhiCal, Calpro AS, Norway) and VEGF (Quantikine, R&D systems, USA). Samples of venous blood and bile were collected from consecutive patients were analysed for calprotectin and VEGF. Measurement was also made of serum CA19.9 a with standard commercial assay.
Results: Both assays were assessed as suitable for use in the study, after testing for: detection limit, linearity on dilution, inter- and intra-assay precision and recovery of analyte from a spiked sample. 21 patients were recruited, 6 had pancreatobiliary carcinoma (2 cholagiocarcinoma, 2 panceatic, 2 ampullary carcinoma). There was a significant difference between levels of serum CA 19.9 between malignant and non-malignant groups, $p=0.006$, but not for serum VEGF or plasma calprotectin, or VEGF or calprotectin in bile, $p>0.4$, Mann–Whitney test. Differences between malignant and non-malignant samples were twofold or less for calprotectin and VEGF compared to over 100-fold for CA 19.9. No combination of the three markers was better than CA 19.9 alone.
Conclusion: Calprotectin and VEGF do not look to be promising candidates for distinguishing between pancreatobilary carcinomas and non-malignant processes. Their performance was considerably inferior to the tumour marker CA 19.9, which is in day-to-day use. It remains possible that a subgroup of tumours might be identified better, for example cholangiocarcinoma, but our sample was too small to determine this. Efforts towards non-invasive diagnosis of pancreatobiliary malignancy should probably focus on other candidate molecules.

232 PANCREATIC FUNCTION TESTS FROM PATIENT POINT OF VIEW: A QUESTIONNAIRE SURVEY

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Introduction: Pancreolaural (PRL) test, butter fat test (BFT) and faecal elastase (FE-1) test are commonly used non-tube tests in the evaluation of the exocrine pancreatic insufficiency. Although straight forward, they can be very difficult from the patient point of view with regards to stopping the medication, food restrictions, understanding the instructions and duration of the tests.
Aims & Methods: To compare the three tests, PRL, BFT and FE-1 from patient point of view with regards to the degree of difficulty. This questionnaire survey was done along with the comparative study of the above mentioned tests in the evaluation of exocrine pancreatic insufficiency.

Abstract 231

Assay	Median carcinoma	Median non-malignant	Sensitivity%	Specificity%	PPV%	NPV%
VEGF bile (pg/ml)	150	78	17	93	50	74
VEGF serum (pg/ml)	681	569	17	93	50	74
Calprotectin bile (pg/ml)	2006	2761	17	80	25	71
Calprotectin plasma (pg/ml)	999	2152	40	87	50	81
CA 19.9 serum (U/ml)	4136	27	100	57	50	100

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All the study subjects were given following questionnaire prior to the tests along with a self addressed envelope to return the answers.
Results: Regarding overall difficulty of having PFTs, they have felt that tests were very easy (38%), easy (42%), moderately difficult (15%) and difficult (5%). Regarding straight forwardness of the tests, they have responded in favour of FE (31%), BFT (30%) PRL (23%) and all tests (8%). Regarding most difficult part of individual test, in PRL group, food and medication restriction was thought to be difficult (54%) followed by urine collection (23%). In BFT group, eating test meal was thought to be difficult (62%) followed by overnight fasting (23%). In FE group, transfer of sample into the pot was thought be difficult (54%) followed by collection of stool (31%).
Conclusion: Overall these tests were perceived as easy by 80% of the study group and FE-1, BFT were considered straightforward compared to PRL.

1. How easy was it to perform the test? (PRL, BFT and FE-1) very easy/easy/moderately difficult/difficult.
2. What did you consider to be the most difficult part of the PRL test? (A) food/medication restriction, (B) urine collections, (C) two day duration, (D) technical details.
3. What did you consider to be the most difficult part of the BFT test? (A) overnight fast, (B) eating the test meal, (C) blood sampling, (D) technical details.
4. What did you consider to be the most difficult part of the FE-1 test? (A) collection of stool sample specimen in the pot (B) transfer of sample into container, (C) technical details, (D) Other—please specify.
5. Of the three tests which did you find was the most straight forward to perform? (A) pancreolauryl, (B) butter fat, (C) faecal elastase.

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233 CLINICAL IMPACT OF SYMPTOMATIC RECURRENT CHRONIC PANCREATITIS IN PATIENTS WITH CYSTIC FIBROSIS

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Introduction: The majority of patients with cystic fibrosis (CF) are pancreatic insufficient by the perinatal period. 10–15% are pancreatic sufficient for a variable period. A subgroup of these develop symptomatic chronic recurrent pancreatitis.
Aims & Methods: The Royal Brompton Hospital CF database of adult patients (>16 years, 1986–2005) was searched to identify all patients with symptomatic pancreatitis.
Results: Sixteen of 1012 patients (1.6%) were identified, 9 male and 7 female. Diagnosis of CF had been confirmed by sweat chloride in all. The mean age a presentation with pancreatitis was 27 (range 12–53). All presented with characteristic pain and imaging. Six had elevated amylase. 15/16 were pancreatic sufficient at the time of presentation. Of the 10 patients with both CF genes identified, 6 carried a class IV or V mutation. There was a median of 3 hospital admissions (range 1–10) with symptomatic pancreatitis. Median hospital stay was 16 days (range 5–65). A specific complication occurred in 3 cases: bile duct obstruction, a 5 cm pseudocyst and a subphrenic abscess (1 each). Another patient developed pancreatic cancer 23 years after a single episode of pancreatitis. Pancreatic insufficiency developed in 12 (75%) a mean of 6 (range 0–23) years after pancreatitis and coincided with pain resolution. 7 had gallstones, 6 patients having a cholecystectomy. Three had bile duct stones and clearance at ERCP. Four had pancreatic stones managed with pancreatic duct stenting and lithotripsy. One case required bile duct stenting.
Conclusion: Symptomatic chronic pancreatitis is a significant problem in a small group of patients with CF. Most have severe mutations. In most cases this occurs as pancreatic insufficiency develops. An expectant approach is appropriate. Complex pancreatobiliary intervention may be required with close cooperation between specialist hepatobiliary and CF centres.

234 ARE THE BSG GUIDELINES ON PANCREATIC CANCER ACHIEVABLE?

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Introduction: Pancreatic cancer is currently the sixth commonest cause of cancer death in UK. In June 2005 the BSG published guidelines aiming to standardise the management of patients with pancreatic, periampullary and ampullary carcinomas across the UK.[1] We assessed clinical practice within our trust comprising two small district hospitals against these guidelines and compared our results to the minimum standards set out by the BSG.
Aims & Methods: A retrospective analysis of case notes of all patients with pancreatic, peri-ampullary and ampullary carcinomas between April 2005 to March 2006 was carried out using a standard audit proforma. Cases were identified by ICD10 coding system.
Results: Forty six patients were identified. 18 (39%) were males and 28 (61%) were females. Mean age at presentation was 75 years with most (68%) patients presenting between 70 and 90 years. Out of 46, 12 (26%) were referred under 2 week rule, 8 (17%) as routine outpatient, 20 (44%) as direct inpatient while 6 (13%) presented themselves directly to A&E. Weight loss (74%) was the most common presenting symptom followed by epigastric pain (54%), jaundice (46%), anorexia (41%) and backache (30.5%). CT scan (47%) was the most commonly used modality to confirm diagnosis followed by cytology (31%), EUS FNA (17%) and USG scan (5%). 67% patients had metastatic disease on presentation while 24% and 9% had locally advanced and localised disease respectively. 11% patients underwent surgical resection, 22% had chemotherapy, 43.5% underwent palliative stenting (24% via ERCP and 19.5% via PTC) while 23.5% were supported by general palliative care alone. 74% of patients consulted clinicians within 40 days of onset of symptoms. 83% of patients were diagnosed within 20 days of presentation to the local cancer unit. Majority (66%) of patients were referred to the specialist centre within 30 days of presentation to the cancer unit. 50% of patients underwent definitive treatment within 40 days of being referred to the specialist centre. 37 (80%) patients died and 9 (20%) are still alive. 36% patients survived more than 200 days and most of these had definitive treatment in the form of surgery and or chemotherapy. Mean duration of hospital stay was 18 days.
Conclusion: Overall the trust performed well against BSG guidelines. We had accurate demographic information on all cases. All patients referred under the 2 week rule were seen within 2 weeks. Following referral, the specialist centre responded within 2 weeks in all cases. However mean duration from referral to definitive treatment was 52.5 days. Resection rate was 11% and there was no post-operative hospital mortality.

1. **British Society of Gastroenterology**. *Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinomas*, June, 2005.

235 ENDOSCOPIC ULTRASOUND GUIDED TISSUE SAMPLING BY COMBINED FINE NEEDLE ASPIRATION AND TRUCUT NEEDLE BIOPSY FOR THE DIAGNOSIS OF PANCREATIC NEUROENDOCRINE TUMOURS

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Introduction: The role of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in the preoperative diagnosis of pancreatic neuroendocrine tumours (PNETs) is well established. In an effort to increase the diagnostic accuracy of EUS-guided tissue sampling, a 19G trucut-type needle (EUS-TNB) has been designed, but its efficacy in the diagnosis of PNETs has not been reported.
Aims & Methods: We investigated the accuracy and safety of EUS-FNA alone versus combined FNA/TNB in the diagnosis of PNETs. Over a four-year period, 132 patients underwent EUS-guided pancreatic sampling at our Unit. Lesions <1.5 cm in size underwent EUS-FNA with a maximum of 4 passes. For lesions ⩾1.5 cm, EUS-TNB with a maximum of 3 passes was also performed. All results, including technical aspects of the EUS FNA/TNB, were recorded prospectively.
Results: In 11 patients (M/F: 5/6, median age 54 years, range 30–71 years), a final diagnosis of PNET was confirmed by histopathological examination of surgical resection specimens (8 non-functioning PNETs, 3 gastrinomas). Both EUS-guided sampling modalities were used in 9 patients, while EUS-FNA alone was used in 2. The sensitivity of EUS-FNA and EUS-TNB alone was 64% and 78%, respectively. The combination of both sampling modalities established the diagnosis preoperatively in all cases (sensitivity 100%). There was a trend towards an increased sensitivity using both EUS-guided sampling modalities as opposed to EUS-FNA alone ($p = 0.09$). There were no complications.
Conclusion: EUS-TNB is feasible, safe and confers additional clinical benefit to cytological assessment for the preoperative diagnosis of PNETs.

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Radiology posters

236 WIDE ANGLE 3D ENDOLUMINAL CT COLONOGRAPHY: IMPACT ON MISSED AREAS AND POLYP CONSPICUITY

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Introduction: Ability to comprehensively visualise the colonic luminal surface at optical or virtual colonoscopy with a uni- or bidirectional view is dependant on the viewing angle used.[1] Recent data suggests even with a bidirectional 90° view, 5.9% of the surface remains unseen, with a mean of 16 missed regions 300–1000 mm^2 and 4 over 1000 mm^2.[2] Most CT colonography (CTC) software however does not alert the reader to regions of unseen mucosa, risking missed neoplasia. We hypothesised that increasing the 3D endoluminal angle of view to 140°, matching that of optical endoscopy, would ensure adequate mucosal visualisation using a 3D bidirectional flythrough.
Aims & Methods: CTC software (Viatronix V3D colon) was customised such that the endoluminal viewing angle could be altered, and the size and number of missed regions could be recorded. Missed areas were subdivided into size categories: >1000 mm^2, 300–1000 mm^2 and all areas, and documented after bidirectional flythrough at 90 and 140°. 3D polyp conspicuity was assessed on a 4 point scale (1, not or barely visible; 4, very well seen) by a blinded experienced radiologist using snapshots of 12 colonoscopically confirmed polyps, median size 6 mm (range 2–20 mm), taken at both viewing angles. Polyps were assessed in isolation and then in a side by side comparison.
Results: Twenty datasets were reviewed, mean age 66 years (range 41–81), 11 female; prone acquisition unavailable in 2. Supine data presented (table 1) prone result were not significantly different to supine, $p>0.2$ (Wilcoxon signed-rank test). When polyps were viewed in isolation there was no statistical difference in conspicuity between the two viewing angles, $p=0.38$ (Mcnemar test); however when viewed as image pairs, 8 of 12 were considered more conspicuous at 90° compared to 140.
Conclusion: Bidirectional 3D endoluminal flythrough with a 140° viewing angle almost eliminates missed areas and increases confidence for adequate mucosal visualisation, particularly if software does not provide a ''missed regions tool''. Polyp conspicuity however is reduced at 140°, an observation only apparent after direct side-by-side comparison. The clinical impact of this requires further study, but suggests optical colonoscopists using very wide angle (170°) colonoscopes might suffer similar changes in conspicuity.

1. **East JE**, *et al. Endoscopy* 2006;**63**(Suppl II):A77.
2. **Pickhardt PJ**, *et al. Gastroenterology* 2006;**130**:1582–1587.

237 SMALL BOWEL IMAGING: COMPARISON OF SMALL BOWEL MAGNETIC RESONANCE IMAGING WITH SMALL BOWEL FOLLOW THROUGH

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Introduction: Small bowel follow through (SBFT) is widely available and well tolerated by patients[1] but risks overlooking important abnormalities[2] and uses ionising radiation. High soft tissue contrast, multi planar imaging and ability to provide functional information[3] with no use of ionising radiation make magnetic resonance imaging (MRI) increasingly popular.
Aims & Methods: To compare small bowel MRI findings with those of SBFT and to determine clinical usefulness of MRI. Retrospective review of MRI reports and comparison of MRI and SBFT findings on patients who underwent MRI at Western General Hospital between July 2004 and April 2006.
Results: MRI findings: 71 patients, majority (54) females, underwent MRI. Average age was 39.9 years. The main indication (43, 60.6%) was Crohn's disease and 35 (49.3%) had previous bowel surgery. Small bowel dilatation was detected in 19 (26.8%), wall thickening in 14 (19.7%), strictures in 9 (12.7%), lymphadenopathy in 3 (4.2%), enterocutaneous or enterorectal fistulae in 3 (4.2%) and intra-abdominal abscess in 1 (1.4%). Active Crohn's disease was diagnosed in 10 (14.1%). Extra intestinal findings were present in 43 (60.6%). SBFT *v* MRI: Of the 71 who underwent MRI, only 38 (53.5%) had had SBFT. The average interval between MRI and SBFT was 20.1 months. 28 (73.7%) of the 38 were known to have Crohn's disease and 20 (52.6%) had previous bowel surgeries. Of the 14 with small bowel dilatation in MRI, only four had dilatation in SBFT. Strictures were demonstrated in 7 MRIs; 5 of them were also detected in SBFTs. Of the 10 who had strictures on SBFT, only 5 were detected on MRI. Bowel wall thickening was found in 8 patients on MRI; only one of them had similar finding on SBFT. Two patients had fistula on MRI; none were detected on SBFT. Eight had active Crohn's disease on MRI but only one of them had active disease on SBFT. Three had ulcers seen on SBFT which were not seen on MRI. 24 (63.2%) had extra intestinal findings on MRI.
Conclusion: MRI was more sensitive than SBFT in detecting small bowel wall thickening and fistula. Disease activity was better assessed with MRI. MRI was unable to detect mucosal ulcers, due likely to its low spatial resolution. Although MRI was less able to detect strictures, it gave more information on disease activity and helped characterise strictures. MRI was also able to provide extra intestinal information. Taking into account the young age, complicated disease course and the functional and extra intestinal information it provides MRI is definitely a better test.

1. **Carlson HC**. Perspective: the small bowel examination in the diagnosis of Crohn's disease. *AJR* 1986;**147**:63–5.
2. **Wills JS**, Lobis IF, Denstman FJ. Crohn disease: State of the Art. *Radiology* 1997;**202**:597–610.
3. **Laghi A**, Paolantonio P, Passariello R. Small bowel. *Mag Reson Imaging Clin N America* 2005;**13**:331–48.

238 DETERMINING THE PROXIMAL EXTENT OF ULCERATIVE COLITIS: WHITE CELL SCAN CORRELATES WELL WITH HISTOLOGICAL ASSESSMENT

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Introduction: Assessing the extent of ulcerative colitis (UC) determines therapeutic strategies and provides prognostic information. Colonoscopy with mucosal biopsy is usually considered unsafe in patients with severe disease. The aim of this study was to assess the correlation between the proximal extent of UC as determined by Technitium-99m hexamethylpropylene amine oxime labeled leucocyte scan (white cell scan) with that determined by histological assessment.
Aims & Methods: 135 patients with histologically-confirmed UC in the computerised histopathology database who had both white cell scan and histological assessment of colonic inflammation (either by multiple mucosal biopsies during colonoscopy or by colectomy) during the years 1991–2004 were included. Both assessments were performed within 6 months of each other. Overall agreement, quadratic weighted kappa (κ) and polychoric correlations (ρ) were calculated to estimate the interrater reliability (extent based on histology and leucocyte scan) of the ordered categorical rating of proximal extent of colitis.
Results: Correlation between white cell scan and histological extent was excellent ($\kappa=0.72$; $\rho=0.82$), while macroscopic appearance on colonoscopy did not correlate as well with histological extent ($\kappa=0.62$; $\rho=0.67$).

Abstract 236 Missed areas at bidirectional 3D endoluminal flythrough

Area size	Viewing angle	Mean (SD)	Range	Median	IQR
>1000 mm^2	140°	0.1 (0.4)	0–2	0	0–0
	90°	4.1 (1.8)	1–6	4	3–5
300–1000 mm^2	140°	1.1 (1.4)	0–6	1	0–1.3
	90°	15.4 (7.4)	7–32	13	8.8–20.3
All areas	140°	8.6 (8.5)	1–38	6	4.8–9.3
	90°	71.8 (21)	40–115	67.5	58.6–78

All comparisons 140 *v* 90, $p<0.001$.

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Abstract 239

	Pre-nurse	Post-nurse	Significance
No of patients	64	77	
Drug stopped (WBC<3)	4 (6.3%)	3 (3.8%)	
Drug stopped (S-E)	1 (1.6%)	1 (1.3%)	
Drug stopped (other)	1 (1.6%)	–	
Longest gap between FBC (weeks) Median (range)	13 (6–26)	9 (6–20)	p=0.001
No with gap between FBC >10 weeks	42 (65.6%)	29 (37.7%)	p=0.001
No with <3 FBCs during 6 months	40 (62.5%)	28 (36%)	p=0.002

Higher C- reactive protein (CRP) values were not significantly associated with better concordance between histological and white cell scan based estimation of proximal extent of disease (p=0.34). White cell scans correlated significantly better in patients with more extensive disease (p=0.02), while colonoscopy predicted disease extent significantly more accurately in patients with more limited colitis (p=0.002).
Conclusion: The proximal extent of UC determined by white cell scans correlates well with histological assessment especially in patients with more extensive disease. White cell scans offer a reasonable alternative to colonoscopy in determining the proximal extent of colitis, not only in patients with active disease but also in those who do not tolerate or decline colonoscopy.

Service development posters

239 BLOOD COUNT MONITORING OF AZATHIOPRINE IS IMPROVED BY INFLAMMATORY BOWEL DISEASE NURSE SUPERVISION

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Introduction: With increasing use of azathioprine in inflammatory bowel disease, robust monitoring systems are required to ensure blood tests are taken and bone marrow suppression acted upon promptly.[1] Inflammatory bowel disease (IBD) specialist nurses are able to take on this role, and coordinate blood count monitoring. Previous studies have shown that IBD nurses can reduce hospital visits and hospital length of stay, and undoubtedly improve patient understanding and satisfaction with their care.[2] We are not aware of studies showing benefit in terms of azathioprine monitoring.
Aims & Methods: 181 patients with Crohn's or ulcerative colitis were taking azathioprine or 6-mercaptopurine at some stage between 1999 and 2006 at the University Hospital of Wales in Cardiff. Monitoring of blood counts was previously done by doctors in clinics, and shared with GPs. In July 2003 a specialist nurse was appointed, and took over the role, maintaining a list of patients on azathioprine, ensuring they were supplied with blood request forms, and contacting them if blood results were not available via the laboratory results reporting system. Our local recommendations are for a full blood count every 8 weeks in patients on a stable dose, and we instruct patients to stop the drug if the total white cell count falls below 3×10^9. We reviewed effectiveness of monitoring for a 6-month period prior to the nurse appointment, (Jan–Jul 2003) and after (Jul–Dec 2005), including only those patients on a stable dose of thiopurine for >2 months at the start of these 6-month periods. We recorded the longest gap without blood tests, the number with a gap of >10 weeks between tests, and those who had <3 tests in the six months. Comparisons by Mann–Whitney test.
Results: No patients in either period experienced problems as a result of leucopaenia. In the nurse-monitored group, the 3 patients with leucopaenia were contacted to stop their drug after 1, 4 and 7 days. This information was not available in the pre-nurse group.
Conclusion: Nurse-led monitoring significantly improved thoroughness of monitoring, but 1/3 patients still do not have blood tests as regularly as intended, (even allowing 2 weeks leeway beyond an 8-weekly target). With increasing emphasis on GP-led monitoring, IBD nurses may still have an important role in coordinating monitoring and ensuring compliance.

1. **Carter MJ**, *et al. Gut* 2004;**53**(Suppl 5):v1–16.
2. **Nightingale AJ**, *et al. Eur J Gastroenterol Hepatol* 1999;**9**:967–73.

240 FEASIBILITY OF USING AN ELECTRONIC HRQOL QUESTIONNAIRE ROUTINELY IN PATIENTS ATTENDING A BUSY GASTROINTESTINAL OUTPATIENTS DEPARTMENT: TIME INVOLVEMENT AND SYMPTOM REPORTING

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Introduction: Electronic data capture to assess health-related quality of life (HRQOL) using validated questionnaires allows real time analysis and presentation of results to clinicians prior to the consultation. Their implementation however is still poor with very few data on their use routinely especially within busy medical or gastroenterology clinics.
Aims & Methods: We are currently involved in a pragmatic single-centre RCT to assess the suitability of measuring HRQOL data routinely in busy medical clinics and its impact on the clinical process and cost implications. We are using the Gastrointestinal Symptom Rating Questionnaire (GSRQ) as the intervention instrument. It is a validated GI system-specific HRQL questionnaire for assessing GI symptoms developed during the MINuET study (*Health Technol Assess* 2006;**10**:1–214). 20 items within 4 dimensions underlie the GI symptoms (upper GI, lower GI, wind and defecation related). Randomised patients complete the questionnaire while in the waiting room prior to clinic consultation. Completion times are recorded and family/friends may assist. A research officer, involved in recruiting, is available to provide minimal help. We aimed to analyse the first 150 patients to use this intervention and assess its feasibility. The questionnaire is a HTML based program with a mouse-based simple point and click. Results are recorded on Access database and standardised dimension and total GSRQ scores are calculated.
Results: 157 patients were randomised to complete the questionnaire during the first 2 months of the study (age range 17–87 years). All patients completed the questionnaire. Only 5 patients took >15 mins to complete questionnaire (3%). Majority required no or minimal help. The table

Abstract 240 Electronic GSRQ completion times and mean HRQOL scores

Age range	Patient numbers	Age median	Time median	Upper GI	Lower GI	Wind	Defec	Total GSRQ
<40	30	34	4:24	27.3	34.2	46.0	18.1	32.3
40–49	29	44	5:47	25.3	33.3	47.1	22.0	32.6
50–59	36	56	6:59	19.5	29.4	50.3	19.1	29.4
60–69	29	66	6:34	16.2	26.7	40.7	18.3	24.5
⩾70	33	76	7:34	18.2	34.8	46.5	21.8	29.2
All	157	56	6:00	21.1	31.5	46.4	19.7	29.5

GSRQ scores (0–100): 0 no symptoms, 100 max symptoms.

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summarises the completion times and GI symptom scores between the different age groups. 41.4% of patients reported sleep disturbance due to symptoms. Questionnaire completion time does have a positive correlation with increasing age groups but times are still acceptable.
Conclusion: Despite the range of computer expertise amongst patients, completion of electronic GSRQ questionnaire is feasible among all age groups including the elderly attending busy GI clinics and will assist in the collection of HRQOL routinely. Younger patients tend to report more GI symptoms with wind-related symptoms being by far the commonest reported symptoms in all groups.

241 IS OUTSOURCING OF DICTATION CHEAPER THAN MEDICAL SECRETARIES?

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Introduction: In the current circumstances of significant cost pressures on the NHS, digital dictation and international outsourcing of medical transcription has been shown to be an effective and viable method enabling faster turnaround and accurate transcription. Nevertheless, the implications of rolling out such a service on the current job roles of medical secretaries are unclear. Indeed concerns have been raised as to whether such a service will erode rather than transform these job roles. Moreover the financial implications associated with international outsourcing of medical transcription have not hitherto been published.
Aims & Methods: To calculate the costs associated with the provision of medical transcription by international outsourcing. Data were retrospectively collected from a comprehensive database of a single consultant gastroenterologist using digital dictation/outsourcing system from an established service provider (ScribeTech UK Ltd) from June 2005–August 2006. Dictation was performed with a digital voice recorder (Olympus DS-330). The anonymous files were downloaded to the hospital server and routed via secure FTP to a transcription centre in Bangalore, India. The transcription was then routed back to the hospital, merged with patient demographics on the hospital electronic patient record (EPR), and was then available for review before approval and printing. Data were collected on the number of transcriptions, total lines, turnaround time, cost data, and error rate.
Results: 1566 transcriptions (36 782 lines) were sent through the system over 15 months (mean 32 letters/week). All transcriptions were processed within prescribed times, no files were lost, and clarity of dictation was excellent. Total cost for all transcription was £3310.38 that was equivalent to £0.09 pence/line. The assumptions on cost for medical secretaries included: (1) mean secretary salary £2166 per month (full time); (ii) 50% of secretarial time spent on analogue system; (3) 2800 lines typed per month/consultant. Using these assumptions, the comparative cost for producing letters the traditional analogue way cost £0.39 per line.
Conclusion: In summary, digital dictation and international outsourcing of transcription is 77% cheaper than the cost of analogue dictation per line. This may have implications in redefining the role of medical secretaries in the future.

242 COPY LETTERS TO PATIENTS: USE AND IMPACT ON WORKLOAD

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Introduction: Copying all outpatient letters to patients helps meet the requirements for good communication but potentially altering the style of the letter to aid patient understanding, and resultant enquiries, could impose a considerable extra workload. We assessed the impact of copying letters to all patients and undertook a re-audit at 2 years
Aims & Methods: All new and follow-up patients seen by consultant were included. The purpose of the copy letter as an information sharing exercise was explained and a header on the copy letter repeated this. Planned study size was initially 200, later extended to 311. The consultant noted changes in letters including text content or additional length used to provide clarification for the patient (2 lines or more). The length of text in the body of the letter was compared with a pre-study sample of letters and a post study sample at 2 years. The personal assistant noted the number of enquiries related to the study sample letters, their nature and how long they took to be dealt with.
Results: We sent copy letters to 311 study patients. None indicated they did not want a letter. The first 200 letters generated no enquiries, extending the study to 311 letters generated one enquiry. 6% of letters were consciously lengthened for clarification, 4% had substantial language modification. 1% of letters were censored as having information which had not been discussed with the patient and which was not suitable for notification other than by face-to-face contact. Length of follow-up letters was little changed in the pre-study sample, study sample and re-audit sample at an average of 8.2, 8.7 and 7.4 lines. New patient letters increased from an average of 12.1 lines pre-study to 18.7 lines during the study, indicating some unconscious tendency to lengthen text, but in the re-audit had dropped back to 15.9 lines. Patient enquiries remain negligible. Informal patient comment indicated during the study (and continues to indicate) that they find the copy letter useful to summarise clinic discussion and management plans.
Conclusion: Patient enquiries related to copy letters were, and remain, negligible in terms of frequency and extra workload. This may be because the explanation in clinic was followed quickly by the letter in 2–4 working days and it contained little new material. Increase in length of new patient letters since the study is modest and follow up letters are slightly shorter than before. Letters were appreciated as providing a summary of sometimes complex information, reassurance of ''openness'' by the doctor and, in a few cases, a means of convincing a partner absent from clinic that all relevant issues had been addressed. A copy letter from clinic should routinely be sent to each patient.

243 AN ''ENDOSCOPY OUTCOMES SHEET'' IMPROVES PATIENT EXPERIENCE AFTER ENDOSCOPIC PROCEDURES: RESULTS OF A PILOT STUDY AT A DISTRICT GENERAL HOSPITAL

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Introduction: Patients in the UK are traditionally given a verbal report of their endoscopy findings before discharge from the unit. However, most patients when reviewed in clinic admit to remember very little about the result of their endoscopy. There is a need for a better system of communicating results of endoscopic procedures to our patients.
Aims & Methods: A pilot project was prospectively carried out between July–August 2006 to provide consecutive patients on a consultant endoscopy list with a single A4 sheet containing information of the outcome of endoscopy and colonoscopy in lay and medical terminology including intended follow-up. The discharging nurse also verbally explained the outcome sheet to the patient. A Patient Satisfaction questionnaire containing 4 structured questions was also provided, to be returned in a Freepost envelope. Results were analysed by the Clinical Governance department in a blinded manner.
Results: 36% completed questionnaires were returned. 97.2% respondents felt that it was a good idea to provide information after the endoscopy in lay terminology. 44.1% felt that they preferred the sheet to take away; 74.4% felt that they would prefer to have a nurse explain the results to them and 18.5% felt that they would prefer to get both kinds of information. 38.8% felt that they would not like to receive information in medical terms, as it would worry them. Overall 91.7% respondents felt that this service was satisfactory to very satisfactory.
Conclusion: The result of this pilot study shows that providing a written explanation of the results of the endoscopy is welcomed by most patients and improves their experience of the procedure. It should be the standard of care for all endoscopy units.

244 THE INVESTIGATION OF IRON DEFICIENCY WITH OR WITHOUT ANAEMIA

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Introduction: In June 2000 the British Society of Gastroenterology published guidelines for the investigation of iron deficiency (ID) with or without anaemia. Patients above the age of 45 years old with ferritins below the normal range should be investigated with upper endoscopy (OGD) and barium enema (+/− sigmoidoscopy) or colonoscopy. In 2003 a retrospective study at the Bristol Royal Infirmary over a three month period, was published showing that only 49% of patients with iron deficiency were being investigated according to the BSG guidelines. Changes were implemented where by the BSG guidelines were automatically typed on the computer report of any patient with a low ferritin result; this study aims to evaluate the effectiveness of this change.
Aims & Methods: A retrospective study was undertaken identifying patients with iron deficiency using the hospital pathology computer. Data were collected using a proforma including age, sex, symptoms, investigations, diagnosis and follow-up. Drug and medical histories were also recorded. Patients below the age of 45 years were excluded from the study.

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Results: Fifty seven patients were identified over a three month period in 2005. 20 with iron deficiency (ID) and 37 with iron deficiency anaemia (IDA). Male:female 24:33; age range 45–92 years. Most presented with an incidental finding of ID or anaemia; some had symptoms such as tiredness, abdominal pain, bloating or weight loss. Those with anaemia were more likely to complain of symptoms than those with isolated ID. 15 (26%) were asymptomatic; 12 patients (21%) were on some form of NSAID at the time of presentation. Of those patients with IDA only 9 had OGD and colonoscopy or barium enema (24%). Three patients with isolated ID were investigated (15%) according to guidelines. Diagnoses included peptic ulcer disease, microscopic colitis, oesophagitis and diverticula disease. Four patients had celiac disease (3 IDA; 1 ID). One patient presenting with IDA had colonic carcinoma.
Conclusion: The results fall far short of the expected improvement following wider distribution of the BSG guidelines. Specialities outside that of gastroenterology are less likely to be familiar with the BSG guidelines and patients with ID present to a wide variety of specialities. With clear instructions printed on the hospital results page, it would appear that the guidelines were either not read or ignored. Despite efforts to improve the service to these patients, the investigation of iron deficiency has deteriorated since the publication of the 2003 study. These guidelines need to find a wider audience outside those with an interest in gastroenterology. Pathology may be going undiagnosed for longer and treatment delayed, because early warning signs (such as ID) are being ignored.

245 INFORMED CONSENT: DO SUBJECTS UNDERSTAND THE INFORMATION SHEETS?

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Introduction: Information sheets for clinical research are becoming increasingly complex but the extent to which they are understood is uncertain.
Aims & Methods: We assessed comprehension by healthy volunteers of a patient information sheet in a phase 3 clinical trial. Healthy volunteers participating in a capsule endoscopy study were given a standard 13 page written information sheet, as per COREC guidelines, and allowed to asked questions. The trial compared as a primary endpoint the incidence of small bowel erosions or ulcers in subjects randomised to take a selective COX2 inhibitor, non-steroidal anti-inflammatory (NSAID) plus proton pump inhibitor, or placebo. After indicating they were ready to give consent and had read and understood the information sheet, the volunteers were asked to complete a 6-item questionnaire covering the identity and adverse effects of trial treatments and of the procedure, the duration of the trial and value of the inconvenience allowance.
Results: Eighty two healthy volunteers were approached and all completed the questionnaire. 74 (90%) of the volunteers had university level education and 49 (60%) were clinical medical students. Only 10 subjects (12%) could name the three trial drugs. Only 14 (17%) could name 3 or more potential risks of the medication they might be exposed to, whilst 17 (20%) could identify none. Most subjects (77/82, 90%) identified capsule endoscopy as the trial procedure and impaction/obstruction as its main risk (52/82, 64%). The maximum number of potential adverse events recalled was 6 (n = 2) of 23. All but one subject (98.8%) could recall the exact value of the inconvenience payment (table). While accurate recall was higher in the medical students than non-medical volunteers, both groups showed deficiencies of understanding (table).
Conclusion: A comprehensive information sheet resulted in limited understanding or recall of trial risks. Shorter information sheets with a test and feedback session should be trialled so that informed consent becomes valid informed consent.

246 THE CHANGING PATTERN OF REFERRALS FOR UPPER GASTROINTESTINAL CANCER 2001–5

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Introduction: The two week wait target for all suspected cancers was implemented at our institution in January 2001. A rapid access proforma was introduced enabling patients with suspected upper gastrointestinal (GI) malignancy to be fast tracked directly to endoscopy within 2 weeks. This is part of the pathway to ensure all cases are diagnosed and treatment is commenced within 62 days. In 2002 we retrospectively analysed all patients diagnosed with oesophageal or gastric cancer and the number of cases diagnosed via the rapid access proforma.
Aims & Methods: To see if the number of two week wait referrals has changed since 2002 and to find out if there has been a significant change in the number of upper gastrointestinal cancer cases diagnosed by this route. A retrospective review of all two week wait referrals for 2005 was carried out. All upper GI referrals were identified and the number diagnosed with gastric or oesophageal malignancy were compared with a database of all upper GI cancers diagnosed at our instituition in 2005 and cross referenced with pathology records, endoscopy records and the local cancer registry. Patients with suspected pancreatic or biliary cancer were excluded from the analysis. These results were compared with those from 2002.
Results: In 2005 a total of 261 patients were referred under the two week rule. 24 (9.2%) of these cases were diagnosed with having upper GI malignancy. A total of 62 cases were diagnosed over this time period. Therefore 39% of all upper GI malignancies were referred and diagnosed via the two week proforma. Figures from 2002 demonstrate a diagnostic yield of 3.8% when 6 out of 157 two week rule referrals were found to have upper GI malignancy. A total of 57 upper GI malignancies were diagnosed. Thus only 10.5% of all upper GI malignancies were identified under the two week rule in 2002. The total number of referrals has increased by 166% over the 4 year period and the ''positive yield'' of malignancy has increased by 28% overall and by 5.4 per 100 referrals. The total number of upper GI malignancies diagnosed remained unchanged.
Conclusion: Demand on the service provided by the two week wait initiative has increased significantly since its introduction. All patients were seen within two weeks in 2005 in our institution. The vast majority of two week referrals (90%) still do not result in a diagnosis of malignancy, although a much greater proportion of the cancers diagnosed are now referred by this route (increase from 3.8% to 9.2%). This partly reflects the increased number of cases seen by this route; modification of the referral proforma; awareness and increased uptake of the form; and education and feedback given to local GPs. This has resulted in a larger number investigated with increased pressure upon endoscopy and outpatient services for the same number of cases diagnosed in the local population.

247 THE IMPACT OF A 24-HOUR TELEPHONE HELPLINE ON THE MANAGEMENT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: BSG Guidelines recommend that an inflammatory bowel disease (IBD) service should allow ''rapid access to advice and clinic appointments in the event of a relapse''. We introduced an IBD nurse-led 24 hour telephone helpline in order to improve accessibility to advice and reduce the number of patients requiring urgent outpatient (OP) review.

Abstract 245 Comprehension of medical *v* non-medical volunteers

	Correct, n	%	Medical, n	%
Able to name all drugs	10	12	8	16
Can name any drugs	65	79	43	88
Can name ⩾3 adverse events (AE)	14	17	10	20
Can name any drug AE	66	80	43	88
Can name the procedure	77	94	47	96
Can name possible risk of procedure	52	64	37	74
Duration of study	79	97	47	97
Payment	81	99	49	100

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Aims & Methods: We audited use of a 24-hour telephone helpline on management and OP attendance in a large teaching hospital setting. Patient satisfaction with the service was also evaluated. We reviewed all calls received by the IBD helpline over a 1-year period. Individual calls are recorded in a standard manner with reason for call, advice provided and outcome documented. If treatment change resulted from the telephone consultation, it was considered to have avoided an OP review. To investigate patients' views on quality of service, questionnaires were randomly sent to 150 patients that had contacted the helpline during the 12 month study period.
Results: In total 709 patients (ulcerative colitis, n = 405) made 2087 calls. Admission as a result of the call was required in 45 (6%) patients. Investigations were arranged in 335 (47%) cases and early review in 84 (12%). Treatment was changed in 285 (40%) patients. Completed questionnaires were returned by 100 (66%) of the 150 patients. 88 patients (88%) said the helpline avoided them seeing their GP and 98 (98%) felt their disease was managed more effectively as a result of the helpline. The quality of care provided by the helpline was considered excellent or good by 95 (95%) of respondents.
Conclusion: A dedicated telephone helpline is an important addition to specialist IBD services. It is valued by patients and the advice and treatment changes suggested can significantly reduce the need for primary care consultation and specialist OP review.

248 OUTCOME OF A NURSE-LED OUTREACH SERVICE FOR PRISON INMATES WITH CHRONIC HEPATITIS C INFECTION

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Introduction: UK prison inmates have a relatively high prevalence of hepatitis C (HCV) infection, most acquired from past intravenous drug use. In 2004, a dedicated nurse-led HCV service was established in Bristol to address the needs of inmates at 5 prisons (4 male, 1 female). Previously, inmates' accessibility to HCV clinics had been restricted; patients often missed hospital appointments due to prison staff shortages, or inter-prison transfers.
Aims & Methods: To evaluate the clinical outcome of patients referred to a nurse-led prison outreach HCV service. Inmates with past intravenous drug use were advised to be tested for bloodborne viruses at prison entry by the prison healthcare team. Those found to be HCV antibody positive (Ab+) at initial testing were referred to the HCV specialist nurse for further management. Those inmates whose remaining sentence exceeded 2 years were considered eligible for HCV treatment whilst in prison. Outcome data were recorded for all patients referred from 1 July 2004 to 31 July 2006.
Results: 247 HCV Ab+ patients were seen by the specialist nurse, 200 (81%) of whom were PCR positive (+). Hepatitis B or HIV coinfection was found in 6 patients (3 and 3, respectively). 174 HCV PCR+ patients were male (87%), with mean ages of 34.8 years (range 17–65 years) and 30.7 years (range 17–53 years), for males and females, respectively. The majority of PCR+ patients were white (n = 194). 72 patients (31%) had short sentences (<2 years) and were referred to their own GP or to hospital outpatient services post-release, while 58 (29%) did not wish further intervention. 70 patients (35%) were considered for treatment whilst in prison and underwent liver ultrasound and/or liver biopsy. 15 of these (21%, 7.5% of total seen) commenced HCV treatment (response rates to be presented). 22 patients being assessed for HCV therapy were transferred to other Bristol prisons after initial assessment.
Conclusion: Nurse-led prison outreach clinics for patients with chronic HCV may improve the accessibility of this high-risk group to specialist services. Sentence length may be used to help target HCV specialist resources.

249 A WEB-BASED ENDOSCOPY REFERRAL AND TRIAGE SYSTEM FOR QUALITY ASSURANCE

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Introduction: Endoscopy referrals are generated from multiple sources including hospital and community physicians with varying levels of clinical experience. The evidence base and consensus statements regarding indications and risk management of endoscopic procedures evolve over time. The current guidelines are perceived to be complex and difficult to access and hence may not be routinely reviewed prior to requesting endoscopy. A web-based referral form with embedded guidelines was developed and published on the intranet in our hospital.
Aims & Methods: Intervention 1: The BSG guidelines regarding dyspepsia, iron deficiency anaemia, GI bleeding and surveillance endoscopy procedures were reviewed and summarised. The Rockall score was used to determine prognosis in GI bleeds. Protocols were developed to optimise pre-procedure management in those requiring antibiotic prophylaxis, diabetics, anticoagulated patients and for ERCP, to maximise day case procedures within limits of safety. All of the above guidelines were made available as summary sheets or simple flow charts. A new unified referral form was developed for inpatient and out patient referrals with prompts to refer to the guidelines. Rockall scoring table was added. This form was made available in electronic format on the hospital intranet in addition to print format. The guidelines could be accessed from intranet version by clicking on the embedded hyperlinks. The medical staff were sent a web link via email and requested to use these guidelines. Intervention 2: All procedure requests were triaged by the physician or nurse assessor using the above system. Booked surveillance colonoscopy procedures were reviewed and the responsible referring consultant was contacted if indications were not in conformity with the published guidelines, with a view to cancelling or rescheduling them.
Results: An audit done in 2005 showed that 60% of the surveillance colonoscopies were being done prematurely or were not necessary. This represented 30% of all colonoscopy procedures. Re-audit for the month of November 2006 (after the introduction of the web-based system) has shown that a total of 73 procedures were booked. 30 were surveillance colonoscopies (41%). After nurse triage, 6 procedures were found to be inappropriately requested (20% of surveillance procedures, 8% of all colonoscopies) and these were cancelled or deferred. Prospective audits are under way to assess the impact of above interventions, in terms of quality assurance, resource utilisation and user satisfaction. Initial indications are positive in all these areas.
Conclusion: Due to the large amount of information needed for decision making in endoscopy referral, hospital intranets offer a very useful resource, in terms of ease of access and the ability to regularly update information.

250 A PROSPECTIVE AUDIT OF A NURSE-LED IRON DEFICIENCY ANAEMIA SERVICE IN COMPLIANCE WITH THE BSG GUIDLINES

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Introduction: Following increasing demands on the gastroenterology service, a specialist nurse-led iron deficiency (IDA) service was established. The aim of this service was to diagnose, investigate and provide treatment options for GP referrals with a provisional diagnosis of IDA. A prospective audit was carried out to determine the safety and appropriateness of treating this group of patients within a nurse-led setting and to audit the service against the BSG guidelines.
Aims & Methods: A prospective audit of the first 53 patients referred to the nurse-led service, 3 of which proved not to have IDA based on haematinics, leaving a study group of 50. Evidence of IDA was documented in the notes of all patients. Risks of investigations were outlined to each patient, who was subsequently able to make an informed choice between barium or endoscopic investigations. The investigations were carried out and outcomes recorded.
Results: A total of 50 patients were included in the audit. 39 female (18 pre-menopausal), and 11 male. The median age was 64 years (range 28–83). Six patients had FOBs performed by GP prior to referral. Only 9 patients had a cause for IDA identified. Two patients had gastric cancer (both inoperable) and one patient had a treatable rectal cancer. One patient had Crohn's disease and 1 patient had gastritis identified as the cause of anaemia. Coeliac pathology was identified in 4 of the pre-menopausal women. Of the pre-menopausal women, 3 had +FOBs and were investigated, nil on pathology. Other pre-menopausal women investigated all had upper or lower GI symptoms and investigated appropriately. Four pre-menopausal women were not investigated as per BSG guidelines. 41 (82%) of patients had no findings for the cause of their anaemia. All patients had appropriate investigations including screening for coeliac disease. All patients received iron replacement therapy. The 8 (16%) patients not responding to iron therapy were investigated further.
Conclusion: The nurse-led service rigorously followed the BSG IDA guidelines and complied with them in all cases. All IDA patients were diagnosed and treatment instigated within 6 weeks of referral, complying with the 18 week government target due in November 2008. The specialist nurse can play a safe and essential role in developing gastroenterology services.

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Abstract 250 Investigations

	OGD Bx, colonoscopy	OGD Bx, Ba enema, Sig	Ba meal, Ba enema, SBE	OGD, Bx Ba enema	Ba enema, Ba meal, Sig	OGD Bx
Men	8	15	1	0	0	0
Post-menopause women	15	3	0	2	2	0
Pre-menopause women	2	6	0	0	0	6

Ba, barium; Bx, biopsy; OGD, gastroscopy; SBE, small bowel enema; Sig, sigmoidoscopy.

1. **Goddard AF**, James MW, McIntyre AS, *et al*. Guidelines for the management of iron deficiency anaemia. BSG Guidelines in Gastroenterology, 2005.

251 RED CELL DISTRIBUTION WIDTH: ANOTHER USEFUL INDEX FOR IRON DEFICIENCY

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Introduction: The BSG guidelines for management of iron deficiency anaemia (May 2005), suggest confirmation of the iron status with the use of mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) or serum ferritin. In the last decade, the measurement of soluble transferrin receptor (sTfR) and its calculated ratio to Log10ferritin (sTfR/Log10ferritin→Index) provides a useful alternative to bone marrow examination (the gold standard test for determination of iron status).
Aims & Methods: Red cell distribution width (RDW) is like MCV and counter measurement. It provides MCH and other Coulter information about the homogeneity of the produced red cell population. It is raised when red cells are produced under precarious iron stores. The BSG guidelines, on the other hand, suggest that high RDW indicate coexistent B12 or folate deficiency. We aimed to examine the validity of RDW as indicator of iron deficiency. We used the Index as surrogate ''gold standard'' of iron deficit. A total of 68 patients from gastroenterology and rheumatology clinics were included in the study. They were all anaemic with normal MCV.
Results: Forty two patients were iron deficient (Index $\geqslant$2). Twenty five of them had high RDW, 17 had normal RDW. Six patients were iron-repleted (Index$<$1). All six had normal RDW values. The use of RDW (on the above cohort) had 59.52% sensitivity and 100% specificity in the detection of iron deficiency, while its positive predictive value (PPV) and negative predictive value (NPV) were 100% and 26.09%, respectively.
Conclusion: RDW is highly specific for iron deficiency. Its better use would be in combination with MCV and MCH values and not as a surrogate index of B12 or folate deficiency.

252 THE DEVELOPMENT OF A COUNTYWIDE LONG-TERM FOLLOW-UP SERVICE FOR PATIENTS WITH GASTROSTOMY TUBES RESULTS IN SIGNIFICANT BENEFITS FOR PATIENTS AND CARERS, THE LOCAL PRIMARY CARE TRUSTS AND THE DISTRICT GENERAL HOSPITAL

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Introduction: Historically, following the insertion of a gastrostomy tube, patients would be discharged to the community with little or no instructions for management of the tube and stoma site. Gastrostomy tubes can cause long-term problems if not managed properly. There was also no routine follow-up and no planned replacement for short term tubes nor any formal training for staff in the acute and community hospitals or in the community. These factors resulted in frequent admissions usually after accidental tube displacement, and accounted for 128 bed nights per annum.
Aims & Methods: A Gastrostomy Tube Follow-up Service has been run by the Nurse Consultant in Stroke (NCiS) for 18 months, managing community-based patients in a population base of 500 000. The service was set up in conjunction with the medical gastroenterologists and the Dietetic Department. The aim of the clinic was to proactively manage the gastrostomy tubes, routinely replacing balloon gastrostomy tubes and providing informal patient, carer and staff training and information. A record was kept of the time spent in direct contact with gastrostomy patients (planned as 1 session per week), together with projected savings from prevented admissions.
Results: On average there were between 175 and 200 patients with gastrostomy tubes at any one time (initially only 70 of these were known), though this is a fluid population. In the first year of the pilot there was a reduction in admissions for PEG complications (predominantly accidentally displaced PEGs) of 100 bednights. The number of ''emergency'' endoscopy appointment slots for replacing displaced balloon gastrostomies fell from 84 to 7 (with resultant reduction in ambulance/transport costs). Few patients could visit outpatient clinics and the service is now totally domicilliary. Urgent referrals are forwarded from, and telephone advice is frequently sought by: community nurses, dieticians, GPs, nursing home staff, learning disability staff, acute and community hospital staff and by patients and carers.
Conclusion: There were many patients across the county with gastrostomy tubes in situ than had been previously known and they required a great deal more support than was originally envisaged. Savings in reduced admissions and emergency gastrostomy replacements in endoscopy unit have been considerable. Long term, following a countywide rolling training programme for all relevant staff, care of these patients will transfer to locally-based teams with support from the NCiS for complex patients.

Abstract 252 Number of interventions between 1/1/05 and 1/1/06

Intervention	n
Planned visits	362
Referrals for urgent/prompt visits	287
Telephone advice	402

253 VALIDATING THE PLANNED COLONOSCOPY WAITING LIST: WORTH THE EFFORT?

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Introduction: In 2002, the British Society of Gastroenterology issued guidelines for colorectal cancer screening in high-risk groups. These were designed to reduce inappropriate screening/repeat colonoscopies to reduce risks and ensure efficient use of resources as well as identifying those who would benefit from repeat procedures.
Aims & Methods: We reviewed the casenotes of 418 patients on the planned (repeat) colonoscopy waiting list to determine whether their procedure was appropriate and timely based on the guidelines. Where apparently inappropriate, the referring clinician was asked to review the notes and the patient was removed or had their appointment altered accordingly.
Results: There were 202 males, 198 females, mean age 62.7 years (range 18–87). 278 (66%) were being followed-up for polyps, 55 (13%) for colitis, 54 (13%) for family history of cancer, 18 (4%) previous colorectal cancer, 9 (2%) for renal transplant, 3 (1%) for acromegaly and 1 for hyperplastic polyposis syndrome. 18 patients were over 80 years old. 37 patients (8.8%) were removed from the waiting list mainly because of inappropriate follow-up following polyp removal (13), inappropriate family history follow-up (10), and also because of development of advanced malignancy (5), patient request (5) and limited proctitis (2). 18 patients had their procedures expedited and several more had theirs delayed giving a net reduction in colonoscopy of ''45 patient years''. Several patients were left on the waiting list outside the BSG guidelines at their Consultant's discretion. In particular, patients with strong family history but not HNPCC or FAP had 5 years colonoscopies until aged 55 years. Patients were

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generally not removed from the planned waiting list on the basis of age alone (BSG guidelines advise patients follow-up stop aged 70 years after cancer, or after 75 years for polyp surveillance). Renal transplant guidelines suggest surveillance for colorectal cancer but do not state how this should be done.
Conclusion: Waiting list validation resulted in a significant removal of patients from a medical planned waiting list and a slight overall reduction in frequency of follow-up. Greater reduction could have been achieved with complete adherence to the guidelines.

254 DYSPHAGIA HOTLINE: THE FIRST 600 PATIENTS

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Introduction: The ''one-stop'' dysphagia hotline (DHL) service allows rapid access to investigation of dysphagia and has now seen over 600 patients. These patients are investigated by consultation, barium swallow and/or upper GI endoscopy. Latterly a nurse endoscopist telephones patients to determine the best means of investigation. We studied which symptoms are most predictive of cancer, and whether the likely diagnosis was best assessed by a medical consultation, or telephone interview by Consultant or nurse.
Aims & Methods: The DHL database was analysed for patients referred March 2003–May 2006. The health professional interviewing patients was asked to give a provisional diagnosis prior to investigation and this was compared with the final diagnosis.
Results: Of 625 patients referred, 69 were excluded from further analysis, due to admission or death before investigation, patient declining investigation or no telephone. Mean age was 68.4 years (range 21–103 y). 12.0% had cancer, 1.8% pharyngeal pouch and 9.0% peptic stricture. The majority of the remainder had gastro-oesophageal reflux disease, oesophageal dysmotility or both, although 4.7% had Barrett's oesophagus, 1.1% achalasia and 1.4% peptic ulcer disease. 21% of patients referred denied dysphagia. True dysphagia was commonly found in serious pathology (cancer OR 1.78, benign stricture OR 3.67) but not in minor pathology (OR 0.32). 8% of patients with cancer presented without dysphagia, although only 1 did not have symptoms fulfilling the 2 week wait criteria (back pain). Cancer more commonly presents with progressive dysphagia (OR 2.36). Weight loss is significantly more likely with cancer (OR 4.2) compared to other pathologies. Dysphagia to liquids and solids was more likely to be indicative of cancer than for solids alone (OR for solid dysphagia was 1.3) however this was also true for peptic stricture and pharyngeal pouch. Cancer was more likely to present with a shorter duration of dysphagia, with only 2.8% of all the referrals after 6 months diagnosed with cancer. Nurse endoscopist telephone calls predicted more patients to have cancer (30.3% *v* 16.3 and 20.5% for Consultant telephone or direct review) although the PPV for each methods was very similar (29.0% *v* 26.7% and 32.1% respectively). Cancer was correctly predicted in 46.8% of cancer patients by nurse endoscopist *v* 66.7% and 64.3% by other methods respectively.
Conclusion: Over 20% of patients referred to DHL had peptic stricture or cancer. Progressive dysphagia, weight loss and dysphagia to both solids and liquids were predictive of significant pathology. Nurse endoscopist telephone triage for DHL has similar PPV and NPV for malignancy as medical triage.

255 GASTROINTESTINAL TRACT PATHOLOGY IN PATIENTS WITH ASYMPTOMATIC ANAEMIA AND CHRONIC KIDNEY DISEASE

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Introduction: Anaemia frequently complicates chronic kidney disease (CKD) and the prevalence significantly increases when the glomerular filtration rate (GFR) falls below 60 ml/min/1.73m^2. Although anaemia in this setting is most likely due to intrinsic renal disease, laboratory markers of iron deficiency are less reliable in this group and consequently upper and lower gastrointestinal (GI) endoscopy is often performed to exclude bleeding lesions. The diagnostic yield and justification of GI investigations in this group of patients is unclear.
Aims & Methods: We conducted a retrospective, case control study of patients referred for endoscopic investigation of asymptomatic anaemia. We identified 94 patients with anaemia and CKD (estimated GFR <60 ml/min/1.73 m^2 based on the abbreviated MDRD equation). The group was subdivided into patients with supporting evidence of iron deficiency (serum ferritin <30 g mg/l) and those without. The control group comprised 217 patients with normal serum creatinine and iron deficiency anaemia (IDA) low haemoglobin and ferritin. All patients underwent OGD and 92.2% of control patients and 55.3% of CKD patients underwent a colonic investigation. The prevalence of lesions potentially accountable for the anaemia was then calculated.
Results: In patients with CKD without supporting evidence of iron deficiency there were significantly fewer upper (11.5% *v* 24.4%, OR=0.40 95% CI 0.20 to 0.83) and lower (6.5% *v* 19.8%, OR=0.28 95% CI 0.10 to 0.79) GI lesions potentially accountable for IDA as compared to controls. The prevalence of GI malignancy was 0% in patients with CKD without evidence of iron deficiency as compared to 17.1% in controls ($p<0.0001$). In patients with CKD and evidence of iron deficiency the number of benign and malignant lesions with potential to cause IDA was statistically equivalent to control patients with normal renal function and IDA.
Conclusion: The prevalence of GI lesions potentially accountable for IDA is low in patients with asymptomatic anaemia and CKD, unless typical laboratory features of iron deficiency are present.

256 IMPROVING COLONOSCOPY SERVICES USING ACTION AUDIT

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Introduction: Colonoscopy is the accepted gold standard for investigating the lower gastrointestinal tract but considerable variation in clinical practice has been reported. Endoscopy services have undergone significant changes driven by the national modernisation programme (http://www.endoscopy.nhs.uk) and the patient centred quality assurance web tool (http://www.grs.nhs.uk). The National Bowel Cancer Screening Programme (BCSP) requires endoscopists to demonstrate both adequate numbers and competency in order to apply for Colonoscopy Accreditation Test (CAT). An audit was performed to bench mark the colonoscopy services for Surrey and Sussex to estimate the number of eligible colonoscopists and improve poor performance.
Aims & Methods: The audit was planned using nationally agreed criteria and standards (http://www.iog.nhs.uk) which included: number of colonoscopies performed, completion rate - intention to reach caecum (IRC), sedation used and complications. The audit was anonymous, voluntary, and all endoscopists were required to sign up to the action outcome agreement. Data were collected prospectively by the nursing staff in each endoscopy unit for a three month period (Jan to Mar 2006) using standard data collection forms which were returned centrally on a weekly basis. Each endoscopist was coded and at the end all the data were validated. The final coded results were presented as summary document for each Trust and codes only revealed to the individual endoscopists.
Results: All the endoscopy units in the region participated and results are outlined in the table. The sedation used was also reported with the majority using recommended drugs and amount. One serious complication (perforation) occurred during the audit period.
Conclusion: Improving performance in healthcare is an important and challenging goal and audits often identify but do not change either individuals or organisations. Expecting endoscopists to sign up to agreed action plans provided a different approach. The audit identified that Surrey and Sussex had enough colonoscopists eligible to apply for CAT but not always in centres ready to apply for BCSP. Detailed results of change in practice of individual endoscopists not reaching standards are awaited, as Chief Executive of Organisations were asked to formally respond to the

Abstract 256

	Surrey	Sussex
Number of colonoscopists	36/48 (75%)	43/54 (80%)
Overall intention to reach caecum (%)	90%	87%
Gold >150/year & IRC>90% (eligible for BCSP)	10 (28%)	9 (21%)
Green 100/year & IRC>90% (increase numbers)	4 (11%)	6 (14%)
Amber <100 &/or IRC 80–90% (improve performance)	14 (39%)	18 (42%)
Red <100 & IRC<80% (retrain or stop)	8 (22%)	10 (23%)

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SHA after 6 months of the data being circulated. Repeat audits have been recommended with an annual update regarding actions outcomes being sent to stakeholders including SHA and Cancer Networks.

257 THE GENDER IMBALANCE IN ACADEMIC MEDICINE: HAVE WE BRIDGED THE GAP OVER 35 YEARS? A UK PERSPECTIVE

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Introduction: Historically there has been a shortfall in the number of women in senior academic posts. Currently the number of female medical students in the UK has increased and now represent up to 60% of the yearly intake. However, despite this there continues to be a perceived disparity between the sexes in academia. A recent publication from the US made an assessment of this problem by using genders of authors in peer reviewed journals as a surrogate marker for representation of women in academia. No such study has ever been conducted in the UK and no data exist for gastroenterology.
Aims & Methods: To determine the degree of UK female author representation in two peer-reviewed British journals. Data were collected for first and senior authors of *Gut* and the *British Journal of Surgery* (*BJS*) for the years of 1970, 1980, 1990, 2000 and 2004. The sexes of British authors were identified by inspection of their first name. In cases where it was unclear, the gender was determined using the medical directory, internet search engines, Medline, Embase, institutional websites or by direct contact with the individual institution.
Results: We determined the sex of 93.9% of British authors in the two journals over the period of 35 years. In 1970, 65% & 84% of the total number of original articles originated from the UK compared to 23% and 36% in 2004 for *Gut* ($p<0.001$) and *BJS* respectively ($p<0.001$) There was a significant rise in the number of female first authors for both journals: from 7.7% in 1970 to 19% in 2004 ($p=0.002$). The number of female senior authors has remained relatively constant over this period ($p=0.8$). Individual comparisons made between the two journals between 1970 to 2004 showed a fourfold rise in the number of female first authors in *BJS* (4% to 15.6%, $p=0.0072$) compared to a two fold increase in *Gut* (12% to 26%, $p=0.052$). While for senior authors, a rise of 1.52% was noted in *BJS* ($p=0.74$) and in contrast, a decline of 1.43% was noted in *Gut* ($p=1$). When comparing the number of female first authors between the two journals, there was a significant difference in 1970 ($p=0.04$) but this is no longer the case in 2004 ($p=0.14$).
Conclusion: There has been an encouraging increase in the number of female doctors who participate in academic medicine (as judged by first authorship). In contrast, the number of senior female authors has stayed relatively the same for both divisions of gastroenterology and surgery. Despite an attempt of narrowing the gap in the field of academic surgery, women still comprise a minority of original research in the UK. Further evaluation at national level such as the Athena and WAM (Women in Academic Medicine) project would help to address factors that could narrow the gender gap.

258 CAPSULE ENDOSCOPY: IS FORMAL TRAINING NECESSARY FOR SPECIALIST REGISTRARS IN GASTROENTEROLOGY?

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Introduction: Capsule endoscopy (CE) has become an important modality to investigate the small bowel. Reading of the video images is time consuming and interpretation of the findings requires expertise. Small studies have shown that physician extenders (nurses) can be used in CE reporting to save physician time.
Aims & Methods: To assess the ability of Specialist Registrars (SpRs) to interpret CE videos and compare against controls (medical students). Six SpRs in gastroenterology and four final year medical students were asked to read and interpret 10 CE videos. The gold standard was taken as the CE findings reported by a gastroenterology consultant with CE expertise (MEM). All of the SpRs (3rd–5th year) had performed more than 1000 gastroscopies. One SpR had already read 50 CE videos under supervision whereas the others were naïve of any CE reporting. All participants were given the same introduction to the CE software and were blinded to the referral indications and each other's findings. Parameters assessed were time taken to read, gastric emptying time (GET), small bowel transit (SBT), number of thumbnails (TN) including false positives and negatives, pathology missed and the ability to make the appropriate diagnosis. The data were analysed using SPSS version 12.0.
Results: The average time taken for the SpRs to read the videos was 54 minutes (range 45–69) as compared to 56 minutes (range 46–73) for the controls. There was no significant difference in minutes to the accepted GET between the two groups ($p=0.133$). However the mean difference in minutes to the accepted SBT (within 1 minute) was 20 minutes for the SpRs and 89 minutes for the students ($p=0.046$) in all 10 videos. SpRs were more likely to record true positives and less likely to record false positives when compared to controls ($p=0.011$ and $p=0.005$ respectively). The SpRs were also more likely to reach the correct diagnosis ($p=0.007$). On comparison between the individual SpRs, the SpR with CE experience had a detection rate of 100% while for the other five SpRs this ranged from 50–90%. There was no significant correlation in time taken to read the videos and the number of true positives for both groups (students: $p=0.92$, SpRs: $p=0.424$).
Conclusion: Our study has shown that SpRs in gastroenterology had a significantly higher pick up rate for pathology on CE when compared to controls (with no endoscopic experience). However, SpRs failed to reach the correct diagnosis in some cases. This study has shown that prior endoscopic experience is beneficial but focussed training would enable SpRs to reliably identify and interpret small bowel pathology on CE.

259 PATIENT ACCESS TIMES AND SURVIVAL BEFORE AND AFTER INTRODUCTION OF A RAPID ACCESS UPPER GASTROINTESTINAL CANCER SERVICE

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Introduction: The ''Improving outcomes'' guidance for upper GI cancer (DoH, 2001) led to major changes in the organisation of cancer services in the UK. The ''two week rule'' (TWR) aimed to encourage rapid diagnosis of suspected cancer. Our centre in North Liverpool receives the highest volume of TWR referrals in the UK and we have reported that <4% of patients with alarm features have oesophagogastric cancers.[1] However, not all cases of cancer will access care via the preferred fast-track route. A key question is whether service redesign and the provision of the Rapid Access Upper Gastrointestinal Cancer Service (RAUGICS) has led to an overall improvement in cancer processes and outcomes.
Aims & Methods: (1) To compare waiting times and survival before and after implementation of the RAUGICS system; (2) To compare survival according to route of diagnosis in the post-RAUGICS era. A cancer centre serving a local population of >330 000. All cases of oesophageal or gastric cancer identified via pathology records during two 2-year periods: Period 1 (Pre-RAUGICS), Period 2 (Post-RAUGICS). Hospital IT systems and case notes audited to establish access times (GP referral to endoscopy; GP referral to histological diagnosis), tumour type, stage, treatment outcome,

Abstract 259 Impact of RAUGICS on process and outcome of care

	Pre-RAUGICS	Post-RAUGICS
Number of cancers (oesophageal:gastric)	152 (71:81)	181 (92:89)
Age (mean, years)	70	71
Referral to endoscopy (median (range), days)	14 (0–470)	12 (1–402)*
Referal to diagnosis (median (range), days)	30 (4–485)	16 (4–434)*
Potentially curative surgery (%)	31.6	30.4
3-year survival (%)	16.4	17.1

*$p<0.05$.

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3-year survival. For the Post-RAUGICS period, route of diagnosis was designated as: ''RAUGICS'' (fast-track; n = 3008 total referrals); ''Other'' (includes non-urgent open access endoscopy, GI clinic and emergency admission) and Barrett's surveillance (BarS; n = 420 patients; cancer rate 0.5% pa).
Results: See table. In the Post-RAUGICS era, only 43.1% of all cancers were diagnosed by fast-track route. Survival was not significantly different for symptomatic patients diagnosed via the ''other'' referral routes. BarS patients had better survival than symptomatic cancer cases ($p<0.025$).
Conclusion: Service reorganisation has led to significantly improvement in overall access times, reducing the median delay from referral to diagnosis by two weeks. This provides prompt treatment decisions and more rapid palliation. However, the fast-track system selects patients with poor survival. Overall 3-year survival from these tumours in our locality is unaltered. Patients on BarS have significantly better survival than others. Screening programmes for these cancers are needed if outcomes are to improve.

1. **Kapoor N**, *et al. Gut* 2005;**54**:40–5.

260 EVALUATION OF EFFICACY OF AN ENDOSCOPE STORAGE AND DRYING CHAMBER IN AN ENDOSCOPY UNIT AND ITS IMPACT ON WORKING PRACTICE

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Introduction: Exogenous infection transmitted during endoscopy is rare. The current BSG guidelines stipulate that all scopes to be used on each day must have been exposed to a cycle of automatic reprocessing not more than 3 hours prior to use. This caused problems with utilisation of endoscopes in morning lists and for emergency procedures. Taking this into consideration the endoscopy unit at Kettering general hospital purchased an endoscope drying and storage cabinet. (Lancer FD8 hereafter will be called FD8). Due to lack of data on microbiological safety we subjected the FD8 to in house tests.
Aims & Methods: Tests for drying were conducted on internal channels and external surfaces of endoscopes stored in FD8. Tests were also conducted on sterility after normal processing and disinfection. Tests on external surfaces used tests to detect protein (Protect M) and ATP (Lighting MVP) in addition to standard microbiological testing at 0.5, 12, 24, 36, 48, 72 h intervals. Tests were conducted after external contamination of endoscopes using standard microbiological tests at regular intervals as above. Tests were also run on simulated parts of endoscopes after contamination by known amount of Pseudomonas aeruginosa. This was to mimic a situation where dismantled parts of endoscopes were contaminated by waterborne bacteria during the last rinsing stage. Tests were also conducted when endoscope channels were contaminated after standard cleaning and disinfection with, water containing known amount of Pseudomonas aeruginosa. The endoscopes were tested using standard microbiological tests at regular intervals as above.
Results: FD8 was very efficient in keeping the external surfaces and internal channels of endoscopes dry. The FD8 also kept external surfaces of all the different types of endoscopes sterile up to the period of 72 h as confirmed on routine microbial cultures. These were reconfirmed by tests for protein and ATP. Following contamination the simulated parts of endoscopes there was reduction of bacterial contamination depending on storage time in the drying chamber. Following internal contamination the number of viable bacteria initially decreased at 30 minutes. However there was an increase in viable bacteria in the first 12 h of storage time when endoscopes were stored at 37˚C. Therefore the test was redone at a reduced temperature of 30˚. This showed reduction of bacterial contamination depending on storage time up to 72 h.
Conclusion: FD8 was very effective in drying the external and internal surface of endoscopes. It also maintained sterility of washed and disinfected endoscopes. BSG guidelines caused duplication of work in endoscope reprocessing. Nursing staff had to turn up at work at 7 am each working day to put the endoscopes in the reprocessor. Also caused wastage of disinfectant and wear and tear to the endoscopes. FD8 had an impact on working practices and working life of the staff at Kettering in last year. Staff are redeployed in a more productive way improving patient care. Also clean endoscopes are always available for emergency procedures. There are also savings on the cost of disinfectant.

261 USEFULNESS OF A DEDICATED NURSE SPECIALIST-LED CLINIC FOR FAMILIAL COLORECTAL CANCER

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Introduction: Risk stratification of patients with a family history of colorectal cancer (CRC) can be time consuming. A hospital based nurse led familial colorectal cancer service (FCRCS) can be useful in identifying and providing specific information to patients who are predisposed to such risk.
Aims & Methods: To determine the usefulness of a hospital based nurse led FCRCS and the diagnostic yield of screening colonoscopies in patients with a familial risk of colorectal cancer. Patients referred from the community with a family history of CRC were identified from the FCRCS database from March 1996–2006. Patients without polyposis syndromes were risk stratified based on the Amsterdam criteria 2.[1] A dedicated nurse specialist confirmed the presence of tumour in families and counselled patients accordingly. Information on screening colonoscopy and histology were obtained from the endoscopy and histology database.
Results: Of the 339 patients 200 were females with a median age of 48 years (IQR 39–58). Risk stratification was as follows: low-risk: 17.4%, moderate: 5%, low–moderate: 19%, high–moderate: 30% and high-risk: 25.3%. Overall 123/339 (36%) patients had 165 screening colonoscopies (low-risk: 8/59, low–moderate: 23/64, high–moderate: 45/102, and high-risk: 46/85). Four patients refused screening and 12 patients did not attend. If 59 patients in the low-risk group who did not warrant screening are excluded, 107/265 (40%) remaining patients were too young for screening to be initiated. No pathology was encountered on screening the low and low–moderate risk group.
Conclusion: More than a third of the patients referred with familial cancer are in the low or low–moderate risk group. A nurse-led FCRCS can avoid unwanted colonoscopies in 17.4% of low-risk cases and in addition delay the inception of screening in 40% of the referred cases. We therefore recommend all patients be risk stratified in a nurse led FCRCS prior to initiating screening.

1. **Myrhoj T**, Bisgaard ML, Bernstein I, *et al.* Hereditary non-polyposis colorectal cancer: clinical features and survival. Results from the Danish HNPCC register. *Scand J Gastroenterol* 1997;**32**:572–6.

262 A MULTIDISCIPLINARY APPROACH TO PERCUTANEOUS ENDOSCOPIC GASTROSTOMY REDUCES THE NUMBER OF INAPPROPRIATE PROCEDURES AND DECREASES MORTALITY

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Introduction: The National Confidential Enquiry into Patient Outcome and Death[1] indicated that outcomes from percutaneous endoscopic gastrostomy (PEG) insertion are poor and many inappropriate procedures are being performed (19%). A 6-month audit in 2005 at St Mary's Hospital concluded that 26% of inpatient PEG referrals were inappropriate.
Aims & Methods: In order to reduce the number of inappropriate referrals a formalised PEG referral form was designed for completion by the referring team. The form required signatures from the dieticians and speech and language therapists as appropriate. Over a 10-month period all patients referred for PEG insertion used a formal PEG request form. The patients were then prospectively evaluated by a gastroenterology SpR or consultant. If the patient was felt appropriate a PEG was booked and the details of the procedure recorded. At 30 days all patient outcomes were reviewed by case note examination or by telephone consultation.
Results: All 38 patients referred for a PEG feeding tube used the formal request form. Two patients were deemed inappropriate for PEG insertion by the gastroenterology team (×1 of these patients died within 30 days). In a further 6 patients, endoscopic placement of a PEG tube was not possible as a safe insertion site could not be identified. These patients were referred for radiologically inserted gastrostomy. A total of 30 patients had PEG tubes inserted. There was ×1 death within 30 days of PEG insertion and ×1 major complication (buried bumper with sepsis that required surgical removal). Rates of local and systemic sepsis were low following the procedure (6.6%). There was no statistical difference in infection rates related to antibiotic prophylaxis, but the sample size was small.
Conclusion: A formal PEG referral form requiring input from all members of the multidisciplinary team significantly reduced the number of inappropriate referrals. The form in combination with pre-assessment by a member of the gastroenterology team limited 30-day mortality to 3.3%. A formal PEG referral form should be standard practice with all patients being pre-assessed prior to PEG placement.

1. **National Confidential Enquiry into Patient Outcome**, Death (NCEPOD). Scoping our Practice (PEG Subgroup) 2004.

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263 NURSE SPECIALIST IRON DEFICIENCY ANAEMIA SERVICE ARISING FROM AUDIT FINDINGS

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Introduction: Iron deficiency anaemia (IDA) is common and can indicate serious pathology. It is frequently misdiagnosed and inappropriately investigated. In 2002, all referrals to endoscopy for anaemia were audited. 36% of patients referred had no evidence of iron deficiency, either because iron and ferritin had not been measured or because they were normal. 41% of patients had been referred for gastroscopy only, 17% for colonoscopy only and 6% for gastroscopy and flexible sigmoidoscopy.
Aims & Methods: The aim of the development was to reduce unnecessary endoscopies, ensure complete investigation and reduce times to cancer diagnosis. To do this we formulated local guidelines, based on BSG recommendations, and set up a Specialist Nurse IDA clinic which takes place twice a week alongside gastroenterology outpatients. Patients are referred via a structured referral form and seen and investigated under the two week rule, with dedicated endoscopy slots allocated. The clinic has 40 minute appointments to allow time for a full history and examination (based on a proforma) and to give patients sufficient information and time to decide on whether to go ahead with invasive testing. Gastroenterology and haematology physicians are available for advice if needed.
Results: The IDA clinic has become well-established in the hospital. It receives referrals from other consultants as well as from GPs. A total of 555 new patients have been seen in 2 years with 11% having a gastrointestinal malignancy. The median wait between referral to the clinic and diagnosis of cancer is 2.5 months, compared with 4.5 months prior to the clinic being set up. The ''Did Not Attend'' rate for patients referred for endoscopy from the IDA clinic is low at 2%. An anonymous questionnaire-based survey of local GPs revealed that 93% were happy to refer to a nurse led clinic. 31% of GPs felt that the service had improved their diagnosis and management of IDA. We repeated the initial 2002 audit of referrals to endoscopy for anaemia in 2005, after the clinic had been established. Patients with anaemia were referred for endoscopy from the IDA clinic, direct from GPs and from other consultant teams. Only 2% of this group of patients had no evidence of IDA (0% of patients referred from IDA clinic). 82% were optimally investigated (ie gastroscopy with D2 biopsies and colonoscopy combined).
Conclusion: We have demonstrated significant improvements in the management of IDA by setting up a dedicated IDA nurse-led service. There has been a significant reduction in unnecessary endoscopic investigation of non-iron deficiency anaemia (mainly anaemia of chronic disease, an improvement in completeness of investigation and a fall in the delay between referral and diagnosis of GI malignancy. Interestingly, improvements were seen across all routes of referral, not just those that came through the IDA clinic. The service is well received in primary care, based on the survey of GPs. In addition, there have been improvements in attendance rates for endoscopic investigation. This may reflect the increased time spent discussing the investigations in the clinic.

264 IMPROVING OUTCOME IN UPPER GASTROINTESTINAL HAEMORRHAGE BY SERVICE DEVELOPMENT: A PROSPECTIVE AUDIT IN A DISTRICT GENERAL HOSPITAL

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Introduction: In 1993 Rockall *et al* undertook the national upper GI bleed audit. The overall mortality was found to be 14%. The Royal Bolton Hospital undertook an audit of acute gastrointestinal haemorrhage (AGIH) in 2001. Mortality was 16%—comparable to the national average. Several issues were highlighted including time taken from diagnosis to endoscopy and poor assessment of patient risk. Several changes were made: junior doctors were educated in the assessment and management of AGIH; the Rockall GI bleed score was printed onto endoscopy request cards to aid in the triage of requests; 4 slots per day were reserved to facilitate early endoscopy of high risk patients and a ''bleed board'' was installed on the medical assessment unit (MAU) to highlight patients with suspected AGIH. In 2006 a second audit was undertaken to assess the impact of these changes and to highlight additional areas for improvement.
Aims & Methods: A prospective audit of 100 consecutive patients with AGIH was undertaken. Patients were identified from endoscopy and MAU records. The medical notes and endoscopy reports were reviewed and data collected. In addition to demographics information regarding presentation, management, diagnosis and outcome was collated and reviewed. Comparison then took place with the previous 2001 audit.
Results: The demographic distribution of patients in the 2 audits was similar with 60% male patients and 60% over 60 years of age in 2001 and 61% male patients and 51% over 60 years of age in 2006. The percentage of inpatients was 13% in 2001 and 8% in 2006. The percentage of patients scoped within 24 hours in 2001 and 2006 was also similar at 57% and 60% respectively. The mortality in the 2006 audit was only 7% compared to 16% in 2001. 3% died directly as a consequence of uncontrolled haemorrhage. These patients all suffered from oesophageal varices and 2/3 died as a result of rebleeding.
Conclusion: This audit indicates that it is possible to improve the outcome from AGIH with a combination of education and service development. The time to endoscopy appears unchanged despite the introduction of dedicated endoscopy slots; however improved access during the week may be offset by lack of emergency endoscopy at the weekend. The ''bleed board'' on MAU has increased awareness amongst all staff and, in conjunction with education of junior doctors, may have led to improved resuscitation. There remain areas for development. An AGIH rota may lead to further improvement in mortality with improved access to endoscopy out of hours. Significant mortality is from variceal bleeding. Education regarding care of cirrhotics, pharmacological strategies and the use of balloon tamponade may improve the outcome in this group.

Endoscopy posters

265 SELF APPRAISAL AND ASSESSMENT OF TECHNICAL SKILLS IN ENDOSCOPIC PROCEDURES

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Introduction: Evaluation of technical skill is notoriously difficult, due to its subjectivity and the need for time-consuming expert analysis. The use of the endoscopists themselves to evaluate their own technique, employing objective analysis techniques would circumvent the need for constant external analysis.
Aims & Methods: This study is designed to examine whether endoscopists' self assessment accurately reflects their actual endoscopic competence and whether self appraisal using the assessment tool in endoscopy is feasible, accurate and practical in the real life and simulated settings. It also aims to determine if assessing endoscopic technical skills in a structured manner has face, construct and predictive validities and to assess the reliability of the assessment tool. The study was performed Using 3 endoscopic techniques (OGD, flexi-sigmoidoscopy, and colonoscopy). Global generic and specific technical skills rating scales and error checklist scales were constructed individually for each endoscopic procedure. The main researcher and endoscopist assessed the performance by completing the performance assessment tool independently. 60 real live endoscopies were assessed using the global technical skills and error check list scales, performed by 5 consultants and 5 trainees. 60 simulated endoscopies were assessed using the same assessment tool as the live group and the generic markers used by the simulator such as operating time, percentage of mucosa surface examined, efficiency of screening, time spent with clear view, time patient was in pain, time to reach (the second duodenum-transverse colon-caecum), and total time with loop, performed by 5 consultants and 5 trainees.
Results: There was a good reliability for generic and specific global score of the performance assessment tool in the three live procedures. In live OGD (for generic score Cronbach $\alpha=0.689$, $p<0.05$, and for specific score Cronbach $\alpha=0.621$, $p<0.05$), in live Flexi sigmoidoscopy (for generic score Cronbach $\alpha=0.729$, $p<0.05$ and for specific score Cronbach $\alpha=0.725$, $p<0.05$), and in live colonoscopy (for generic score Cronbach $\alpha=0.847$, $p<0.05$, and for specific score Cronbach $\alpha=0.847$, $p<0.05$). Also there was a good validity for generic and specific global score of the assessment tool in the three live procedures ($p<0.05$). There was good validity for generic and specific global score when used for assessment on the simulator ($p<0.05$) except for specific global score in simulated OGD ($p>0.05$). There was not a good validity for the parameters of the simulators ($p>0.05$).
Conclusion: The performance assessment tool was able to differentiate between subjects with different endoscopic experience which indicates that performance assessment tool evaluates skills relevant for gastrointestinal endoscopy. Further studies are required to determine the validity of this tool in training that may be achieved by the junior endoscopists.

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266 ENDOSCOPY IN PEOPLE AT RISK OF VCJD: FROM SCOPE QUARANTINED TO ACCESS DENIED

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Introduction: In 2005 the Advisory Committee on Dangerous Pathogens (ACDP) defined classes of patients at potential risk of variant CJD (vCJD). These include up to 6500 recipients of blood products prepared from large pools of donated plasma during the time when individuals with preclinical vCJD may have donated blood (1980–2001). Consensus was reached with the BSG in defining an ''invasive procedure'', the most frequently performed being mucosal biopsy. A biopsy could potentially contaminate the working channel of an endoscope with gut lymphoid tissue and pose a potential risk of infection to others. Quarantine of endoscopes used for invasive procedures is advised, because there is no certain method for decontaminating prion particles.
Aims & Methods: Two independent surveys of Haemophilia Centres and the endoscopy units serving them were undertaken to determine: (1) whether access to endoscopy is being restricted in people with bleeding disorders; (2) what precautions endoscopists are taking to avoid endoscope contamination; and (3) the extent to which endoscopes are being quarantined.
Results: The United Kingdom Haemophilia Centre Doctors Organisation (UKHCDO) conducted a survey of the impact of recommendations made for high risk endoscopic procedures. 43 Haemophilia Centres responded. There was evidence that referrals for endoscopy in ''at risk'' patients are being delayed or declined by endoscopy units serving 25 of these 43 Centres. A BSG survey found that 10 responding endoscopy units commonly endoscope people with haemophilia (median 10 such patients per year, range 3–20) and one unit routinely scopes other patients with or at risk of vCJD. Of these 11 units, two do not perform any mucosal biopsy, four do perform biopsy but take no special precautions against endoscope contamination, two use a dedicated endoscope, one unit performs one biopsy per procedure and withdraws the endoscope with forceps protruding, and two quarantine endoscopes after biopsy in such patients (as per the ACDP/BSG guidelines). From the survey findings it is understood that at least 10 units have quarantined at least 33 endoscopes, but only one of these has access to dedicated resources for replacing quarantined endoscopes.
Conclusion: There is wide variation in the interpretation of national recommendations and in clinical practice, both in the acceptance of patients at risk of vCJD for endoscopy and in the precautions taken to avoid the theoretical risk of vCJD transmission. Endoscopists must balance the need for endoscopic biopsy and therapy against any alternative avenues for diagnosis and therapy. Access to endoscopy for patients at risk of vCJD would probably improve if central funding were to be made available for the replacement or refurbishment of quarantined endoscopes.

267 COLONOSCOPIC SURVEILLANCE FOR ULCERATIVE COLITIS IN A LARGE DISTRICT GENERAL HOSPITAL: IS THE JUICE WORTH THE SQUEEZE?

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Introduction: Current BSG guidelines recommend regular colonoscopic surveillance for dysplasia and cancer in patients with a long history of extensive colitis. The guidelines also suggest four biopsies are taken every 10 cm on extubation. Colonoscopy time is precious and waiting list targets and the introduction of bowel cancer screening will put more pressure on already busy endoscopy services.
Aims & Methods: Our aims were to identify yield for dysplasia and cancer in our IBD population undergoing surveillance at the two main Derby Hospitals. We identified patients undergoing surveillance colonoscopy for ulcerative colitis (UC) between 2001 and 2006 from our endoscopy database and identified any cases of dysplasia and cancer from pathology results. We also correlated pathological findings with endoscopic appearances.
Results: Over a 5-year period 340 colonoscopies were performed for colitis surveillance (male 184, female 166, median age 56). The caecum was reached in 82% of cases. 2322 biopsies were taken (median six per colonoscopy, range 0–30). One cancer (Dukes A rectum) was found and twelve cases of dysplasia (two severe/high grade, one moderate, nine low grade) reported from biopsies. Six colectomies were performed (one for cancer, five for dysplasia). Of the colectomies performed for dysplasia, three showed dysplasia but no cancer, and two no evidence of dysplasia or cancer. The other seven patients with dysplasia have undergone further colonoscopic examination (n = 11, 1–3 per patient) with no more evidence of dysplasia in any of the cases. Of the four patients with proven cancer or dysplasia on histology of colectomy specimens, three had visible mass lesions at colonoscopy.
Conclusion: In our population we found one cancer and three definite cases of dysplasia as a result of 340 colonoscopies in a 5-year period. There was wide variation in the amount of biopsies taken and we identified only one case of definite dysplasia when taking over 2000 routine biopsies from colons without a visible mass lesion- this is similar to recent published data (Hurlestone. *Endoscopy* 2006) and would support the need for use of targeted biopsy techniques (eg chromoendoscopy) to detect dysplasia.

268 IS FLUID DEPRIVATION REQUIRED PRIOR TO ENDOSCOPY?

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Introduction: There are no national guidelines for the length of time patients should be starved prior to upper GI endoscopy. Indeed there are very few papers in anaesthetic journals examining the period of starvation prior to general anaesthesia. Even in our own trust practice varies widely as it does nationwide. We examined the effect of allowing patients to drink 500 ml of clear fluids in the 4 h prior to upper GI endoscopy.
Aims & Methods: We performed a prospective single blind controlled study in which half the patients attending for upper GI endoscopy were starved for 4 h and half were allowed to drink 500 ml of clear fluids. Particular reference was given to the ease and safety of the procedure, degree of patient discomfort and overall patient satisfaction. Data were collected using visual analogue scale based questions, via questionnaires. Gastric fluid volume and pH was also recorded. Ethical approval was granted by the South East Wales ethical committee.
Results: Of 41 patients, 18 in group A were starved and 23 in group B were allowed to drink. We demonstrated that patients in Group B tolerated the preparation better and found it more acceptable than those in group A ($p < 0.05$ and $p < 0.05$ respectively). Following the endoscopy the thirst score was significantly less in group B ($p < 0.05$). Thirst was also reduced prior to endoscopy but this was not significant. The volume aspirated from the stomach was higher in group B (34 ml *v* 19 ml) ($p < 0.05$) however there was no difference in pH and the endoscopist reported no difference in patient distress or difficulty in performing the procedure. There were no adverse events recorded.
Conclusion: Permitting patients to drink up to 500 ml of clear fluid prior to endoscopy make the procedure better tolerated, more acceptable and also reduces thirst. There is a small increase in gastric fluid volume (15 ml) which does not adversely affect the procedure. We propose that this practice would improve patient experience during diagnostic endoscopy.

269 THE NEED FOR NURSE-LED PRE-ASSESSMENT IN A COMMUNITY BASED ENDOSCOPY CLINIC

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Introduction: Flexible sigmoidoscopy is an invaluable investigation for change in bowel habit, PR bleeding and surveillance of the distal colon. This has historically been carried out in the hospital setting but with increasing pressures to reduce waiting times and improve access, this service is now being offered in community based clinics.
Aims & Methods: This study attempts to quantify the effect of a nurse-led pre-assessment service on ''Did Not Attend'' (DNA) rates in a community based endoscopy unit in Newcastle upon Tyne. A prospective database of all patients attending for flexible sigmoidoscopy was kept for 26 months, 13 months with the pre-assessment service and 13 months without. These data were then used to compare the DNA rates with and without the pre-assessment service. The phone based pre-assessment service was costed at £3.36 per patient. An endoscopy appointment whether it is used or wasted costs £470. A total of 1539 patients were included in the study, 820 with pre assessment and 719 without.
Results: With the pre-assessment service there were 53 DNAs, 28 cancellations and 5 appointments not used for other reasons, representing a total of 86 (10.5%) wasted appointments. Without the pre-assessment service there were 88 DNAs, 36 cancellations and 10 unused appointments for other reasons, representing a total of 134 (18.6%) wasted appointments.
Conclusion: If entirely attributable to the pre-assessment service being withdrawn then the increase in wasted appointments translates into a cost of £32,195. The cost of providing the pre-assessment service for those 719 people would have been £2416.

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270 SUCCESS OF REPEAT ERCP FOLLOWING INITIAL THERAPEUTIC FAILURE

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Introduction: The recent BSG national audit shows that endoscopic retrograde cholangio-pancreatography (ERCP) is performed with therapeutic intent in 90% of cases in the UK, but is unsuccessful in 29%. Optimal further management for these patients remains unclear. While percutaneous transhepatic drainage (PTD) is one therapeutic option, this may not be definitive and carries a risk of complications. We report the outcome of repeat ERCP in a tertiary centre, following failed ERCP elsewhere.
Aims & Methods: All patients referred to our centre for therapeutic ERCP following a previous failed procedure from Sept 2002–Sept 2005 were included. Indications for ERCP and reasons for failure in the referring unit were documented. Difficulty of the procedure was graded according to the Schutz grading system as modified by Cotton.[1] Repeat ERCP was defined as successful when biliary drainage was achieved. Reasons for failure in our centre, complications, and subsequent management and outcome were recorded.
Results: 121 patients were referred from 27 hospitals, after a median of 1 ERCP (range 1–4). Indications: obstructive jaundice, 95 (79%); bile duct stones without jaundice, 18 (15%); biliary dilatation and abnormal liver biochemistry, 2 (1.7%); biliary leak, 6 (5%). 76 procedures (63%) were Schutz grade 1, grades 2 and 3 accounting for 12 (10%) and 33 (27%) respectively. At repeat ERCP, therapeutic success was achieved in 106 patients (88%) after a median of 1 procedure (range 1–2). Two patients sustained retroperitoneal perforations which resolved with conservative management. Endoscopic biliary drainage was unsuccessful in 15 patients. Predictors of failure included polya gastrectomy (failed in 1/8 patients, 13%), duodenal obstruction/distortion (1/7, 14%), duodenal diverticulum (3/19–17%), bile duct transection (1/1, 100%), and overall Schutz grade 3 (4/33, 12%). Of the failures, further management included PTD in 9 patients, surgery in 2 (biliary reconstruction for CBD transection; CBD clearance at cholecystectomy), and conservative/expectant management in 4.
Conclusion: In a high volume tertiary centre, repeat ERCP may be successful in the great majority of cases following initial therapeutic failure, even in those with apparently unfavourable indicators of difficulty.

1. **Cotton PB**. Income and outcome metrics for the objective evaluation of ERCP and alternative methods. *Gastrointest Endosc* 2002;**56**:S283–90.

271 DO UC WHAT I SEE? IMPACT OF ENDOSCOPY SCORING ON THE OUTCOME OF A CLINICAL TRIAL

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Introduction: The impact of interobserver variation in endoscopy on trial outcomes to our knowledge has not been previously explored. A clinical study of a peptide versus mesalazine provides evidence of the influence of the variability of endoscopic scoring on clinical outcome.
Aims & Methods: To investigate the efficacy of a peptide over mesalazine, 335 patients with moderately active ulcerative colitis (UC) were randomised in two independent cohorts to receive peptide 200 mg or 600 mg daily plus mesalazine 2.4 g daily, or mesalazine 4.8 g daily for 8 weeks. Moderate UC was defined as a Mayo score 7–11, with a sigmoidoscopy score (SS) endoscopic, histologic and clinical data were collected at entry and 8 weeks. To minimise variability, investigators (INV) and an independent blinded observer (Central) were trained to score sigmoidoscopies to prespecified standards. Three definitions of remission were used: clinical (stool frequency (SF) subscore 0 and rectal bleeding subscore (RB) 0); complete (SF 0, RB 0 & SS <1) and registration (RB 0 and SS <1). Data were analysed for 305 patients with >14 days of treatment and adequate endpoint information.
Results: Central disagreed with INV scoring for endoscopic disease severity at entry by 12–23% across both cohorts. The impact of the ''observer'' on the treatment effect of peptide versus 5-ASA control for absolute clinical, complete and registration remission rates within each cohort was a median difference of 9.5% (range 6.6 to 41.2%). Results were more variable for registration remission than clinical or complete remission outcomes.
Conclusion: Observer assessment of endoscopic activity for UC needs to be validated and techniques standardised. It is possible to conduct clinical trials with an independent observer. Absolute remission rates defined by regulatory authorities for registration trials are highly dependent on the observer. Standards of quality of UC trials will benefit from trial design using independent observers and internationally accepted definitions of disease activity and remission.

272 MANAGEMENT OF BENIGN BILIARY STRICTURES: ENDOSCOPY VERSUS SURGERY, INSTITUTIONAL EXPERIENCE

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Introduction: The effectiveness of various benign biliary stricture treatments has not been evaluated systemically. The authors reviewed the treatment and outcome of patients with benign biliary stricture who underwent surgical treatment, minimally invasive treatment (ERCP, PTCD) or both.
Aims & Methods: Between 2002 and 2006 Patients(n = 49) treated for benign bile duct strictures due to chronic pancreatitis (17), sclerosing cholangitis (12), bile ducts injuries (11), choledochal cysts (3), pancreatic pseudocyst (3), Crohn's disease of the duodenum (2) and aberrant anatomy (1). Surgery and/or endoscopic treatment were performed according to the degree, the level (Bismuth-Collins classification) and the aetiology of the stricture. Multivariate and univariate analysis of clinical and pathologic factors in relations to patient's outcome, hospitals stay and survival were done.
Results: Twenty eight patients had only endoscopic intervention (stenting, balloon dilatation). 16 patients were managed with both surgical and minimally invasive procedure. 5 patients underwent only surgical treatment. Repeated minimally invasive treatments gave less complications (4/28) than surgery alone (4/5) or surgery and endoscopy (15/16); as well as were correlated to a less initial hospital stay ($p<0.01$) and total hospital stay ($p<0.01$). There was no difference in the outcome according to the aetiology and the level of the stricture. Recurrence rate was less in patients treated by surgery and endoscopy ($p<0.01$).
Conclusion: Successful management of benign biliary stricture requires a multidisciplinary approach. Initial endoscopic treatment should be attempted and repeated minimally invasive procedures are a real option. Combination of surgery and endoscpic intervention provides the best outcome.

273 IS THERE EVIDENCE FOR MYOCARDIAL DAMAGE IN PATIENTS UNDERGOING ERCP?

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Introduction: Cardiac arrhythmias and ischaemia have been reported during endoscopic retrograde cholangio pancreatogram (ERCP). The

Abstract 271 Central and investigator readings agree (difference when readings disagree)

Outcome measure of remission	Peptide 200 + 2.4 g 5-ASA	Placebo + 4.8 g 5-ASA	Peptide 600 + 2.4 g 5-ASA	Placebo + 4.8 g 5-ASA
n (n disagree)	68 (20)	73 (18)	51 (9)	60 (6)
Clinical	22.4% (+2.6%)	23.3% (−6.6%)	24.0% (+20.4%)	30.0% (+3.0%)
Complete	7.7% (+7.3%)	11.1% (0.0%)	6.3% (+15.9%)	13.6% (+19.7%)
Registration	15.9% (+4.1%)	14.7% (+18.6%)	10.6% (+11.6%)	25.5% (+41.2%)

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extent of this relationship and risk conferred to patients undergoing ERCP is uncertain. Cardiac troponin T (cTnT) is a highly sensitive and specific marker of myocardial injury, allowing detection of minor degrees of myocardial damage. This study examines whether there is evidence of myocardial damage in patients undergoing ERCP, assessed by measurement of cTnT.
Aims & Methods: 181 ERCP procedures in 163 patients were studied. Pre-endoscopy assessment included resting ECG and routine bloods with extra bloods pre and post (>12 h) procedure for cTnT. ERCP was performed as per standard procedure. Where resources allowed, continuous cardiac monitoring was performed with a Lifecard Holter monitor, for development of tachycardia (>100 beats/min) and arrhythmia and with 12 lead ECG for ST segment changes.
Results: Age of the study populaiton (105F/76M) was 25–100 (median 77). Continuous cardiac monitoring was performed in 99 (54%) procedures. No significant differences were found in baseline data between the group who had monitoring and those who didn't. 47 had sinus tachycardia, 14 of whom had arrhythmias (8 atrial fibrillation, 4 bundle branch block, 1 Wenkebach and 1 SVT). Nine (9.1%) patients had signifcant ST depression (> than 1 mm depression for >1 minute). Post ERCP blood results were available for 150 patients, 141 had a post procedure cTnT below the assay detection limit (<0.03 μg/l). Of 9 patients with detectable cTnT, 6 were marginally increased (<0.1 μg/l) and 3 were significantly increased (>0.1 μg/l), a level suggestive of myocardial infarction. Of the 6 with a marginal increase, 3 had detectable cTnT pre-procedure. Of the 3 patients with cTnT levels >0.1 μg/l, only one was a rise from an undetectable level. In the second, the post procedure level rose from 0.06 μg/l to 0.19 μg/l, while in the third it fell from 0.30 μg/l to 0.19 μg/l.
Conclusion: Our study is the only one measuring cTnT as a marker of myocardial damage in patients undergoing ERCP. Cardiac monitoring identified evidence of ischaemia in a similar proportion of patients to that reported in previous studies. These results suggest a small risk of myocardial damage in patients undergoing ERCP. However the number of positive findings appears too small to be conclusive. In view of our findings, it may be worthwhile considering cardiac monitoring and troponin measurement in patients undergoing ERCP who are deemed to be at risk of myocardial ischaemia.

274 OPEN ACCESS ENDOSCOPY: ARE PATIENTS BEING APPROPRIATELY REFERRED AND PRIORITISED ACCORDING TO NATIONAL GUIDELINES?

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Introduction: Many Trusts provide an ''open access'' upper GI endoscopy (UGIE) service to primary care, allowing direct access to UGIE. The level of pre-procedure screening of these referrals for appropriateness, based on national guidelines, varies between units. Two recent developments have highlighted the importance of examining these services. Firstly, NICE has issued streamlined guidance on the management of dyspepsia and referral for suspected UGI cancer (two-week rule, 2WR). Secondly, the Global Rating Scale (GRS) in endoscopy has emphasised the need for appropriateness of referrals and the need for all procedures to be performed in a timely fashion. Finally, timely access to diagnostic services is an essential step in achieving targets on diagnosis and treatment (2WR and 18 week targets). Current UK data show that 14 935 people are waiting more than 13 weeks for UGIE (July 2006).
Aims & Methods: We performed a prospective 3-month audit of referrals to the open access endoscopy service of an NHS Trust in the North of England using NICE guidelines as the gold standard. Information on patient symptoms, H pylori status and drug treatment was collected from the referral form, and checked with the patient at the time of endoscopy. The result of the endoscopy was also noted.
Results: 383 referrals were identified. 51% were male, 49% female, median age 52 years. 219 (65%) were over 55 years. 97 (25%) had symptoms requiring a 2WR referral. Of 164 patients under 55 years, 124 (76%) had dyspepsia with no alarm symptoms. Helicobacter status/Test and Treat were performed in only 20% of patients. 36% had received no drug therapy, 46% had received PPI prior to endoscopy. 21 patients were referred with haematemesis. Endoscopy results were obtained in 374 patients. In 95% these were normal or revealed minimal changes (gastritis or minimal oesophagitis). Three patients (1%) had an UGI malignancy, 2 were referred with dyspepsia and no alarm symptoms, 1 with weight loss. The ''DNA'' rate was 8%.
Conclusion: Our audit identified poor adherence with national guidelines. Many patients referred for open-access UGIE should have been referred under the 2WR system, and most patients under 55 referred for UGIE did not conform to NICE guidance on management of dyspepsia. Rates of ''test and treat'' and appropriate trials of medical therapy prior to endoscopy were low. These problems impact on clinical governance, lead to increased waiting times for UGIE and result in poor performance on the GRS scale. This audit highlights the need for Endoscopy units to examine their open-access services in light of new national guidelines, and stresses the importance of clear communication between primary and secondary care to develop robust treatment and diagnostic pathways.

275 REFINING THE INDICATIONS FOR USAGE OF WIRELESS OESOPHAGEAL VIDEO CAPSULE ENDOSCOPY IN THE INVESTIGATION OF THE UPPER DIGESTIVE TRACT

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Introduction: Wireless oesophageal video capsule endoscopy (WOVCE) is a non-invasive, disposable imaging methodology for visualisation of the upper GI tract specifically the oesophagus. The clinical use of the oesophageal capsule is not yet routine practice with expanding indications, which are currently under evaluation.
Aims & Methods: To report the Edinburgh experience in the use of oesophageal capsule (Pillcam).
Methods: WOVCE was performed after a standard 6-hour fast, correct placement of the recording electrodes and ingestion of 100 ml of water to clear saliva and debris from the oesophagus. The capsule was ingested in a supine position, with sequential elevations of 30, 60 and 90 degrees over a period of 5 minutes. In order to enhance visualisation of the stomach the patients that could easily mobilise were asked to rotate at 1 minute intervals right and left laterally. At the end of this period each patient remained seated upright until capsule battery depletion and end of recording.
Results: We have investigated 17 patients since March 2005. They fell into 3 groups: (1) high risk for vCJD patients to establish diagnosis and assess the need for conventional endoscopy or help planning other investigations (10); (2) patients with liver cirrhosis requiring surveillance for varices who were unfit/not keen or high risk for vCJD for conventional endoscopy (4); (3) patients with upper gastrointestinal symptoms who were unable to tolerate a gastroscopy (3). In all cases excellent views of the oesophagus were obtained and in 85% adequate views of the stomach were obtained. In 69% of patients the investigation was adequate to guide patient management without further investigations. In 75% of the patients with gastrointestinal symptoms the combination of capsule endoscopy and a C13 BT was adequate to provide the diagnosis and treatment.
Conclusion: From our experience we consider that WOCVE is a valuable oesophageal imaging modality of particular value in high risk of vCJD patients and for those patients who cannot tolerate conventional endoscopy and may otherwise require the test under GA. In both patient groups WOCVE is not only a useful diagnostic modality but it is particularly cost effective.

276 TRENDS IN UPPER GASTROINTESTINAL BLEEDING: A SINGLE CENTRE EXPERIENCE OF OVER 1200 PATIENTS

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Introduction: Acute upper gastrointestinal bleeding (UGIB) is a common medical emergency with an incidence ranging from 50 to 150 per 100 000 of the population each year. A UK audit, published in 1995, reported 11% mortality in patients admitted to hospital because of bleeding (primary) and 33% mortality in those who developed gastrointestinal bleeding whilst hospitalised for other reasons (secondary). Our hospital is a large district general hospital serving a population of approximately 250 000 with over 11 000 medical admissions per year.
Aims & Methods: To identify changes in the presentation, demography, referral patterns and clinical management from October 1998 to May 2005 (80 months) in those presenting with suspected UGIB. All patients with acute upper GI bleeding were identified prospectively at the time of referral for endoscopy and an initial proforma was completed as part of an ongoing audit. Case notes were later retrieved to capture other data.
Results: We identified 1237 patients (age range 17–100 years) during this period; 1114 case notes were retrieved for analysis (90.1%). Over this time many of the parameters have remained remarkably similar—these include

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Abstract 276 The changing trends

Time	10/98–5/99	6/99–5/00	6/00–5/01	6/01–5/02	6/02–5/03	6/03–5/04	6/04–5/05
n (total)*	120 (139)	165 (185)	184 (205)	194 (209)	162 (191)	160 (178)	129 (140)
Primary/secondary	106/14	140/25	164/20	153/39	121/43	130/30	97/32
No on warfarin	7	6	20	25	17	26	25
PPI prior to OGD	34	47	73	15	29	64	62
OGD by consultant	61	66	94	136	126	111	103
OGD out of hours	NA	NA	2	16	20	19	9
Endoscopic therapy	14	20	21	52	33	32	26
Units of blood used	5.9	5.5	5.2	5.0	4.8	4.5	3.8
Surgery/survival	6/3	9/4	7/3	7/1	4/3	6/3	2/2

*Number analysed (total number of patients).

a mean age of 66 years (range 63–69 years and 70% were over 60 years), sex ratio (1.4M:1F), mean mortality 11% (range 10–17.2%), Rockall score (⩾3) 85%, proportion with peptic ulcers (33%) and varices (6%). There have also been no significant changes in haemodynamic parameters, haemoglobin and urea results and the presence of major comorbidities. There have been a few apparent changes and these are summarised in the table above. In addition the proportion of normal OGD has decreased from 25.8% to 12.4%, mean duration of stay has decreased from 6 days to 4 days and H pylori eradication rates have increased from 40% to 78%.

Conclusion: As with other published studies we have shown that the majority of patients with UGIB are elderly with significant comorbidities. We have shown a few potentially important trends over this time period including a greater proportion of patients who bleed after admission for other reasons and a higher number of bleeds occur whilst taking warfarin—these areas merit further exploration. The increase in cases done out of hours, with more endotherapy but increasingly performed by consultants, has important implications for training our juniors.

277 POLYP DETECTION RATE IS IMPROVED WITH POSITION CHANGES DURING COLONOSCOPE WITHDRAWAL: A RANDOMISED, CROSSOVER TRIAL, MID-POINT ANALYSIS

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Introduction: Changing patient position during colonoscope withdrawal is recommended by some experts to improve mucosal visualisation, but anecdotally this is not routine in most units. We have previously demonstrated that changing patient position during the withdrawal phase of colonoscopy improves visualisation through better luminal distension;[1] however it is not clear that this translates into improved polyp and adenoma detection rates.

Aims & Methods: A randomised, crossover trial was perfomed. The proximal colon was examined in three segments: caecum to hepatic flexure; transverse; splenic flexure to descending colon. Patients were randomised to either examination in left lateral position alone or with position changes first. Each segment was examined twice for 2 minutes, either in left lateral then with position changes or vice versa. Position changes were: caecum to hepatic flexure, left lateral; transverse, supine; splenic to descending, right lateral. After examination with both options with recording of all polyps, polyps were then removed and sent for histological analysis.

Results: Sixty four patients (of a planned 130) were randomised, mean age 63 years, 29 male. Median sedation: midazolam 1.25 mg, pethidine 25 mg IV. Data are expressed as the number of patients with at least one polyp detected by segment in each position (see table). When transverse, splenic and descending polyp counts were combined (areas where positions were different between examinations) the difference in patients with at least 1 polyp detected, 21 (33%) left lateral *v* 30 (47%) position changes, was significant, p = 0.03. The total number of polyps in these areas was 31 *v* 42, and total adenomas 18 *v* 26, for left lateral *v* position changes respectively. There was no significant difference in the number of patients with at least one polyp for caecum, ascending and hepatic combined, 32 (50%) *v* 34 (53%), left lateral *v* position changes (left lateral in these areas) respectively, p = 0.75.

Abstract 277 Polyp detection rate by colonic area

	Left lateral, n (%)	Position changes, n (%)
Caecum	18 (28)	19 (30)
Ascending	16 (25)	17 (27)
Hepatic flexure	13 (20)	15 (23)
Transverse	12 (19)	19 (30)*
Splenic flexure	8 (13)	12 (19)
Descending	4 (6)	4 (6)

*p = 0.04 for difference.

Conclusion: Changing the patient's position during colonoscope withdrawal, a cost-neutral intervention, improves polyp detection rates overall in the transverse colon, splenic flexure and descending colon combined. This intervention has the potential to improve the effectiveness of the National Bowel Cancer Screening Program without increasing costs.

ClinicalTrials.gov Identifier:NCT00234650.

1. **East JE**, *et al.* Position changes improve visibility during colonoscope withdrawal: a randomized, blinded, crossover trial. *Gastrointest Endosc* (in press).

278 FACIAL RESPONSE TO ANAESTHETIC SPRAY IS A PREDICTOR OF PATIENT TOLERANCE FOR GASTROSCOPY

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Introduction: Upper GI endoscopy is a high volume, high turnaround procedure. Many units encourage topical pharyngeal anaesthesia alone rather than sedation. The advantages include shorter procedure time and quicker recovery time, in addition to the lower incidence of respiratory complications and lack of antegrade amnesia. Predictors of poor tolerance to the procedure have included female patients, young age and high level pre-test anxiety.[1]

Aims & Methods: To determine whether the immediate response to throat spray can predict the patient tolerability of unsedated gastroscopy. Consecutive day case patients referred for a gastroscopy who had selected to receive throat spray alone were assessed. All patients had received written information in the post and had opportunities for further discussion with the admitting nurse and the endoscopist prior to giving consent to the procedure. The endoscopy nurse allocated a spray score (1 = smile or neutral; 2 = grimace; 3 = cough or choke). The endoscopist (SM) allocated an endoscopy score whilst blinded to the spray score (1 = well tolerated; 2 = poorly tolerated: retching >50% of the time, panicking, pulling out scope). Chi-squared tests were used to analyse the data.

Results: 121 patients were assessed (M = 65, F = 56). A total of 82 (group 1), 26 (group 2) and 13 (group 3) patients received a spray score of 1, 2 or 3 respectively. In group 1, 95% (n = 78) tolerated the procedure with ease (endoscopy score 1) compared with 73% (n = 19) for group 2 and 38% (n = 5) for group 3 (p<0.001). Of 102 patients with an endoscopy score of 1, 76.4% (n = 78), 18.6% (n = 19) and 5% (n = 5) had a throat spray score of 1, 2 and 3 respectively (p<0.001). Of the 19 patients with an endoscopy score of 2, 21% (n = 4), 36.8% (n = 7) and 42.1% (n = 8) had throat spray scores of 1, 2 and 3 respectively. Among female patients, 25% (n = 14) poorly tolerated the procedure compared with 8% of men (n = 5) (p<0.01). The male-female differences were independent of their spray score. The mean age of females with poor tolerance was 49.8 years versus 61.9 years if it was tolerated.

Conclusion: This prospective blinded study has demonstrated a reliable means of predicting tolerance to unsedated gastroscopy by noting the facial reaction to topical pharyngeal anaesthesia. The study also confirms previous reports that young female patients are less likely to tolerate the procedure. This should be incorporated into the informed consent

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discussion permitting a switch from spray to sedation if required prior to intubation.

1. **Campo R**, Brullet E, Monteserrat A, *et al*. Topical pharyngeal anaesthesia improves tolerance of upper gastrointestinal endoscopy: a randomised double-blind study. *Endoscopy* 1995;**27**:659–64.

279 LEEDS DISCOMFORT SCORE IN COLONOSCOPY: PATIENTS AND NURSES DISAGREE

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Introduction: A recent national colonoscopy audit (Healthcare Commission) required an assessment of comfort during colonoscopy using Leeds discomfort scale.
Aims & Methods: The aim of our study was to determine if these scores accurately reflect patients' discomfort level. Data were collected by an independant observer from 150 consecutive colonoscopies. The sedation and discomfort scores were recorded by the nursing staff using the Leeds criteria. After colonoscopy each patient used the Leeds criteria to rate their own experience of colonoscopy.
Results: The overall caecal intubation rate on an intention to treat basis was 90% with an average time to caecum of 15.2 minutes. 74 females and 76 males completed the study. The correlation coefficient between the nurses and patients score for discomfort (D) and sedation (S) was 0.34 and 0.28 respectively (not significant). Nursing staff consistently underestimated the patient level of discomfort. The patient D score was >2 points above the nurse's score in 35% and was >1 point above the nurse's score in 60% of the cases.
Conclusion: Discomfort and sedation scores assessed by nurses showed little correlation to the patient's score in our study. We propose that discomfort score should be recorded by the patient if it is to be included as a criteria for assessing the performance of units.

280 PAEDIATRIC ENDOSCOPY PERFORMED BY GENERAL GASTROENTEROLOGISTS

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Introduction: Children requiring endoscopy in district hospitals have to travel to teaching centres for endoscopic procedures by paediatric gastroenterologists. In some district hospitals, general gastroenterologists provide endoscopic services for children as well as adults. We report our experience of general adult gastroenterologists endoscoping children over a 10-year period.
Aims & Methods: Patients younger than 16 years old having an endoscopic procedure from 1997 to 2006 at Wycombe Hospital, a district hospital serving a 300 000 population were identified from a computerised endoscopy database. Case notes were retrieved for referral details, indication, histology results, etc.
Results: A total of 174 procedures (118 gastroscopies, 41 colonoscopies, 15 flexible sigmoidoscopies) were performed. The median (IQ range) age was 11.5 (5–14) years. 69% (120) children were referred by paediatricians, 31% from general practitioners/other adult specialties. The median number of endoscopic procedures was 16.5 per year. Despite increased serological testing for coeliac disease, the numbers of serologically positive children referred for endoscopic biopsies remained constant over the decade at approximately 25% of referrals. Children referred as outpatients waited a median (IQ range) of 23.5 (12–43) days to be seen in the gastroenterology clinic and waited 32 (16–52) days for their procedure, the total time from referral to procedure being 50 (23.5–95) days. Inpatient children waited 3 (1–4) days for their procedure. 89% (63) of 71 children aged 10 years or younger (and 100% of 47 children aged 5 years or younger) had general anaesthesia for their endoscopic procedure. In contrast, 96% (99) of 103 children aged 11 years or older had their procedure in the endoscopy unit with intravenous sedation. Median midazolam doses for gastroscopy, colonoscopy and flexible sigmoidoscopy were 5 mg, 5 mg and 4 mg respectively. Children having colonoscopy also received a median dose of 50 mg pethidine. Paediatric endoscopes were used in 82% of those 10 yrs or younger, and in 19% of those over 10 years. Organic disease was identified from 90 of 174 (52%) endoscopic procedures. The most common diagnoses were coeliac disease (41 children), inflammatory bowel disease (26 children), gastro-oesophageal reflux (6 children). 7 endoscopies were for foreign body removal. No endoscopic complications occurred. Subsequent management of chronic gastrointestinal disorders was shared between paediatric and adult gastroenterology teams.
Conclusion: General gastroenterologists can provide endoscopic services for children safely and promptly in their local hospital. This would seem to be appropriate in the management of common gastrointestinal problems affecting children.

281 LACK OF ALARM SYMPTOMS AT FIRST PRESENTATION IS COMMON IN PATIENTS SUBSEQUENTLY FOUND TO HAVE GASTRIC OR OESOPHAGEAL CARCINOMA

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Introduction: In August 2004 NICE guidance advised that endoscopy was not routinely indicated in patients over 55 years who developed new dyspepsia without alarm symptoms.[1] This was amended in June 2005[2] to advise endoscopy in such patients because of limited evidence available on how patients with gastric or oesophageal cancer initially present to primary care. Indeed in a recent study alarm features have been found to have only limited value in the diagnosis of upper gastrointestinal (GI) cancer.[3]
Aims & Methods: The aims of this study were to assess how patients subsequently found to have gastric or oesophageal carcinoma first present and whether lack of alarm symptoms at presentation confers any survival advantage. 216 patients with a diagnosis of upper GI cancer were identified from hospital records between January 1999 and December 2003. The notes of 199 patients (124 males, 75 females, mean age 72 (range 39–98) years) were available and 21 General Practices were visited to consult Primary Care records. Data on symptoms at first presentation, attempted curative surgery and length of survival up to October 2006 were retrieved.
Results: 177 (88.9%) patients were over 55 years. Alarm symptoms were absent in 51/199 (25.6%). Endoscopy was undertaken after a mean of 53 days in this group and after 39 days in those with alarm symptoms. 33.3% without, compared to 22.3% patients with alarm symptoms underwent attempted curative surgery (NS, $p<0.05$). All patients were followed up for at least 2 years and 99 patients for at least 5 years. Those presenting without alarm symptoms had a tendency towards greater survival than those with such features but this did not reach statistical significance (table).

Abstract 281 Survival of patients with and without alarm symtoms

Presenting symptoms	Alive at 2 years	Alive at 5 years
Non-alarm	29.4%	20.0%
Alarm	23.0%	14.9%

Conclusion: This study has identified that approximately 26% patients subsequently found to have upper GI cancer presented without alarm symptoms. There was a tendency for a greater suitability for curative surgery and longer survival in this group but statistical significance was not reached with the number of patients in this study. Endoscopy should continue to be offered to those patients over 55 presenting with new onset dyspepsia irrespective of whether alarm symptoms are present.

1. **National Institute for Health and Clinical Excellence**. *Dyspepsia. Managing dyspepsia in adults in primary care*, Clinical guideline 17, NICE August, 2004.
2. **National Institute for Health and Clinical Excellence**. *Referral guidelines for suspected cancer*, Clinical guideline 27.NICE June, 2005.
3. **Vakil N**, Moayyedi P, Fennerty MB, *et al*. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy; systematic review and meta-analysis. *Gastroenterology* 2006;**131**:390–401.

282 JAG COLONOSCOPY TRAINING GUIDELINES ARE NOT BEING MET BY TRAINEES FOLLOWING A ONE-TO-ONE HANDS-ON COLONOSCOPY TRAINING COURSE

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Introduction: Manual dexterity and hand-eye coordination skills can be acquired to a high level of competence in a brief course, unrelated to previous experience.[1] Improvement in these skills is significantly greater when individuals have ongoing practical experience and training.[2] The

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intensive one-to-one hands-on colonoscopy training course includes 3 micro-teaching, 2 computer simulator and 4 hands-on training sessions within 4 days, and has been shown to improve core knowledge and clinical skills in colonoscopy.[3] JAG guidelines state that trainees should be performing at least 100 colonoscopies within the course of a year,[4] which equates to less than two procedures per week.

Aims & Methods: The aim of the study was to assess whether trainees continue to practise in accordance with JAG guidelines and improve their skills following the course. The first 50 trainees were asked to complete and return a questionnaire asking how many colonoscopies they had performed during the 6 months following the course and the frequency of training lists. If they were not receiving regular training, explanations were recorded. Individual trainees' caecal intubation rates were compared with their pre-course rates.

Results: Twenty questionnaires (40%) were returned. Fewer than half the trainees had performed over the minimum 50 colonoscopies recommended by JAG within 6 months (mean 60.5, range 12–130). Five trainees (25%) did not have a regular training list. Military service, a research post and a specialist hepatology post were given as explanations in three of the cases. Despite this, caecal intubation rates improved by a mean of 11.8% (71.6% *v* 83.4%), with no significant difference in improvement between those who performed over 50 procedures and those who did not (10.4% *v* 13.8%, $p=0.78$). Less experienced trainees (<100 previous colonoscopies) showed the most improvement, from 46.3% to 75.5%, but those with moderate previous experience (101–200 colonoscopies) achieved caecal intubation rates consistent with independent practice, with the mean improving from 77.5% to 93%.

Abstract 282 Number of colonoscopies within 6 months of the course

Colonoscopies (n)	0–25	26–50	51–75	76–100	>100
Trainees (n)	3	8	3	3	3

Conclusion: Trainees are falling far short of JAG guidelines with regard to adequate experience and supervised lists. However, following an intensive training course, juniors appear to make good progress and more senior trainees may become independent despite low numbers of procedures. This highlights the continuing need for ongoing procedure exposure and training after intensive training courses.

1. **Rosser**, *et al. Arch Surg* 1998.
2. **Tsai**, *et al. J Am Assoc Gynecol Laparosc* 1994.
3. **Suzuki N**, *et al. Gut BSG abstracts* 2006.
4. Guidelines for the Training, Appraisal and Assessment of Trainees in Gastrointestinal Endoscopy, Joint Advisory Group 2004.

283 HAVE CHANGES TO SEDATION PRACTICE IN ENDOSCOPY AFFECTED THE INCIDENCE OF SEDATION OVERDOSE

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Introduction: Significant changes in UK sedation practice have occurred in recent years. The BSG guidelines on sedation and safety in 2003 were followed recently by the NCEPOD data which highlighted the risks associated with sedation. Most complications are secondary to benzodiazepines, and flumazenil use has been shown to be a surrogate marker for sedation overdose.

Aims & Methods: The aim of this audit was to determine whether previously documented changes to sedation practice in endoscopy at Charing Cross Hospital had altered the use of reversal agents. A retrospective analysis of the endoscopy unit database was performed (2000–5) and the hospital notes were analysed for each patient requiring sedation reversal.

Results: There was no significant difference between the number of endoscopic procedures requiring reversal in 2000 (11) versus 2005 (9). On comparing data for the year 2000 to that for 2005, there was no significant difference in the median midazolam dose used for those procedures that had been reversed (5 mg in 2000 and 2 mg in 2005) versus non-reversed (5 mg in 2000 and 2 mg in 2005). The median midazolam dosages for both reversed and non-reversed procedures had significantly decreased from 5 mg in 2000 to 2 mg in 2005 ($p<0.05$). For all patients requiring reversal (2000–5) 37.5% had an ASA grade of 3 or more and the 30-day mortality was 19%.

Conclusion: The median sedation dose administered during endoscopy at Charing Cross Hospital has significantly decreased for all procedures over the last 6 years. Despite this the number of procedures requiring sedation reversal has not decreased; this was not due to excessive amounts of sedation being use in those cases. Over one third of the patients who required reversal had an ASA grade of 3 or more. We therefore conclude that high ASA grade is more likely to be associated with complications from sedation than the sedation dose itself. More emphasis should be placed on accurately assessing and documenting the ASA grade of the patient before endoscopy, and adjusting the dose of sedation appropriately.

1. **British Society of Gastroenterology**. BSG guidelines on sedation, safety and monitoring, Nov 2003.
2. **Scoping Our Practice**. Available at http://www.ncepod.org.uk.
3. **Lord DA**, Bell GD, Gray A, *et al.* Sedation for gastrointestinal endoscopic procedures in the elderly: getting safer but still not nearly safe enough..

284 DEXTROSE SOLUTION IS AS EFFECTIVE AS SODIUM HYALURONATE FOR THE RESECTION OF COLORECTAL PARIS TYPE I AND 0-II LESIONS: A RANDOMISED BLINDED STUDY

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Introduction: Loss of mucosal ''lift'' prior to submucosal dissection or EMR increases the risk of complications. Given the significant costs associated with many commercial submucosal solutes we conducted a randomised control trial of dextrose solution (DS) versus sodium hyaluronic acid (SHA) for the en bloc EMR of Paris 0-II/Is and LSTs of the colorectum.

Aims & Methods: To investigate the efficacy of DS versus SHA for the en bloc resection of Paris type I/0-II and LST lesions (<30 mm). Primary endpoints were histologically proven R0 resection and complication rates. A power calculation ($\alpha=0.05$; $\beta=0.2$) indicated that a sample size of 80 lesions per group was sufficient to detect a 5% difference in resection completeness and recurrence rates. Inclusion criteria were a Paris type Is/0-II/LST lesion <30 mm diagnosed using double contrast barium enema or index colonoscopy. Patients were randomised in a 1:1 ratio by random number codes: group A, EMR using DS; and group B, EMR using SHA.

Results: 193 patients fulfilled eligibility criteria (19 exclusions; 17 on table staging compatible with stage T2 disease/2 participant refusers). 174 patients were therefore randomised in a 1:1 ratio (87 patients per group) to receive EMR using DS or SHA. The median age of the SHA and DA group was 58 years (range 32–83) and 56.5 years (range 29–84) respectively. There were no statistically significant differences between the SHA and DB group regarding baseline demographical characteristics or when comparing morphological Paris class, anatomical location or post resection histopathology. R0 resection was achieved in 59/82 (72%) of lesions in the DS group versus 56/81 (69%) in the SHA group ($p>0.1$) with no significance reached when comparing the median lesion diameters (DS group median 18 mm; range 6–35 mm/SHA group median 20.2 mm; range 4–40 mm)—$p>0.1$. 163 (100%) patients randomised attended for post EMR surveillance. The median number of post resection surveillance colonoscopies in the DS and SHA group were 3 (range 1–6) and 4 (range 2–6) respectively (p=NS). The median post index EMR resection follow-up period in the DS group was 20 months (range 4–26) and 18 months (range 3–22) in the SHA group (p=NS). Recurrence rates were 4/82 (5%) and 5/81 (6%) is the DS and SHA group respectively (p=NS). There was no significance reached when comparing bleeding (immediate/delayed) or perforation rates between the two study groups ($p>0.1$/$p>0.5$) respectively.

Conclusion: EMR using dextrose solution is as effective as hyaluronic acid comparing the end-point parameters of resection completion, recurrence rates and complications. Significant cost savings can be achieved.

285 MAGNETOCOLONOSCOPY

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Introduction: Magnetocolonoscopy is used to take photographs of the colon and also to ablate polyps using laser.

Aims & Methods: Structural components: Internal elecromagnets inside the cylinder; camera; light emitting diodes; laser; wire supply to magnetocolonoscopy in its posterior end to feed camera, laser, diodes; external elecromagnets mounted on robotic arm outside body; joystick for physician to direct movements; computer system to control current flow and movement; monitor to visualise camera output. Fed up with the large tube-like colonoscopy, pain and discomfort? Now there is a small cylindrical structure with blunted anterior and

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posterior ends. The anterior end consists of a camera, laser and light-emitting diodes. The cylinder consists of electromagnetic coils in its anterior, posterior and sides. The currents passing through these coils are individually controlled by sophisticated computer software. The colon is washed with enema and a long catheter with an inflatable balloon in its tip is passed through the anus until it reaches the ileocaecal valve region, and inflates it so that it seals the ileocaecal region. Then the lumen of the colon is filled with saline to dilate it. The magnetocolonoscopy passed into the colon through the anus and the anal opening sealed with watertight anal cap. Now the internal electromagnets are activated by passing electric current through it. Electromagnets that are fixed and moved on a robotic arm are placed on the external surface of the body. When these external magnets are activated and moved on a robotic arm both its polarity and movement will guide and direct the magnetocolonoscopy inside the colon. Magnetocolonoscopy can be moved and used to take photographs and video of the colon; also the in-built laser can be used to destroy any polyp or other growths in the colon.
Results: Guided capsule colonoscopy is achieved.
Conclusion: The advantages are: (1) small size, with no discomfort, unlike tube colonoscopy; (2) guided and controlled, unlike capsule endoscopy; (3) in-built camera and light source; (4) in-built laser for polypectomy.

286 INTEROBSERVER AGREEMENT IN CAPSULE ENDOSCOPY REPORTING BETWEEN TRAINEE AND CONSULTANT GASTROENTEROLOGISTS

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Introduction: Video capsule endoscopy is a safe and effective test for assessing the small bowel. It is particularly useful in the investigation of patients with unexplained iron deficiency anaemia. Training in capsule endoscopy for gastroenterology registrars in the UK is limited to a few centres. Previous studies have suggested that with minimal training, nurses and novice readers were able to detect positive findings with good interobserver agreement with a trained consultant gastroenterologist.[1 2] We perform about 100 capsule endoscopies per year in our institution and are interested in assessing the outcomes of training. In particular this study was performed to assess the effects of basic training in capsule endoscopy for specialist registrars who are competent in gastroscopy and colonoscopy.
Aims & Methods: To assess agreement on positive diagnostic findings and pyloric and caecal detection times for 12 patients capsule videos between two trainee gastroenterologists with minimal training in capsule endoscopy and a consultant gastroenterologist with experience of 280 capsule endoscopies. 12 capsule endoscopy studies were selected randomly and basic clinical information was provided to all three authors. We then reviewed the images independently and recorded positive findings, pylorus and caecal entry times and a provisional diagnosis. Each author recorded their confidence in each diagnostic finding on a standardised ordinal scale at the time of reporting. The data were then analysed for agreement with kappa statistics.
Results: There was excellent agreement between all three authors for both positive findings and pyloric detection times. There was less agreement on caecal entry times between the trainees and the trainees and the consultant.
Conclusion: Minimal training in capsule endoscopy for gastroenterology trainees who are already trained in conventional diagnostic endoscopy is effective and allows reliable clinical reporting with good agreement with an experienced capsule endoscopist. This has positive implications for training in capsule endoscopy and on the potential provision of this service in hospitals in the UK.

1. **Chen GE**, Enayati P, Tran T, *et al*. Sensitivity and inter-observer variability for capsule endoscopy image analysis in a cohort of novice readers. *World J Gastroenterol* 2006;**12**:1249–54.
2. **Niv Y**, Niv G. Capsule endoscopy examination -preliminary review by a nurse. *Digest Disc Sci* 2005;**50**:2121–4.

287 DOES MANAGEMENT OF AN ACUTE UPPER GASTROINTESTINAL HAEMORRHAGE WARRANT THE NEED FOR A 24-HOUR ENDOSCOPY SERVICE?

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Introduction: National guidelines suggest that the majority of patients who are admitted to hospital with upper gastrointestinal (GI) haemorrhage should have an endoscopy within 24 hours. The NCEPOD report in 2004 (*Scoping our practice*) and BSG in 2002 recommended that Trusts should have an out of hours on call rota for emergency upper GI haemorrhage.[1, 2] NCEPOD also reported that 62% of Trusts across the UK do not provide a 24-hour on-call service.
Aims & Methods: To ascertain the local management of upper GI haemorrhage within the available resources of our Trust against the published and recommended guidelines. A total of 125 patients admitted to Morecambe Bay NHS Trust during the period July 2005 to December 2005 were audited retrospectively. The patients were managed at three hospital sites: 70 at Royal Lancaster Infirmary (RLI), 39 at Furness General Hospital (FGH) and 16 at Westmorland General Hospital (WGH).
Results: Endoscopy was performed within 24 hours in 46% of patients at RLI, 31% at FGH and 33% at WGH. In the Trust overall, endoscopy was conducted within 24 hours in only 44% of patients, while 29% had endoscopy within three days, 22% within seven days and in 5% the procedure was performed as an outpatient. Endoscopy revealed: hiatus hernia (32%), duodenal ulcer (28%), gastric ulcer (8%), oesophageal varices (8%), Mallory–Weiss tear (2%), oesophagitis and gastritis (5%), and 17% were normal. Nine patients had findings warranting endotherapy of whom 5 had adrenaline injected into the ulcer bed. 43% of patients had a haemoglobin of less than 10 g/dl of whom 93% had a blood transfusion. 8% had features of shock on admission and all were appropriately managed with colloid and blood. Of the 20 patients who met the criteria for surgical assessment, 7 were referred. All were reviewed by the surgeons. Five of the 7 had a laparotomy, 4 of whom survived. The overall mortality of upper GI haemorrhage was 8.8% and the mean Rockall score was 2.5. Of the 11 patients who died, only 4 underwent emergency endoscopy. Severe comorbidity precluded intervention in the remaining seven patients. Ten of 11 deaths were secondary to comorbid disease and 1 patient died postoperatively within 30 days.
Conclusion: In our Trust where an emergency endoscopy service has not yet been instituted patient care was not compromised. No patient died of uncontrolled upper GI haemorrhage where intervention was possible. While taking into account the NCEPOD and BSG recommendations, our audit findings now question the absolute necessity of a 24-hour on-call service for our Trust. However in Trusts where the mortality rate is unacceptable, the NCEPOD and BSG recommendations should be implemented.

1. **British Society of Gastroenterology**. *Management of non-variceal upper GI haemorrhage*. BSG, 2002.
2. **NCEPOD**. *Scoping our practice* 2004.

288 IS POOR ENDOSCOPIC TECHNIQUE LEADING TO MISSED CANCER DIAGNOSES?

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Introduction: Upper gastrointestinal (GI) cancers progress rapidly and most cases are advanced at diagnosis.[1] Despite implementation of ''Early Access Endoscopy'' detection rates of early cancers have not improved.[2] Evidence in the literature suggests early cancer may be missed at initial endoscopy.[3–7]
Aims & Methods: Our aim was to identify the number of oesophago-gastric cancers missed at St Mary's Hospital, London between January 2000 and June 2006. We investigated for any contributing factors, in an attempt to reduce the risk of missed diagnoses in the future. We performed a retrospective analysis of the histological and endoscopic databases to collect information on all oesophageal and gastric cancers diagnosed within the time scale. We identified patients who had undergone an endoscopy within 3 years of their diagnosis and these patients were separated into definite and potential missed diagnoses. Data collected included indication for endoscopy, sedation, endoscopist grade, initial and final endoscopy findings, number of biopsies, histology, duration between diagnostic and previous endoscopy and reason for missed diagnoses.
Results: Within the time period, a total of 248 cancers were diagnosed: 85 oesophageal and 163 gastric. The oesophageal cancers had 6 definite missed diagnoses and 2 potential misses. The gastric cancers had 11 definite and 6 potential missed diagnoses. In total there were 25 potentially missed diagnoses; approximately 10% of all cancer diagnoses, which compares favourably with other studies. The majority of misses were due to inadequate biopsy sampling or endoscopist failure to identify the lesion. Alarm symptoms were more prevalent at the time of diagnostic endoscopy. None of the definite misses were due to pathologist error. Sedation did not contribute to missed cancer risk.

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Conclusion: These data suggest a significant number of lesions are missed at initial endoscopy. Our recommendations are to ensure precision during endoscopy, with clear mucosal views especially in the setting of ''alarm symptoms'', and adequate biopsy sampling.

1. **Auld**, *et al*. Missed diagnoses in patients with upper gastrointestinal cancers. *Endoscopy* 2004;**36**:874–9.
2. **Paterson**, *et al*. Impact of open-access endoscopy on detection of early oesophageal and gastric cancer 1994–2003: population-based study. *Endoscopy* 2006;**38**:503–7.
3. **Amin**, *et al*. Gastric carcinoma missed at endoscopy. *JR Coll Surg Edin* 2002;**47**:681–4.
4. **Yalamarthi**, *et al*. Missed diagnoses in patients with upper gastrointestinal cancers. *Endoscopy* 2004;**36**:874–9.
5. **Voutilainen & Juhola**. Gastric cancers missed on endoscopy. *Eur J Gastroenterol Hepatol* 2005;**17**:1345–9.
6. **Suvakovic**, *et al*. Improving the detection rate of early gastric cancer requires more than open access gastroscopy: a five year study. *Gut* 1997;**41**:308–13.
7. **Hosokawa**, *et al*. Diagnosis of gastric cancer up to three years after negative upper endoscopy. *Endoscopy* 1998;**30**:669–74.

289 DIAGNOSTIC YIELD OF COLONOSCOPY IN CHRONIC DIARRHOEA

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Introduction: Diarrhoea is one of the most common symptoms for referral to gastroenterology department. Full colonic survey is usually recommended in those >45 years of age. In patients less than 45 years, diagnostic yield of flexible sigmoidoscopy is not substantially different when compared with colonoscopy.
Aims & Methods: To assess the diagnostic yield of colonoscopy in patients with chronic diarrhoea, to assess the diagnostic yield of biopsies taken from right and left sides of the colon and total number of microscopic colitis in the study sample. It was a retrospective study carried out at West Cumberland Hospital (District General Hospital). Data were collected from the Endoscribe/Revive databases and patients' notes. All patients who underwent Colonoscopy for investigation of chronic diarrhoea during 2004 and 2005 were included in the study. Patients were categorised as those <45 years of age and those >45 years.
Results: Colonoscopy was performed by consultant gastroenterologist in 90% of the cases (n=140) with caecal intubation rate of 93% (n=144). Colonic biopsies were taken in all of the patients (100%). Mean age was 55 years (range 16–86). 46% (n=71) of the patients were male and 54% (n=84) were female. Basic investigations including FBC, U&E, LFTs, TFT, CRP, ESR and Albumin were normal in 66% of patients. None of the patients was positive for endomyseal IgA antibody. C-reactive protein and erythrocyte sedimentation rate were raised in 21% (n=32) and 19% (n=30) patients respectively. Colonoscopy was found to be normal in 62% (n=96) patients. Colonic histology was normal in 63.9% (n=99). Ulcerative colitis, Crohn's disease, microscopic colitis, colonic polyp, tubular adenoma and cancer were diagnosed histologically in 3.9% (n=6), 8.4% (n=13), 2% (n=3), 5.2% (n=8), 5.2% (n=8) and 3.2% (n=5) respectively. Histological diagnosis of borderline significance was found in 8.39% (n=13) cases. Number of patients <45 years of age with normal or abnormal basic investigation were 28% (n=49) and out of these 84% (n=41) had normal biopsy results. Among the remaining, 8% (n=4) had unclassified inflammatory changes, 8% (n=4) had IBD (one indeterminate colitis) on histology. Microscopic diagnosis was apparent both in left and right sided colonic biopsies in these patients. 100% of the cancers were found in patients >45 years. Out of a total of 19 cases of IBD 79% (n=15) were found in >45 years age group.
Conclusion: Diagnostic yield of colonoscopy is low in patients aged <45 years. Hence flexible sigmoidoscpy should be considered as the initial endoscopic investigation. None of the cancer was found in patients under 45 years. Three patients were diagnosed with microscopic colitis. Endoscopically they had normal colons.[1 2] Microscopic findings were similar in biopsies taken from both left and right side of the colon. Hence full colonoscopy was not necessary to reach this diagnosis.

1. **Saurine TJ**, Brewer JM, Eckstein RP. Microscopic colitis with granulomatous inflammation. *Histopathology* 2004;**45**:82–6.
2. **da silva JG**, *et al*. Histologic study of colonic mucosa in patients with chronic diarrhoea and normal colonoscopic findings. *Journal Clin Gastroenterol* 2006;**40**:44–8.

290 LONG-TERM FIVE-YEAR PROSPECTIVE FOLLOW-UP OF ENDOCINCH THERAPY FOR GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD): RETENTION OF PLICATIONS ARE ESSENTIAL TO CONTROL GORD

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Introduction: Endocinch therapy for gastro-oesophageal reflux disease (GORD) has been reported to be effective in the short term. However recently long-term failure of Endocinch has been reported due to loss of stitches. This is the first long-term five year prospective follow-up study to assess the efficacy of Endocinch and an impact of retention of stitches on GORD.
Aims & Methods: To evaluate the long-term benefit of Endocinch technique in patients seen up to five years post procedure and also to assess the GORD in patients who retained stitches and those who lost stitches at five years post procedure. Twenty two patients were prospectively studied who had Endocinch therapy in year 2000 and 2001 and had up to one year post procedure follow-up previously. Three patients were lost to follow-up. One patient had successful anti-reflux surgery and one failed to submit the data. Seventeen patients successfully completed their symptom scoring, proton pump inhibitors requirement and quality of life (QOL) questionnaires. However only 13 patients agreed for follow-up endoscopy. Five years post procedure data were compared with baseline pre-procedures parameters.
Results: Mean age 44 (27–65 years), female:7 male:10. Heartburn symptom score significantly reduced from mean of 18.55 at baseline to 8.4 at 5 year post procedure (p=0.002). Regurgitation score also reduced significantly from mean of 2.27 at base line to 1.17 at five years (p=0.001). Similarly all QOL assessments remained significantly better (p=0.01) and use of PPI was reduced by 53% at 5 year post procedure. Only 13 patients agreed for endoscopy (F: 5; M: 8). Both plications were present in 70% (n=9; group-1) of cases whereas 30% (n=4, group-2) lost all the plications. An improvement in oesophagitis grades, symptom scoring (p=0.01), regurgitation score (p=0.007) and quality of life (p=0.02) remained significantly better in those who retained plications at five years post procedure.
Conclusion: The Endocinch procedure is an effective out patients therapy that offers GORD patients significant long-term improvement in symptomatology, QOL and reduced requirements for PPIs at five-year period. Retention of plications seems to be an important factor in maintaining significant long-term improvement in symptom scores, QOL and reduced requirement of PPIs.

291 A STUDY TO ASSESS EXPERTISE AND TRAINING IN SENGSTAKEN–BLAKEMORE TUBE PLACEMENT AMONG TRAINEE GASTROENTEROLOGISTS

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Introduction: The average mortality of the first episode of variceal bleeding in most studies is 50%. BSG guidelines on the management of variceal haemorrhage state that balloon tamponade with a Sengstaken–Blakemore (SB) tube is highly effective and controls acute bleeding in 90% of patients, although 50% rebleed when the balloon is deflated.[1] Although the use of SB tubes in the management of variceal haemorrhage has reduced with the advent of vasoactive treatments and endoscopic advances, it is still an effective treatment. Despite clear reference to its value in the control of variceal haemorrhage in BSG guidelines, the JCHMT gastroenterology curriculum 2005 makes no recommendation on gastroenterology SpR training in this subject.
Aims & Methods: This study aims to determine the level of training and competence in SB tube placement among gastroenterology SpRs in a training region (Wessex). All gastroenterology SpRs in the Wessex deanery received a questionnaire to assess their training in SB tube placement and clinical expertise.
Results: Thirty one SpRs were eligible for the study and 71% responded. Only 57% had practical experience of SB tube placement. None had a written training record of their experience, and none had been formally assessed using DOPs or an equivalent assessment format. 10% had never seen a senior colleague deploy an SB tube and only 36% felt confident using an SB tube independently. Although 42% had placed a SB tube within the last year only 5% currently worked in a hospital with local guidelines on SB tube placement. With regards to clinical expertise, 31% felt the gastric balloon should be inflated with water rather than air and only 31% would inflate the balloon to 300 ml. Other answers to this question varied from 20 ml to 500 ml in volume! No trainees knew the maximum time an oesophageal balloon should be inflated, and only 30% gave correct figure

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for the gastric balloon. 80% could not quote the correct percentage of patients that develop serious complications such as aspiration pneumonia and oesophageal ulceration in association with SB tube placement. Importantly all trainees felt gastroenterology SpRs should be trained in SB tube placement.
Conclusion: This study shows that trainees in gastroenterology have a low level of practical and theoretical knowledge with regards to SB tube placement. SB tube placement is still an essential skill for gastroenterologists involved in the management of acute variceal haemorrhage. The JCHMT gastroenterology curriculum does not currently give guidance on the training of SpRs in the use of SB tubes. Neither JAG or the BSG has published guidelines on this topic. If gastroenterology SpRs in the UK are to be safely trained in SB tube placement, a more formal framework of educational guidelines and methods of assessment are required.

1. **Jalan R**, Hayes PC. UK Guidelines on the management of variceal haemorrhage in cirrhotic patients. *GUT* June, 2000;**46**:1–15.

292 ABDOMINAL PRESSURE DURING COLONOSCOPY: A SURVEY TO ASSESS ATTITUDES AND TRAINING AMONG ENDOSCOPY NURSES

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Introduction: Abdominal pressure is a valuable way to facilitate complete colonoscopy. In the majority of endoscopy departments this vital adjunct to colonoscopy is carried out by endoscopy nurses. Formal training in colonoscopy is mandatory and well structured but the role of training for endoscopy nurses is less well defined. This survey aims to assess endoscopy nurses level of training in abdominal pressure and their attitudes and understanding of the technique and its rationales.
Aims & Methods: Endoscopy nurses, in five UK hospitals were asked to complete a postal questionnaire.
Results: In total 59 endoscopy nurses were surveyed and 69% replied. Of these 98% performed abdominal pressure on a regular basis. None had read, or been presented with any evidence based literature on the subject. Only 2% had received formal training in the technique whilst 43% had received informal or ''on-the-job training''. 100% felt endoscopy nurses should have formal, structured training in abdominal pressure. Only 39% had any understanding of terms used in the literature to describe different manoeuvres in abdominal pressure such as the ''caecal lift'' or ''sigmoid lift'', and 30% felt they didn't understand what the term ''looping of the colonoscope'' meant. Interestingly 71% felt competent to perform abdominal pressure but none had any formal objective assessment of their competence. Only 30% always understood the anatomical terms used to describe areas of the abdomen by the endoscopist, when asked to perform abdominal pressure.
Conclusion: Endoscopy nurses are frequently asked to perform abdominal pressure during colonoscopy as a recognised manoeuvre to improve chances of satisfactory completion and patient comfort. Neither the BSG nor JAG provides any guidance on how this technique should be applied. Quality and effectiveness of colonoscopy in all its aspects is important and education of the whole endoscopy team is necessary to achieve best clinical outcomes. This survey would suggest training and assessment amongst nurses performing abdominal pressure is inadequate. Endoscopy nurses should have guidelines and training on the application, contraindications and complications of abdominal pressure. Such training is not currently undertaken in the UK despite endoscopy nurses' apparent willingness to participate in an educational programme.

1. **Waye JD Yesayan SA**. The technique of abdominal pressure in total colonoscopy. *Gastrointest Endosc* 1991;**37**:147–51.
2. The importance of abdominal pressure during colonoscopy: techniques to assist the physician and to minimize injury to the patient and assistant. *Gastroenterol Nurs* 2005.

293 AUDIT OF 30-DAY MORTALITY FOLLOWING PEG INSERTION AT A DISTRICT GENERAL HOSPITAL, THE KENT AND SUSSEX HOSPITAL TUNBRIDGE WELLS, KENT: COMPARED WITH NCEPOD RESULTS

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Introduction: Percutaneous endoscopic gastrostomy (PEG) was first described in 1980. A large number of PEG procedures are performed in hospitals throughout the UK. There are no national guidelines regarding the use of PEG tubes. Mortality post procedure is currently a concern for the BSG, following the recent first ever NCEPOD audit on endoscopy.[1]
Aims & Methods: To establish the 30-day mortality following PEG at our institution.
Methods: Data on indication, demographics, anaesthetic spray, sedation, complications and cause of death collected from the endoscopy department computer system on all patients who had a PEG inserted during 2003. Medical notes of all patients who died following the procedure were reviewed and data compared with NCEPOD findings.
Results: Of the 66 patients who had a PEG tupe inserted during 2003, 28 are still alive 18–24 months later. 30-day mortality, 24% (16 pts); national 30-day mortality, 6%; 1-year mortality, 53% (34 pts). Indication for procedure: CVA, 26; head injury, 2; cancer oesoph, 1; unclear, 1; poor oral intake, 1; poor swallow, 1; dysphagia, 1. Anaesthetic technique: 64 patients received both lignocaine throat spray and sedation; 1 patient required naloxone; 1 patient required flumazenil. Causes of death at 30-days: pneumonia, 6; aspiration, 6; stroke, 2; sepsis, 1; sedation, 1. Causes of death at 1 year: pneumonia, 14; aspiration, 8; unknown, 8; stroke, 2; sepsis, 1; sedation, 1.
Conclusion: The 30-day mortality in this study is higher than that reported by NCEPOD, possibly because of an open access service. Our deaths also occur later and this may be because following PEG most of our patients are discharged to a nursing home. The mortality falls dramatically after 50 days and is highest within the first 21 days (where most deaths are due to comorbidity rather than the procedure itself). Therefore more care needs to be taken over both timing and selecting patients for PEG in order to reduce this early mortality. This could be achieved by introducing a PEG referral protocol, reviewing all patients by a MDT on a nutritional ward round and increasing the time between referral and procedure. Urgent review of current PEG policy should be undertaken. Throat spray and sedation should not be co-administered due to the increased risk of aspiration. Ultimately we should almost certainly be inserting fewer PEGs. A further audit should be performed following change in practice to confirm a positive outcome.

1. **Percutaneous endoscopic gastrostomy**. See http://www.ncepod.org.uk/2004report/pegs.intro.htm.

294 LONG-TERM, FIVE-YEAR FOLLOW-UP OF PATIENTS WITH IRON DEFICIENCY ANAEMIA AFTER A NEGATIVE GASTROINTESTINAL EVALUATION

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Introduction: Current guidelines suggest that OGD and a lower gastrointestinal (GI) investigation (colonoscopy or barium enema with or without sigmoidoscopy) are sufficient in the evaluation of iron deficiency anaemia (IDA). These guidelines are based on two small studies from the mid 1990s which concluded, after long-term follow-up of patients with IDA, that this approach was safe.
Aims & Methods: Patients who had negative upper and lower GI investigations for IDA between 1997 and 2000 were identified. Our aim was to determine if these patients subsequently developed recurrent anaemia or significant pathology. Patients with overt GI bleeding or a positive diagnosis (gastric Ca, colorectal Ca, colonic polyps, coeliac disease, inflammatory bowel disease) were excluded. 67 patients were included and their hospital records were reviewed. Where these were incomplete the patient's primary physician was contacted. Two patients were excluded because of inadequate follow-up data.
Results: Sixty five patients (52 female, 13 male), with a mean age of 65.6 years (range 29–87), were followed up long term. Follow-up was for a median of 5 years and nine months (range 7–109 months). In 54 patients (83%) the anaemia resolved after the initial treatment period. Five patients (8%) developed chronic IDA severe enough to require recurrent blood or iron transfusions. Two of these were pre-menopausal women with menorrhagia. Four patients (6%) were diagnosed with GI malignancies during follow-up. One of these was diagnosed with colonic carcinoma on barium enema 9 months after a normal OGD and barium enema. Another patient was diagnosed with a small bowel adenocarcinoma 13 months after initial investigations, which included a small bowel series, and a third patient was found to have a gastric tumour 42 months after a negative evaluation. One other patient was diagnosed with a malignant colonic polyp 7.5 years after her first presentation. 11 patients (17%) died of other illnesses during the follow-up period, 4 of these (6%) of a non-GI malignancy.
Conclusion: For the majority of patients with a negative GI evaluation for IDA the outcome is favourable although a small percentage may subsequently be found to have significant GI pathology. The current approach to IDA investigation is probably safe but a change in symptoms

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or persistent anaemia should prompt further investigations. We suggest long-term annual FBP check.

295 SEDATION FOR ENDOSCOPIC PROCEDURES: ARE WE SAFE ENOUGH?

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Introduction: Previously published reports have shown that excessively high doses of benzodiazepines and opiates were used to sedate patients for endoscopic procedures, particularly in the elderly,[1] which leads to increased morbidity and mortality. This has led to British Society of Gastroenterology (BSG) recommendations[2] on safe sedation dosage for elderly patients which were recently highlighted by the National Patients Safety Association (NPSA). In particular, a change in benzodiazepine (midazolam) concentration was advised in order to allow smaller doses to be easily titrated in elderly patients. Patient Comfort Scores assess patients' overall comfort before, during, and after endoscopic procedures and give a good indication of a patient's perception of the procedure and appropriateness of sedation. Flumazenil has also been established to be a good surrogate marker of over sedation.
Aims & Methods: To determine whether endoscopic sedation practice has improved in our department since recent recommendations were issued, and to compare Patient Comfort Scores over this time period. A retrospective analysis of endoscopic reports (for colonoscopy and gastroscopy) was carried out during two months prior to, and two months after, the introduction of change in midazolam concentration. Mean sedation doses and flumazenil usage were recorded. Patient Comfort Scores were recorded for a period of two weeks before and after the recommendations.
Results: A total of 2332 procedures were reviewed. An overall reduction in midazolam use for all procedures was observed. This was demonstrated in both those <70 years (mean midazolam dose 4.0 mg (SD 2.7) *v* 3.0 mg (SD 2.8); $p=0.0001$), and in those >70 years (3.0 mg (SD 2.2) *v* 2.7 mg (SD 2.2); $p=0.02$). A decrease in midazolam use in elderly patients undergoing gastroscopy was also seen (2.3 mg (SD 1.9) *v* 1.9 mg (SD 1.7); $p=0.011$). There was no significant reduction of midazolam dose in both patient groups undergoing colonoscopy. Pethidine use did not fall. There was no significant change in Patient Comfort Scores or flumazenil use during the period studied. Flumazenil was used in 0.6% of patients receiving midazolam.
Conclusion: By highlighting recommendations for safe sedation use, a reduction in midazolam use is demonstrated in our unit. Patients' overall comfort levels are not compromised by this reduction in use. The sedation doses used are also in line with BSG recommendations, and the overall use of flumazenil is low.

1. **Lord DA**, *et al*. Sedation for gastrointestinal endoscopic procedures in the elderly. BSG Guidelines, 2006.
2. **Teague, R**. The British Society of Gastroenterology (BSG) guidelines on safety, sedation and monitoring. (Updated) November, 2003.

296 FIVE-YEAR EXPERIENCE WITH ENDOCLIPS IN THE MANAGEMENT OF GASTROINTESTINAL BLEEDING

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Introduction: Endoscopic therapy is first line treatment for upper gastrointestinal (GI) bleeding. Adrenaline injection alone leads to high rebleeding rates and addition of a second method particularly heater probe is advocated. Endoscopic application of endoclips provides an alternative method of achieving haemostasis in upper GI bleeding (UGIB) but published experience is limited compared with other haemostatic methods.
Aims & Methods: To evaluate the use of endoclips over a 5-year period (2001–6) with reference to appropriateness and outcomes from their use. Endoscopy report database analysed for reports containing the term ''endoclip''. Patients identified and their notes or computer records (Isoft) reviewed. Ulcer lesions classified according to Forrest's classification and rebleeding risk calculated by Rockall scores.
Results: Forty six reports identified with the term ''endoclip'' of which 3 stated that endoclips could not be deployed successfully. Another 3 were outside the criteria for inclusion in the audit (1 after bleed from oesophageal biopsy, 1 after bleed from puncture for PEG insertion, 1 after gastric polypectomy). 40 patients had acute UGIB (29M, 11F). Age range was 24–89 years (mean 66.3). Mean pre-endoscopy Rockall score was 3.52 (range 0–6) and mean final Rockall score was 6.5 (range 3–9). At first endoscopy there were 20 duodenal ulcers, 7 gastric ulcers and 13 miscellaneous lesions. 27 patients had endoclips (range 1–4, mean 2.14) applied at first endoscopy and only 7 (26%) of these rebled of which 3 went directly to surgery. Of the 13 who did not have endoclips at first endoscopy 11 (85%) rebled. 15 patients who rebled had a second endoscopy and endoclips (range 1–7, mean 3) were applied to 14. Haemostasis was achieved in 12 of these while 2 proceeded to surgery. There were a total of 6 deaths in the audit population but only one of these was due to uncontrolled bleeding. There were no complications from endoclip application.
Conclusion: Over a 5-year period endoclips have proven to be a safe and effective method of achieving haemostasis in high risk UGIB in combination with adrenaline injection.

Abstract 296 Forrest classification of ulcers at first endoscopy

Forrest classification score	Patients (n)
1a: active bleeding (spurting)	3
1b: active bleeding (oozing)	5
2a: non-bleeding visible vessel	11
2b: adherent clot	7
2c: flat pigmented spots	0
3: clean ulcer base	1
Total	27

297 DIRECT PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY: TECHNIQUE AND A FIVE-YEAR REVIEW

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Introduction: Direct percutaneous endoscopic jejunostomy (DPEJ) is a potentially valuable technique for artificial nutrition in selected patients, particularly those who require palliative nutritional support due to inoperable or recurrent upper gastrointestinal (GI) malignancy, where a PEG may not be feasible. We review here our technique and outcome.[1 2]
Aims & Methods: The procedure is done with a gastroscope, paediatric colonoscope or enteroscope, under conscious sedation, and with fluoroscopy available. The endoscope is advanced into a loop of jejunum and an appropriate point for abdominal wall puncture identified by finger indentation and/or fluoroscopy. A conventional Fresenius PEG kit is used and puncture is done with either the conventional PEG trochar or a long drainage access (Kellett) needle, prior to completion of the procedure as for a PEG.
Results: Twenty eight cases were done between 2001 and 2006. 23/28 cases had malignant disease (oesophagus 5, stomach 15, pancreas 3); 12 had inoperable disease and 11 were postoperative; 7/11 postoperative cases had recurrent malignancy (median interval from surgery to PEJ was 12 months). Median DPEJ endoscopy time was 20 mins and there were no procedural complications. 12/28 patients (35%) died within 30 days although 20/28 patients (71%) were discharged from hospital with the PEJ in use. 5/20 PEJs were removed (no longer used, 3, infected, 2). Median survival was 83 days.
Conclusion: DPEJ placement is safe and has a role in selected patients, particularly for palliative nutritional support in patients with advanced malignancy. Discharge from hospital is feasible in most cases and a minority of cases have long-term survival.

1. **Shetzline MA**, Suhocki PV, Workman MJ. Direct percutanous endoscopic jejunostomy with small bowel enteroscopy and fluoroscopy. *Gastrointest Endosc* 2001;**5**:633–8.
2. **Leichis L**, Patel R, Johnlin F. Percutanous endoscopic gastrotomy/jejunostomy tube placement: a novel approach. *Gastrointest Endosc* 1997;**45**:79–81.

298 PREOPERATIVE STAGING OF PANCREATICOBILIARY TUMOURS: THE ROLE OF ENDOSCOPIC ULTRASOUND (EUS) WITH EUS FINE NEEDLE ASPIRATION WHEN COMPUTED TOMOGRAPHY IS INCONCLUSIVE

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Introduction: Multislice computed tomography (CT) and endoscopic ultrasound (EUS) are both used for the local staging of pancreatic malignancies.[1] However there is little published data on the additional

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diagnostic power and benefit offered by EUS fine needle aspiration (FNA) performed concurrently for cases where CT imaging is inconclusive.
Aims & Methods: This was a retrospective study of data collected prospectively via the hepatobiliary unit database between January 2004 and January 2006. We analysed the CT and EUS findings, EUS FNA cytology and final histology after surgery. The aim of the study was to determine if the combination of EUS and FNA assisted diagnosis and therefore surgical decision making in cases where CT imaging was inconclusive. CT and EUS reports were classed as definite, inconclusive or benign. Only definite reports were taken as indicative of malignancy.
Results: We identified 65 patients who had pancreatic and biliary resections during this period. Male to female ratio was 1:5. All patients had CT scans and 60 patients had EUS performed. 51 patients had a definite diagnosis of malignancy on CT scan alone. 14 patients had lesions identified as benign or indeterminate on CT and these made up the study group. Of these 14 patients, the combination of EUS and EUS FNA confirmed a diagnosis of malignancy in 10 (77% sensitivity, 100% specificity, positive predictive value (PPV) 100%, negative predictive value (NPV) 25%). Of these 10 patients, 3 had malignancy confirmed on both FNA cytology and EUS morphology, 5 on EUS morphology alone and 2 on cytology alone. Of the remaining 4 patients who had inconclusive CT, EUS and FNA cytology in the study group, 2 had malignant adenocarcinomas of the head of pancreas, 1 had a cholangiocarcinoma and the other, a benign stricture on final surgical histology.
Conclusion: In patients where CT findings are inconclusive, the combination of EUS and EUS FNA cytology is useful in establishing the diagnosis of pancreatic and biliary lesions and thus provides additional information to guide surgical decision making.

1. **Dewitt J**, *et al*. Comparison of endoscopic ultrasound and computed tomography for the preoperative evaluation of pancreatic cancer: a systematic review. *Clin Gastroenterol Hepatol* 2006;**4**:717–25.

299 SENSITIVITY AND SPECIFICITY OF ERCP BRUSHINGS OF SUSPECTED MALIGNANT BILIARY STRICTURES

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Introduction: There are a wide range of values quoted in the literature for sensitivity and specificity for ERCP brushings. We wished to assess the specificity and sensitivity for ERCP brushings performed in our hospital.
Aims & Methods: To assess the sensitivity and specificity of ERCP brushings in patients presenting with suspected malignant biliary strictures over a five year period. A retrospective search was performed using an endoscopy database over a five-year period between 2000 and 2005 for patients with suspected malignant biliary strictures. Endoscopic and demographic data were obtained from charts and a pathology database. Brushings results were compared with biopsy results where available.
Results: 102 ERCPs and brushings were performed on 93 patients during this period. Eight patients had repeat ERCPs, 44 brushings were malignant (43%), 24 were suspicious for malignancy (24%), 19 showed cellular atypia (19%) and 15 showed benign epithelial cells only (14%). 22 patients had both brushings and biopsies to compare with, 4 of whom had two ERCPs. 14 brushings were malignant or were suspicious for malignancy and were found to be malignant at surgery/biopsy. Four brushings showed normal epithelial cells or cellular atypia, which were found to be malignant at surgery. Six patients had brushings which showed benign epithelial cells with benign findings at surgery/biopsy and 2 had brushings suspicious for malignancy with benign surgery/biopsy findings. Sensitivity, specificity, positive predictive value and negative predictive value for ERCP brushings were 78%, 75%, 88% and 60% respectively. Overall accuracy of brushings at ERCP compared to final histology was 77%. In 45 (48.4%) patients there was a stricture at lower 1/3 bile duct, 27 (29.0%) had a stricture at mid bile duct, 13 (14.0%) had a stricture at junction of hepatic and bile ducts (hilar stricture), and 8 (8.6%) had a stricture at the ampulla. 30 patients had a mass seen on abdominal imaging and of these 20 had malignant/suspicious brushings (67%) and 10 had normal/atypia brushings (33%). There were 9 patients who had a normal Ca 19-9 value but malignant brushings (20.5% of those with malignant brushings). The average age of the patients was 72 years (range 35–95). Duration of presenting symptoms were less than 1 week in 25%, 1 week to 1 month in 35%, and greater than 1 month in 35%. Symptoms at presentation were as follows jaundice (53%), weight loss (24%), pain (28%) and nausea (9%). Mean bilirubin prior to ERCP was 212.23 μmol/l. Mean survival for patients post ERCP was 209 days (74 patients).
Conclusion: In our hospital the accuracy of biliary brushings at ERCP in patients presenting with suspected malignant biliary strictures was 77%. This compares favourably with other published studies.

300 ROLE OF REPEAT ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION IN OBTAINING TISSUE DIAGNOSIS IN SOLID PANCREATIC LESIONS: IS IT WORTHWHILE?

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Introduction: Endoscopic ultrasound fine needle aspiration (EUS-FNA) is established as an effective technique for tissue diagnosis of solid pancreatic lesions. Sensitivity of 64% to 96% and specificity ~ 95% is reported in the literature. In general higher sensitivities are reported by units with the availability of an in room cytopathologist. There are limited published data on the utility of a repeat procedure in individuals with initial negative cytology and a residual suspicion of malignancy. Definite cytological diagnosis is particularly required in inoperable patients being considered for chemotherapy.
Aims & Methods: We report our experience of repeat EUS-FNA in a tertiary referral centre in patients who did not have a definite tissue diagnosis after the first FNA. We retrospectively analysed data from all patients who had a repeat EUS-guided FNA performed between January 2004 to April 2006.
Results: 440 patients had EUS guided FNA performed for various lesions during the study period. Of these 24 patients had 48 procedures performed for solid pancreatic lesions (21), hilar lesions (1) and a suspected cholangiocarcinoma (2). The reasons for repeat sampling were either inadequate tissue for diagnosis (PANC 0/1/2 =13) or atypia (PANC 3/4 =11) in the first sample. The mean age was 59.92 years (range 36–70). There was equal M:F distribution. The average number of passes was 2.75 (range 1–4). Mean follow-up period was 15.6 months (range 4–38). Repeat EUS guided FNA provided a final diagnosis in 20 (83%) patients. These include: adenocarcinoma (12), metastatic disease (2), and benign (6). The sensitivity, specificity, positive predictive value and negative predictive value were 93.3%, 100%, 100% and 90% respectively. Surgical pathology was obtained in 4 patients.
Conclusion: Our data support repeat pancreatic EUS-FNA in individuals with inconclusive cytology in whom there remains a suspicion of malignancy.

301 FLEXIBLE SIGMOIDOSCOPY IN THE COMMUNITY: IS MEDICAL SUPERVISION NECESSARY?

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Introduction: In March 2004 Newcastle Hospital Trust established a nurse-led flexible sigmoidoscopy service to complement existing endoscopy facilities. The aim was to allow direct access referrals to sigmoidoscopy for GP and hospital referrals, provide prompt investigation, and where appropriate offer treatment and advice that may reduce the burden on existing hospital outpatient services. Initially the service was supervised by medical staff, but for the last 16 months the service has been exclusively run by nurse endoscopists.
Aims & Methods: To audit the activity of the nurse-led endoscopy service and compare 12 months under medical supervision with the same period run independently. Since the service was established all referral data, patient histories, procedure findings and outcomes have been prospectively entered into a database. This study assesses whether the effectiveness of the nurse-led service has changed with respect to outcomes.

Abstract 301

	June 2004–5	September 2005–6
Sigmoidoscopies (n)	776	754
Mean waiting times	43 days	34 days
Completion rate (40+cm)	88.3%	94.2%
Biopsy rate	46.5%	50.5%
Complication (bleed/perf)	0	0
Polyp diagnosis	13.4%	12.5%
Outcomes		
Discharge	28.5%	26.5%
Outpatient clinic fo	32.6%	31.6%
Colonoscopy	18.4%	14.2%
Barium enema	10.9%	1.6%
Nurse clinic	2.6%	19.1%
Notes to consultant	1.9%	5.6%
Further Ix	1.8%	0.3%
Repeat flexi	0.9%	0.8%

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Results: See table.
Conclusion: Community flexible sigmoidoscopy run by nurse endoscopists is safe and effective. There is no significant difference between completion rates and diagnosis of serious pathology when nurse endoscopists have medical supervision. Most common outcomes have remained unchanged including hospital outpatient follow up, discharge and colonoscopy referral. Decrease in number of barium enemas and other investigations ordered may reflect the corresponding increase in number of cases requiring discussion with a consultant.

302 PERCEPTION OF THE MALIGNANT POTENTIAL OF GASTRIC ULCERS IS INFLUENCED BY ACID SUPPRESSING MEDICATION

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Introduction: Approximately 10% of malignant lesions are ''missed'' at endoscopy. Even when lesions are seen, misdiagnosis occurs because of insufficient biopsies. The number of biopsies taken depends on the suspicion of malignancy which in turn may be affected by changes in appearances due to acid-suppressing therapy (AST).
Aims & Methods: To determine how reliable endoscopic opinion was at determining whether an ulcer was benign or malignant and the effect of AST. A prospective study of all patients diagnosed with a gastric ulcer at gastroscopy over a 20-month period were identified (mucosal breach >5 mm). The endoscopist's macroscopic judgement of the ulcers was recorded (benign, suspicious or malignant) and correlated with both prior AST and histology results.
Results: 196 ulcers were included. The predictive value of the endoscopist's macroscopic judgement regarding the ''suspiciousness'' of an ulcer can be estimated as the proportion of correct macroscopic diagnoses (PV pos) (table).
Conclusion: The ability of the endoscopist to determine whether an ulcer was benign or suspicious/malignant appears to be influenced by treatment with antisecretory drugs prescribed prior to endoscopy. In this situation the endoscopist was less likely to recognise the ulcer as malignant suggesting that these agents alter the endoscopic appearance of malignant ulcers. The PPV of endoscopy in suspicious ulcers fell from 0.65 to 0.3 if patients had received prior AST. Clinicians need to be aware of this and adopt a more rigorous biopsy protocol.

Abstract 302 Positive predictive value of macroscopic judgement

	Benign	Suspicious/malignant
All (overall)	0.96 (131/137)	0.58 (26/45)
All +AST	0.93 (27/29)	0.3 (3/10)
All −AST	0.97 (102/105)	0.65 (20/31)
List (overall)	0.94 (45/48)	0.59 (14/24)
List +AST	0.85 (11/13)	0.67 (2/3)
List −AST	0.97 (31/32)	0.61 (11/18)
OAG (overall)	1.0 (21/21)	0.71 (5/7)
OAG +AST	1.0 (13/13)	0.5 (1/2)
OAG −AST	1.0 (8/8)	0.8 (4/5)
Emergency (overall)	0.95 (63/66)	0.50 (7/14)
Emergency +AST	1.0 (3/3)	0.4 (2/5)
Emergency −AST	1.0 (61/61)	0.5 (4/8)

303 INADEQUATE NUMBERS OF BIOPSIES RESULTS IN DELAYED DIAGNOSIS OF UPPER GASTROINTESTINAL ADENOCARCINOMA

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Introduction: Up to 30% of patients diagnosed with an upper GI adenocarcinoma have had a prior gastroscopy in the 3 years before diagnosis. The inference is that the abnormality was missed.

Abstract 303 Number of biopsies taken at prior OGD

Principal finding at prior endoscopy (n = 183)	n	Mean number of biopsies taken (median, range)
Normal/HH/DU	19	0
Oesophagitis	25	2.3 (2, 0–14) (n = 23)
Oesophageal stricture	21	1.1 (1, 0–3)
''Gastritis''	14	1.9 (1.5, 0–6)
Gastric ulcer	71	2.0 (1, 0–7)
Benign looking polyp	1	1
Suspicious mass	10	2.9 (3, 1–5)
Pyloric stenosis	6	2.3 (2.5, 0–5)

Aims & Methods: To determine the nature of the findings at the initial gastroscopy, the time interval between gastroscopy and diagnosis and the biopsy rate. Endoscopy records from 685 patients diagnosed in South Tees Health District (population ~ 350 000) over a 10-year period were analysed having been identified from the pathology and NYCRIS databases.
Results: 747 patients were identified (April 1991–April 2001). 92% had primary adenocarcinomas (29% oesophageal; 71% gastric). Of the 685 patients, 183 (26.6%) had a prior endoscopy in the 3 years before diagnosis. Of the 685 patients, 183 (26.6%) had a prior endoscopy in the 3 years before diagnosis. However 120 of these had a planned follow-up endoscopy at which the diagnosis was made. In only 63 (9.2%) was no abnormality seen or other diagnosis made, not requiring follow-up. Inadequate biopsy numbers account for the high incidence of failure to diagnose malignancy first time round, influenced by previous antisecretory therapy. The table shows the findings at the prior endoscopy.
Conclusion: In the majority of cases lesions were seen at the first gastroscopy but many were thought to be benign. Inadequate numbers of biopsies were taken and so the opportunity to diagnose the cancer at initial gastroscopy was missed. It must be emphasised that benign looking ulceration in patients on antisecretory therapy should be regarded as potentially malignant and an adequate numbers of biopsies must be taken to avoid delayed diagnosis. The ''true'' miss rate for gastric cancer is the same as in Japan.

304 SIZE DOESN'T MATTER: SAFETY AND EFFICACY OF ERCP IN A SMALL DISTRICT GENERAL HOSPITAL

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Introduction: It has been suggested that an annual ERCP caseload of less than 200 is an independent risk factor for complications.[1] In 2005 the BSG Endoscopy Committee recommended an annual caseload of 150.[2]
Aims & Methods: To determine the safety and efficacy of ERCP in our small volume practice, a retrospective 7-year casenote analysis was carried out on all ERCPs performed between January 1998 and December 2004. Cotton criteria were used to categorise post-ERCP complications.[3]
Results: 685 ERCPs were attempted; 47 were unsuccessful, 136 were diagnostic. Median (range) age of patients was 73 (22–94). Most requests were for gallstone disease (63%) or malignant common bile duct obstruction (16%). Complications occurred in 6.3% of all procedures. 47% of complications occurred after sphincterotomy and 21% after stenting.
Conclusion: Over a 7-year period, rates of success and complication in our unit with an annual caseload of around 100 compare well with published data from larger units. This suggests an annual ERCP caseload of approximately 100 can be effective and safe.

1. **Loperfido**, *et al. Gastrointest Endosc* 1998;**48**:1–10.
2. **Quality and safety indicators for endoscopy**. *BSG* 2005.
3. **Cotton**, *et al. Gastrointest Endosc* 1991;**37**:383–93.
4. **Schutz**, *et al. Gastrointest Endosc* 2000,51;535–9..
5. **Masci**, *et al. Eur J Gastro Hepatol* 1999;**11**:781–4.
6. **Hui**, *et al. Ali Pharm Thera* 2004;**19**:1153–8.
7. **Poon**, *et al. Gastrointest Endosc* 1999;**49**:593–8.
8. **Ho**, *et al. Gastrointest Endosc* 1999;**49**:587–93.
9. **Shalilesh**, *et al. Gastrointest Endosc* 1996;**44**:443–9.
10. **Christensen**, *et al. Gastrointest Endosc* 2005;**60**:721–31.
11. **Vandervort**, *et al. Gastrointest Endosc* 2002;**56**:652–6.
12. **Halme**, *et al. Ann Chir et Gynaecol* 1999;**88**:127–31.

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Abstract 304 Comparisons with published data (%)

	Results at Weston (all ERCPs)	Results at Weston (therapeutic ERCPs only)	Published data ranges[4–12]
Cannulation of desired duct	95.8		89–99
Mortality (30-day all cause)	0.9	1	0–4.2
Pancreatitis	2.2	2.6	0.8–10
Cholangitis	2.2	5	0.4–5.0
Haemorrhage	1.6	2	0.7–3.9
Perforation	0.3	0	0.1–2.4

305 DO VARIABLE STIFFNESS COLONOSCOPES IMPROVE EXAMINATION COMPLETION RATES? ANALYSIS OF 4463 CASES

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Introduction: Variable stiffness colonoscopes have theoretical advantages over standard instruments in negotiating variable colonic anatomy and fixation due to the ability to vary shaft flexibility. It is unclear whether this characteristic results in a clinically significant difference in caecal intubation rates.

Aims & Methods: Analysis of endoscopy database of 4463 fully documented colonoscopic examinations at our unit between 2003 and 2006. Completed examination rates for cases performed with variable (VSC) and normal stiffness scopes (NC) were assessed (the scopes used were Olympus 240 AL and 240 S respectively). Sex of patient and reason for failure (where documented) were also analysed.

Results: 4463 cases were analysed. 1871 in males and 2412 in females. The total completion rates for the VSC (all operators) were 3006 of 3579 (83.99%). This compares to 577 of 704 (81.96%) in the NC group ($p=0.121$, Fischer's exact test). In male patients 1370 of 1570 (87.26%) were completed using the VSC. 256 of 301 (85.05%) were completed using the NC. In females, 1636 of 2009 (81.43%) cases were completed with VSC compared to 321 of 403 (79.65%). Therefore, successful colonoscopy appears more likely in males than females for each type of instrument ($p<0.001$ and $p=0.004$ for VSC and NC respectively). When comparing completion rates in patients of the same sex for the different scopes, the results failed to show a significant difference between the two instruments ($p=0.171$ for males, 0.249 for females). In considering the causes of failure reported, there were similar proportion of failures attributed to looping or discomfort (31% and 30% in VSC and NC respectively) and prep (26% *v* 21%). Examinations limited by pathology and adverse events were similar in both groups (40% and 45%).Cases where the cause of failure could not be determined from the report were also similar (3% *v* 4% for VSC and NC) between the two groups. None of the causes of failure reached statistical significance between VSC and NC groups.

Conclusion: In this large sample, there were no significant differences between completion rates for either the VSC or NC. Colonoscoping male patients resulted in higher completion rates ($p<0.001$) for each scope. Variable stiffness scopes do not appear to offer any advantage over standard scopes in terms of colonoscopy completion rates, despite theoretical benefits.

306 EXPLORING THE UTILITY OF THE GIVEN PATENCY CAPSULE IN PATIENTS AT RISK OF CAPSULE RETENTION

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Introduction: Capsule retention (CR) is a concern when considering capsule endoscopy (CE) for patients with ''high-risk'' indicators—Crohn's disease, obstructive symptoms, heavy NSAID usage, prior abdominal surgery or abnormal small bowel radiology.[1] For these patients it is prudent to perform a patency capsule (PC) test or small bowel *x* ray (BFT) beforehand. However, a normal BFT does not exclude significant stricturing or CR—one study showed CR in 6.7% of patients with known Crohn's disease despite a normal BFT, questioning the validity of the test.[2] We reviewed our experience with the PC and with BFT in patients at risk of CR.

Aims & Methods: We aimed to compare the utility of the Given PC system with BFT in patients at high risk of CR. We reviewed the records of all patients referred for CE at our institution between July 2004 and August 2006. During this period, any patient considered high risk for CR received a PC prior to CE. An abdominal *x* ray (AXR) 36 h after ingestion was used to confirm PC passage. If the PC was visible, gastrograffin was used to confirm position (small or large bowel). If the PC was retained in the small bowel, CE was not performed and a BFT was carried out.

Results: In each case comparison was made between the PC result, prior radiology, and subsequent BFT (if performed). 324 patients were studied over 26 months. 275 (85%) low-risk patients did not receive a PC, with no cases of CR at CE. 49 (15%) high-risk patients received a PC. The PC passed in 38 (77%)—at CE: 35 passed easily; 1 transient hold-up; 1 retained in stomach; 1 retained in small bowel (but AXR review showed PC in small bowel, ie false negative). 25 of 38 had prior radiology, with significant strictures in 3. PC retained in 11 (23%) with no resulting complications. Four had no prior radiology: 1, subsequent BFT showed jejunal adhesions; 2, BFT showed Crohn's stricture; 3, false+ PC (actually a calcified fibroid); 4, lost to follow-up. Five had prior normal radiology: 1, subsequent BFT normal, repeat PC retained, CT showed active Crohn's; 2, PC in caecum ie false+; 3, subsequent BFT normal, awaiting repeat PC; 4, awaiting BFT; 5, lost to follow-up. Two had prior minor abnormalities at radiology: tight strictures found at DBE in 1; tight Crohn's stricture at BFT in other.

Conclusion: (1) Patients without high-risk indicators for CR do not require a PC prior to CE. (2) The reliability of BFT for determining PC passage through the small bowel is poor. (3) In our experience, the PC can be used safely as a 1st line investigation in patients with high-risk indicators for CR without a prior BFT. (4) Retention of the PC is highly suggestive of significant underlying pathology. PC use helps to avoid the inappropriate and potentially dangerous application of CE in these patients. (5) Interpretation of PC location on AXR can be difficult, and false positives or false negatives may result.

1. **Cave D**, Legnani P, Lewis B, *et al.* ICCE consensus for capsule retention. *Endoscopy* 2005;**37**:1065–7.
2. **Buchman AL**, Miller FH, Wallin A, *et al.* Video capsule endoscopy versus barium contrast studies for the diagnosis of Crohn's disease recurrence involving the small intestine. *Am J Gastroenterol* 2004;**99**:2171–7.

307 A SINGLE-BLINDED RANDOMISED CONTROLLED TRIAL ASSESSING OPTIMAL BOWEL PREPARATION FOR THE CAPSULE ENDOSCOPY TEST

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Introduction: The diagnostic accuracy and patient acceptablity of the capsule endoscopy (CE) test has led to an exponential increase in its use since its introduction in 2002. However the test may be limited by poor luminal views, and by incomplete small bowel transit in up to 25% of cases.[1] Standard preparation consists of clear fluids from 12 pm the day prior and then nil-by-mouth from midnight. The use of bowel preparation and prokinetic agents has been studied but the results are inconclusive and the trials often limited by small numbers and retrospective design.

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Aims & Methods: We aimed to assess the optimal method of bowel preparation for the capsule endoscopy test. We prospectively randomised patients to four groups: standard preparation as above (S); standard preparation plus 10 mg metoclopramide 15 mins before the test (M); Senna tablets with 2 l of Citramag the day before (CS); Citramag and Senna as above plus metolcopramide before the test (CSM). The studies were reviewed by a single investigator, blinded to the preparation used. The gastric (GTT) and small bowel transit times (SBTT), completion rate (CR), and significant findings were recorded. The view quality (VQ) was assessed on a scale from 0 (poor) to 4 (good) dependant on percentage of the luminal view obscured (0–20%, 20–40%, 40–60%.). The score was applied to 5 minute segments assessed every 10% of the SBTT (max score = 44). Patient acceptance of the preparation was assessed using a visual analogue scale questionnaire. The study was powered for 150 patients.
Results: An interim analysis of 76 patients recruited to date was performed (18 in S, 17 M, 24 CS and 17 CSM). No significant difference in age, in-patient status or diabetes prevalence was noted between groups, but significantly fewer men were found in group S and M. The GTT and SBTT were significantly reduced in the CSM group compared with S (GTT 591 s *v* 1012 s, p = 0.03, SBTT 184 min *v* 258 min p = 0.01), but this was not the case in groups M or CS. No significant difference in CR was noted between groups (range 82–94%). VQ was significantly improved in the CSM group *v* S (overall score 41 *v* 36 p = 0.04) but no difference was seen in the CS or M groups. No association was noted between VQ and number of findings or rate of positive diagnosis in any of the groups. Patients found the CSM group significantly less comfortable (52% *v* 93% comfort p = 0.04). There was a trend towards CS being less comfortable and both CS and CSM being less convenient. 90% of patients would agree to the same preparation again, and would forego more comfortable preparation for a more accurate test.
Conclusion: Citramag and Senna with Metoclopramide pre-procedure results in significantly reduced transit times and better small bowel visualisation than standard preparation. Although it is less comfortable and convenient, patients may overlook this for a more accurate diagnosis.

1. **Rondonotti E**, Herrerias JM, Pennazio M, *et al*. Complications, limitation and failures of capsule endoscopy: a review of 733 cases. *Gastrointest Endosc* 2005;**62**:712–16.

308 COMMON BILE DUCT WIDTH, AS MEASURED BY ENDOSCOPIC ULTRASOUND, INCREASES WITH AGE AND POST-CHOLECYSTECTOMY

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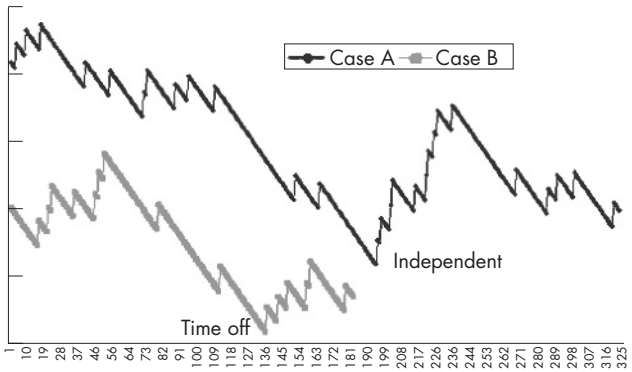
Introduction: The diameter of the common bile duct (CBD) frequently triggers further, often more invasive, imaging of the biliary tree. At what width is the CBD significantly dilated? Are there any variables that need to be taken in to account when considering this measurement? Existing literature on the subject of CBD calibre has used both transabdominal ultrasound and cholangiography. Endoscopic ultrasound (EUS) enables a more accurate method of measuring CBD diameter, as it can image the entire CBD in a single real-time image.
Aims & Methods: This series set out to define the relationship between age and CBD diameter as measured by EUS. The influence of previous cholecystectomy and gender was also assessed. Prospective data were collected from consecutive patients undergoing EUS for non-biliary indications between March 2005 and May 2006. Exclusion criteria were: biliary or head of pancreas abnormalities; previous sphincterotomy; and abnormal liver function tests. At the time of EUS the CBD was identified at its ampullary distal origin and its proximal course mapped. The point of maximum diameter was recorded. This was correlated with age, gender and cholecystectomy status using the SPSS statistical package.
Results: 143 subjects were evaluated (90 females, 53 males). Their mean (SD) age was 62 (14) years. 35 were post-cholecystectomy. Overall the mean CBD diameter was 5.7 (2.4) mm. The Pearson correlation coefficient between age and CBD diameter was 0.285 (p = 0.01). Mean CBD diameters for gallbladder intact and post-cholecystectomy patients were 4.88 (1.5) mm and 8.1 (3.1) mm respectively ($p<0.001$). Mean CBD diameters for males and females were 5.2 (1.6) mm and 5.9 (2.8) mm respectively (p = 0.10). On multivariate analysis, cholecystectomy (p = 0.001) and age (p = 0.037), but not gender (p = 0.296), were found to be predictors of CBD diameter.
Conclusion: In agreement with the existing literature, CBD diameter as measured at EUS is increased post-cholecystectomy. However, the correlation with age is not as strong, and a dilated CBD in an elderly patient should therefore not be solely attributed to age.



Abstract 309.

309 THE ADDITIONAL VALUE OF CUSUM CHARTS FOR COLONOSCOPY TRAINING

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Introduction: The Cusum (cumulative sum) chart gives a graphical representation of colonoscopy success rates. The graph line rises if trainee fall short of 90% caecal hit rate (CHR), and falls if CHR consistently exceeds 90%. Their use is promoted in JAG colonoscopy courses but few trainees or trainers use them. Here we share our unit's experience of Cusum charts, and describe their value in highlighting potential problem areas for colonoscopy trainees and trainers.
Aims & Methods: All colonoscopy trainees in our hospital maintain a Cusum chart of CHR. These charts are reviewed quarterly as part of broader one-to-one endoscopy trainee meetings. Over the past 18 months, several interesting findings have been highlighted by the Cusum charts that would otherwise have been overlooked.
Results: Case A. Completed one-to-one training after 200 cases with clear evidence of >90% CHR. Performance dropped for first 40 procedures performed without trainer in room, only recognised on reviewing Cusum at next quarterly review. Action proposed: Phased withdrawal from room after signing off trainee. Trainer to review initial progress more regularly. Case B. Trainee practising without one-to-one supervision demonstrating >90% CHR. However following 3 week period of absence from colonoscopic practice, CHR dropped to <90% for next 30 cases. Action proposed: highlight potential issue to future trainees/trainers. Consider list size reduction or brief period one-to-one training on return.
Conclusion: The value of Cusum charts extends beyond simply tracking CHR. In our experience their use has highlighted potential training/performance issues in colonoscopy and has refined the unit's training practice. We encourage all trainees and all units who train colonoscopists to adopt them.

310 DIAGNOSTIC YIELD OF INVESTIGATIONS IN PATIENTS WITH HEPATIC METASTASIS

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Introduction: Patients with hepatic metastasis from unknown primary have a short-term prognosis. The dilemma is how to obtain information identifying a primary site with minimal inconvenience and delay.
Aims & Methods: To evaluate the diagnostic yield of investigations, looking for a primary, in patients with proven hepatic metastasis of unknown origin. Retrospective case notes review of patients with hepatic metastasis proven by liver biopsy attending Stobhill Hospital, Glasgow, between 2001 and 2006. Information was collected regarding liver biopsy, CT scan and investigations of the gastrointestinal (GI) tract.
Results: We found 52 cases, of which 47 were eligible for the study. The group had 22 (47%) women. The mean age was 65 (range 26–86) years. The mean survival after liver biopsy was 15 weeks. Liver biopsy of these 47 patients showed adenocarcinoma in 47%, non-small cell and large cell carcinoma in 6%, poorly differentiated carcinoma in 4% and 2% each of squamous cell carcinoma, carcinoid, pancreatic/neuroendocrine

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carcinoma. 85% of 47 had CT scan of chest and abdomen +/− pelvis. In 80% of scans a possible primary was identified. 49% of 47 were referred for GI investigations (upper GI endoscopy, ERCP, flexible sigmoidoscopy, colonoscopy or barium enema). A total of 44 procedures were carried out on these 23 patients. 21% of the patients were found to have GI primaries. The mean survival in those who had GI investigations and those who did not was 19.81 and 9 weeks respectively. However, it may be that those who did not have GI investigations were considered unsuitable for invasive investigations. 22 (47%) of all the biopsies were diagnosed as adenocarcinoma. 81% underwent CT scan. 78% of scans a possible primary was identified. 50% underwent 13 GI investigations. 18% tests yielded GI primary.
Conclusion: Mean survival in liver biopsy-proven patients with hepatic metastasis is extremely poor. Non-invasive investigation using CT scan appears to be more productive in diagnosing a possible primary site than invasive GI investigations.

311 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: IMPROVED PATIENT SELECTION AND 30-DAY MORTALITY RATES AFTER A CHANGE IN CLINICAL PRACTICE

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Introduction: Following the National Confidential Enquiry into Patient Outcome and Death (NCEPOD)[1] of perioperative mortality following percutaneous endoscopic gastrostomy (PEG) insertions, a retrospective audit of our practice was undertaken before and after a change in clinical practice.
Aims & Methods: Case notes, endoscopy records and endoscribe computer database searches were reviewed of PEG insertions from January to September 2004. Re-audit occurred from January to September 2006. We aimed to show a decrease in mortality through improved patient selection.
Results: Case notes, endoscopy records and endoscribe computer database searches were reviewed of PEG insertions from January to September 2004. 43 cases were identified. The 30-day mortality rate, indication for PEG and use of prophylactic antibiotic were recorded for each. Of these, 6/30 (20%) patients died in 30 days or less. These results were presented to the general internal medicine staff and a dedicated referral form was created that focussed on the indication for PEG, current patient status (including the American Society of Anaesthesiology grading) and any complicating factors that might make the procedure high risk, such as recent abdominal surgery, MRSA colonisation and clostridium difficile infection. In addition, all referrals were assessed either by a specialist gastrointestinal nurse or gastroenterology registrar. Re-audit occurred from January to September 2006 and showed a decrease in total number of procedures (27) and 30 day mortality rates (2/27 or 7.4%). The indications for PEG insertion were similar in both groups.
Conclusion: In conclusion, clinician education, a dedicated referral form and specialist review of patients prior to PEG insertion resulted in improved patient selection, fewer procedures and a reduced mortality rate.

1. **Department of Health**. *National Confidential Enquiry into Patient Outcome and Death*, DOH, 2004.

312 SINGLE-CENTRE, SINGLE-OPERATOR ERCP EXPERIENCE IN A DISTRICT GENERAL HOSPITAL

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Introduction: Multicentre series carried out by multiple operators may have confounding factors in determining the risks and benefits of endoscopic retrograde cholangio-pancreatography (ERCP). Data from single-centre, single-operator series can provide a useful estimate of the average risk of complications and failure, and can be used in obtaining informed consent in patients undergoing this procedure.
Aims & Methods: The ERCP experience of a single operator (RS) carrying out over 97% of these procedures in a district general hospital is reported. Preliminary imaging always included transabdominal ultrasonography and may have included computerised tomography, but magnetic resonance cholangio-pancreatography was not routinely available. A total of 638 procedures were carried out for the period December 2000–October 2006. Patient characteristics, indications, procedures, complications and failure rates is reviewed.
Results: Patient demographics: 261 males, 377 females; mean age 59.9 years, range 20–94. Indications (%): gallstone disease, 434 (68.0), carcinoma of the pancreas 37 (5.8), chronic pancreatitis 56 (8.8), pancreatic pseudocyst 30 (4.7), postoperative biliary injury 28 (4.4), cholangiocarcinoma 25 (3.9), ampullary neoplasia 15 (2.4), miscellaneous 13 (2.0). Therapeutic procedures: 577 (90.4). Endoscopic sphincterotomy: 412 (64.6). Needle knife papillotomy, 173 (27.1). Stone extraction, 281 (44.0). Endoscopic stenting: 149 (23.4) (Amsterdam 65, Pigtail 52, Metallic 32). Mechanical lithotripsy: 26 (4.1). Pancreatic endotherapy: 32 (5.0). Previous polya gastrectomy: 6 (0.9). Failed procedures: 9 (1.4). Complications: 14 (2.2) (pancreatitis 5, perforation 4, haemorrhage 3, cholecystitis 1, cholangitis 1).
Conclusion: Patients referred appropriately for ERCP are likely to undergo a therapeutic procedure in over 90% of cases, overall have a 2.2% risk of serious complications requiring in-patient stay and a 1.4% risk of failure. All serious complications were associated with therapeutic intervention except post-ERCP pancreatitis.

313 FIBRED CONFOCAL ENDMICROSCOPY: A FEASIBILITY STUDY TO ENHANCE ROUTINE ENDOSCOPY

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Introduction: The incorporation of magnification and chromoendoscopy has increased the ability of routine endoscopy to detect subtle abnormal lesions in the gastrointestinal tract. However, characterisation of these lesions is difficult even with the use of pit pattern description. The Cellvizio-GI F400 (developed by Mauna Kea Technologies, Paris, France) is a through the scope device with the ability to characterise lesions in vivo by providing ''virtual histology''.
Aims & Methods: The aim of this study was to assess the potential of fibred confocal endomicroscopy for prediction of histology during routine endoscopy. 62 patients underwent endoscopies using the Olympus Lucera video endoscopy system, (gastroscopy 22; colonoscopy 40) and confocal images were obtained using the CellVizio fibred confocal endomicroscopy system. Prior to obtaining confocal images the mucosa was washed with 10% N-acetyl cysteine to clear mucus. Either 10 ml of 0.8% fluorescein intravenously or 0.6% fluorescein topically was given as a fluorophore. ColoFlex S and HD confocal miniprobes were used which have a lateral resolution of 5 μm and 2.5 μm respectively. The Laser Scanning Unit (LSU) functions at 488 nm. Confocal images were graded according to structural and cellular changes.
Results: Digital video images of confocal endomicroscopy were obtained at 12 f/second during the endoscopies from normal and abnormal mucosa. Corresponding biopsies were taken to allow histological comparison with endomicroscopy. The endomicroscopy images obtained resembled the histological appearance allowing in vivo diagnosis of Barrett's oesophagus, intramucosal carcinoma of the oesophagus and stomach, tubular villous adenoma and ulcerative colitis in the colon. 0.8% iv fluorescein gave the best images. No complications resulted from using this imaging system.
Conclusion: In vivo virtual histology can now be obtained using Cellvizio GI confocal endomicroscopy system. This imaging modality may have potential uses in surveillance endoscopies for Barrett's oesophagus and ulcerative colitis. It may also help distinguish hyperplastic from dysplastic adenomas. Further studies are needed in these areas to investigate the possibility of enhancing routine endoscopies.

314 THE SAFETY, EFFICACY AND CLINICAL OUTCOMES OF ENDOSCOPIC MUCOSAL RESECTION: EXPERIENCE FROM A TERTIARY REFERRAL CENTRE

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Introduction: Endoscopic mucosal resection (EMR) has gained increasing acceptance as a minimally invasive approach to the management of superficial carcinomas or premalignant lesions in the gastrointestinal tract. Our aim was to assess the safety, efficacy and clinical outcomes of EMR in our institution.

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Aims & Methods: One hundred consecutive EMRs in 82 patients over a period of 35 months were prospectively analysed. Early (up to 24 h), and delayed (upto 4 weeks) complications were recorded. Completeness of resection (CR) was also assessed based on the histologic specimen and negative biopsy findings on follow-up endoscopic examination.
Results: A total of 51 males and 31 females with a mean (SD) age of 67 (14) (34–87) years underwent the procedure. The lesions were located in the oesophagus (10), stomach (8), duodenum (4), caecum (11), ascending colon (16), transverse colon (15), descending colon (4), sigmoid colon (14), recto-sigmoid (5) and rectum (13). Morphologically, 72 flat, 23 sessile and 5 subpeduncalated lesions measuring 16.6 (9.8) (3–50) mm were resected. Minor bleeding occurred in 12 patients (11 intraprocedure, 1 delayed) of which hemostasis was successfully achieved. Two patients developed perforations that required surgery and recovered. There were no procedure related mortality. Post-EMR histopathology was low-grade dysplasia (55), high-grade dysplasia (HGD) (23), carcinoma (3), carcinoid (3), serrated adenoma (3), metaplastic polyp (7) and unknown (6). Histology was upgraded to either invasive adenocarcinoma or HGD in 13% of the lesions. CR was achieved in 65% as per intention-to-treat analysis and 80% as per protocol analysis.
Conclusion: EMR is a safe and effective technique for resection of superficial GI neoplasms with low complication rates. Long-term follow-up and outcome data are needed.

315 BENEFITS OF PRE-ASSESSMENT IN PEG PATIENTS

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Introduction: A percutaneous endoscopic gastrostomy (PEG) assessment service was set up in our hospital in 2001 to assess all referrals for PEG placement. Prior to this they were performed on an ''on-demand'' basis, when requested by a patient's clinical team. Consequently patients were arriving in endoscopy ill prepared and for ''inappropriate'' reasons. The aim of the service was to reduce these inappropriate referrals, prioritise and ensure all patients were prepared for the procedure.
Aims & Methods: All patients referred between October 2001 and September 2006 were pre assessed by a Nutrition Nurse Specialist (NNS). Those felt to be unsuitable were discussed with the referring team. All patients receiving PEGs were given written information; a pre procedure label was entered into the notes to ensure consent, prophylactic antibiotic treatment, FBC, INR and IV access were all completed before the procedure. Post procedure the endoscopist placed a second label into the notes with detailed after care advice. Patients were followed-up with daily care records by ward staff and a weekly review by the NNS. A comparison between the number of PEG insertions before and after the introduction of pre assessment was made.
Results: In the year prior to pre-assessment 78 PEGs were inserted. The table shows the numbers inserted during the five-year period, the number of unsuitable patients referred for PEGs and the 30-day mortality rate. Reasons for which patients were declined included patients being unfit for the procedure, patient deterioration/death, improvement in patient condition, family decision and medical team decision. The main indications for the PEG procedures over the five year period were cerebrovascular accident (CVA) (43%), general deterioration (9%), MS/MND (8%), lung pathology (7%), head and neck malignancy (6%), dementia (5%) and Parkinson's (4%). Other indications included oesophageal stricture and psychiatric causes. The highest mortality was in stroke patients (63%). All the patients had undergone pre-procedure checks.
Conclusion: Since introduction of a pre-assessment service of PEG patients the number of PEGs being carried out in the hospital has decreased. Also there has been a reduction in 30-day mortality suggesting a better preparation and selection of patients.

316 CHANGE IN BOWEL HABIT TO CONSTIPATION: IS FLEXIBLE SIGMOIDOSCOPY INDICATED?

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Introduction: Change in bowel habit is a common cause of referral to gastroenterology clinics. The prevalence of constipation is higher in women than men and increases with age.[1] National guidelines have defined high risk groups who warrant endoscopic investigation to exclude colorectal carcinoma and include patients over 60 years with a persistent change in bowel habit to looser stools and/or more frequent stools without rectal bleeding.[2] However, there is no consensus on the investigation of change in bowel habit to constipation. A previous study has shown that the yield of endoscopy for investigation of isolated constipation may be comparable with asymptomatic patients who undergo colon cancer screening.[3]
Aims & Methods: We looked at constipation as an indication for flexible sigmoidoscopy, with or without other symptoms. A retrospective case series report was conducted for all flexible sigmoidoscopies between 3 February 1997 and 27 October 2006 performed for a change in bowel habit to constipation alone, or in association with other symptoms including bleeding, weight loss, anaemia and abdominal pain. Cases were found using Endoscribe database. A review of the patients' medical notes and histology was also performed.
Results: 327 patients had a flexible sigmoidoscopy for constipation. The median age was 73 years (range 26–96). The male to female ratio was 1:1.3. In 57.0% cases, isolated constipation was the only indication for endoscopy, and of the remainder, 18.6% were associated with pain, 16.2% overt rectal bleeding, 4.0% weight loss, 1.2% anaemia, and 6.1% other symptoms. Seven cases of colorectal carcinoma were seen (2.14%). However, in all of these cases there was another independent indication for endoscopy: constipation + overt rectal bleeding, 5 cases; constipation + colonic obstruction, 1 case; constipation + weight loss, 1 case. Overall, sigmoidoscopy was normal in 72.0% cases. Other diagnoses included diverticular disease (14.6%), polyps (9.8%) and colitis (1.5%). A review of histology and further imaging is also presented.
Conclusion: Our results confirm that the incidence of colorectal cancer in patients referred with constipation is low. Flexible sigmoidoscopy should only therefore be performed in patients presenting with constipation if other high-risk features are present.

1. **ASGE Guideline**. Guideline on the use of endoscopy in the management of constipation. *Gastrointest Endosc* 2005;**62**:199–201.
2. **National Institute for Health and Clinical Excellence**. *Referral for suspected cancer. a clinical practice guideline*, NICE, June, 2005.
3. **Pepin C**, Ladabaum U. The yield of lower endoscopy in patients with constipation: a survey of a university hospital, a public country hospital and a veterans administration medical center. *Gastrointest Endosc* 2002;**56**:325–32.

317 GASTROINTESTINAL BLEEDING AND COAGULOPATHY: WORTH GETTING OUT OF BED FOR?

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Introduction: Upper gastrointestinal bleeding (UGIB) in the setting of coagulopathy is most often a consequence of liver disease and portal hypertension. The role of immediate, therapeutic endoscopy in this population is paramount. However, UGIB also occurs in a fifth of patients with bleeding disorders or on long-term anticoagulation.[1] Immediate endoscopy has been shown to have a lower yield in this group of patients.[2]
Aims & Methods: The aim of this study was to establish the yield of upper gastrointestinal endoscopy for UGIB in the presence of coagulopathy at a

Abstract 315

Year	01/02	02/03	03/04	04/05	05/06
Total referrals (n)	85	59	50	52	55
PEGs inserted (n)	61	47	36	34	40
Unsuitable patients (n)	22	7	13	14	15
Failed procedures (n)	2	5	1	4	0
30-day mortality rate (%)	20	32	17	21	10

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Abstract 317

	Significant findings	Non-significant findings	Total
Normal coagulopathy*	30	44	74
Coagulopathy*	8	30	38

*p<0.05.

single UK centre. A retrospective analysis of all patients presenting with haematemesis or melaena within a six month period was conducted. Patients with portal hypertension evidenced by oesophageal varices, gastric varices or portal hypertensive gastropathy were excluded. Patients were defined as having coagulopathy if the prothrombin time (PT) or activated partial thromboplastin time (APTT) were prolonged immediately prior to endoscopy. Charing Cross Hospital haematology laboratory reference ranges were used. Significant endoscopic findings were defined as: oesophageal ulcer, gastric ulcer, duodenal ulcer, carcinoma, angiodysplasia and Mallory–Weiss tear. The presence of significant endoscopic findings was compared between the two groups. Statistical analysis was performed on the data using Fisher's exact test.
Results: Of the cases reviewed, 112 were eligible for inclusion in the study. There was no significant difference in demographics between the patient groups. Abnormal coagulation was found in 38 (34%) of patients. Significant endoscopic findings were present in 21% of patients with abnormal coagulation compared with 40% of patients with normal clotting ($p = 0.032$).
Conclusion: With the exception of portal hypertension, endoscopy for UGIB in the presence of coagulopathy has a lower yield. Furthermore, the group of patients with negative initial endoscopy have been shown to have a favourable outcome.[2] Clinical prognostic markers remain the most accurate method of risk stratification for endoscopy in UGIB. Nevertheless, these data remind us of the importance of reversal of coagulopathy in UGIB of any cause.

1. **Levine MN**, *et al. Chest* 1995;**108**(Suppl 4):276S–290S.
2. **Thomopoulos KC**, *et al. World J Gastroenterol* 2005;**11**:1365–8.

318 ACUTE OESOPHAGEAL NECROSIS OR JUST ANOTHER BLACK OESOPHAGUS?

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Introduction: The literature suggests that black oesophagus or acute oesophageal necrosis (AEN) is a rare condition. It was our impression that it is a more common phenomenon, particularly in inpatients.
Aims & Methods: We prospectively collected cases of ''black oesophagus'' identified during endoscopy at the Royal Berkshire Hospital (RBH) January 2005–July 2006. The RBH is a district general hospital serving a population of over 500 000; the unit performs >3000 OGDs annually. Endoscopic images and histology were obtained where possible
Results: Nine cases (6 men) were identified, median age 85 (52–93), see table. In six patients (* in table) the oesophagus was biopsied and all comprised predominantly acutely inflamed ulcer slough. In four cases (2, 3, 8, 9) there was also acutely inflamed oesophageal squamous mucosa; in two cases (4, 7) there was no epithelium. There was no evidence of Barrett's oesophagus or malignancy. Special stains for iron, melanin, and bile were all negative. Three cases (4, 8, 9) contained hyphae and spores compatible with fungal infection.
Conclusion: True AEN is confirmed by diffuse oesophageal necrosis and is reportedly rare. The appearance of a black oesophagus however appears more common and the underlying pathogenesis may be difficult to ascertain. The histology from all these cases confirmed ulceration. Microscopic presence of abundant extracellular yellow/brown pigment in three cases is significant but the special stains were inconclusive and do not discount extrahepatic bile or exogenous pigment. There was insufficient non-ulcerated tissue to reliably assess for ischaemia. One final consideration is that the black appearance is not due to pigment but rather reflects the state of ischaemia within the tissue, in a manner analogous to gangrenous necrosis. Black oesophagus may represent a spectrum of pathologies but also may represent true AEN more commonly than previously thought. This may be due to poor recognition, underreporting or difficulty in obtaining diagnostic histology. Although the natural history is poorly understood and some cases heal completely, black oesophagus and AEN appear to be generally associated with significant comorbidity which may dictate outcome. Histology should be obtained to help clarify the diagnosis.

319 WHAT ARE THE KEY COMPONENTS OF HANDS-ON COLONOSCOPY TRAINING?

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Introduction: Existing colonoscopy training may be poor and little is known about the components of good training, with much of the endoscopy literature based on expert opinion. Practical skills training is a major component of learning colonoscopy. The sport and motor skills literature contain an extensive evidence-base relating to this, some of which may be relevant to endoscopy.
Aims & Methods: The aim was to identify the key components involved in hands-on colonoscopy training and to examine training from three viewpoints. Firstly evidence to support endoscopic expert opinion; secondly the relevance of data from the sport and motor skills literature and lastly any other concepts not previously considered. Qualitative research was used to identify the key components of hands-on colonoscopy training and how these components relate to each other. Twenty hands-on training sessions and feedback from colonoscopy training courses were observed and analysed in depth. Framework analysis was used and data analysis followed the process of familiarisation; identifying a thematic framework; indexing; charting and mapping and interpretation. Trainers and learners also used visual analogue scales to assess their training and feedback sessions for 60 procedures on training course and 60 procedures on service lists.
Results: Fifteen key components of hands-on training were identified. The most prevalent of these were the use of description; directions; questions; motivation; explanation of a principle and patient related. Many of the components, such as using questions for training, have previously been identified as being important by expert endoscopists' opinion. Some components, such as the importance of dual task interference, have been recognised in the sport and motor skills literature. Other components, such as the role of explanation, have not previously been demonstrated elsewhere. These components were used differently by trainers and learners. The correlation between trainers' and learners' assessment of training and feedback was poor but both groups regarded these elements to be better on courses than on in-service lists.

Abstract 318

Patient (age)	Underlying diagnosis	Indication for endoscopy	Survival post-endoscopy
1 (85)	Back surgery	Haematemesis	Well at 18 months
2* (86)	Metastatic cancer	Jaundice	RIP 24 days
3* (68)	Bladder cancer	Haematemesis	RIP 38 days
4* (79)	Diarrhoea	Haematemesis	RIP 1 day
5 (85)	Fracture neck femur	Haematemesis	RIP 22 days
6 (81)	Pancreatic cancer	Jaundice	RIP 4 days
7* (52)	Diabetic ketoacidosis	Melaena	Well at 4 months
8* (93)	Dysphagia	Dysphagia	None available
9* (90)	Fracture neck femur	Haematemesis	RIP 34 days

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Conclusion: This is the first study to establish the key components of hands-on training for colonoscopy. The components identified included novel considerations as well as those present in expert endoscopy opinion and the sport and motor skills literature. In general the study supports the notion that critical components of skills training outside medicine may be applicable to endoscopy. Knowledge and awareness of the components identified has implications for colonoscopy training and perhaps more broadly in other medical skills training.

320 TRAINEE COLONOSCOPY AUDIT: NORTH EAST THAMES

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Introduction: Highly competent colonoscopists will be required to deliver the national colorectal cancer screening programme. A recent national audit demonstrated caecal intubation rates significantly below the 90% target set out by JAG. A study of North West Thames trainees concluded that a combination of improved training and self directed learning was required to increase competence.
Aims & Methods: Our aim was to assess North East Thames (NET) trainees' level of expertise in colonoscopy and the nature of their training. NET trainees were assessed retrospectively using a 21 point questionnaire designed to assess trainees overall endoscopy experience, record keeping, self-assessment of performance (using the ''cusum'' method) and the nature of their supervision, training and assessment. It was sent by email on three occasions (July–Sept 2006) and completed electronically.
Results: 29/61 (47.5%) trainees responded. The median year of training was 3.5 (range 0.33–7.17). 28/29 respondents were training in colonoscopy with 20/28 trainees performing colonoscopy independently. 10/20 (50%) had performed fewer than 100 procedures before being left unsupervised. The level of supervision for trainees first 100 colonoscopies was assessed by reviewing 66 trainee-trainer experiences. The trainer was in the room, in the department, in the hospital or unavailable in 31 (47%), 30 (45%), 5 (8%), and 0 experiences respectively. The quality of training for trainees first 100 colonoscopies was assessed by reviewing 61 trainee-trainer experiences: the trainer explaining and talking the trainee through overcoming the problem in 39/61 (60%), taking the scope and overcoming the problem prior to explaining in 17/61 (27%), taking the scope but not explaining in 3/61 (5%) or taking the scope and completing the procedure in 5/61 (8%). 18/28 trainees had attended a colonoscopy course and 4/28 were using the ''cusum'' method. All 20 independent trainees had been confirmed as competent in intubation technique. 6/20 and 3/20 had not been assessed as competent in polypectomy and extubation technique respectively. 16/28 trainees kept a record of their complication, caecal and ileal intubation rates. For independent trainees the average caecal and ileal intubation rates were 90.2% and 63.4% respectively.
Conclusion: Trainees are not performing enough fully supervised colonoscopies prior to independent practice. Trainers are taking the scope in 40% of experiences when a problem is encountered suggesting there is potential to improve training. Record keeping, course attendance and use of the ''cusum'' method are under utilised. Assessment of competency is not yet being undertaken in all aspects of colonoscopy. However, the recommended caecal and ileal intubation rates are being met by independent trainees. Thus, although there is still some way to go, an overall improvement in colonoscopy training is evident.

321 A RANDOMISED, SINGLE-BLIND COMPARISON BETWEEN A LOW VOLUME POLYETHYLENE GLYCOL AND ASCORBIC ACID BOWEL PREPARATION (MOVIPREP) AND PICOLAX IN GUT CLEANSING PRIOR TO COLONOSCOPY

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Introduction: Colonoscopy is an important tool for the diagnosis and evaluation of diseases of the colon. For a successful colonoscopy, it is essential that complete cleansing of the colon is achieved prior to the procedure with minimum inconvenience to the patient. If all the mucosa cannot be seen, the colonoscopy may need to be repeated as pathological findings might have been missed. Currently available bowel preparations are unsatisfactory.
Aims & Methods: This was a single-blind, parallel-group study comparing Moviprep (polyethylene glycol 3350 solution plus ascorbic acid and electrolytes) with Picolax (sodium picosulfate + magnesium citrate) in 65 adult male and female patients undergoing elective colonoscopy. Patients were randomised to treatment allocation in a 1:1 ratio. The physicians who performed the colonoscopy and rated the cleansing were unaware of the preparation allocated. The degree of cleansing was scored for each colonic segment, and the overall success of treatment for each patient was based on these individual scores. The treatment was defined as an overall success (100% colonic mucosa visualised) if all segments had Grade A or Grade B, indicating a good cleansing. Preparation was defined as a failure if one or more segments had bad cleansing (Grade C or Grade D).
Results: The percentage of patients who had an overall successful preparation was comparable for Moviprep (27/32 patients; 84.4%) and Picolax (24/33 patients; 72.7%) 11.2, +34.5; $p=0.367$) (Fisher's exact test: treatment difference +11.6, 95% CI). However, the quality of colon cleansing was significantly better following Moviprep (Wilcoxon signed rank test: $p=0.018$); 46.9% of patients who received Moviprep received a grading of ''A'' compared with 15.2% of patients who received Picolax. Furthermore, analysis of the individual colon segments showed a significant difference in the quality of cleansing for the ascending colon (Wilcoxon signed rank test: $p=0.024$) and caecum ($p=0.003$) in favour of Moviprep. Patient acceptability ratings tended to favour Picolax, but the patients were not blind to treatment allocation and different dietary regimens were adopted for the two compounds. The safety and tolerability profile of the two treatments was similar, with headache, nausea and anal discomfort, being the most frequent adverse events (Moviprep 9, 7 and 2 patients and Picolax 12, 5 and 4 patients respectively). One patient in the Picolax group, who was hyponatraemic prior to the bowel preparation, experienced worsening of hyponatraemia. This was classed by the investigator as probably related to treatment.
Conclusion: Moviprep provides gut cleansing that is at least as good as Picolax. Moviprep offers superior cleansing in the proximal colon, which offers important advantages in the clinical setting.

Gastrointestinal physiology posters

322 JNK MAPK AND CPLA2 REGULATE CHLORIDE SECRETION IN T_{84} COLONIC EPITHELIAL CELLS

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Introduction: Inflammation of the intestine is typically associated with increased fluid secretion, manifesting clinically as diarrhoea. Chloride (Cl-) secretion is the predominant driving force behind this fluid secretion. Activation of G_q Protein Coupled Receptors (G_qPCRs) by neuroimmune mediators induces transient Cl-secretory responses in intestinal epithelial cells. These responses are limited by an antisecretory pathway mediated by epidermal growth factor (EGFR) and mitogen activated protein kinases (MAPKs) including ERK1/2 and p38. c-Jun N-terminal kinase (JNK) is also a member of the MAPK family while cytosolic phospholipase A_2 ($cPLA_2$) is a common downstream effector of EGFR and MAPK signalling in other systems. Their roles in regulating epithelial secretion are unknown.
Aims & Methods: The aim of this study was to determine if JNK and $cPLA_2$ regulate G_qPCR-induced Cl- secretion in intestinal epithelia. Experiments were performed on monolayers of T_{84} colonic cell lines grown on permeable supports. Protein phosphorylation was analysed by Western blotting. Cl- secretion was measured as changes in short-circuit current (Isc) across voltage-clamped T_{84} cells mounted in Ussing chambers.
Results: Western blot analysis revealed that the prototypical G_qPCR agonist carbachol (CCh; 100 μM) induced phosphorylation of both 46 kDa and 54 kDa isoform of JNK ($n=5$; $p<0.01$) and of $cPLA_2$ ($n=3$; $p<0.05$). Furthermore, pretreatment of voltage-clamped T_{84} cells with SP600125 (2 μM), a specific JNK inhibitor, and with AACOCF3 (100 μM), a specific $cPLA_2$ inhibitor, significantly potentiated Isc responses to CCh. The maximal response to CCh in SP600125-pretreated cells was 54.1 (5.8) $\mu A/cm^2$ compared with 34.0 (3.5) $\mu A/cm^2$ in control cells ($n=6$;$p=0.01$) while maximal responses to CCh in AACOCF3-pretreated cells increased by 45.2 (7.8)% compared to those in control cells ($n=5$; $p<0.05$).
Conclusion: Both JNK and $cPLA_2$ are components of a signalling pathway that limits the extent of G_qPCR-induced Cl- secretory responses in intestinal epithelial cells. Pharmacological manipulation of MAPKs and/or $cPLA_2$ may prove useful in the treatment of transport disorders assocaited with diarrhoea.

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Abstract 323

Symptom subtype	% with spasm	% with disordered peristalsis	% with abnormal LOSP	% with abnormal reflux	% with normal findings
Reflux	18.3	50.7	37.3	51.1	11.9
Atypical chest pain	33.9	32.2	19.0	23.9	37.2
Dysphagia	47.0	57.6	12.9	30.0	7.6
Achalasia	40.4	82.5	66.7	No pH studies	1.8

323 DIAGNOSTIC VALUE OF OESOPHAGEAL PHYSIOLOGY STUDIES: AN EIGHT-YEAR PROSPECTIVE STUDY

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Introduction: Physiology studies are an aid in the diagnosis and management of patients who suffer from gastro-oesophageal symptoms. The purpose of this study was to evaluate the diagnostic value of oesophageal pH and manometry at a university hospital physiology unit over an eight-year period.
Aims & Methods: Between July 1996 and October 2004 there were 1116 referrals for 24 h oesophageal pH/manometry to investigate four cardinal symptoms. These were symptomatic gastro-oesophageal reflux (n = 802), atypical chest pain (n = 137), dysphagia (n = 153), and achalasia (n = 74).
Results: Studies were successfully completed in 92.4%. Reasons for failure were patient intolerance (3.3%) and recording malfunction (4.3%). Results are shown in the table.
Conclusion: Symptoms alone are a poor predictor of abnormal oesophageal function. 24 h pH and manometry studies are valuable in defining the physiological abnormality in order to allow appropriate treatment.

324 ASSESSMENT OF RECTAL SENSORY AND MOTOR FUNCTION USING TWO DIFFERENT BAROSTAT SYSTEMS

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Introduction: Barostat studies have been used extensively to study visceral sensori-motor function in man. Currently, two devices are commonly used: the dual stage rigid cylinder type (capacity 100 ml; Synectics) and the single stage matched reservoir type (capacity 1200 ml; G&J). The former has the theoretical disadvantage of error due to non pre-pressurising of that cylinder excluded from the circuit. Comparing the two systems in vivo is important to determine the validity of comparisons of data, especially contemporary versus historical, within retrospective comparisons, multicentre studies, and meta-analysis of literature.
Aims & Methods: The aim of the study was to determine the reproducibility of assesment of rectal sensory and motor function using the two systems in healthy volunteers. Four rectal barostat studies were performed on 7 healthy volunteers (3F, 4M; median age 46 years), using the 2 barostat systems (dual stage (system A) and single staged matched reservoir (system B)) randomly twice (on two consecutive days, repeated two weeks apart). After conditioning distension, and determination of the operating pressure (minimum distending pressure +2 mm Hg), an ascending method of limits phasic distension protocol was used, with 4 mm Hg increments up to maximum tolerated pressure. Between phasic distensions, baseline pressures were maintained at operating pressure, and volumes (residual volume) recorded. Pressures and volumes at different sensory thresholds (first sensation, defaecatory desire, maximum toleration), as well as residual volumes, were compared between the two systems within individuals. Compliance curves were also assessed.
Results: Operating pressures (A: 6.4 ± 0.2 mm Hg, B: 6.7 (0.2) mm Hg, p = 0.84) and compliance (A: 7.7 (0.6) ml/mm Hg, B: 7.9 (0.6) ml/mm Hg, p = 0.42) within subjects were equivalent (paired t test); Bland-Altman statistic showed a mean difference in compliance of −0.2 ml/mmHg (95% limit of agreement −2.3 to 1.9). Similarly, pressures and volumes at sensory thresholds were similar within subjects using the two barostat systems ($p>0.05$). Residual volumes at operating pressures were also similar: A: 109 (14) ml, B: 120 (13) ml ($p>0.05$).
Conclusion: In vivo assessment of rectal biomechanical properties was equivalent when determined by the two most commonly used barostat systems. At least with regard to the ascending method of limits, studies performed using these different systems are comparable.

Inflammatory bowel disease posters

325 MTHFR POLYMORPHISMS ARE OF PHARMACOGENETIC VALUE IN AZATHIOPRINE TREATMENT IN INFLAMMATORY BOWEL DISEASE

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Introduction: Polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene has clinical implications in vascular disease (through hyperhomocysteinaemia) and immunosuppression (primarily methotrexate). Importantly, the two common polymorphisms, MTHFR 677C>T and 1298A>C are predicted to have different metabolic consequences. The MTHFR 677TT encodes a thermolabile variant and has been associated with hyperhomocysteinaemia and toxicity to methotrexate, and decreased red cell TPMT activity. The MTHFR 1298CC variant genotype has been associated with methotrexate toxicity but not homocysteinaemia. This raises the possibility that MTHFR 677C>T impacts on both red cell and nucleated cell activities while the MTHFR 1298A>C may be more relevant in nucleated cells. We have investigated the influence of MTHFR polymorphism on tolerance and clinical response to azathioprine treatment for inflammatory bowel disease (IBD).
Aims & Methods: 216 patients were entered into a prospective study of 2 mg/kg azathioprine in IBD. All patients were genotyped for the MTHFR 677C>T and 1298A>C polymorphisms and haplotypes correlated with strictly defined clinical response and risk of withdrawal due to adverse effects.
Results: A protective effect of the MTHFR 677C>T polymorphism against adverse effects was noted (15.7% *v* 5.3%, p = 0.032 for homozygous, p = 0.067 for heterozygous), not present for MTHFR 1298A>C. Conversely, there was a strong relationship between MTHFR 1298A>C and improved clinical response (64% *v* 39%, p = 0.002, OR 3.35). No relationship was observed for MTHFR 677C>T and clinical response.
Conclusion: Contrary to a recently published study, our results suggest that genetic variation in folate metabolism influences clinical response to azathioprine therapy. The MTHFR 677C>T polymorphism offers some protection from adverse effects on azathioprine, perhaps by restricting red cell S-adenosylmethionine (SAM) pools, which in turn may decrease TPMT activity and the production of toxic methylated thiopurine metabolites. The MTHFR 1298A>C polymorphism, on the other hand, appears to confer improved clinical response to azathioprine, possibly by reducing thiopurine methylation and inactivation in nucleated cells, and may be an important pharmacogenetic marker in addition to TPMT.

326 GENOMIC DNA HYPERMETHYLATION IN COLORECTAL MUCOSA OF PATIENTS WITH ULCERATIVE COLITIS (THE BORICC STUDY)

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Introduction: Alterations in DNA methylation patterns are seen commonly in tumours and may be affected by folate status. Folate deficiency can result

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Abstract 326

Subject group	Age (SD)	Genomic DNA methylation (DPM $\times 10^3/\mu g$ DNA)	RCF concentrations (ng/ml)
Ulcerative colitis (n = 24) 17 male: 7 female	58 (12)	4.1* (2.6–6.3)	190* (160–227)
Control (n = 220) 118 male: 102 female	51 (13)	14.5 (13–15.8)	346 (330–370)

*Statistically significant. Figures in brackets indicate 95% confidence interval.

in both genomic DNA hypomethylation as well as aberrant methylation of specific genes. Global DNA hypomethylation has previously been reported in rectal mucosa of patients with active and quiescent ulcerative colitis (UC) but folate status was unknown[1] In UC, folate status may be adversely affected by chronic inflammation, malabsorption and certain drugs.
Aims & Methods: To assess the genomic DNA methylation status in the macroscopically normal mucosa and folate status in a cohort of UC patients. 244 subjects were recruited (24 UC patients and 220 normal controls). Colorectal mucosal biopsies were obtained and DNA extracted. Genomic DNA methylation was measured using the tritium-labeled cytosine extension assay (3[H] dCTP) as described by Pogribny *et al*.[2] In this assay, the extent of 3[H] dCTP incorporation into DNA is inversely proportional to the global DNA methylation status.
Results: Mean duration of UC was 9 years with on average 1 flare-up/year and mean SCCAI score was 2. Genomic DNA methylation (as measured by 3[H] dCTP incorporation) was higher in UC patients than in control subjects ($p<0.001$). Folate status was lower in UC patients ($p<0.001$) compared with controls.
Conclusion: Low folate status and genomic hypomethylation have both been shown to be associated with colorectal cancer[3] although recent data have challenged this concept, suggesting a protective effect of low folate status on risk of colon cancer.[4] We have shown a higher methylation status in UC patients, with a corresponding lower folate status compared to control subjects. Our findings are in contrast with a previous report,[1] but our study size was significantly larger, involved quiescent UC and used a more reproducible assay. Further investigation is required to determine the precise effects of folate status on genomic methylation and its association with colorectal cancer.

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1. **Gloria L**, *et al. Cancer* 1996;**78**:2300–6.
2. **Pogribny I**, *et al. Biochem Biophys Res Commun* 1999;**262**:624–8.
3. **Pufulete M**, *et al. Gastroenterology* 2003;**124**:1240–8.
4. **Van Guelpen B**, *et al. Gut* 2006;**55**:1461–6.

327 USE AND SAFETY OF INFLIXIMAB FOR INFLAMMATORY BOWEL DISEASE IN SOUTH EAST ENGLAND (2): PREDICTORS OF RESPONSE, SAFETY AND USE OF IMMUNOSUPPRESSION IN CLINICAL PRACTICE

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Introduction: Infliximab (IFX) is now well established as treatment for moderate to severe IBD in the UK. However, use in practice varies considerably particularly as optimal usage based on clinical trials is at variance with NICE guidance upon which local protocols are often based.
Aims & Methods: To assess the impact of local variations in treatment regimes for IFX on broad clinical outcome and to identify clinical characteristics that may predict the likelihood of remission. A retrospective multicentre audit of clinical notes was performed.
Results: 122 (55%) were females. 200 (90%) had Crohn's disease and 22 ulcerative colitis. 152 (69%) patients responded to IFX (assessed by HBI/CDAI/arbitrary physician assessment). 40 (18%) patients had a primary non-response and 20/152 responders (13%) suffered a secondary loss of response to therapy. A comparison of episodic and scheduled infusions for both induction and maintenance of a response showed no difference between the two approaches ($p=0.4$ for response induction and $p=1.00$ for response maintenance). Concurrent immunosuppression did not affect success of induction (immunomodulators *v* none $p=1.00$), however, concurrent azathioprine use prevented a loss of response when compared with no immunomodulation ($p=0.001$). No significance was noted for the other immunomodulators. Early Infliximab use and current smoking status did not influence response. Patients with isolated ileal disease (12/19 patients) had a lower chance of response than patients with isolated colonic disease (40/45 patients) ($p=0.03$, RR 0.3, CI 0.19 to 0.7). 57 episodes of side effects were noted (0.6%). Side effects led to treatment withdrawal in 8 patients. Concurrent Azathioprine increased the risk of minor infectious complications when compared with Infliximab monotherapy (25/39 *v* 11/34, $p=0.0098$, RR = 1.98, CI 1.1 to 3.4). Methotrexate appears to protect against minor infections when compared in a similar fashion (1/20 *v* 11/34, $p=0.0215$, RR = 0.15, CI 0.2 to 1.1). Regular scheduled infusion protocols did not reduce risk of hypersensitivity reactions when compared with infusions on relapse ($p=0.9$). Regular scheduled infusions appeared to increase the risk of infectious complications ($p=0.0003$, RR = 0.16, 95% CI 0.05798 to 0.4806).
Conclusion: This suggests interesting possibilities for optimising infliximab use in IBD. Isolated colonic disease increases chances of a response and concurrent Azathioiprine use helps maintain that response with a higher likelihood of infectious complications. Low dose Methotrexate, on the other hand, may offer a previously unsuspected protection against minor infections. The incidence of adverse effects is reassuringly low.

328 THE PHARMACOGENETICS OF FOLATE AND PURINE METABOLIC PATHWAYS IN METHOTREXATE THERAPY OF INFLAMMATORY BOWEL DISEASE

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Introduction: Methotrexate acts by inhibiting dihydrofolate reductase and the purine and pyrimidine biosynthetic pathway. Methotrexate (MTX) acts by inhibiting dihydrofolate reductase and the purine and pyrimidine biosynthetic pathway. Response in inflammatory bowel disease can be limited by side effects leading to drug withdrawal (10% of patients) or non-response (45%). Polymorphisms in enzymes involved in folate metabolism and transport have been shown to predict clinical outcome. In this retrospective study, clinical outcome and tolerance to MTX were correlated to genetic variation in MTHFR, ATIC (purine synthesis), and TS (pyrimidine synthesis).
Aims & Methods: Data were available on 171 patients with inflammatory bowel disease treated with methotrexate for more than 12 weeks. Response was defined as a withdrawal of steroids with a Harvey–Bradshaw Index <4. Hepatotoxicity (ALT>3 times the upper limit of normal); neutropaenia and other less frequent side effects were recorded. Patients were genotyped for the MTHFR 677C>T, ATIC 347C>G, TSER*2/*3 and TYMS 3′-UTR 6 bp in/del genotypes. Genotypes were tested for association with clinical outcomes and side effects using recessive and dominant models.
Results: Forty five patients suffered side effects. Five patients experienced leucopenia and 12 developed abnormal liver function tests during therapy. 101/171 (60%) of patients responded to therapy. The ATIC 347C>G mutation correlated with response to therapy as a recessive trait. 39/54 (72%) of homozygous mutants responded to treatment compared with 8/18 wild types ($p=0.04$, RR = 1.6, CI 1.925 to 0.9407). The MTHFR 677C>T SNP correlated with a lack of response. 41/65 (65%) of wild types responded compared with 10/26 (38%) of homozygous mutants ($p=0.03$, RR = 1.340, CI 1.005 to 1.785). No other associations were found in recessive or dominant models with either response to therapy or occurrence of side effects.
Conclusion: These findings suggest that genetic variation in folate metabolism does influence response and tolerance to MTX. Further studies may define those loci which are of true clinical importance or which might have an additive effect as part of a pharmacogenetic index as proposed for MTX use in rheumatoid arthritis.

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329 HLA-G 14BP INSERTION-DELETION POLYMORPHISM INFLUENCES RESPONSE TO METHOTREXATE IN INFLAMMATORY BOWEL DISEASE

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Introduction: HLA-G antigens have a recognised role in chronic inflammation and auto-immune diseases. Membrane bound and soluble HLA-G has been shown to correlate with increased IL-10 levels. A 14-bp deletion polymorphism in exon 8 at the 3′ UTR of the HLA –G gene has been associated with the development of auto immune disease. It has also been associated with efficacy of Methotrexate (MTX) therapy in rheumatoid arthritis possibly via increased IL-10 levels. MTX is well established as a standard second line immunosuppressant in the treatment of inflammatory bowel disease (IBD).
Aims & Methods: The aim of this study was to determine the influence of the HLA-G 14 bp ins-del polymorphism on clinical response to MTX in patients with IBD and compare this to any effect amongst those receiving azathioprine (AZA). 171 patients with IBD treated with Methotrexate and 96 treated with Azathioprine were included. Clinical response was defined as complete steroid withdrawal for at least 3 months with a duration of immunomodulatory therapy of at least 3 months. Genotyping was performed by fluorescent PCR and size-based allelic discrimination by capillary based liquid polyacrylamide gel electrophoresis. The two-sided Fisher's exact test was used to calculate significance. Odds ratios are reported.
Results: The polymorphism correlated significantly with response to therapy in the MTX treated group. No correlation was found in the AZA treated group (p = 0.5238, RR = 0.8373, 95% CI 0.5696 to 1.23).
Conclusion: The hypothesis that the 14 bp ins/del mutation influences clinical response to MTX therapy is confirmed and suggests that upregulation of IL-10 expression plays an important role in the mechanism of action of MTX in IBD. The lack of a correlation with response to AZA, which has a differing mode of action, is in keeping with this. The SNP will require further validation in a large series to confirm its role as a clinically useful pharmacogenetic marker of MTX efficacy.

Abstract 329 Methotrexate-treated group

Genotype	Responders	Failed	Total
14 bp del/del	41 (38%)	22 (20%)	63 (58%)
14 bp ins/ins	17 (16%)	28 (26%)	45 (42%)
Total	58 (54%)	50 (46%)	108 (100%)

p value = 0.0063, RR = 1.723, CI 0.136 to 2.613.

330 USE AND SAFETY OF INFLIXIMAB FOR INFLAMMATORY BOWEL DISEASE IN SOUTH EAST ENGLAND (1): ADHERENCE TO RECOMMENDED GUIDELINES

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Introduction: Few data exist reporting the use in practice of infliximab in the UK with much emphasis placed on registry data reported from the US. Here we report the preliminary results of a regional audit.
Aims & Methods: The aim of this study was to undertake a regional audit of infliximab usage in South East England assessing adherence to NICE guidelines and recommended protocols for safe and effective use.
Results: 222 patients (122 females) were included from 7 centres. 200 (90%) had Crohn's disease and 22 ulcerative colitis. 129 (58%) were less than 40 years of age. 986 infusions were recorded. Adherence to NICE guidance was variable. Objective pre-treatment scoring systems (HBI/CDAI) were used in 112/222 patients (51%) with a recorded pre-treatment HBI>8 in 61/112 (55%) patients. Failure/intolerance of immunosupression was documented in 201/222 (91%) and unsuitability/unwillingness for surgery in 66 patients (30%). Pre-treatment tuberculosis screening was performed in only 108/220 patients (49%). Active IBD in 165 patients (75%) and fistulising disease in 39 patients (18%) were the chief indications. 62 (28%) patients were on concurrent steroids at induction, of whom 9 (14%) remained steroid dependent. Azathioprine was the predominant immunomodulator (101 patients—46%) used for antibody suppression. Methotrexate (19/220 patients) and 6-Mercaptopurine (21/220 patients) were less frequently used. 40 patients (18%) were not on immunomodulators. Induction was performed as per NICE guidelines in 89 (40%) patients and on a regular schedule in 52 (24%) patients. The remainder (40 patients) received a single infusion. Of the 152 responders, 31 (33%) were maintained on a variety of regimen. Pre-treatment with IV hydrocortisone was used in 21 patients (12 as local hospital policy, 7 after a prolonged interval between infusions and 2 after an infusion reaction). 152 patients (69%)responded to Infliximab (assessed by HBI/CDAI/arbitrary physician assessment).
Conclusion: Considerable variation exists between centres in the use of Infliximab for IBD. Adherence to NICE Guidance is variable and pre-treatment screening for tuberculosis is often lax. The take up of maintenance infusions has been poor in the past but is now increasingly seen. There is an underrepresentation of fistulising disease among the indications for therapy.

331 POLYMORPHISMS IN THE PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA GENE ARE ASSOCIATED WITH ILEAL CROHN'S DISEASE

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Introduction: Peroxisome proliferator-activated receptor (PPAR) gamma is a nuclear receptor with inhibitory effects on NFkB, c-Jun and c-Fos signalling. It is expressed in the colon and ileum but is impaired in inflammatory bowel disease.[1, 2] It is activated through bacterial TLR4 signalling as well as directly by bacterial products and components of food.[3] Linkage to a region incorporating the PPARγ gene has been demonstrated in a mouse model of ileitis[2] and is syntenic to the 3p21–26 IBD susceptibility locus in humans. A small case-control study has shown significant association between polymorphisms in this gene and CD.[2]
Aims & Methods: Our aim was to study PPARγ polymorphisms in cohorts of well characterised CD and ulcerative colitis (UC) patients. Haplotype tagging single nucleotide polymorphisms (SNPs) were genotyped in 608 CD patients, 670 UC patients and 1131 controls using the MALDI-TOF iPLEX platform. All patients and controls were unrelated, white, non-Jewish and from Oxfordshire. Five intronic SNPs were identified from the two major haplotype blocks in the PPARγ gene (3 in block 1 and 2 in block 2). The genotyping rate was >96% and the genotypes were all in Hardy–Weinberg equilibrium.
Results: No association with individual SNPs was seen overall although a weak association with a common 2 SNP haplotype in block 2 was seen in CD (p = 0.05). For block 1, subphenotype analysis, showed a protective effect of the minor allele of each SNP (the SNPs being in tight linkage disequilibrium, r^2 0.95) for ileal CD (p<0.005, OR>0.59, CI 0.4 to 0.86), stricturing behaviour (p<0.006, OR>0.57, CI 0.37 to 0.87) and the need for ileal resection (p<0.008, OR>0.46, CI 0.25 to 0.84) although these three variables were not independent of each other. Stratification of the cohort by known variants demonstrated that the ileal association was seen in those carrying the IBD5 risk haplotype and was strongest for the block 1 SNPs (p = 0.001, OR 0.51, CI 0.32 to 0.78). There was a trend for a protective effect of the block 1 SNPs and ileal disease in patients negative for the common NOD2 variants (p = 0.02, OR 0.60, CI 0.37 to 0.95).
Conclusion: SNPs in a single haplotype block of the PPARγ gene are dependently associated with ileal CD, stricturing behaviour and ileal resection and there is epistasis with the IBD5 risk haplotype. These disease associated SNPs are unlikely to have functional effects on the PPARγ gene themselves but may be in LD with functional SNPs either within the gene or in neighbouring genes. Direct sequencing and further fine mapping in CD is required.

1. **Dubuquoy L**, *et al. Gastroenterology* 2003;**124**:1265–76.
2. **Sugawara K**, *et al. Gastroenterology* 2005;**128**:351–60.
3. **Dubuquoy L**, *et al. Gut* 2006;**55**:1341–9.

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332 EFFECT OF ANTI-TNF ANTIBODIES ON T LYMPHOCYTE CELL CYCLE AND RELATION TO APOPTOSIS

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Introduction: Crohn's disease is characterised by an excess of lamina propria lymphocytes. Anti-TNF agents have had variable clinical efficacy in the treatment of Crohn's disease but not in rheumatoid arthritis. Considerable work to explain the differential efficacy of these agents has focused on the induction of lymphocyte apoptosis. We investigate the differential effects of three anti-TNF agents (infliximab, adalimumab and etanercept) on stimulated lymphocyte cell cycling.
Aims & Methods: Peripheral blood mononuclear cells were isolated from four healthy individuals using lymphoprep separation. CD4 lymphocytes were then isolated by positive selection using beads. T-lymphocytes were stimulated using antibodies against CD3 and CD28. Medium alone, human control IgG1 or anti-TNF agent at 10 μg/ml was added to the cells. After 72 h the cells were fixed. DNA staining was performed using propidium iodide. Samples were run on a flow cytometer and data analysed using cell cycle analysis software to give the percentage of cells in G1/0, S and G2 phases. For apoptosis studies CD4 lymphocytes were stimulated with antibodies for 7 days in the presence of anti-TNF agent or IgG1 at 10 μg/ml. Apoptosis was measured using annexin V and topro3.
Results: Cell cycle results are shown in the table and are expressed as the mean percentage of cells (+/−standard deviation (SD)) in each cell cycle phase (n=4) for each of the conditions. The increase in lymphocyte apoptosis was measured (n=7 healthy subjects) and expressed as a percentage of background apoptosis rate of stimulated cells with medium alone added. The increase in apoptosis compared to baseline as −2% for human IgG1 control antibody, +76% for etanercept, +110% for adalimumab and +132% for infliximab.
Conclusion: Both infliximab and adalimumab cause significantly greater G1/G0 cell cycle arrest (p=0.007) when compared to etanercept. With adalimumab and infliximab but not etanercept there is a corresponding decrease in the percentage of cells in the S phase (p=0.05). Infliximab and adalimumab cause greater apoptosis than etanercept. The induction of apoptosis may be related to the degree to which the anti-TNF agent induces cell cycle arrest. The variable effects of different anti-TNF agents on lymphocyte cell cycling may contribute to the differential efficacy of anti-TNF agents in Crohn's disease.

Abstract 332 Cell cycle percentages at 72 h after drug exposure

	% cells in G1/ phase (SD)	% cells in S phase (SD)	% cells in G2 phase (SD)
Unstimulated cells alone	90.6 (6.3)	8.6 (6.3)	0.7 (0.6)
Stimulated plus medium	46.6 (12.8)	45.6 (10.1)	7.8 (4.3)
Stimulated plus IgG1	52.6 (17.9)	39.2 (12.7)	8.1 (7.7)
Stimulated plus infliximab	75.0 (7.8)	21.3 (7.2)	3.7 (1.4)
Stimulated plus adalimumab	73.7 (11.6)	22.9 (10.1)	3.4 (2.5)
Stimulated plus etanercept	58.0 (5.5)	33.8 (8.4)	8.2 (8.9)

333 RECENT-ONSET CROHN'S DISEASE SHOWS HIGHER REMISSION RATES AND DURABILITY OF RESPONSE TO TREATMENT WITH SUBCUTANEOUS MONTHLY CERTOLIZUMAB PEGOL: RESULTS FROM AN ANALYSIS OF THE PRECISE 2 PHASE III STUDY

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Introduction: Certolizumab pegol is a PEGylated Fab' fragment of a humanised anti-TNF monoclonal antibody. Efficacy of subcutaneous (sc) certolizumab pegol in patients with active Crohn's disease (CD) was shown in a large Phase III, randomised, controlled trial (PRECiSE 2). Mean duration (SD) of CD for patients in the certolizumab pegol group was 8.6 (7.1) years (range <1–33 years)). The objective of this analysis was to asses the effect of CD duration on efficacy.
Aims & Methods: Patients with active CD (CD Activity Index score (CDAI) 220–450 points) received open-label sc certolizumab pegol 400 mg at Weeks (Wks) 0, 2 and 4, followed by randomisation of responding patients (at least 100-point decrease from baseline in CDAI) at Wk6 to certolizumab pegol 400 mg or placebo every 4 wks from Wk 8–24. Exploratory analyses were performed to determine rates of response (defined above) and remission (CDAI of at least 150 points) at Wk26 in the overall intent to treat (ITT) population according to disease duration at baseline.
Results: Certolizumab pegol induced and maintained response and remission compared with placebo irrespective of disease duration in the overall ITT population (tables). In patients with <3 years' disease duration, Wk26 maintenance of response rates reached 75.9% with certolizumab pegol (n=58) and 39.5% with placebo (n=81; p<0.001). Certolizumab pegol long-term response rates increased to 89.5% (placebo 37.1%; p<0.01) in patients with disease <1 year (tables). Remission rates at Wk26 follow the pattern of the response data with 58.6% remission in the <3-year group (placebo, 33.3%; p<0.01) and 68.4% remission in the <1-year group (placebo 37.1%; p<0.05).
Conclusion: Efficacy of certolizumab pegol in CD was shown irrespective of disease duration at baseline. The analysis also indicates higher rates of clinical response and remission at Wk26 in patients who were treated with sc certolizumab pegol 400 mg early after disease commencement. These data suggest a benefit of early intervention with monthly sc certolizumab

Abstract 333 Table 1

CD duration (years)	Placebo (n)	Placebo response rate* (%)	Certolizumab pegol (n)	Certolizumab pegol response rate* (%)
Any	210	36.2	215	62.8†
<1	35	37.1	19	89.5‡
1–<2	22	50.0	20	75.0
2–<5	55	36.4	45	62.2§
≥5	98	32.7	131	57.3†

*Wk26 overall ITT population; †p<0.001; ‡p<0.01; §p<0.05 *v* placebo.

Abstract 333 Table 2

CD duration (years)	n	Remission rate* (%)	n	Remission rate* (%)
Any	210	28.6	215	47.9†
<1	35	37.1	19	68.4§
1–<2	22	36.4	20	55.0
2–<5	55	29.1	45	46.7
≥5	98	23.5	131	44.3†

*Wk26 overall ITT population; †p<0.001; ‡p<0.01; §p<0.05 *v* placebo.

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pegol 400 mg for the long-term maintenance of response and remission in patients with active CD.

334 CERTOLIZUMAB PEGOL ADMINISTERED SUBCUTANEOUSLY IS EFFECTIVE IN ANTI-TNF NAÏVE PATIENTS AND IN PATIENTS PREVIOUSLY TREATED WITH INFLIXIMAB

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Introduction: Certolizumab pegol, a PEGylated Fab' fragment of a humanised anti-TNFα monoclonal antibody, is currently being developed for the treatment of Crohn's disease (CD) and other autoimmune diseases. The PRECiSE 2 maintenance trial assessed the efficacy and safety of certolizumab pegol 400 mg given subcutaneously (sc) every 4 weeks (wks) (after a 4-wk open-label induction phase) in patients with active CD (CD Activity Index (CDAI) score of 220-450 points, inclusive) compared with placebo (PBO). Patients who had previously received infliximab (IFX) entered the study provided that a response to treatment was observed after the first dose and there was no severe hypersensitivity or anaphylactic reaction.
Aims & Methods: We aimed to assess the efficacy of certolizumab pegol in the PRECiSE 2 study in IFX-naïve patients and in patients previously treated with IFX. Patients received open-label certolizumab pegol 400 mg sc Wks 0, 2, 4. CDAI responders (decrease from baseline in CDAI score at least 100 points) at Wk 6 were randomised to receive double-blind certolizumab pegol 400 mg or PBO every 4 wks, Wks 8–24.
Results: Overall, 474/668 patients were IFX-naïve and 193/668 had a history of prior IFX use at baseline (data for 1 patient unavailable). Of those, 324 (68.4%) IFX-naïve patients and 104 patients (53.9%) with prior IFX use responded at Wk 6. The percentages of patients maintaining response at Wk 26 and achieving remission (CDAI score at least 150 points) were significantly greater with certolizumab pegol than with PBO irrespective of prior IFX use. Similar results were observed with the IBD Questionnaire (IBDQ) for response (increase from baseline of at least 16 points) at Wk 26 (table).The proportion of patients experiencing adverse events (AEs) was similar in the certolizumab pegol and PBO groups in IFX-naïve (61.6% *v* 65.6%, respectively) and prior IFX (75.0% *v* 73.1%) cohorts. Serious AEs were observed in 4.3% (certolizumab pegol) and 5.6% (PBO) of IFX-naïve patients and in 9.6% in both groups for prior IFX patients.
Conclusion: Certolizumab pegol is a safe and effective sc administered anti-TNF treatment for patients with CD, irrespective of whether they are IFX-naïve or have received previous treatment with IFX.

335 RAPID INDUCTION OF REMISSION AND CLINICAL RESPONSE WITH ADALIMUMAB IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE AND SECONDARY FAILURE TO INFLIXIMAB THERAPY: RESULTS OF THE GAIN STUDY

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Introduction: Hypersensitivity and loss of response are associated with antibodies to infliximab (IFX) in the treatment of patients with Crohn's disease (CD).[1] Adalimumab (ADA), a self-injectable, fully human anti-TNF monoclonal antibody, is approved for treating rheumatoid arthritis (RA), psoriatic arthritis, and ankylosing spondylitis in the EU, US, and elsewhere. This study assessed the impact of secondary failure to IFX therapy on the induction of remission and clinical response in patients with active CD.
Aims & Methods: Patients with moderate to severe CD (CDAI 220–450) and secondary failure to IFX therapy (intolerance and/or loss of response) were enrolled in GAIN, a Phase III, double-blind, placebo-controlled study, and were randomised to receive ADA, 160 mg sc at Wk 0 (BL) and 80 mg sc at Wk 2, or placebo (PBO) at both time points. Primary endpoint was remission (CDAI<150) at Wk 4. Secondary endpoints were clinical response (CR) defined as a decrease from BL CDAI of ⩾70 or 100 (CR-70/CR-100) at Wk 4. Safety was assessed throughout the study.
Results: Patients received ADA (n=159) or PBO (n=166). Baseline characteristics were similar between treatment arms: mean age, 38 years; female, 65%; mean CDAI, 313; median CRP, 0.8 mg/dl; immunosuppressant use, 48%. Clinical remission and response rates observed in the ADA arm were significant versus PBO. Serious adverse events were observed in 4.8% of PBO patients (abscess, 3; sepsis, 1; CD flare, 2; abdominal pain, 2) and in 1.3% of ADA patients (dehydration, 2). No delayed-hypersensitivity (serum sickness) reactions or deaths occurred. The overall safety profile of ADA was consistent with prior CD trials and the existing RA database.
Conclusion: Adalimumab rapidly and significantly induced clinical remission and response in patients with moderate to severe CD who had secondary failure to infliximab. Adalimumab was well-tolerated.

1. **Baert F**, *et al. N Engl J Med* 2003;**348**:601–8.

Abstract 335 Remission and clinical response in GAIN, n (%)

	Week	PBO, n=166	ADA, n=159
CDAI<150	4	12 (7%)	34 (21%)*
CR-100	2	30 (18%)	58 (37%)*
	4	41 (25%)	61 (38%)**
CR-70	2	55 (33%)	82 (52%)**
	4	56 (34%)	82 (52%)*

*p⩽0.001; **p⩽0.01; both *v* PBO.

336 LEUKOCYTAPHERESIS FOR ULCERATIVE COLITIS: CORRELATION OF CLINICAL RESPONSE WITH IMMUNE REGULATION

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Introduction: Leukocytapheresis (LCAP) has been shown to be a safe and effective treatment for ulcerative colitis (UC). The mechanisms of action are unknown. A cellular pathway which may be affected by LCAP involves regulatory T cells (Treg). FOXP3+CD4+CD25+ T cells have been shown to be potent suppressors of immune responses.
Aims & Methods: The aim of this study was to assess the effect of leukocytapheresis on Treg cells and correlate the changes with clinical response. Patients who had not achieved remission (Colitis Activity Index (CAI) >4) after at least 4 weeks of >20 mg of oral prednisolone or who had relapsed when the prednisolone dose was reduced to <10 mg per day were eligible for the study. Inclusion criteria included a CAI of 5–12 and disease extent >15 cm. Twelve patients underwent 1 treatment session a week for 5 weeks. Response to treatment was assessed by CAI, ESR and CRP. Sigmoidoscopy and biopsy were performed at the beginning and end of the study and the endoscopic index (EI) was calculated. Outcome measures were compared using a paired t-test. Results are given as mean (SEM). The frequency of CD4, CD8 and regulatory FOXP3+CD4+ T cells

Abstract 334 Patients (%) (ITT population) for certolizumab pegol (CZP) or PBO

Wk 26 endpoint	IFX-naïve CZP (n=163)	IFX-naïve PBO (n=159)	Prior IFX CZP (n=52)	Prior IFX PBO (n=51)
Clinical response	68.7*	39.6	44.2‡	25.5
Remission	52.8*	33.3	32.7§	13.7
IBDQ response	64.8†	47.8	46.2¶	27.5

p Values *v* PBO: *<0.001; †0.002; ‡0.018; §0.008; ¶0.014.

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from PBMC was determined by flow cytometry on samples collected before and after the initial (week one) and final (week five) LCAP sessions.
Results: Two patients were withdrawn from the study due to worsening of their condition and underwent surgery. 11/12 patients were on immunomodulator therapy. The total activity scores (CAI+EI) improved on per protocol analysis (17.3 (1.1) *v* 13.4 (1.3), p=0.01). LCAP was associated with a decrease in the absolute number of CD3+ T cells without a change in the ratio of CD4:CD8 T cells. There was a reduction in the proportion of CD19+cells. Over the 5 week period of treatment there was an increased proportion of naïve T cells (CD4+CD45RA+) 27.2% *v* 29.9% p=0.3 and a reduction in the proportion of memory cells (CD4+CD45RO+) 46.1% *v* 41.6% p=0.07. Successful outcome correlated with the proportion of FOXP3+CD4+CD28- Treg cells (r=0.66 p=0.018) and was inversely correlated with the proportion of a subset of memory cells (CD69+CD4+CD45RO+).
Conclusion: This pilot study provides evidence for the use of LCAP in refractory UC and suggests that response to therapy may be regulated through Treg cells.

337 DEVELOPMENT, VALIDATION AND TESTING OF A NEW SOCIAL QUALITY OF LIFE MEASURE FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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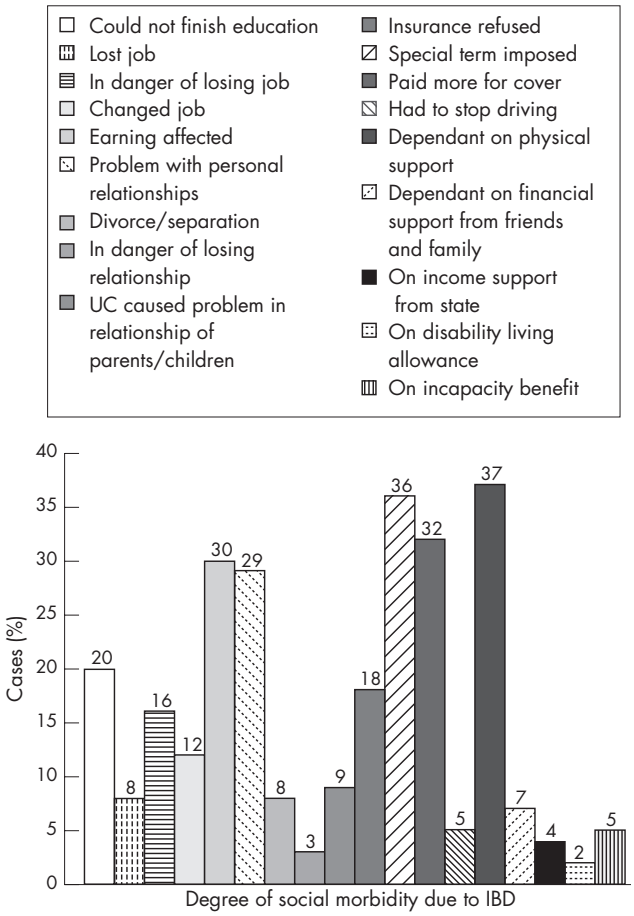
Introduction: Present quality of life (QOL) instruments for inflammatory bowel disease (IBD) fail to evaluate aspects of patients' life such as education, job/earning, personal relationships, finance and independence. We have developed a new QOL instrument to assess the impact of IBD on these domains.



Abstract 337.

Aims & Methods: A 14-item questionnaire was extended to include 33 items after a pilot assessment by surgeons and gastroenterologists on 39 patients. This was then completed by 148 IBD patients (median age 54 (24–78) years: 83 males) who had never had surgery. Median duration of disease was 24 (5–56) years. Patients also completed a SF-36 v2 and IBDQ.
Results: There was high level of inter-item correlation with the severity of colitis to: education (p=0.421–0.916), job/earning (p=0.003–0.838), human relationship (p=0.004–0.832), finance (p=0.120–0.727) and independence (p=0.003–0.613). The items correlated well with the eight domains of SF-36 v2 and also with IBDQ. The questionnaire had a high level of reliability (Cronbach's α=0.731).
Conclusion: The items correlated with the clinical status of patients with IBD and the SF-36v2. The questionnaire may have a role in identifying IBD patients whose medical treatment is no longer effective in maintaining satisfactory life goals.

338 EFFECTS OF ANTI-TNF ANTIBODIES IN VITRO ON DENDRITIC CELL APOPTOSIS AND FUNCTION

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Introduction: Anti-TNF therapy is effective in the treatment of IBD. Its effect on dendritic cells (DCs) is not fully understood. DCs are important antigen presenting cells and are activated via toll-like receptors (TLR) by TLR ligands such as LPS. It has been demonstrated recently that DC apoptosis is an important mechanism of immunoregulation. It is not clear whether infliximab causes apoptosis of DCs.
Aims & Methods: Blood from 7 patients, 4 with IBD and 3 controls was used to isolate monocytes. These were cultured in serum free medium in the presence of GM-CSF and IL-4 to derive DCs. Monocyte derived-DCs from the above patients were activated with LPS and exposed to etanercept, adalimumab or infliximab. Cytokine profile of the culture supernatants were studied for IL-12p70, IL-10 and TNF. DCs were assessed by flow cytometry after staining with Annexin V and Propidium Iodide in a calcium rich medium. The remaining DCs were subjected to an mixed lymphocyte reaction (MLR) with allogeneic lymphocytes (CD4+). Post proliferation IFNγ(Th1) and IL-13(Th2) levels from lymphocytes were assessed.
Results: There was no apoptosis seen in LPS activated DCs at increasing concentrations of infliximab 1, 10, 100 μg/ml. In contrast, we were able to demonstrate apoptosis of CD4 lymphocytes at concentrations of 0.1 to 10 μg/ml infliximab. The cytokine profile of the anti-TNF exposed LPS activated DCs showed that IL-10 conentration was reduced, which was greatest with adalimumab followed by etanercept and then infliximab. IL-12p70 concentration were also reduced, the greatest reduction being with etanercept, followed by adalimumab and infliximab. TNF concentrations were reduced and the greatest reduction was with infliximab followed by adalimumab. Etanercept did not show a change in TNF levels. In the MLR reaction infliximab pulsed LPS activated DCs demonstrated a reduction in proliferation with increasing concentrations. Finally the cytokine concentrations from supernatants after proliferation of CD4+ T cells by infliximab pulsed LPS activated DCs demonstrated reduction in IL-13 and IFNγ at concentrations of infliximab 1 to 10 μg/ml.
Conclusion: Unlike monocytes and lymphocytes, LPS activated (or immature) DCs do not undergo apoptosis when exposed to anti-TNF agents.[1,2] Anti-TNF agents do however cause a reduction in DC derived IL-12, TNF and IL-10 and also reduce T-cell activation in an MLR in a dose dependent manner. DC driven T lymphocytes show inhibition of both IL13 and IFNγ.

1. **Shen C**, *et al.* Caspase activation and apoptosis induction by adalimumab: demonstration in vitro and in vivo in a chimeric mouse model.Inflamm. *Bowel Dis* 2006;**12**:22–8.
2. **Shen C**, *et al.* Infliximab induces apoptosis of monocytes and T lymphocytes in a human-mouse chimeric model. *Clin Immunol* 2005;**115**:250–9.

339 INCIDENCE OF CROHN'S DISEASE STILL RISING IN CARDIFF: 1931–2005

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Introduction: Crohn's disease (CD) incidence in the City of Cardiff is documented from 1931, and the steep rise in incidence seemed to peak in the early 1980s.[1, 2] There has been debate about whether the incidence is still increasing in industrialised countries.[3] We collected incidence data and

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disease patterns for 1996–2005 to confirm whether incidence continues to rise, and investigate changes in clinical features with time in a defined population-based cohort.
Aims & Methods: To report the incidence of CD in Cardiff City for 1996–2005. Using the same methods as in past studies, cases were identified from weekly pathology meetings, computerised pathology and discharge diagnosis records, IBD database, clinic letters, paediatric IBD database and a questionnaire sent to all Cardiff GPs. New cases resident in the City, fulfilling Lennard-Jones CD criteria,[4] and diagnosed 1996–2005 were identified. Cases were reviewed where necessary by pathologist and radiologist and cases excluded if features were indeterminate. Information was collected on clinical features. Incidence figures were corrected to the age and sex distribution for England and Wales population 2001.
Results: 1739 case notes were reviewed, and 212 cases identified. Corrected incidence for 1996–2005 was 66/106/year (95% CI 57 to 76), compared to corrected incidences of 58.8, 70.9, and 44.0 for the previous 3 decades. Female:male ratio was 1.6:1, as previously with the excess females mainly in young adults. The incidence in children <16 is rising: 27/106/year (95% CI 14 to 40), compared to 15.6 (1.9 to 29) and 16.4 (2.0 to 31) for 1991–5 and 1986–90 respectively. More striking is the increasing spread in age range at diagnosis (ages from 7 to 86 for 1996–2005, compared to age 3–83, 10–77, 9–71, 12–59 and 13–44 for successive past decades back to 1946–55). Colonic location at diagnosis continues to increase in frequency (38%) and terminal ileum decreases (29%), followed by small and large bowel (13%) and other sites (9%). Colonic location is commoner in older patients.
Conclusion: CD incidence in Cardiff continues to rise. CD is more commonly diagnosed in elderly and the young and colonic location continues to rise and terminal ileal fall in frequency, particularly in older patients.

1. **Rose JDR**, *et al. Gut* 1988;**29**:346–51.
2. **Yapp TR**, *et al. Eur J Gastroenterol Hepatol* 2000;**12**:1–5.
3. **Logan RFA**. *Gut* 1998;**42**:309–11.
4. **Lennard-Jones JE**. *Scand J Gastroenterol* 1989;**24**(S170):2–6.

340 STANDARD AND ALTERNATIVE THERAPIES FOR INFLAMMATORY BOWEL DISEASE: THE PATIENT'S PERSPECTIVE

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Introduction: Patient experience and perception of drug treatments will have profound effects on compliance and may influence use of alternative therapies. In a postal survey of 567 patients with inflammatory bowel disease (IBD) we assessed experience/attitudes to traditional medical therapies and the use of alternative treatments.
Aims & Methods: All patients with IBD treated at the Royal Cornwall Hospital were sent a questionnaire regarding attitudes to and experiences of standard medical therapies and alternative treatments. Attitudes were assessed with a linear score (1–10). Extensive demographic details were recorded. All responses were anonymised.
Results: 329 patients responded (58%), 44% had Crohn's disease (CD), 52% had ulcerative colitis (UC). 52% felt their treatment was very effective and 8% perceived little benefit. Response to steroid and 5 Aminosalicylate (5ASA) therapy reflected published data (62% and 48% respectively reporting a ''very good'' effect). However, 77% were concerned about potential side effects from steroids and 24% reported these. 5ASAs were felt to be less effective than steroids (48% ''works very well'' *v* 67%), but better tolerated (11% ''bad side effects'' *v* 24%) and safer (33% showing concern *v* 77%). 47% of patients had exposure to immunosuppressants. 66% of patients worried about side effects and 41% reported severe problems. A positive clinical effect was reported by 54% of those on Azathioprine, compared to 35% on 6-Mercaptopurine. No significant difference was reported in efficacy between CD and UC. 19% of patients took alternative therapies. These therapies were perceived to be ''very effective'' in 27% and included aloe vera, hemp, kombucha and tumeric. Aloe vera was the most commonly used and 30% reported an improvement in symptoms. Only 6% reported poor tolerability. Acupucture, reflexology and reiki were used by 11% of patients of whom 57% improved. Probiotics were used by 32% and led to an improvement in 36%, although this was only ''helped a lot'' in 8%; 3% reported poor tolerability. 10% patients felt their doctors would support this treatment compared to 75% for the other alternative therapies. Although not in clinical practice, worm therapy was known to 24%. 47% felt they would take this therapy.
Conclusion: IBD patients are well informed regarding the safety profile of their medical treatment. Concurrent with clinical practice, patients feel it safer to take immunotherapy than repeated courses of steroids. 19% use alternative therapies and more than half perceive a worthwhile improvement with excellent tolerability. 75% of IBD patients felt they could approach their hospital team to try these treatments.

341 THE HUMAN ATP-BINDING CASSETTE TRANSPORTERS SUPERFAMILY AND XENOBIOTIC-TRANSCRIPTION REGULATORS: ANALYSIS OF INTESTINAL EPITHELIAL GENE EXPRESSION IN INFLAMMATORY BOWEL DISEASE

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Introduction: The ATP-binding cassette (ABC) transporters regulate many important physiological processes, such as gut barrier defence, bile acid/lipid homeostasis, and innate immunity. Inherited variations of ABC transporters (ABCB1/MDR1 and ABCC3) and the transcriptional regulator, PXR have been implicated in IBD susceptibility. Functional studies have also demonstrated a role in transcriptional factors such as FXR, in small intestinal defence.
Aims & Methods: The aim of this study was to characterise comprehensively the gene expression patterns of the entire ABC superfamily (48 genes) and their respective key transcriptional mediators (PXR, FXR, LXR and CAR) in human IBD based on the Agilent whole human genome oligonucleotide microarray chip. Mucosal biopsy specimens (colon and terminal ileum) from 53 Crohn's disease (CD) and 67 ulcerative colitis (UC) individuals were subjected to DNA microarray analysis. We performed comparative analyses with subanalyses for regional expression, inflammation status with healthy and non-IBD inflammatory controls (30 individuals).
Results: Overall, 15 (31%) ABC genes were differentially expressed in IBD. In non-inflammatory states, 7 ABC transporters (3 members of sub-family B, ABCB1/MDR1,ABCB4&5) were significantly downregulated in UC and CD compared with healthy controls (p values 0.05–0.0001; ABCB1/MDR1 in UC, $p=0.003$). In inflammatory states, a further 6 and 2 genes were significantly down- and upregulated in UC/CD respectively (p values 0.04–0.0001; CFTR in UC and CD, $p=0.008$) compared with inflammatory controls. Three ABC transporters were significantly expressed differentially irrespective of inflammation status (ABCE1, ABCF1/2). Of interest, there were no differences in the expression of PXR between IBD and controls (with subanalyses for disease location and activity). In contrast, the transcriptional regulator LXR, was significantly expressed differentially in inflamed states (upregulated in CD, $p=0.008$) and FXR downregulated in non-inflamed states ($p=0.02$) in IBD. Multiple logistic regression analyses revealed significant contribution of inflammatory status to the expressions of ABCB1/MDR1, ABCB2, ABCE1 and transcription factors, PXR, FXR, CAR and LXR irrespective of disease phenotype and control status ($p=0.02$-0.005). In addition, ABCB1/MDR1, ABCC3, ABCC6 and ABCE1 genes display differential expression gradients independent of disease phenotype and control status ($0.01>p>0.001$). Of interest, ABCB1/MDR1 and ABCC3 demonstrated a similar expression pattern from proximal to distal colon (decreasing gradient respectively).
Conclusion: The current data show significant alterations in key ABC genes and xenobiotic transcriptional factors in IBD. Previously implicated genes such as ABCB1/MDR1 along with novel transporters emphasised the importance of this class of proteins/transporters in the maintenance of epithelial defence and provide further insights for the pathogenesis of IBD.

342 THE ROLE OF DIET IN THE AETIOLOGY OF ULCERATIVE COLITIS: A EUROPEAN PROSPECTIVE COHORT STUDY

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Introduction: The causes of ulcerative colitis are unknown, although it is plausible that dietary factors are involved. Case-control studies of diet and ulcerative colitis are subject to recall biases.
Aims & Methods: The aim of the study was to examine the prospective relationship between the dietary intake of food groups and nutrients and the development of ulcerative colitis. Dietary information was collected on 263 824 men and women aged 40–65 years, participating in a large prospective cohort study (EPIC Study, European Prospective Investigation into Cancer and Nutrition). The participants were residents of the UK, Sweden, Denmark, Germany or Italy). Participants supplied information on diet at recruitment and were followed up for the development of ulcerative colitis. Each incident case was matched with four controls and dietary

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groups divided into quartiles. An analysis was performed using multivariate conditional logistic regression adjusting for total energy intake.
Results: 134 incident patients with ulcerative colitis (69 women, 65 men) were identified with a median age at diagnosis of 59.0 years (range 28.0–80.8 years). No significant trends for food groups or nutrients were identified, apart from a significant positive association with an increasing consumption of total polyunsaturated fatty acids (OR = 2.33, 95% CI 1.15 to 4.73, for highest *v* lowest quartile of intake).
Conclusion: Increased total polyunsaturated fatty acid intake was associated with an increased risk of developing ulcerative colitis. A possible biological mechanism exists in that polyunsaturated fatty acids are metabolised to proinflammatory mediators. The study is ongoing to identify more study participants developing ulcerative colitis to increase the statistical power for further analyses.

343 INFLIXIMAB FOR THE TREATMENT OF ULCERATIVE COLITIS: OUTCOMES IN OXFORD OVER A SIX-YEAR PERIOD

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Introduction: Infliximab (IFX) has been shown to be of benefit in the treatment of both moderate and severe ulcerative colitis, but long-term colectomy rates are not known. The aims of this study were to review the rate of colectomy after infliximab and try to identify factors that might predict the need for colectomy.
Aims & Methods: We conducted a retrospective cohort study of all patients with active ulcerative colitis who were treated with infliximab between 2000 and 2006. The primary outcome measure was colectomy-free survival. Cases were identified from pharmacy records and checked against ward and surgical records. Disease duration, activity, extent, indication for IFX, previous therapy, number of doses of IFX and complications were documented. Colectomy-free survival was analysed by a Kaplan–Meir curve; quantitative data were compared by a two-tailed Student *t* test; qualitative variables and differences were analysed by χ^2 analysis.
Results: From 2000–6, 30 patients were treated with IFX for active ulcerative colitis refractory to steroids and immunomodulators. Sixteen (53%) came to colectomy a median of 140 days after their first infusion (range 4–607), the most common indication being intractable symptoms (14/16 patients, 88%). Only 16.6% (5/30) maintained a steroid-free remission. All were non-smokers except one and all were white except 2 Jews, an Indian and an Iranian. 14/30 (47%) received IFX (5 mg/kg, single infusion) for severe colitis refractory to intravenous steroid therapy, after a mean 7 days from admission. 16/30 (53%) had their first IFX (5 mg/kg) for moderate, outpatient refractory disease. Disease distribution was distal in 10%, L-sided in 33%, or extensive in 57%. All were on immunomodulators (AZA 11, MP 3, MTX 9) except 6 who were intolerant or refractory and one who was newly diagnosed. All but 3 were either steroid dependant or refractory. 11/30 (37%) had previously been treated with ciclosporin. The median follow up was 1.1 years (range 57 days to 6 years). Postoperative complications including sepsis occurred in 4/16 (25%).Earlier age at diagnosis of colitis was significantly associated with an increased rate of colectomy (27.5 years *v* 38.7 years (p = 0.011))
Conclusion: Over half the patients studied with refractory UC treated with IFX came to colectomy, but of those avoiding colectomy only five (16.6% of all patients) sustained a steroid-free remission. Younger age at diagnosis was significantly associated with colectomy. Long-term outcomes are similar to those for ciclosporin. There did not appear to be an increased risk of postoperative complications. IFX delays colectomy but probably does not alter the long-term pattern of disease and it role may be in providing time for patients to come to terms with the need for colectomy.

344 VALIDATION OF THE NEW ''PHICAL'' FAECAL CALPROTECTIN TEST AS A DIAGNOSTIC TOOL FOR POUCHITIS

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Introduction: One of the hallmarks of pouchitis is the polymorphonuclear (PMN) infiltration of the mucosa, thought to be driven by dysbiosis. Calprotectin is a stable antimicrobial protein produced by activated PMN. Faecal calprotectin is already well established as a diagnostic tool in inflammatory bowel disease. We aimed to validate its use in pouchitis.
Aims & Methods: 54 stool samples were obtained: 46 from ulcerative colitis (UC) patients and 8 from familial adenomatous polyposis (FAP) coli patients. These samples were processed and analysed using a qualitative type enzyme linked immunosorbant assay (''PhilCal ELISA New Method'', Eurospital, Italy). Pouchitis was defined as an objective pouchitis score (OPS) of ⩾5/12 (endoscopic score of ⩾3/6 and an acute histological score of ⩾2/6) or a pouch disease activity index (PDAI) of ⩾7/18. Statistical analysis was performed using Spearman Rank and Mann–Whitney.
Results: The faecal calprotectin concentration correlated well with the OPS ($r = 0.68$, $p < 0.0001$), PDAI ($r = 0.7$, $p < 0.0001$), endoscopy score ($r = 0.6$, $p < 0.0001$), acute histological score ($r = 0.71$, $p < 0.0001$) and neutrophil score ($r = 0.68$, $p < 0.0001$), but correlated poorly with patients' clinical symptoms ($r = 0.3$, $p = 0.03$). Using the OPS, 6 patients were diagnosed with UC pouchitis (+ pre-pouch ileitis), 13 with UC pouchitis alone, 27 had a healthy UC pouch, 1 had FAP pouchitis (+ pre-pouch ileitis) and 7 had a healthy FAP pouch. Respectively, median faecal calprotectin values (mg/kg) for these groups were 865, 145, 56, 305 and 9, with means (95% confidence intervals) of 1073 (188.5 to 1958), 888.8 (174.1 to 1603), 147 (71.8 to 222.2), 305 and 12.86 (5.1 to 20.6). Statistically significant differences were noted when comparing inflamed and non-inflamed pouches ($p < 0.0001$). The pre-pouch ileitis group had higher values than those with pouchitis alone but this proved non-significant ($p = 0.2$). Using the upper normal limit for calprotectin as 50 mg/kg, the receiver operating characteristic analysis revealed a sensitivity of 90%, a specificity of 53%. Using a higher threshold of 92.5 mg/kg a sensitivity of 90% was maintained with a specificity of 76.5% demonstrated. Similar results were obtained using the PDAI, albeit with a slightly lower specificity level.
Conclusion: The new ''PhiCal'' faecal calprotectin test is a useful non-invasive diagnostic tool for differentiating between healthy and inflamed ileal pouches. In addition, the quantity of faecal calprotectin directly correlated to the objective markers of disease severity. This simple test could be use to rationalise the management of ileal pouch patients before exposing them to the potential risks of empirical antibiotic therapy and endoscopic investigations with biopsies.

345 AZATHIOPRINE INDUCED HEPATOTOXICITY IN INFLAMMATORY BOWEL DISEASE: IS IT AS RARE AS WE THINK?

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Introduction: Azathioprine is widely acknowledged as the benchmark therapy for maintenance of long-term symptomatic remission in inflammatory bowel disease (IBD). However, the concern for both the clinician and the patient are the well documented side effects. Hepatotoxicity is of concern but is said to be rare in adults with reported rates of 0–2.75%.
Aims & Methods: Blood monitoring was performed on 55 consecutive patients with IBD (24 UC; 31 Crohn's disease) started on Azathioprine. All

Abstract 345 ALT and Alk Phos in patients with Azathioprine induced hepatotoxicity

	ALT (0–35)	Alk Phos (30–100)	Week	Symptoms
Patient 1	120	233	2	Vomiting
Patient 2	142	527	5	Vomiting
Patient 3	124	159	1	Flu-like symptoms
Patient 4	73	180	2	Vomiting
Patient 5	78	81	5	Vomiting
Patient 6	251	229	6	Vomiting
Patient 7	265	519	6	Vomiting

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had normal liver function tests (LFTs) on initiation of therapy. Thiopurine methyl transferase (TPMT) levels were assayed on all patients. Azathioprine was prescribed at 2–2.5 mg/kg with dose reduction in patients with low TPMT levels. LFTs and full blood count (FBC) were taken weekly for eight consecutive weeks. The aim was to identify patients with significant myelosuppression or increase in alanine transaminase (ALT) or alkaline phosphatase (Alk Phos) to twice the upper limit of normal.
Results: Forty two patients (76%) completed the eight-week induction period. All patients complied with blood testing and this was closely monitored and supported by a nurse specialist (HEJ). No patients developed myelosuppression. Six (11%) stopped treatment with Azathioprine for a number of reasons (flu-like symptoms, abdo pain, infection) with normal blood tests. Seven (13%) developed hepatotoxicity. In all patients LFTs returned to normal after stopping Azathioprine.
Conclusion: The results from this study demonstrate that hepatotoxicity can occur in excess of 10% of IBD patients within eight weeks of starting Azathioprine. All patients were symptomatic with this. Although there were no long-term complications, the elevation in LFTs was often significant and concerning. These results challenge the belief that Azathioprine induced hepatotoxicity is rare.

346 MMX MESALAZINE IS WELL TOLERATED DURING 12 MONTHS' MAINTENANCE TREATMENT OF MILD-TO-MODERATE ULCERATIVE COLITIS

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Introduction: Current 5-aminosalicylate formulations for the maintenance of remission of ulcerative colitis (UC) require multiple-daily dosing regimens. Patient compliance with these regimens is poor, resulting in reduced drug efficacy and an increased risk of disease flare. MMX mesalazine is a high strength (1.2 g/tablet) 5 ASA formulation designed for once-daily (QD) dosing. Two pivotal phase III studies (SPD476-301 (301) and SPD476-302 (302)) have shown MMX mesalazine to be efficacious and well tolerated for the induction of remission (clinical and endoscopic) of active, mild to moderate UC. Here we report a further study, SPD476-303, assessing the safety of MMX mesalazine for the maintenance of remission of UC.
Aims & Methods: Study 303 was a randomised, multicentre, open label, extension study. Patients not in remission after the two phase III studies (301 and 302) could enrol into the acute phase of study 303 and receive 8 weeks' MMX mesalazine 4.8 g/day (2.4 g given twice daily (BID)). Patients in remission after the pivotal studies or the acute phase of 303, could enter the maintenance phase of 303 and were randomised to 12 months' MMX mesalazine 2.4 g QD or 1.2 g BID. The primary objective was to assess safety and tolerability in the maintenance phase.
Results: 459 patients entered the maintenance phase (246 from studies 301/302; 213 via the acute phase of study 303). Treatment-emergent adverse events (AEs) were experienced by 88/225 (39.1%) and 86/234 (36.8%) patients taking MMX mesalazine 2.4 g/day QD or BID, respectively. The most commonly reported AE was UC flare (coded ''aggravated UC'' (29 cases) or ''UC'' (11 cases)). 22 serious AEs (SAEs) were reported by 18 patients (9 in each treatment arm). Only one SAE (abnormal liver function test) in the QD group was considered possibly treatment-related. 21 patients experienced 23 AEs that led to withdrawal (11 patients and 10 patients in the QD and BID groups, respectively). Of these, 2 cases of aggravated UC, 1 abnormal liver function test and 1 case of arthralgia were assessed as probably or possibly related to treatment.
Conclusion: Long-term therapy with MMX mesalazine 2.4 g/day given QD or BID is well tolerated for the maintenance of remission of mild-to-moderate UC.

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347 DIFFERENT DEFINITIONS OF REMISSION FOR ULCERATIVE COLITIS RESULT IN LARGE VARIATIONS OF CLINICAL OUTCOME SCORES

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Introduction: [Introduced by Dr S Riley] One of the treatment goals for ulcerative colitis (UC) is to induce remission. Currently, there is no standard/accepted definition of remission for UC. Thus, the definition of remission differs among clinical trials supporting various therapies for UC. The purpose of this analysis was to estimate remission rates using several different definitions of remission.
Aims & Methods: Data from two Phase III, multicenter, randomised, double-blind, 6-week, controlled studies of similar design (ASCEND I and II) were pooled and analysed using different definitions of remission. Definitions varied from complete resolution of clinical assessments to still having mild UC signs and symptoms. Remission rates of delayed-release oral mesalazine in patients with mildly to moderately active UC taking 2.4 g/day were examined using several different definitions used by various UC therapies.
Results: A total of 687 patients with mildly to moderately active UC were included in the study, of which 349 received 2.4 g/day. Depending on the definition of remission used in the analyses (see table), the percentage of patients in remission varied from 22–54%.
Conclusion: Remission rates vary widely depending on the definition of remission used. As there is no standard/accepted definition of remission for UC, physicians and other healthcare professionals should pay attention and be aware of the definition of remission being used when evaluating clinical efficacy in addition to different patient populations and treatment duration.

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Definition	Rate
Complete resolution (score = 0) of SF, RB, Sig score, PFA and PGA	22%
UCDAI $\leqslant$1, RB and SF = 0, at least 1 point decrease in Sig score from baseline	28%
RB = 0 and SF = 0 or 1	49%
UCDAI $\leqslant$2 and no individual subscore >1	50%
UCDAI $\leqslant$2	54%

348 THE ALPHA7-NACHR RECEPTOR MEDIATES INHIBITION BY NICTOINE OF TNFα-INDUCED IL-8 PRODUCTION BY HT29 COLONIC EPITHELIAL CELLS

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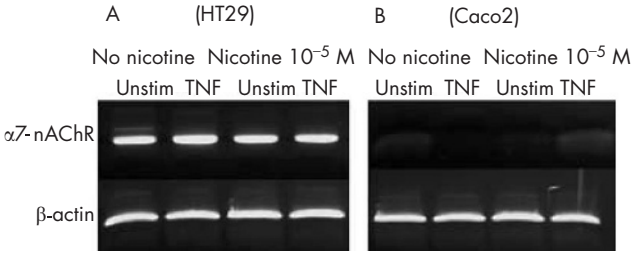
Introduction: Why smoking and nicotine patches are beneficial in ulcerative colitis, while smoking is deleterious in Crohn's disease, is unknown. We previously reported (Khatab *et al*, *Gut* 2005;**54**:A97) that nicotine downregulates IL-8 production by epithelial cells with a colonic phenotype (HT29), but has no effect on those of small intestinal phenotype (Caco2). Nicotine exerts its effects via nicotinic acetyl choline receptors (nAChR); these have 17 subunits but it is not clear which subunit mediates the effects of nicotine in the gut. In macrophages, α7-nAChR mediates cholinergic inhibition of proinflammatory cytokine synthesis.
Aims & Methods: We aimed to explore the role of α7-nAChR in mediating the effects of nicotine in HT29 and Caco2 cell lines. HT29 and Caco2 cells were grown to confluence and stimulated with TNFα (0–100 ng/ml) in the presence of nicotine (10^{-9}–10^{-5}M). After 24 h, total RNA was isolated by Trizol. mRNA expression of α3, α4, α5, α7 and η2-nAChRs by HT29 and Caco2 were analysed using RT-PCR. Supernatants were assyed for IL-8 by ELISA.
Results: RT-PCR analysis showed that α7-nAChR was expressed by HT29 cells (fig 1A), but not Caco2 cells (fig 1B). α3, α4, α5, and η2-nAChRs were expressed by neither HT29 nor Caco2. ELISA showed that TNFα dose-dependently stimulated IL-8 production by HT29 and Caco2 cells. In



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HT29 cells, but not Caco2 cells, nicotine (in concentrations resembling those found in the serum) significantly inhibited IL-8 production.
Conclusion: Of the five receptors assessed, only α7-nAChR is expressed by HT29 colonic epithelial cells and is likely to mediate the inhibitory effect of nicotine on IL-8 production by this cell type. In contrast, epithelial cells with a small intestinal phenotype (Caco2) do not express any of the receptors sought, and did not respond to nicotine. These results suggest that the beneficial effects of nicotine in UC may be attributed in part to its inhibition, via the α7-nAChR receptor, of IL-8 production by colonic epithelial cells.

349 RANDOMISED PLACEBO-CONTROLLED TRIAL OF CLARITHROMYCIN IN ACTIVE CROHN'S DISEASE

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Introduction: Crohn's disease (CD) is characterised by defective innate immune responses to intestinal bacteria. Clarithromycin is a broad-spectrum antibiotic that has particularly good penetration into macrophages and may therefore be effective at eradicating the organisms at the centre of the granulomatous reaction in Crohn's disease. There is also evidence suggesting that macrolide antibiotics can stimulate macrophage proliferation, phagocytosis, chemotaxis and cytocidal activity.
Aims & Methods: Patients with active Crohn's disease (Crohn's disease activity index (CDAI) >200 and a CRP >10 mg/l) were allocated either clarithromycin 1 g od or identical placebo for three months in a single-centre randomised double blind controlled trial. Inclusion criteria included a stable dose of corticosteroid (<10 mg prednisolone or <3 mg budesonide) and a stable dose of other medication (azathioprine for at least 3 months and 5-ASA preparation for at least one month). Randomisation was by blinded pharmacist independent from the trial. Primary outcome measure was remission (CDAI<150) or response (fall in CDAI >70 from pretreatment level) at three months.
Results: The trial was stopped after 41 patients had been randomised because of poor overall efficacy (initially assessed blinded to treatment allocation). Baseline characteristics were similar in the two groups except baseline CDAI (mean (SD)) was 246 (28) in the clarithromycin group (n = 19) and 280 (68) in the placebo group (n = 22) (p = 0.04). There were no other significant differences between the groups at baseline. Median CRP at baseline was 28 mg/l (range 10–200) in the clarithromycin group and 26 mg/l (range 10–109) in placebo group. By intention to treat analysis there was no difference in remission or response rates at week 12: clarithromycin 5/19, placebo 6/22 (p = 1.00). The mean (SD) fall in CDAI was 35 (80) for clarithromycin and −2 (114) for placebo. There was a significant difference in response/remission after one month: 10/19 clarithromycin versus 3/22 placebo (p = 0.01).
Conclusion: Clarithromycin 1 g for three months is ineffective in achieving remission in active Crohn's disease. However a significant response/remission rate was observed at one month. This suggests that an initial antimicobial effect is attenuated by bacterial resistance to clarithromycin. Combination or rotating antibiotic therapy may be a more effective therapy.

350 AN ASSESSMENT OF BACTERIAL DYSBIOSIS IN ILEAL POUCH INFLAMMATION USING TERMINAL RESTRICTION FRAGMENT LENGTH POLYMORPHISM

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Introduction: The results from previous studies on dysbiosis and pouchitis using conventional culture techniques have been disappointing because of inherent limitations associated with the technique. We used terminal restriction fragment length polymorphism (T-RFLP) (a novel molecular method) to assess bacterial diversity and counts in patients who had either pouchitis or a healthy pouch.
Aims & Methods: Bacterial flora in 20 pouch patients (15 healthy; 5 inflammed) were studied. DNA was extracted from faeces and PCR was performed using pan-enteric primers (V6-V8 region) that were modified at the 5′ end with CY5 dyes. Amplicons were digested with the enzyme MSP-1. The restricted fragments were analysed by capillary electrophoresis (CEQ 8000 Genetic Analysis System, Beckman Coulter) and the electrophenograms generated were studied. Electrophenograms provide information about operating taxonomic units (OTUs) which correspond with specific organisms. Principal component analysis was performed to identify dominant and important OTUs in the 20 patients. Bacterial diversity and counts of these OTUs were compared in the two groups of patients.
Results: Bacterial diversity in patients with pouchitis was similar when compared with patients with healthy pouches (16 (11–20) *v* 12 (9–13), p = 0.279). Bacterial counts of dominant organisms (OTU 79 (Enterococci), 88 (Enterobactericea), 146 (Clostridia) and 148 (Bacilli)) in pouchitis patients were similar when compared with patients with healthy pouches (p = 0.306, 0.735, 0.800 and 0.735 respectively). However, eight organisms (OTU 100 (Sulphate reducing bacteria), 137, 193 (Methylobacter), 232, 376, 381, 414 and 465 (Microbacterium)) were seen exclusively in patients with pouchitis.
Conclusion: Using T-RFLP, bacterial diversity and counts of predominant organisms in patient with pouchitis was similar when compared with patients with healthy pouches. However, T-RFLP identified eight candidate organisms (of which five were novel) which may be responsible for pouchitis.

351 A RAPID, NON-INVASIVE TEST FOR THE QUALITATIVE DETECTION OF ELEVATED FAECAL LACTOFERRIN IN ILEAL POUCH PATIENTS WITH INFLAMMATION

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Introduction: Pouchitis is a common long term complication of ileal pouch surgery. Currently, diagnosis requires a triad of clinical symptoms, endoscopic appearance and histological confirmation of inflammation. Elevated lactoferrin, a marker of intestinal inflammation, can be measured in faeces and may be a useful adjunct. The IBD EZ VUE test, an immunochromatographic assay, is non invasive, easy to perform and provides a result within 10 minutes. Visual interpretation of positive and negative results is simple because of the membrane cassette format of the test.
Aims & Methods: We studied the sensitivity and specificity of the IBD EZ VUE faecal lactoferrin kit (TechLab) in diagnosing pouchitis. Consecutive ileal pouch patients with change in pouch function were recruited from a colorectal outpatients department. A faecal sample was collected from each patient prior to examination and biopsy of the pouch. An IBD EZ VUE test was performed by a person blinded to the patient's symptoms and pouch appearance. Pouch disease activity indices (PDAI) were calculated for each patient. Pouchitis was defined as a PDAI of 7 or greater. Results of the IBD EZ VUE test were correlated with the PDAI for each patient.
Results: There were 32 ileal pouch patients (11 with and 21 without pouchitis). Median PDAI was significantly higher in those with pouchitis compared with those with healthy pouches (8 (7–9) *v* 3 (2–4), p = 0.001). Overall the IBD EZ VUE test had a sensitivity of 100% and a specificity of 86% for diagnosing pouchitis. The positive predictive value was 79%. The three elevated lactoferrin results in the non-inflammed pouch group occurred in (1) bleeding haemorrhoids, (2) a pouch anal anastomotic stricture and (3) a patient with cuffitis. All three causes were readily apparent on clinical examination.
Conclusion: IBD EZ VUE is a simple, non-invasive and rapid test for indicating pouchitis. It is a sensitive method for diagnosing pouch inflammation without the need for routine endoscopic pouch examination or biopsy. Antibiotic treatment can be commenced with greater confidence and is appropriate in more than three quarters of patients. Further investigations can be reserved for those patients who have a positive lactoferrin test that fail to respond to standard antibiotic treatment.

352 A COMPARATIVE STUDY OF LUMINAL AND MUCOSAL ASSOCIATED FLORA IN PATIENTS WITH ILEAL POUCHES

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Introduction: The luminal associated flora of patients with healthy and inflammed pouches has been previously studied. However, inflammation of the ileal pouch often involves the mucosa, and flora at the mucosal interface may be more important clinically. We therefore studied mucosal associated flora in ileal pouch patients
Aims & Methods: Bacterial flora were studied in 20 consecutive ileal pouch patients. As with previous studies, luminal associated flora (LAF) were obtained from pouch effluent. Mucosal associated flora (MAF) were extracted from pouch biopsies using the vortex technique. Best culture methods (complete preservation of sample anaerobia and use of wide range of media) and genotypic confirmation of all phenotypically identified organisms was performed. Diversity indices and counts (log colony forming units/per gram sample) of bacteria were compared between LAF and MAF. Wilcoxon's statistical test was performed, a p value of <0.05 was statistically significant.

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Variable	LAF (Median (IQR))	MAF (Median (IQR))	p Value
Total diversity index	5 (4–6)	3 (2–4)	0.008
Total counts	8.71 (7.84–8.92)	7.41 (5.49–8.37)	0.012

Results: Total bacterial diversity indices and counts were all significantly lower in MAF when compared with LAF. When data were analysed according to individual organisms, there were significantly more enterococci (5.9 (IQR 0.0–6.8) *v* 0.0 (IQR 0.00–0.0)) and bacteroides (IQR 6.9 (0.0–7.7) *v* 0.0 (IQR 0.0–5.4)) in LAF when compared with MAF.
Conclusion: Using best culture techniques, bacterial diversity and counts are significantly lower in mucosal associated flora when compared with luminal associated flora. There are inherent differences in bacterial yield and populations between the lumen and the mucosa of ileal pouch patients. These differences may be important in the planning and comparison of future studies.

353 SATISFACTION WITH HEALTHCARE IN INFLAMMATORY BOWEL DISEASE: INFLUENCE OF PATIENT CHARACTERISTICS

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Introduction: Interest in measuring satisfaction with healthcare (SwH) is growing. Better information about factors affecting SwH should help providers and planners to improve service quality. Factors that may affect SwH include those that relate to patient characteristics and those that relate to features of the healthcare system itself. If ratings of SwH are to be used as a measure of healthcare quality we need to understand the confounding influence of measurable patient factors. There is poor knowledge of the factors that determine SwH in IBD.
Aims & Methods: To identify patient variables associated with variation in SwH among subjects with ulcerative colitis (UC) and Crohn's disease (CD) attending GI clinics at a university hospital. Subjects: outpatients attending for follow-up. Primary outcome: global SwH measured using a visual analogue scale (''feeling thermometer'') consisting of a 100mm scale anchored between 0 (completed dissatisfied) and 100 (completely satisfied) (''SwH%''). Data collected: Age, sex, occupation, educational level, disease history (IBD type, duration, complications, surgery, drugs), activity score (Harvey Bradshaw Index (HBI) or Simple Colitis Activity Index (SCAI)), global health state (''utilities'', using Time Trade Off (TTO) and EQ5D), health-related QoL (IBD-Q), Hospital Anxiety & Depression Scale (HADS), IBD knowledge questionnaire (CCKNOW), NACC membership.
Results: Data for the first 149 patients (CD, n = 70; UC, n = 79): mean (SD) SwH%: 79 (19.8); range: 10–100. SwH% was independent of age, disease type, disease duration, immunosuppressant use, surgery, recent hospitalisation and HADS scores. Mean SwH% was lower in those who ''Stayed on at School'' (74.5 *v* 81.8; p = 0.09) or had ''Higher Qualifications'' (62.5 *v* 82.0; p = 0.019) and showed a negative correlation with level of disease knowledge (CCKNOW score; Pearson $r = -0.24$; p = 0.045). SwH% was correlated negatively with colitis activity score (SCAI, Pearson $r = -0.47$; p = 0.001) and positively with utility score (TTO, Pearson $r = 0.29$; p = 0.007).
Conclusion: Overall, SwH was high among IBD patients but SwH rating was influenced by global state of health (utility) and disease activity. ''Better'' educated patients and those with higher levels of disease knowledge appear to report lower SwH, probably reflecting higher expectations of care (as reported in other disease areas). SwH is a potentially useful outcome measure but absolute scores are influenced by patient factors that appear unrelated to service quality.

354 ALTERATIONS IN THE EXPRESSION OF HUMAN DEFENSIN-5 IN ILEOSTOMY FLUID OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Human defensin-5 (HD-5) is a major antimicrobial peptide which is normally present in the lumen in its mature form but stored in small intestinal Paneth cells in its precursor form.
Aims & Methods: To investigate luminal expression of HD-5 in Crohn's disease (CD). Ileostomy fluid samples from 51 CD patients and 20 controls (7 had ulcerative colitis) were collected with protease inhibitors. Concentration of HD-5 in ileostomy fluid samples was determined (blinded) by comparison of immunodot density against a standard curve. Luminal HD-5 was characterised following purification using a cation-exchange matrix and reverse phase-high performance liquid chromatography (RP-HPLC). HD-5 immunoreactive fractions were analysed by acid urea-polyacrylamide gel electrophoresis (AU-PAGE) and SDS-PAGE Westerns, N-terminal amino acid sequencing and ES-QToF mass spectrometry (MS).
Results: Luminal HD-5 levels were lower in CD ileostomy fluid than control (median (range): 7.9 (5.5–35.0) *v* 10.5 (6.0–30.4) μg/ml; p = 0.05). This reduction was most marked in those with active CD (p = 0.01) and in NOD2 mutant homozygotes/compound heterozygotes (p = 0.03). In control group (n = 3), luminal HD-5 had characteristics of the mature form only. By contrast, luminal HD-5 from the CD group (n = 7) appeared to exist in multiple forms on AU-PAGE Western. This was confirmed by RP-HPLC, in which HD-5 eluted from the column at three acetonitrile concentrations: 39% (previously seen with pro-HD-5), 50% (mature HD-5), but the majority eluted at 59% acetonitrile. Further analysis of the latter fraction (from 3 CD patients) by ES-QToF showed sequences for chymotrypsin (confirmed by N-terminal sequencing) and also contained a mass consistent with mature HD-5 (3580.51 Da). In one representative 59% acetonitrile sample, AU-PAGE showed HD-5 and chymotrypsin-specific bands in a similar position. However, in SDS-PAGE (under denaturing/reducing conditions) Westerns, the same sample showed distinct immunoreactive bands consistent with mature HD-5 and chymotrypsin. SDS-PAGE Westerns of ileostomy fluid cation-exchange concentrates (not applied to RP-HPLC) showed chymotrypsin immunoreactive bands in samples from CD and controls. Western blot analyses of control and CD Paneth cell extracts showed chymotrypsin immunoreactive bands.
Conclusion: (1) HD-5 levels in CD ileostomy fluid samples were lower than in controls (2) in control ileostomy fluid, HD-5 exists in the free mature form (3) in CD ileostomy fluid, majority of the HD-5 was present in a complex with chymotrypsin (which may originate from Paneth cells) (4) reduced total luminal HD-5 levels, and luminal HD-5-chymotrypsin complexes may result in reduced function of this antimicrobial peptide in CD.

355 EFFECTS OF CERTOLIZUMAB PEGOL, ETANERCEPT, ADALIMUMAB AND INFLIXIMAB ON LIPOPOLYSACCHARIDE-INDUCED CYTOKINE PRODUCTION BY HUMAN PERIPHERAL BLOOD MONOCYTES

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Introduction: Monocytes/macrophages secrete a variety of pro-inflammatory cytokines, such as tumour necrosis factor alpha (TNFα) and interleukin-1 beta (IL-1β), which are expressed in increased amounts in the blood and intestinal mucosa of patients with Crohn's disease (CD). It has been suggested that anti-TNF agents induce signalling via membrane TNF alpha, which results in an inhibitory effect on lipopolysaccharide (LPS)-induced cytokine production.
Aims & Methods: The aim of this study was to compare certolizumab pegol (an antibody Fab' fragment conjugated with polyethylene glycol) with other anti-TNF agents in terms of their effect on LPS-stimulated production of TNFα and IL-1β. Human monocytes were selected from peripheral blood mononuclear cells of healthy donors using CD14+ magnetic microbead-associated cell sorting (MACS). Purified monocytes were pre-incubated for 1 h with certolizumab pegol, etanercept, adalimumab, infliximab (at a range of concentrations from 100 μg/ml to 100 pg/ml) or a relevant control. After extensive washing, the monocytes were incubated, with or without LPS (100 ng/ml), for 4 h at 37°C. Supernatants were collected for measurement of TNFα and IL-1β by enzyme-linked immunosorbent assay and a range of chemokines, cytokines and other proteins measured by Luminex at one anti-TNF concentration.
Results: Pre-incubation of monocytes with certolizumab pegol, adalimumab or infliximab appeared to completely inhibit subsequent LPS-stimulated production of TNF alpha and IL-1 beta in a dose-dependent manner. In contrast, etanercept was much less efficient at mediating this activity, causing only partial inhibition of cytokine production. There were no clear differences in potency between infliximab and adalimumab, while certolizumab pegol was approximately 100-fold more potent than infliximab or adalimumab at inhibiting the release of TNFα and IL-1β by monocytes. The Luminex analysis of several cytokines and chemokines showed a range of effects, with inhibition of IL 10 and IL 12 being the most profound. Again, etanercept was not as potent as the other three anti-TNF agents at inhibiting these two cytokines.

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Conclusion: Certolizumab pegol effectively inhibited cytokine production more potently than adalimumab or infliximab. Etanercept showed only partial inhibition of cytokine production even at high concentrations. Although these data were generated in an in vitro system, the comparative trends in the inhibition of cytokine production stimulated by bacterial products appear to reflect the clinical efficacy of these anti-TNF agents in CD. The potent inhibition by certolizumab pegol of cytokine production by monocytes may represent an important mechanism of action in CD.

356 ANTIBODIES TO INFLIXIMAB IN PATIENTS WITH CROHN'S DISEASE DO NOT CROSS-REACT WITH CERTOLIZUMAB PEGOL

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Introduction: Anti-tumour necrosis factor-alpha (TNFα) therapies have shown clinical benefit in a range of inflammatory diseases. Infliximab is a chimeric full IgG1 monoclonal anti-TNF antibody administered intravenously for the treatment of Crohn's disease (CD). Its use may be limited by the induction of antibodies to infliximab, subsequent loss of efficacy and occurrence of infusion reactions.[1] Certolizumab pegol is a PEGylated Fab fragment of a humanised anti-TNF antibody that is administered subcutaneously and is currently in development for the treatment of CD. If the antibody response to infliximab does not cross-react with certolizumab pegol, then patients who develop antibodies following treatment with infliximab may have an opportunity to switch to treatment with certolizumab pegol.
Aims & Methods: The aim of this study was to determine if the antibody response elicited in patients to infliximab cross-reacts with certolizumab pegol. Samples from 20 patients with an antibody response to infliximab were assayed using ELISA plates coated with certolizumab pegol and then blocked with 0.1% bovine serum albumin. Plasma from patients with antibodies to infliximab was then incubated on the plates. Following a wash step, biotinylated certolizumab pegol was added followed by streptavidin horseradish peroxidase. Colour was developed using 3,3,5,5-tetramethylbenzidine (TMB) substrate and the absorbance read at 450 nm with reference at 630 nm.
Results: No cross-reactivity to certolizumab pegol was detected in any of the 20 infliximab antibody-positive samples tested.
Conclusion: The generation of an antibody response to one anti-TNF therapy may not preclude the use of another anti-TNF drug in patients with CD. Subcutaneous certolizumab pegol may provide an alternative therapy for patients who develop antibodies following intravenous treatment with infliximab.

1. **Baert**, *et al. N Engl J Med* 2003;**348**:601–8.

357 ACCUMULATION OF PLASMACYTOID DENDRITIC CELLS IN THE INTESTINE OF ACUTE ULCERATIVE COLITIS

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Introduction: Breakdown of tolerance against the commensal microflora is believed to be a key factor in the pathogenesis of inflammatory bowel disease (IBD). Dendritic cells (DCs) have been implicated in mediating this process in various rodent models, but data on human intestinal DC in IBD are limited.
Aims & Methods: We aimed to identify changes in intestinal DCs in patients with an acute flare-up of ulcerative colitis (UC). Rectal biopsies were obtained from patients with active UC symptomatic for less than four weeks (n = 19; Ulcerative Colitis Disease Activity Index >3; sigmoidoscopy score >2) and controls (n = 7; macroscopically and histologically normal intestine of patients referred for rectal bleeding). DCs were identified in freshly isolated lamina propria mononuclear cells and four colour flow cytometric analysis was used to identify the proportion and number of CD11c+ (HLA-DR+ lin-) myeloid DCs and CD11c- (HLA-DR+ lin-) putative plasmacytoid DCs. Surface expression of activation/maturation markers CD40, CD86, and toll-like receptors (TLR), TLR-2 and TLR-4 was assessed on each cell population.
Results: During acute flare-up, UC patients have a significantly higher number of intestinal DCs compared with controls (456 versus 108 per milligram tissue; p = 0.026). The majority of additional DCs present in inflamed tissue were CD11c- cells. The number of these cells was significantly greater in tissues from UC patients than from controls (403 *v* 51; p<0.005). In contrast, the number of CD11c+ DC did not differ significantly between UC patients and controls. Unlike CD11c+ myeloid DCs, the CD11c- cells from UC patients did not express TLR-2 and TLR-4, and only a few expressed CD40 (22% CD11c-DC versus 60% CD11c+DC) and CD86 (11% CD11c-DC versus 48% CD11c+ DC). Preliminary data also suggested that these CD11c- cells lack expression of the classic blood plasmacytoid DC markers (CD123, BDCA-2 and BDCA-4).
Conclusion: UC patients with acute flare-up have an increased number of intestinal DCs, the majority of which are CD11c- cells and the nature of which remains to be fully determined. The recruitment of this specific group of cells in the intestine probably contributes to gut inflammation and tissue damage. Further characterisation of these cells have therapeutic potential.

358 MANAGEMENT OF POSTOPERATIVE CROHN'S DISEASE IN A SPECIALIST UNIT: NEED FOR A DEFINED STRATEGY

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Introduction: Postoperative clinical and endoscopic recurrence is common in Crohn's disease.
Aims & Methods: We aimed to assess postoperative Crohn's management and recurrence in a cross-sectional patient cohort in our unit, and to define a treatment algorithm for the prophylaxis of Crohn's recurrence after resection. We retrospectively reviewed all patients who had a primary ileo-colonic resection for Crohn's disease between 2003 and 2005 in a secondary and tertiary specialist centre.
Results: Ninety nine patients (42 male; 57 female; mean age 37 years) with a median disease duration of 10 years, were reviewed. Indications for surgery were obstruction (n = 61), failed medical therapy (n = 31) and internal fistula (n = 7). 30 patients (30%) were active smokers. 51 patients (52%) had at least one previous Crohn's resection. Clinical and surgical recurrence rates were 28% and 5% respectively, at one year. Median time to clinical recurrence was 10 months. Only 19% of patients had an ileo-colonoscopy, and 60% had been reviewed by a gastroenterologist after surgery. Nine of the 28 patients (32%) who had clinical recurrence had not had postoperative medical therapy. We have subsequently devised a postoperative treatment strategy to stratify patients to receive no treatment, mesalazine or immunosuppressant based on clinical risk factors and endoscopic findings at 6 and 12 months after surgery.
Conclusion: The rate of postoperative recurrence of Crohn's disease in our unit was high in the short term. Prospective treatment strategies are deficient. We have devised a postoperative treatment strategy which requires further evaluation.

359 ANALYSIS OF DISTINCT GENOME WIDE EXPRESSION PROFILES IN THE TERMINAL ILEUM OF PATIENTS WITH CROHN'S DISEASE

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Introduction: Gene expression technology using microarray allows a comprehensive picture of gene expression at the tissue and cellular level.
Aims & Methods: The aim of this study was to investigate differential gene expression in endoscopic terminal ileal (TI) biopsies of a well phenotyped cohort of Crohn's disease (CD) patients and controls. Paired TI biopsies from 16 patients with CD: 6 non-inflamed biopsies, 7 chronically inflamed biopsies and 3 acutely inflamed biopsies, and 6 healthy control TI biopsies were collected for RNA extraction and histology. Patients symptoms were scored at the time of endoscopy and phenotypic data were collected by patient questionnaire and case note review. Microarray studies were carried out using the Agilent whole human genome oligonucleotide chip. Results were confirmed by real time PCR.
Results: Using unsupervised hierarchical clustering, discrete separation between the female CD TI biopsies and female control TI biopsies was observed. When the CD TI biopsies (16 biopsies) were compared to controls (6), 296 sequences were upregulated and 312 sequences were downregulated (fold change (FC) greater or less than 2, 0.01>p>1×10–45). By removing the acute inflammatory signal to compare quiescent CD TI biopsies (6) to controls (6), 87 sequences were upregulated and 83 sequences were downregulated (FC greater or less than 2, 0.01>p>1.68×10–44). To further investigate the acute inflammatory signal 10 inflamed CD TI biopsies were compared to 6 non-inflamed CD biopsies. 149 sequences were up regulated and 156 sequences were downregulated, (FC greater or less than 2, 0.0095 >p>1×10–45). Gene

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ontology revealed a preponderance of these differentially regulated sequences were associated with endoplasmic reticulum stress when gene pathways were considered and lipid metabolism when biological function was considered. Interestingly, and contrary to previous data,[1] no change in alpha defensin 5 and 6 expression was observed between the CD TI biopsies and controls. This was confirmed by real-time PCR.
Conclusion: Genome wide microarray analysis of CD TI biopsies has allowed us to characterise distinct expression signatures and to identify candidate genes involved in disease pathogenesis that could be considered novel therapeutic targets.

1. **Wehkamp J**, *et al*. Reduced Paneth cell alpha-defensins in ileal Crohn's disease. *Proc Natl Acad Sci U S A* 2005;**102**:18129–34.

360 SERUM AND SALIVARY IGA RESPONSES TO A 200 KD SACCHAROMYCES CEREVISIAE ANTIGEN IN OROFACIAL GRANULOMATOSIS AND CROHN'S DISEASE

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Introduction: Orofacial granulomatosis (OFG) is a rare chronic inflammatory disease of unknown aetiology and has been linked to Crohn's disease (CD). Whether OFG represents a true manifestation of CD or exists as a separate entity remains uncertain. Serological markers such as anti-*Saccharomyces cerevisiae* antibodies (ASCA) have proven useful in defining indeterminate cases of inflammatory bowel disease. Early identification of patients with gut CD presenting as OFG is likely to be beneficial.
Aims & Methods: To investigate whether the immunological response to a specific *S cerevisiae* 200 kd glycoprotein antigen in serum and saliva can predict the presence of gut CD in patients with OFG. Serum and salivary antibodies to a 200 kd *S cerevisiae* antigen were measured by ELISA in 4 distinct groups of patients: OFG alone (n = 10), gut CD alone (n = 10), both oral and gut CD (n = 7) and healthy controls (n = 30). Response to control antigens from SAP2 protein (from *Candida albicans*) and whole cells of *Escherichia coli* (*E coli*) were also determined.
Results: Serum IgA antibodies to *S cerevisiae* 200 kd were raised markedly in the two groups with gut disease compared to controls (OFG + CD, $p<0.005$ and CD, $p<0.001$). Whole saliva IgA antibodies to *S cerevisiae* were raised in the groups with oral involvement but also in CD ($p<0.005$). Specific salivary IgA to SAP2 from *Candida albicans* were also raised in the groups with oral involvement ($p<0.005$) and in CD ($p<0.001$). Serum IgG to SAP2 was raised in the groups with oral involvement whilst serum IgA to SAP2 did not show any difference between the four groups. Specific serum IgG to *E coli* was elevated in all three groups ($p<0.005$) but no difference between the groups was seen with salivary IgA to *E coli*.
Conclusion: These findings suggest that raised serum IgA antibodies to *S cerevisiae* 200 kd may reflect gut inflammation while raised salivary IgA antibodies to *S cerevisiae* 200 kd reflect oral and/or gut disease. High titres of serum IgA to *S cerevisiae* 200 kd antigen might be of predictor of gut involvement in OFG, identifying a subgroup of patients that may benefit from early gastrointestinal investigations and possibly treatment.

361 THE DIETARY MANAGEMENT OF OROFACIAL GRANULOMATOSIS

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Introduction: Orofacial granulomatosis (OFG) is a rare chronic inflammatory disease of unknown aetiology that typically presents with lip swelling in young adulthood. Management of OFG remains a challenge but recent evidence implicates dietary antigens, in particular cinnamon and benzoate, as a possible trigger of the chronic inflammatory process. At our institution dietary manipulation, in the form of a cinnamon and benzoate free diet (CB-free), is used as a standard first line treatment. Failing a CB-free diet, a more formal dietary approach with liquid enteral diet as a sole source of nutrition is offered. In this study we review the impact of a dietary approach to OFG.
Aims & Methods: A retrospective case note review to determine the utilisation and efficacy of dietary manipulation in patients with OFG. Patients attending a combined Oral Medicine/Gastroenterology clinic with a diagnosis of OFG confirmed by typical clinical and histological features were advised on a CB-free diet (n = 57) for 12 weeks. Following treatment with a CB-free diet those patients who required further symptomatic control were assessed for suitability of liquid enteral diet (elemental E028 or Modulen IBD) as a sole source of nutrition for 6 weeks followed by a low fat, fibre limited, exclusion (LOFFLEX) reintroduction regimen. A standardised oral disease chart was used to objectively assess the oral features pre- and post all dietary treatments.
Results: Data were available on 57 patients who followed a CB-free diet. The median age was 22 years and 29 patients were male. Improvement in oral activity scores was seen in 39/57 (68.4%) patients following a CB-free diet after 12 weeks. Of the 57 patients, 15 patients with an incomplete or absent response to the CB-free diet were assessed for liquid enteral nutrition. Data were available for 12 of the patients. Three patients could not comply with the diet within the first week and one had no response after six weeks of Modulen IBD. On an intention to treat basis, 8/12 (66.7%) patients had improvement in their oral disease activity scores, two were taking Modulen IBD and 6 were taking elemental E028.
Conclusion: A dietary approach as management for patients with OFG is an effective form of treatment and supports the view that the disease is driven by a dietary antigen(s). The disease typically affects teenagers and young adults making dietary therapy particularly appropriate. In a majority, this avoids the need to consider corticosteroids and immunosuppression.

362 B-CELL INFILTRATES IN OROFACIAL-GRANULOMATOSIS

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Introduction: Orofacial granulomatosis (OFG) is a rare chronic inflammatory disease of unknown cause and which overlaps with Crohn's disease. Recent data suggest a possible dietary link with benzoate. Histologically OFG is characterised by a chronic inflammatory cell infiltrate, non-caseating epithelioid granulomas, lymphoedema of the corium and dilated lymphatics. We have recently observed B-cells with dendritic morphology in the inflammatory infiltrates that have not been described previously.
Aims & Methods: To characterise the B-cell infiltrate in patients with OFG. Serial sections of paraffin embedded lip biopsies from patients with a confirmed diagnosis of OFG were stained for CD20, CD21 and IgD. A frozen lip biopsy sample was also stained for CD138 and CD19. Standard immunohistochemical techniques were applied.
Results: Lip biopsies in OFG contain an infiltrate of subepithelial large dendritic B-cells in all of 12 cases studied. They express the B cell marker CD20, but not markers of naive B-cells such as IgD or CD21. They are not associated with organised follicular lymphoid structures since B-cells expressing IgD and CD21+ follicular dendritic cells were absent in serial sections. The dendritic processes of the B-cells frequently associate with adjacent cells, confirmed to be T-cells in double stained preparations. They are unlikely to represent differentiation of B lineage towards plasma cells since the CD20+ infiltrate is not consistantly accompanied by a CD19+, CD20- B-cell subset or CD138+ cells that would signify local plasma cell differentiation.
Conclusion: B-cells with dendritic morphology that are independent of lymphoid follicular structure are present in the oral mucosa in OFG. These cells resemble large interfollicular B-cells in the T-cell zones of lymph nodes and follicle independent B-cells in the thymus that have been linked with antigen presentation. These B-cells may therefore provide a link between the specific recognition of dietary benzoate within this group of patients and the associated inflammatory response.

363 HIGH THROUGHPUT 16S RIBOSOMAL RNA SEQUENCE ANALYSIS OF THE INTESTINAL MICROBIOTA IN CROHN'S DISEASE

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Introduction: It is generally accepted that alterations in the bacterial microbiota associated with the human intestinal mucosa play a critical role

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in the pathogenesis of IBD. Previous studies on the composition of the bacterial flora in Crohn's disease (CD) patients and healthy controls using fluorescent in situ hybridisation (FISH) or culture suggest higher content of Bacteroides spp and Clostridia in patients with CD. The exact difference in the microbiota between inflamed and non-inflamed mucosal sites in CD patients has not been established.
Aims & Methods: The aim of this study was to undertake detailed molecular characterisation of the mucosal-associated microbiota in inflamed and non-inflamed mucosal sites in CD patients using high throughput bacterial 16S ribosomal RNA sequencing. Total DNA was extracted from paired biopsies of inflamed and non-inflamed mucosa from 6 patients with CD and from biopsies of healthy mucosa of 6 normal controls. Bacterial DNA was amplified using universal bacterial 16S ribosomal RNA gene primers and cloned into a plasmid vector to generate clone libraries. Approximately 620 clones from each clone library or total of 11 160 bacterial clones were sequenced and the data analysed to identify individual operational taxonomic units (OTUs) or phylotypes within the sequence set. Data from the species-level differences between inflamed and non-inflamed sites were analysed using χ^2 test and integral-libshuff analysis.
Results: The clone libraries yielded 11 160 sequenced clones, with up to 101 OTUs per clone library, representing a large sample population. The identified phylotypes included Firmicutes, Fusobacteria, Actinobacteria, Proteobacteria, CFB (Cytophaga-Flavobacterium-Bacteroides) and previously unidentified bacterial phylotypes. Analysis on species level data showed a highly significant difference (p = 8.23 E-52) between inflamed and non-inflamed tissue in all of the CD patients. Higher numbers of Firmicutes, (including all Clostridia spp) were found in the inflamed mucosa of all of the CD patients. The most abundant species in all of the 6 CD patients were Firmicutes and Bacteroidetes.
Conclusion: This is the most extensive 16S ribosomal RNA sequence analysis of the intestinal microbiota in CD undertaken to date and shows a highly significant difference between inflamed and non-inflamed mucosa in CD. The findings of increased numbers of Firmicutes and Bacterioidetes in inflamed mucosa complement those obtained by FISH. Further detailed analysis of these species may reveal phenotypic properties important in the pathogenesis of CD.

364 MOLECULAR CHARACTERISATION OF MUCOSAL ENTEROBACTERERIACEAE ISOLATED FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: A number of groups, including our own, have reported consistent isolation of Enterobacteriaceae (predominanty E coli) from the inflamed mucosa of patients with inflammatory bowel disease (IBD). Previous studies from our group using fluorescent in situ hybridisation suggest these bacteria lie within lamina propria macrophages in both Crohn's disease (CD) and ulcerative colitis (UC). The exact phenotype of these bacteria has not been fully established and any role in the pathogenesis of CD or UC remains uncertain.
Aims & Methods: The aim of this study was to undertake the molecular characterization of Enterobacteriae isolated from mucosa of patients with CD and UC. Paired mucosal biopsies of inflamed mucosa from patients with CD (n = 15), UC (n = 11) and of normal mucosa from healthy controls (n = 8) were cultured in selective liquid media with and without gentamicin (100 μg/ml) for 30 minutes. Samples were then disrupted and transferred to McConkey agar and cultured overnight. Initial typing of resulting colonies was undertaken by API20E strips. Colonies were also sent to the Colindale HPA for serotyping. Finally, bacterial DNA was extracted and used for multi-locus sequence typing (MLST) which types isolates according to the DNA sequence of 7 bacterial housekeeping genes.
Results: All biopsies (CD, UC and controls) cultured without gentamicin produced isolates, with one isolate being typed as Klebsiella and all the rest being typed as E.coli by API20E. Colony numbers from CD and UC were fourfold higher than controls. With gentamicin, isolates were obtained from 12 of 15 (80%) CD, 4 of 11 (36%) UC but none from controls. Higher colony number without gentamicin predicted an isolate with gentamicin. API20E defined these as E coli apart from the one patient with the isolate typed as Klebsiella spp in the non-getamicin culture who again was positive for this species. Standard HPA serotyping of gentamicin E coli isolates defined these as E coli 08, 0 rough or 0 unidentifiable serotype. MLST analysis showed a different allelic profile in each isolate including three previously unreported MLST profiles. Furthermore, in each patient the non-gentamicin and gentamicin isolates were identical.
Conclusion: The MLST profiles suggest that intracellular isolates of Enterobacteriaceae (predominantly E coli) are those resident at the mucosal surface. Some isolates have a unique and previously unidentified serotype and genotype suggesting that certain specific properties, as yet undefined, may permit submucosal access. Alternatively, the colony numbers support an entirely passive phenomenon. Further molecular analysis of known virulence factors may reveal common properties predicting submucosal presence in IBD.

365 THALIDOMIDE IN LUMINAL AND FISTULISING CROHN'S DISEASE RESISTANT TO STANDARD THERAPIES

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Introduction: Thalidomide has been shown to be an effective treatment in patients with Crohn's disease (CD).
Aims & Methods: We retrospectively assessed the efficacy and tolerability of thalidomide in patients with refractory CD. 25 patients with CD (eight luminal, 11 fistulising, 4 luminal and fistulising, 2 perianal ulcerating disease) refractory to standard therapy, including infliximab, were treated for a mean of 32 weeks. All patients had active luminal disease with a Crohn's Disease Activity Index (CDAI)>200 and/or draining fistulising disease. Thalidomide was started at a dose of 50 or 100 mg at night and increased stepwise if tolerated. Retrospective ''estimated'' CDAIs were assessed at baseline and at end of follow-up. Clinical response was defined as a reduction in the ''estimated'' CDAI of >100 points for patients with luminal disease, ⩾50% reduction in draining fistulas or ⩾50% reduction in perianal ulcer size. Clinical remission was defined as an ''estimated'' CDAI <150 points (luminal disease), complete fistula closure (fistulising disease), and complete ulcer healing (perianal ulcerating disease).
Results: Six of 8 patients (75%) treated for luminal disease responded to thalidomide at a median follow-up of 12 months (3 clinical responses, 3 clinical remissions). The median ''estimated'' CDAI was 378 (range 251–600) at baseline and 151.5 (range 98–241; p = 0.005) at the end of follow-up. Nine of 11 patients (81.8%) with active fistulising disease responded to thalidomide (6 responses; 3 remissions). All the patients treated for both luminal and fistulising disease had fistula response (3 clinical responses, 1 complete healing) and 3 of them had a response in luminal disease activity (2 remissions, 1 clinical response). One of 2 patients with ulcerating perianal disease responded. Three of 7 (43%) steroid-dependent patients discontinued steroids. 12 patients (48%) discontinued treatment because of adverse effects (sedation = 3; abdominal pain = 2; leucopenia = 1; neuropathy = 6).
Conclusion: Thalidomide is an effective and relatively safe treatment in selected patients with refractory luminal and fistulising CD. It has a potential role in the short to medium-term use for acute disease, bridging therapy, or fistulising disease. Its long-term use is limited by toxicity.

366 A NON-SYNONYMOUS SNP IN AN AUTOPHAGY-RELATED GENE IS ASSOCIATED WITH CROHN'S DISEASE

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Introduction: A genome-wide association scan of non-synonymous single nucleotide polymorphisms (nsSNP) in Crohn's disease (CD) patients from Germany detected a highly significant association in a gene from the autophagocytosis pathway which is known to participate in the degradation of intracellular pathogens such as bacteria and viral particles. We investigated this SNP in British cases and controls to confirm the association and to examine its effect on clinical phenotype.
Aims & Methods: A total of 1236 British CD cases and 1235 population controls were genotyped for the nsSNP in the ATG-related gene and known

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disease susceptibility variants in CARD15 and IBD5 loci to test for association and interaction with these loci. In addition, genotype data were stratified by clinical phenotype in order to determine if the ATG-related risk variant is associated with a particular subtype of CD based on site of disease and disease behaviour.
Results: The frequency of the ATG nsSNP was 58.1% in CD cases and 51.3% in controls, demonstrating a highly significant association with CD ($p = 2.4 \times 10–6$). Genetic modelling revealed that this trait locus best fits a recessive model with a 1.65-fold increase in risk of disease in individuals homozygous for the risk allele (95% CI 1.32 to 2.07). This risk was increased to 2.6-fold for ileal disease (95% CI 1.59 to 4.31) $p = 8.7 \times 106$, and there was no increase in risk of CD for other disease sites. Analysis of the ATG locus with respect to interaction with the two other well-defined IBD loci, CARD15 and IBD5, indicated independent additive contributions for all three loci to the risk of CD.
Conclusion: These data, together with the recent report of an association of the IL23R locus with CD, strongly support the existence of at least 4 susceptibility genes for this disorder, and indicate a role for processing of intracellular bacteria in the pathogenesis of CD.

367 A GLYCOMIC APPROACH TO THE IDENTIFICATION OF DISEASE BIOMARKERS IN INFLAMMATORY BOWEL DISEASE

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Introduction: Earlier research into IgG glycosylation changes associated with rheumatoid arthritis and other rheumatic diseases has indicated the presence of sugar biomarkers that may be associated with health and disease. Furthermore, a pilot study has demonstrated the possibility of using this technique to differentiate between Crohn's disease, ulcerative colitis and healthy controls. Our aim was to extend these studies using serum to assess the direct diagnostic and prognostic potential for identifying other sugar biomarkers in a cohort of patients with inflammatory bowel disease.
Aims & Methods: High performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD) together with mass spectrometry (MS) was used to compare the overall glycosylation profile of patients with Crohn's disease (CD) (n = 30), ulcerative colitis (UC) (n = 30), indeterminate colitis (IC) (n = 15) and healthy controls (n = 15). The oligosaccharides were enzymatically cleaved from total serum glycoproteins using PNGase-F.
Results: HPAEC-PAD analysis together with MS indicates marked and significant differences in the glycosylation profiles of CD and UC from each other, and from healthy controls. These include changes in the neutral as well as monosialyated and multi- (di-, tri- and tetra-sialyated structures) where the major changes occur. Additionally, in the cohort of patients with IC, the glycosylation profile was often similar to those associated with CD or UC.
Conclusion: We have demonstrated that HPAEC-PAD can be used to provide rapid complete sugar profiles of serum glycoproteins, and that there are marked and significant differences associated with inflammatory bowel disease. The results also suggest that indeterminate colitis may not be a separate entity in patients, and may eventually be diagnosed as either CD or UC after a latent period. We conclude that serum sugar profiles may be of use in the management of patients with inflammatory bowel disease, and further suggest that glycoproteins other than IgG may be undergoing disease-specific sugar variation.

1. **Axford JS**. Glycosylation and rheumatic disease. *Biochim Biophys Acta* 1999;**1455**:219–29.
2. **Watson M**, *et al*. Sugar printing rheumatic diseases: a potential method for disease differentiation using immunoglobulin G oligosaccharides. *Arthritis Rheum* 1999;**42**:1682–90.

368 ENDOSCOPICALLY MEASURED MUCOSAL HEALING CORRELATED WITH RESPONSE TO THERAPY IN MODERATELY ACTIVE ULCERATIVE COLITIS

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Introduction: [Introduced by Dr S Travis] To examine the correlation between endoscopically measured mucosal healing and response to therapy with delayed-release oral mesalamine 4.8 g/day (investigational 800 mg tab) and 2.4 g/day (marketed 400 mg tab) in patients with moderately active ulcerative colitis (UC).
Aims & Methods: Data from 2 Phase III, multicentre, randomised, double-blind, 6-week, controlled studies of similar design (ASCEND I&II) were pooled and analysed. The primary endpoint was treatment success, predefined as improvement from baseline in the Physician's Global Assessment (PGA) accompanied by improvement in at least one other clinical assessment (stool frequency, rectal bleeding, patient functional assessment (PFA), or endoscopy findings) and no worsening in any of the remaining clinical assessments. Mucosal healing was defined as an endoscopy score of 0 or 1. PFA was based on a 4-point scale, 0 (''generally well'') to 3 (''terrible''). Patients with moderately active UC (baseline PGA = 2) and baseline endoscopy subscore >2 were included in this analysis. The correlation between mucosal healing and treatment response and PFA was determined.
Results: 423 analysable patients with moderate UC were randomised in the two studies, of which 391 patients met the criteria for these analyses. The two treatment groups were balanced at baseline with regard to demographic characteristics, disease history, and disease state characteristics. Overall at 6 weeks, 67% of moderate UC patients who achieved treatment success also had mucosal healing ($\kappa = 0.6938$). This finding was consistent regardless of dose of 2.4 g/day or 4.8 g/day ($\kappa = 0.7452$ and 0.6046, respectively). This finding was also consistently present at the 3-week time point ($\kappa = 0.7173$). An endoscopic score of 0 alone was poorly correlated with treatment success but did improve from 3 weeks to 6 weeks ($\kappa = 0.1176$ and 0.2252 respectively). Regardless of dose or time, PFA correlated poorly with mucosal healing. Both doses of mesalamine were well tolerated, with adverse events comparable between 4.8 g/day and 2.4 g/day.
Conclusion: This analysis demonstrates that successful treatment of moderately active UC with mesalamine is associated with improved mucosal integrity as early as 3 and 6 weeks. The lack of association between endoscopic improvement and PFA may be due to the fact that UC patients' general wellbeing involves more than mucosal healing.

369 DIABETIC CONTROL IS NOT DISTURBED BY AN ORAL CORTICOSTEROID (PREDNISOLONE METASULFOBENZOATE) DESIGNED TO TREAT COLITIS

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Introduction: Corticosteroids remain the mainstay of treatment of acute severe ulcerative colitis despite potential side effects, including unmasking latent diabetes or exacerbation of known diabetes. Orally administered Eudragit-L-coated prednisolone metasulfobenzoate (Predocol) has limited absorption but remains effective in treating colitis. The effect of oral Predocol on diabetic control has not been studied.
Aims & Methods: To compare the effects on blood glucose in stable diabetic volunteers of a single dose of prednisolone metasulfobenzoate with a single dose of prednisolone. Blood glucose levels were measured in stable diabetic volunteers following either oral Predocol 30 mg or oral

Abstract 369 Glucose levels pre- and post-treatment in the 24- and 48-h post-dose periods

Blood glucose (mmol/l)	Pre-Predocol (n = 22)	Post-Predocol (n = 22)	Pre-prednisolone (n = 22)	Post-prednisolone (n = 22)
24 hours: mean (SD)	7.7 (1.5)	7.7 (1.4)	7.7 (1.3)	10.8 (2.4)
24 hours: range	5.3–10.3	5.9–11.5	5.4–11.1	6.8–15.5
48 hours: mean (SD)	7.7 (1.5)	7.8 (1.2)	7.7 (1.3)	9.2 (1.9)
48 hours: range	5.3–10.3	5.4–10.9	5.4–11.1	6.3–13.0

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prednisolone 30 mg in a randomised, double-blind, single dose, cross-over study.
Results: The greatest effect on blood glucose occurred in the first 24 h with an increase in mean blood glucose following prednisolone of 3.05 mmol/l with no change following Predocol ($p<0.001$). In the 48-h post-treatment period mean blood glucose increased from 7.7 to 7.8 mmol/l following Predocol and from 7.7 to 9.2 mmol/l following prednisolone (treatment difference 1.44 mmol/l; $p<0.001$).
Conclusion: A single oral dose of Predocol 30 mg has a minimal effect on blood glucose levels in controlled diabetics in contrast to a significant increase seen following a single oral dose of prednisolone 30 mg. This is of importance to diabetic patients requiring steroid therapy for colitis. Predocol may be a preferred alternative to conventional prednisolone in the treatment of acute colitis in diabetic patients. Further work is needed to establish the effect of a course of Predocol on diabetic control.

1. **Ford GA**, Oliver PS, Shepherd NA, *et al*. An Eudragit-coated prednisolone preparation for ulcerative colitis: pharmacokinetics and preliminary therapeutic use. *Aliment Pharmacol Therap* 1992;**6**:31–40.
2. **Darlow SJ**, Simon J, Mandal A, *et al*. The short term effects of Eudragit-L-coated prednisolone metasulphobenzoate (Predocol) on bone formation and bone mineral density in acute ulcerative colitis. *Eur J Gastro Hepatol* 2004;**16**:1173–6.
3. **Cameron EA**, Binnie JA, Balan K, *et al*. Oral prednisolone metasulphobenzoate in the treatment of active ulcerative colitis. *Scan J Gastroenterol* 2003;**38**:535–7.

370 CYCLOSPORINE IN ACUTE ULCERATIVE COLITIS: A RETROSPECTIVE REVIEW OF A TEACHING HOSPITAL CASELOAD OVER AN EIGHT-YEAR PERIOD

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Introduction: Cyclosporine (CsA) has been regarded as rescue therapy in patients with active colitis who would otherwise have surgery. CsA is currently under review since publication of the Janerot Study[1] showing a benefit with infliximab as rescue therapy in moderate to severe ulcerative colitis
Aims & Methods: Retrospective review from 1998–2006. By reviewing clinical records we assessed short and long-term efficacy of intravenous (IV) CsA
Results: Twenty three patients received CsA, 11 female, 12 male. Mean age 44.5 years, mean time from initial diagnosis of ulcerative colitis to CsA treatment was 5.5 years, 7 patients (30%) received IV CsA on their presentation. Mean duration of symptoms prior to hospitalisation was 7 weeks. Two patients (9%) were already taking azathioprine. Mean CRP on admission was 133 mg/l. All patients received IV steroids. CsA was commenced on mean day 12, for a mean duration of 8 days. In 18 (78%) of the cases 4 mg/kg dose was used, in the remaining 5 cases (22%) 2 mg/kg was used. 15 of the 23 patients (65%) responded and did not require colectomy. Eight patients (35%) required colectomy on the same admission, one of whom died postoperatively from sepsis secondary to peritonitis (she had received the longest duration of IV CsA). 14 of the 15 patients discharged with an intact colon were on oral CsA at a mean dose of 6.3 mg/kg. Mean duration of use was 3.6 months. Of the 14 patients discharged on oral CsA, 12 (86%) were on triple immunosuppression (ie prednisolone, CsA and azathioprine). The other 2 patients were commenced on azathioprine on discontinuation of their CsA. 6 out of the 12 patients on triple immunosuppression were on pneumocystis prophylaxis with co-trimoxazole. We had an initial colectomy rate of 35%, 43% at 1 year, 58% at 2 years, 65% at 3 years, 65% at 4 years and 73% at 5 years. With regards to treatment response to CsA in relation to site of the colitis, 1 patient had a proctitis (failed to respond to treatment), 5 patients had proctosigmoiditis (all responded to treatment), 6 had left sided colitis (5 responded) and 11 had pancolitis (only 5 responded).
Conclusion: Our data are consistent with previously reported outcomes. Our policy now is to use the 2 mg/kg dose to start treatment with CsA after day 3 of IV hydrocortisone therapy (if Travis criteria[2] are met) or no later than day 7 if the patient is refractory to IV steroids and for no longer than 7–10 days. By this means, colectomy is not delayed. Our review suggested that patients with a pancolitis were less likely to respond to CsA therapy than limited colitis. We routinely give triple immunosupression (steroids, azathioprine and CsA) with co-trimoxazole prophylaxis and discontinue CsA at 3–6 months in patients who have been discharged with an intact colon. Infliximab is likely to have a role to play in acute severe refractory colitis but despite favourable short-term data,[1] long-term data are awaited.

1. **Jarnerot G**, *et al*. Infliximab as rescue therapy in severe to moderately severe ulcerative colitis: a randomized, placebo-controlled study. *Gastroenterology* 2005;**128**:1805–11.
2. **Travis SP**, Farrant JM, Ricketts C, *et al*. Predicting outcome in severe ulcerative colitis. *Gut* 1996;**38**:905–10.

371 MYELOTOXICITY IS A LATE EVENT IN AZATHIOPRINE TREATED TPMT HETEROZYGOTES

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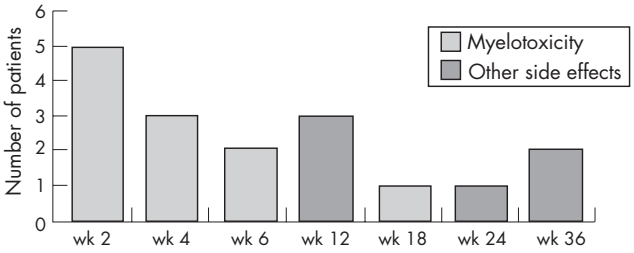
Introduction: Heterozygous TPMT deficiency has been reported to be associated with side effects to azathioprine, particularly myelotoxicity. However, the extent and timing of toxicity when treated with azathioprine at standard dose is not clearly established and as a result take up of TPMT testing pre-treatment remains low.
Aims & Methods: We undertook a subgroup analysis of TPMT heterozygous patients identified in a prospective cohort of 216 inflammatory bowel disease (IBD) patients treated with 2 mg/kg azathioprine. Monitoring included FBC, renal and liver profile, ESR and CRP, (at weeks 2, 4, 6, 12, 18 and 24) and thioguanine nucleotide (TGN) levels and clinical assessment (at weeks 4, 12 and 24).
Results: 19 (9%) of the cohort were TPMT heterozygous (12 CD, 7 UC). All were prescribed azathioprine as a steroid sparing agent. There was 100% concordance between TPMT genotype and phenotype. By 36 weeks, 17/19 patients had withdrawn due to: myelotoxicity (6), gastrointestinal disturbance (6), nausea (4), and rash (1). Myelotoxicity occurred from 12 weeks (mode 12 wks, range 12–36 wks) and all episodes occurred off steroids. In 4 patients myelotoxicity occurred within 4 weeks of steroid withdrawal. In those with normal TPMT, the incidence of myelotoxicity was 1%. The single patient who appeared to tolerate long-term azathioprine was non-compliant (multiple low TGN blood levels (75 pmol/8×108 RBC) and urinary 6-thiouric acid). The average TGN level in the remainder was high (566 pmol/8×108 RBC).
Conclusion: TPMT heterozygous patients do not tolerate full dose azathioprine and in the majority of cases treatment is withdrawn within 6 weeks due to gastrointestinal side effects. This early effect may protect this group from later occurring myelotoxicity. Steroids appear to have a protective effect. The implications for therapy are: (1) TPMT heterozygous patients will not tolerate standard dose azathioprine therapy; (2) conventional early intensive blood monitoring regimens will not detect myelotoxicity in this group; (3) close FBC monitoring when withdrawing concurrent steroids is important to detect late myelotoxicity.



Abstract 371 Side effects experienced by TPMT heterozygous patients on standard dose azathioprine.

372 SERUM PROTEIN SIGNATURES DETERMINED BY MASS SPECTROMETRY (SELDI-TOF) ACCURATELY DISTINGUISHES CROHN'S DISEASE FROM ULCERATIVE COLITIS

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Introduction: Accurate diagnosis of ulcerative colitis (UC) or Crohn's disease (CD) is essential to guide patient management. Current tests are invasive and carry significant risks. A recent meta-analysis suggests that serological diagnosis of CD by ASCA positivity and pANCA negativity has a sensitivity of 54.6% and pANCA positivity has a sensitivity of 55.3% in the diagnosis of UC.
Aims & Methods: In this preliminary study serum was collected prospectively from patients with histological proven UC (n=62) and CD

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(n = 63) and stored at −80°C. Samples were applied to CM10 protein chip arrays and time-of-flight spectra were generated using a PBS-II mass spectrometer (Ciphergen, Freemont, CA, USA). To identify peaks, spectra were normalised to the total ion current in the m/z range over 2000–100 000 after baseline subtraction. Biomarker Wizard version 3.1 was used to identify corresponding peaks in each spectrum (peak clusters) within 0•3% of the molecular mass. Signal-to-noise ratio was set at 5 for the first pass and 2 for the second pass. Preliminary analysis was performed using p value determination of integrated peaks. Statistical analysis was performed using principal components and support vector machine (SVM) classifiers. Classifier performance was measured using 10-fold cross-validation.

Results: A linear kernel SVM classifier working on ten principal components of the original data obtained a sensitivity of 77% (7%), specificity of 79% (5%), accuracy of 79% (4%) and area under the receiver operating characteristic curve of 0.77 (0.04), on a 10-fold cross-validation study. The peaks selected by the SVM were also significantly discriminative when used in individual peak analysis.

Conclusion: Using protein signatures of patients with UC and CD we have developed a classification model which is more accurate and sensitive than currently available serological tests. Characterisation of discriminant peaks is currently underway and may offer serum based diagnostic techniques in the future.

373 INFLIXIMAB THERAPY IN CROHN'S DISEASE: CURRENT PRACTICE FOR FUTURE GUIDELINES

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Introduction: The National Institute of Clinical Excellence (NICE) recommends Infliximab therapy in Crohn's disease (CD) for patients who have severe active disease, who are refractory (or intolerant) to medical therapy and for whom surgery is inappropriate.[1] In addition, NICE recommends that an experienced gastroenterologist prescribes therapy in an episodic regime and not in isolated fistulating CD. Clinical studies have shown efficacy of infliximab as maintenance therapy[2] and for fistulising CD (FCD).[3]

Aims & Methods: To audit the practice of Infliximab prescribing compared to NICE recommendations and to determine the therapeutic response. Data were extracted from the St Mark's Hospital database for the period between December 2001 and June 2006. These were analysed for indications and response to therapy.

Results: A total of 65 patients were included in the database: 40 (62%) were female and 25 (38%) were male. Of those treated, 61/65 (94%) were between 20–59 years of age. An experienced gastroenterologist prescribed infliximab for all the patients and all cases were refractory or intolerant of other medical therapy. With respect to disease activity, therapy was commenced on the basis of symptoms rather than research indices. The symptoms were poor general health (PGH) in 55/65 (85%), abdominal pain in 27/65 (41%) and diarrhoea in 21/65 (32%). More than one symptom was noted with PGH and abdominal pain in 25/65 (38%) patients, and PGH, with abdominal pain and diarrhoea in 15/65 (23%). There were no documented fistulae in 23/65 (35%) cases. Of the remaining patients, 27 (42%) had perianal FCD, 8 (12%) had abdominal FCD and 3 (5%) had both. The remaining 4 cases had isolated perianal FCD without active luminal disease. Maintenance infusions were prescribed in 46 patients (71%) and only 2/46 (4%) lost response to therapy in this group compared to 19 patients given episodic infusion where 7(37%) lost response to therapy. For patients with non-FCD, a clinical response was noted in 19/23 (86%) of the patients. Of the 31 patients (48%) who received infliximab for perianal FCD, a response was noted in 27/31 (90%). A clinical response was noted in 6/8 (85%) patients with abdominal FCD.

Conclusion: This audit shows that compliance with NICE recommendations was 100% for prescribing by a Gastroenterologist and for disease refractory or intolerant to other medical therapy. Our practice deviated from NICE recommendations with a preference for use in maintenance infusion regimes due to increasing evidence that episodic therapy is associated with greater infliximab antibody formation and reduced clinical benefit. There was also a preference for its use in FCD. Infliximab therapy was prescribed before considering surgery in uncomplicated CD due to the high risk of postoperative recurrence. The NICE Infliximab therapy guideline review should consider all clinical evidence to reflect current evidence-based practice.

1. **National Institute for Health and Clinical Excellence**. Guidance on the use of Infliximab for Crohn's disease. Available at http://www.nice.org.uk/page.aspx?o=TA040guidance.
2. **Hanauer SB**, ACCENT I Study Group, *et al.* Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial. *Lancet* 2002;**359**:1541–9.
3. **Present DH**, *et al.* Infliximab for the treatment of fistulas in patients with Crohn's disease. *N Engl J Med* 1999;**340**:1398–405.

374 IN SITU HYBRIDISATION FOR HUMAN DEFENSINS, LYSOZYME, SPLA2 AND TNFα IN CROHN'S DISEASE AND CONTROLS

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Introduction: Paneth cells are located at the base of crypts of Lieberkühn throughout the small bowel and the appendix and in small numbers in the right colon. They are known to secrete a number of antimicrobial peptides in response to bacteria in the crypt lumen. It has been suggested that the amount of human defensin produced by Paneth cells in patients with Crohn's disease is reduced and is particularly low in patients who carry mutations in the *CARD15* gene.

Aims & Methods: Using the technique of in situ hybridisation we investigated the mRNA gene expression in Paneth cells of lysozyme, $sPLA_2$, human defensins 5 and 6 and TNFα. Archival tissue was identified from patients who had had terminal ileal resections for Crohn's disease or right hemicolectomy for cancer. *CARD15* genotyping was carried out for the 3 common mutations found in Crohn's disease; R708W, G908R and 3020insC. All people gave written informed consent. Non-isotopic in situ hybridization was performed using antisense mRNA probes. Density of staining in Paneth cells was measured using Axiovision software.

Results: Ten in situ hibridization was performed on groups of sections with a standard section, control section, wild type Crohn's disease, *CARD15* heterozygotes and *CARD15* homozygotes/compound heterozygote Crohn's disease sections. There was a significant increase in TNFα mRNA expression in Paneth cells as measured by densitometry in Crohn's disease sections compared to controls ($p<0.001$). There was a trend to increased TNFα mRNA expression in *CARD15* heterozygotes, with a further increase in density of staining in *CARD15* heterozygotes/compound homozygotes. No difference was seen between *CARD15* genotypes and density of staining for lysozyme, $sPLA_2$, human defensin 5 and 6 and TNFα mRNA. No difference was seen between controls and Crohn's disease sections and density of staining for lysozyme, $sPLA_2$, human defensin 5 and 6 and TNFα mRNA.

Conclusion: In contrast to previous work this study shows no difference in human defensin 5 and 6 mRNA expression in Paneth cells between *CARD15* genotypes. TNFα mRNA is shown to be increased in the Paneth cells in Crohn's disease sections. A trend to increased TNFα mRNA expression was seen in Crohn's disease sections homozygous/compound heterozygous for CARD15 mutations.

375 CONFIRMATION OF ASSOCIATION BETWEEN TNFSF15 AND CROHN'S DISEASE IN EAST ANGLIA PANEL

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Introduction: Association between variants in TNFSF15 on chromosome 9q32 and Crohn's disease (CD) was recently reported.[1] In this study there was significant association ($p=1.7\times10-11$ OR 2.17) with single nucleotide polymorphisms (SNPs) and haplotypes in Japanese CD patients. Replication in an Oxford, UK population using TDT and case control panels confirmed an association although the effect was weaker (peak allelic OR1.32 $p=0.02$) and a protective haplotype common to both UK and Japanese populations was identified ($p=0.02$ in both Oxford, UK panels).[1] The discrepancy in effect size is consistent with other studies demonstrating heterogeneity at confirmed CD susceptibility loci between western and Japanese populations.[2] TNFSF15 is a strong candidate IBD susceptibility gene encoding a novel TNF-like factor expressed by macrophages and lymphocytes.[3]

Aims & Methods: Our aim was to replicate the association between variants in TNFSF15 and CD in the UK population using a large independent East Anglia case control panel. 756 CD patients and 636 geographically matched controls were genotyped using Taqman for 3 SNPs defining the risk haplotype in TNFSF15. Results were analysed using

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logistic regression methods within STATA. Haplotypes were reconstructed using SNPHAP v1.3.
Results: Two SNPs (rs3810936 and rs7848647) showed significant association between CD and TNFSF15 overall (p = 0.048 and p = 0.033 respectively; table) There was significant LD between these loci (D′ 0.80 r^2 0.61). Construction of 3 locus haplotypes identified a risk haplotype, frequency 0.65 in cases and 0.62 in controls and one protective haplotype, frequency 0.25 in cases and 0.28 in controls. Although similar to the Oxford panel in the index study this is not statistically significant (p = 0.23).
Conclusion: Our results provide independent replication of association between SNPs in TNFSF15 and CD. We also confirm that TNFSF15 has a smaller effect on susceptibility to CD in UK than in Japanese populations and we were unable to identify a significant risk haplotype. Attempts should now be made to fine map the locus and identify the disease causing variants.

1. **Yamazaki K**, *et al. Hum Mol Genet* 2005;**14**:3499–506.
2. **Yamazaki K**, *et al. J Hum Genet* 2002;**47**:469–72.
3. **Bamias G**, *et al. J Immunol* 2003;**171**:4868–74.

376 GERMLINE VARIATION OF NOD1/CARD4 DOES NOT DETERMINE SUSCEPTIBILITY TO INFLAMMATORY BOWEL DISEASE: RESULTS OF A DETAILED HAPLOTYPE-TAGGING INVESTIGATION

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Introduction: NOD2/CARD15 variation has a definite but weak effect on Crohn's disease (CD) susceptibility in Northern Europe. NOD1/CARD4 and NOD2/CARD15 are intracellular pattern-recognition receptors involved in the anti-bacterial innate immune response. The NOD1/CARD4 gene lies within the putative 7p14.3 IBD locus. Data regarding the role of a complex insertion/deletion (+32656) variant of NOD1/CARD4 in IBD from groups in Germany, England and our own Scottish/Swedish data have shown no association in contrast to the index study from Oxford.
Aims & Methods: The aim of this study was to assess the influence of NOD1/CARD4 on IBD susceptibility and phenotype in the Scottish population using a gene wide association approach. 1693 subjects comprising of 1323 IBD patients (662 CD, 628 UC, 33 IC) and 370 controls were genotyped for nine single nucleotide polymorphisms (SNPs) tagging the NOD1/CARD4 gene and the three common NOD2/CARD15 variants. Allelic, genotype and haplotype frequency comparisons between cases and controls using χ^2 and a log-likelihood analysis were used to assess association with IBD. Genotype-phenotype analyses (Montreal classification, need for surgery—including stratification for NOD2/CARD15 variant carriage) were also performed.
Results: After correction for multiple testing, no significant associations were observed between any of the NOD1/CARD4 SNPs studied and IBD, CD or UC ($p \geq 0.10$ for all). Haplotype case-control analysis was also negative ($p \geq 0.20$ in IBD, CD and UC). NOD2 variant carriage did not influence the effect of NOD1/CARD4 haplotype on CD susceptibility. Using log-likelihood analysis (heterogeneity model—1000 permutations), set χ^2 statistics (degrees of freedom = 511) were reached 103, 396 and 35 times for IBD, CD and UC, respectively (corresponding uncorrected p values 0.10, 0.39 and 0.03). Genotype-phenotype analysis in both adult and childhood onset CD did not show any significant influence of NOD1/CARD4. We did not observe any significant effect of NOD2/CARD15 variant carriage on the influence of NOD1/CARD4 on any of the phenotypes studied.
Conclusion: This is the first study using a gene wide haplotype-tagging approach to assess the contribution of NOD1/CARD4 in IBD. In the Scottish IBD population, germline NOD1/CARD4 variation does not represent an important determinant of disease susceptibility.

377 AZATHIOPRINE TOLERANCE IN INFLAMMATORY BOWEL DISEASE: ASSESS TPMT STATUS BY PHENOTYPE OR GENOTYPE?

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Introduction: Azathioprine is a commonly used drug in the management of refractory inflammatory bowel disease (IBD). Although generally regarded as effective, it is associated with a wide range of adverse events, the most serious being myelosuppression, which can occasionally be fatal. The enzyme thiopurine methyltransferase (TPMT) holds an integral role in the metabolism of thiopurine drugs. Its activity can be measured directly or predicted by detection of genetic polymorphisms. 1/300 individuals are homozygous for mutant alleles and have little or absent enzyme activity, and 11% of the population are heterozygotes with more moderate reduction in activity.[1] Reduced activity of TPMT has been associated with an increased risk of side effects, particularly marrow suppression,[2] and it has been proposed that pretreatment assessment of TPMT status can reduce the incidence of side effects and is therefore cost effective.[3 4]
Aims & Methods: The aim or our study was to determine whether measurement of TPMT activity (phenotype) or TPMT gene polymorphisms (genotype) was more effective in predicting azathioprine intolerance in IBD. Sequential patients were identified and tolerance of azathioprine recorded. Patients had been commmenced on therapy without knowledge of TPMT status. Blood was collected for measurement of TPMT activity and for DNA analysis for the commonest TPMT gene mutations (2, 3B, 3C).
Results: 129 patients were recruited. 86 (67%) remained on azathioprine after a median duration of 30 months. 44 patients (34%) experience side effects, forcing 33 (26%) to discontinue treatment. The commonest side effect was gastro-intestinal upset, affecting 11% of patients. Four patients experienced severe leucopenia (WCC<2) with 3 requiring hospital management for the complications of myelotoxicity. There was no association between TPMT activity and all cause side effects. One of the 4 patients with severe myelosuppression was a heterozygote, but with a TPMT level much lower than could have been predicted from the genotype.
Conclusion: Prior knowledge of TPMT status would have avoided side effects in 1 of 129 patients. Moderate reduction of TPMT activity in heterozygotes did not correlate with risk of any adverse event. Very low TPMT activity accounted for one of our four cases of severe myelosuppression. This would have been predicted by measuring TPMT activity but not by genotyping. Very low TPMT activity in the presence of a heterozygous mutation has been previously reported and attributed to novel mutations acting in a compound heterozygous manner.[5, 6] Measurement of TPMT activity may be superior to genotype analysis in assessing risk due to the possibility of rarer gene mutations being missed.

1. *Am J Human Genetics* 1980;**32**:651–2.
2. *Gastroenterology* 2000;**118**:1025–30.
3. *Aliment Pharmacol Ther* 2004;**20**:593–9.
4. *Am J Gastroenterology* 2005;**100**:2239–47.
5. *Leukemia* 2003;**17**:1422–4.
6. *J Hepatol* 2002;**37**:441–7.

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SNP (rs no)	MAF controls	MAF CD	OR (95% CI)	p Value	Genotype	Controls	CD	p Value
3810936	66.8	70.3	1.2 (1.0–1.4)	0.048	T/T	9.11	8.92	0.034
					T/C	48.1	41.5	
					C/C	42.8	49.5	
7848647	65.6	69.4	1.2 (1.0–1.4)	0.033	A/A	10.7	9.0	0.086
					A/G	47.65	43.18	
					G/G	41.65	47.77	
7869487	67.3	70.2	1.15 (0.97–1.4)	0.10	G/G	8. 82	7.79	0.23
					G/A	47.75	44.03	
					A/A	43.43	48.19	

Allele frequencies and genotypes are given for 756 Crohn's disease patients and 636 controls.

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Liver posters

378 RECOVERY OF LIVER FUNCTION FOLLOWING DECOMPENSATED ALCOHOLIC LIVER DISEASE: RELATION TO SUBSEQUENT DRINKING BEHAVIOUR

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Introduction: We have reported (*McFarlane. Gut* 2006;**55**:A36) that following hospital discharge in patients presenting with a first episode of decompensated ALD (defined as Childs grade B or C), 3-year survival was 80% in abstinent patients and was still substantial (44%) in patients who failed to reduce alcohol intake. How often liver function recovers in these patients is unclear.
Aims & Methods: To document the frequency and determinants of liver function recovery in this cohort following hospital discharge. Serum liver tests were extracted from hospital databases; at least one result was available in 195 patients. Recovery was defined as a serum bilirubin of <34 mmol/l *and* a serum albumin of >35 g/l. Three patients, with recovery prior to index hospital discharge were excluded. Drinking behaviour (unavailable in 2 cases) between discharge and either recovery or latest liver tests classified as: 1 (n = 61): completely abstinent, 2 (n = 48): reduction to below safety limits, 3 (n = 44): reduction but above safety limits and 4 (n = 40): no reduction of prior heavy intake.
Results: By life table analysis, recovery rates for patients who failed to reduce alcohol intake were (mean (SE)) 28 (7)%, 38 (9)% and 47 (9)%, after 6, 12 and 24 months, lower (log rank p = 0.021) than corresponding pooled rates of 41 (4)%, 60 (4)% and 68 (6)% for other drinking categories, between which, rates did not differ. Recovery rates were unaffected by either (a) excluding patients (n = 54) whose initial presentation was associated with a GI bleed, or (b) considering only patients (n = 75) with Childs grade C at presentation (6, 12 and 24 month rates in those failing to reduce (a): 23 (9)%, 41 (10)% and 47 (9)% and (b): 27 (13)%, 27 (13)% and 45 (19)%). By Cox multivariate analysis, recovery was negatively associated with heavy drinking (p = 0.029) and older age (p = 0.008) but not associated with Childs score on initial admission or serum bilirubin or albumin on discharge. Five-year survival was 76 (5)% in patients who recovered and 5 (0)% in those who did not (p<0.001).
Conclusion: Over half of patients with a first episode of decompensated ALD show recovery of liver function over 2 years. Recovery is highly predictive of survival and is more likely in patients who either abstain or reduce their alcohol intake and in younger patients, but is unrelated to initial severity of liver dysfunction. Even in patients failing to reduce their drinking, recovery may still occur, suggesting that decompensated ALD is partly influenced by factors other than alcohol intake.

379 LACTATE ALONE IS NOT AN ACCURATE PREDICTOR OF POOR PROGNOSIS IN PARACETAMOL-INDUCED FULMINANT LIVER FAILURE

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Introduction: The Kings College Hospital (KCH) criteria have been used since 1989 to determine need for transplantation in patients with fulminant hepatic failure. These criteria have recently been modified to include lactate in patients with paracetamol induced fulminant hepatic failure.[1] A lactate >3.5 mmol/l 24 h post overdose or >3.0 mmol/l following fluid resuscitation fulfils a separate criterion for poor prognosis and the patient can be listed for super-urgent orthotopic liver transplant (OLT).
Aims & Methods: To assess the sensitivity and specificity of the lactate criteria applied to patients admitted to the Scottish Liver Transplant Unit (SLTU). A retrospective analysis of all admissions to SLTU from 1 September 2004 to 31 October 2006 with paracetamol overdose (POD). The initial lactate on admission and a second sample following fluid resuscitation were recorded. The sensitivity and specificity of lactate in relation to outcome compared with KCH criteria was analysed.
Results: Sixty eight patients were admitted with a diagnosis of POD. Three patients underwent super-urgent OLT and were excluded from further analysis. The admission lactate was available in 53 patients (med 4.1 mmol/l (range 1.1–19.53 mmol/l)). 30 patients had a lactate >3.5 mmol/l. 12 patients subsequently fulfilled KCH criteria (11 died, 1 survived). 18 patients did not fulfil KCH criteria and 17 survived. The sensitivity of initial lactate for predicting death from FHF was 92%, but specificity was 55%. KCH criteria were 92% sensitive and 95% specific for predicting death. Two patients within the lactate<3.5 group subsequently fulfilled KCH criteria. 26 patients had a second lactate value following fluid resuscitation (med time 12.16 (6.4–26.98) h). Within this group 15 patients' lactate was >3.0, (medtime 12.2 h following initial lactate). Five of these patients survived (med lactate 3.34 (3.03–4.67) mmol/l) and 10 died (med lactate 7.07 (3.03–16.86) mmol/l). Of the 5 patients with lactate >3.0 mmol/l who survived, 4 did not fulfil KCH criteria. Of the 10 patients with lactate >3.0 mmol/l who died, 9 fulfilled KCH criteria. Sensitivity and specificity of post resuscitation lactate >3.0 mmol/l in predicting POD mortality was 100% and 66.7% respectively.
Conclusion: The incorporation of lactate into poor prognostic criteria may reduce the time to listing for OLT however, in our experience this test lacks the specificity to be the sole criterion for listing for liver transplantation in paracetamol overdose. KCH criteria remain sensitive and specific in predicting poor prognosis in patients with paracetamol overdose.

1. **Bernal W**, Donaldson N, Wyncoll D, *et al.* Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. *Lancet* 2002;**359**:558–63.

380 13C-METHACETIN BREATH TEST COMPARED TO ALSO NON-INVASIVE, BIOCHEMICAL BLOOD TESTS IN PREDICTING HEPATIC FIBROSIS AND CIRRHOSIS

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Introduction: The 13C-methacetin breath test and several also noninvasive blood tests comprising routine laboratory parameters have been proposed to predict fibrosis and cirrhosis in chronic hepatitis C.
Aims & Methods: The aim of the study was to compare the diagnostic accuracy between these tests. 96 patients with chronic hepatitis C virus infection, but without clinical evidence of cirrhosis underwent percutaneous liver biopsy in Menghini technique and the 13C-methacetin breath test. The AST to platelet ratio index (APRI), and the AST to APT ratio (AAR) were used as parameters for the staging of fibrosis. The main endpoint was the area under the characteristic curves for the diagnosis of advanced fibrosis (F3-F4) and cirrhosis (F4) according to the Batts Ludwig criteria.
Results: Receiver operating characteristics analysis revealed a cut-off >14.6% best with 84.1% sensitivity and 92.6% specificity for the 13C-methacetin breath test in predicting liver cirrhosis. For the APRI >1.0 66.7% sensitivity and 75.4 specificity, and for the AST to APT ratio >1.0 65.4% sensitivity and 59.4% specificity were obtained in predicting liver cirrhosis. The areas under the curve for the breath test, APRI and the AST to APT ratio were 0.957, 0.799, and 0.688, respectively, when predicting cirrhosis. For identifying patients with advanced fibrosis, the areas under the curve were 0.827, 0.779, 0.561, respectively. Discordances between APRI (29%) or AAR (37.6%) and liver biopsy were significantly more frequent than between 13C-breath test (11.6%) and liver biopsy (p<0.005).
Conclusion: The 13C-methacetin breath test is more reliable in predicting advanced fibrosis and cirrhosis than simple biochemical parameters (APRI, AAR).

381 HAEMOCHROMATOSIS: RISING HOSPITAL ADMISSION RATES BUT STABLE MORTALITY 1989/90 TO 2002/03

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Introduction: Awareness of haemochromatosis has increased in recent years. Treatment of the consequences of iron overload and venesection to prevent progression of disease represent significant healthcare burdens.
Aims & Methods: To investigate time trends for hospital admission and mortality rates for haemochromatosis in England. Hospital admission data for haemochromatosis (ICD-9: 2750, ICD-10:E831) were obtained from the Hospital Episodes Statistics service. Both day-case and inpatient admissions were analysed. Mortality rates for haemochromatosis in England and Wales were also studied.
Results: Hospital admission rates for haemochromatosis substantially increased during the period of the study, for both inpatient admissions and day-cases, and for both sexes. Most admissions occurred in patients aged over 24. Directly age-standardised mortality rates from haemochromatosis remained fairly stable from 1979 to 2000, being 0.07 per 100 000 population for men in 2000 and 0.02 for women.

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Abstract 381

	1989/90 male	1989/90 female	2002/03 male	2002/03 female	Change male	Change female
Inpatients	0.64	0.21	2.36	0.81	+269%	+290%
Day-cases	2.78	0.58	34.9	11.67	+1155%	+1924%

Directly age-standardised admission rate per 100 000.

Conclusion: Hospital inpatient and day-case admissions for haemochromatosis increased markedly over the study period while mortality rates remained stable. Both admission and mortality rates were higher in men than women. The huge increase in the admission rate is likely to reflect improved recognition and diagnosis of iron overload disorders following identification of the HFE gene in 1996, rather than the underlying prevalence of disease or the effect of treatment.

382 HEPATITIS E IGG SEROPREVALENCE IN SOUTH WEST ENGLAND

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Introduction: Hepatitis E (HEV) has previously been thought to be rare in the UK and largely confined to travellers returning from endemic areas in the developing world. However, recent data has shown that locally acquired HEV is more common than previously recognised in the UK[1] and, in contrast to developing countries, is caused by HEV genotype 3 and has a predilection for middle aged and elderly males. The source of locally acquired HEV in the UK is not known, but it could be zoonotic from pigs. Little is known about the HEV IgG seroprevalence in the UK.
Aims & Methods: To study the HEV IgG seroprevalence in a group of blood donors (n = 500), patients with stable established chronic liver disease (CLD, n = 126), and asymptomatic individuals >60 years (n = 336). All had sera tested for HEV IgG (WanTai, China), and the >60 years cohort had a dietary history to establish if they were vegetarian or not.
Results: 85/500 (17%) of the blood donor group were HEV IgG positive compared to 86/336 (25.5%) in the >60 years group (p = 0.002). In the >60 years group males had a significantly (p = 0.05) higher HEV IgG seroprevalence (48/157, 30.5%) compared to females (38/179, 21.2%). 17/126 (13.4%) of the CLD group were HEV IgG positive. This is not significantly different from the blood donor group. 5/336 were vegetarian, 1/5 tested positive for HEV IgG.
Conclusion: These data indicate that subclinical and/or unrecognised infection with HEV is common in the UK. HEV IgG positivity seems to be particularly common in individuals >60 years and males. The reason for this observation is not clear, but we (and others) have shown that this group of individuals seems particularly prone to clinically recognisable locally acquired HEV infection.[1] Over 85% of patients with CLD are HEV IgG negative. These patients can be considered an ''at risk'' population, as HEV superinfection in patients with CLD carries a poor prognosis.[2]

1. **Dalton HR**, Thurairajah P, Fellows HJ, *et al.* Autochthonous hepatitis E in southwest England. *J Viral Hepatitis* (in press).
2. **Ramachandran J**, Eapen C, Kang G, *et al.* Hepatitis E superinfection produces severe decompensation in patients with chronic liver disease. *J Gastrohepatol* 2004;**19**:134–8.

383 INDIGENOUS HEPATITIS E: THE SOUTHAMPTON EXPERIENCE

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Introduction: Hepatitis E virus (HEV) is an enterically transmitted RNA virus traditionally associated with disease in endemic areas such as Africa and Asia. HEV infection in developed countries, where the seroprevalence is much lower, is thought to arise in those who have visited endemic areas or had contact with visitors from these areas. As HEV infection is considered rare in the UK, single centre experience of HEV has hitherto been thought to be too low to represent a clinically significant problem. We present data from a single centre covering a population of 220 000, which suggests that HEV has a greater clinical impact than would be implied from centrally reported statistics.
Aims & Methods: Patients diagnosed with HEV in Southampton University Hospital Trust between May 2005–June 2006 were identified from computer records. Their case notes were reviewed and additional information was obtained from HPA questionnaires.
Results: Fifteen patients with HEV were found in this 13 month period. Diagnoses were confirmed by a positive HEV IgM with rising IgG levels on later specimens. 13 of these 15 patients reported no travel to endemic areas or history of contact with affected individuals. Of these, 8 cases had PCR confirmation of HEV RNA; and all 8 were genotype 3. Of the 13 patients with no travel exposure, the median age was 71.4 years (47–85) and 9 were male. All patients were British of white European ethnicity. 11 were retired; 1 was a refuse collector, 1 worked in a depot and another worked in a residential home. Clinical presentations were similar in all cases. Typical features were a 2–3 week prodrome of malaise, jaundice and anorexia. Initial bloods typically showed a transaminitis with ALTs varying between 600–6000 iu/l. Symptoms resolved over 2 weeks. One patient died of an unrelated cause within 3 months of HEV diagnosis. In this same period, only 4 cases of acute hepatitis B and 2 cases of acute hepatitis A were identified.
Conclusion: HEV was the most common cause of acute viral hepatitis in Southampton within this 13 month period. We believe we have identified the largest cohort of non-travel associated HEV infected individuals in a single centre within the UK. This finding has partly been achieved by implementation of a new testing algorithm. Systematic testing for hepatitis E IgM and IgG was carried out in patients with an ALT >300 (norm 5–42) who had no serological markers of acute hepatitis A, B, C, CMV or EBV. We suggest all patients with an acute hepatitis should be tested for HEV if initial investigations are negative.

384 ULTRASOUND GUIDED VERSUS ''BLIND'' DAY CASE LIVER BIOPSY: WHAT WOULD YOU CHOOSE?

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Introduction: Percutaneous liver biopsy is associated with a morbidity rate >5%. Death is rare. At our centre the outpatient liver biopsy service is provided by doctors from gastroenterology, infectious diseases and radiology. Obese patients, those with a abnormal liver ultrasound (US), a targeted lesion or a previous liver transplant are classified as higher risk. These procedures are done under US guidance either by a radiologist or a gastroenterologist.
Aims & Methods: We audited our practice to identify the local complication rates, to compare US guided (non-plugged) and blind biopsy and to assess how practice could be improved. All outpatient liver biopsies from Jan 2000 and Dec 2005 were traced from the biopsy request. Data for procedure indication, pathology and radiology results, possible complications and death were collected. If a possible complication was identified the notes were obtained for further analysis.
Results: Over the 6-year period there were 640 biopsies on 608 patients. No patient had died within 30 days. We found 33 complications (5.2%). 18 patients were admitted within 30 days (2.8%) including 4 pre-planned. Of the 378 unguided biopsies there were 25 complications: 1 transfusion-dependent haemorrhage, 1 pneumothorax , 1 haemoptysis, 6 samples contained viscera, 11 patients had pain (6 requiring admission) and a further 6 patients attended hospital within 30 days, some for unrelated reasons. Of the 262 US guided biopsies there were 8 complications: 2 patients had pain and a further 6 patients attended hospital within 30 days, some for unrelated reasons. 43 attempts were recorded as having failed. 37 of these were to be undertaken blindly: 4 procedures were felt to be unsafe and were abandoned, 7 failed to obtain an adequate specimen, 10 samples contained inadequate liver tissue for histological diagnosis and 16 samples did not contain any liver tissue. The remaining 6 were performed with US guidance: 5 were not adequate for diagnosis and 1 sample was lost.
Conclusion: Day-case liver biopsy appears to be a safe procedure at our centre. The higher risk US guided biopsies are less likely to fail (2.7% *v* 9.5%) and less likely to be complicated (3.1% *v* 6.6%) and this supports the argument for US-guided biopsy.

385 HEPATITIS C PATIENTS: THE MYTH ABOUT POOR DNA RATES

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Introduction: Several studies report poor attendance of hepatitis C (HCV) patients in outpatient clinics. Good attendance is necessary for compliance with treatment and its monitoring.

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Aims & Methods: This study aimed to compare DNA (did not attend) rates in a HCV clinic with DNA rates in a general gastroenterology clinic, and identify risk factors for poor attendance. Attendance records at the HCV clinic in a district hospital over a period of 17 months were scrutinised. The HCV clinic is run simultaneously alongside a general gastroenterology clinic with an identical appointments system. Patients attending both clinics were divided into new, follow-up and total categories. Characteristics of HCV patients wih a DNA record (failed to attend one or more appointments) were contrasted with those of HCV patients attending all appointments.
Results: There were 245 HCV patient and 1741 general gastroenterology patient appointments. Although the DNA rate of 19% for new HCV patients was greater than the DNA rate of 3% for new non-HCV patients ($p<0.01$), the DNA rate of 9.4% for follow-up HCV patients was not different to the DNA rate of 10.5% for follow-up non-HCV patients. Similarly the total (new and follow-up) DNA rates for HCV (10.6%) and non-HCV patients (10.5%) were not different. When comparing the characteristics of HCV patients who missed one or more appointments with HCV patients who kept all appointments, those with a DNA record were more likely to be male ($p<0.01$), younger (median age 43 *v* 48 years, $p<0.05$), and living alone ($p<0.05$). Previous intravenous drug use was found equally in HCV patients with and without a DNA record, but those with a DNA record were more likely to have used intravenous drugs or methadone in the past 12 months ($p<0.001$). Rates of excess alcohol consumption, psychiatric history and previous criminal behaviour were similar in those with and without a DNA record. Racial origin did not influence DNA rates (35% of this HCV clinic population is Pakistani), and attendance records were better in non-English speakers.
Conclusion: HCV patients in general do not have a higher DNA rate than other gastroenterology clinic patients. However HCV patients who are male, live alone or have recently used intravenous drugs or methadone, are more likely to miss clinic appointments.

386 LONG-TERM OUTCOME OF A COHORT WITH AUTOIMMUNE HEPATITIS AT A SINGLE CENTRE

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Introduction: Data on long-term follow-up of patients with autoimmune hepatitis (AIH) are limited. We describe the long-term outcome of a large cohort of patients with AIH from a single centre.
Aims & Methods: Patients: between 1971 and 2005, 216 patients with AIH, defined by the revised criteria of the International AIH Group (IG),[1] have been followed-up. 32 patients were male, 204 white. Median age at diagnosis: 56.63 years (range 2.5–87 years). The median length of follow-up: 9.23 years (0.17–30.01 years), total length of FU was 2178.08 years.
Results: Presentation: 27 patients had signs of advanced liver disease (Ascites, HE, GI bleed) at diagnosis. 43 patients were completely asymptomatic. 74 patients had a positive family history (15) and/or pre-existing autoimmune disorders (66). 169 patients had hypergammaglobulinaemia, 129 had positive antinuclear (⩾40), 48 positive smooth muscle (⩾40), 7 positive liver kidney microsomal, and 13 positive anti-mitochondrial antibodies. 64 patients were cirrhotic at presentation. Treatment: 21 achieved clinical remission with no treatment. 195 patients were treated with prednisolone (median initial dose: 30 mg, median length on >10 mg: 3 months), 157 also received more than 4 weeks treatment with Azathioprine. Of the 195 treated patients 191 achieved biochemical/clinical remission. 82 patients experienced 170 episodes of clinical and biochemical relapse (median 2.5 episodes/patients). Outcome: 130 patients are under follow-up, 36 died of causes unrelated to liver disease, 10 underwent liver transplantation, 20 died from liver disease and 20 were lost to follow-up. 5 patients developed HCC, all died; all were cirrhotic at diagnosis and 2 presented with decompensation. Rates for death (all-causes) or liver transplantation were 13+2%, 22+3%, 37+4% and 48+5% after 5, 10, 15 and 20 years respectively. Corresponding rates for liver-related death or transplantation were, 7+2%, 9+2%, 18+4% and 25+5%. In multivariate analysis, liver-related death or transplantation was associated with decompensation at presentation and with slow or incomplete response to immunosuppression, but was unrelated to sex, ethnicity, age, serum bilirubin, albumin or globulin at presentation, or to number of relapses. The risk of liver death and transplantation was increased if cirrhosis was present at diagnosis ($p<0.0001$ and $p=0.005$, Fischer's exact test).
Conclusion: Although most patients with AIH achieve initial remission, the risk of liver-related death or transplantation is appreciable with prolonged follow-up, especially in those presenting with cirrhosis and/or with decompensation and those with a slow/incomplete response to immunosuppression.

1. **Alvarez F**, Berg PF, Bianchi FP, *et al.* International Autoimmune Hepatitis Group Report: review of criteria for diagnosis of autoimmune hepatitis. *J Hepatol* 1999;**31**:929–38.

387 RISKS OF MORTALITY, MALIGNANCY AND MYOCARDIAL INFARCTION IN PEOPLE WITH PRIMARY BILIARY CIRRHOSIS: A POPULATION-BASED COHORT STUDY

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Introduction: There is debate over the mortality risk in people with primary biliary cirrhosis (PBC) and whether this risk is reduced by use of ursodeoxycholic acid. We have performed a cohort study using the General Practice Research Database to quantify the excess mortality, malignancy and myocardial infarction (MI) risk in people with PBC.
Aims & Methods: We identified 930 people with PBC and 9202 age and sex matched control subjects. We used Cox regression to estimate the hazard ratios for our outcomes in the PBC cohort compared with the general population. We categorised ursodeoxycholic acid as treatment ⩾6 prescriptions and no treatment <6.
Results: There was a 2.7-fold increased mortality for the PBC cohort compared with the general population (adjusted hazard ratio (HR) 2.69 95% CI 2.35 to 3.09) but no increased risk of extrahepatic malignancy or MI (HRs 1.06, 95% CI 0.77 to 1.45, 1.15 95% CI 0.10 to 1.87 respectively). In those treated with ursodeoxycholic acid (43%) the mortality increase was 2-fold (HR 1.90 95% CI 1.47 to 2.46) compared to a threefold increase for those not exposed (HR 3.19 95% CI 2.71 to 3.76). Overall, we found an eightfold increased risk of primary liver cancer (HR 8.56, 95% CI 3.18 to 23.06) which in those not treated with ursodeoxycholic acid was 19.91 (95% CI 4.74 to 83.63).
Conclusion: People with PBC had a threefold mortality increase compared with the general population which was not explained by an excess risk of malignancy or MI. Treatment with ursodeoxycholic acid was associated with reduced mortality and, perhaps, a lower incidence of primary liver cancer.

Abstract 387 Mortality, malignancy and myocardial infarction (MI) in the primary biliary cirrhosis (PBC) cohort compared with matched controls

	⩾6 UDCA prescriptions, number of events	HR (95% CI)	<6 UDCA prescriptions, umber of events	HR (95% CI)
Mortality control cohort	352	1	795	1
Mortality PBC cohort	71	1.9 (1.47–2.46)	179	3.19 (2.71–3.76)
Any malignancy control cohort	184	1	278	1
Any malignancy PBC cohort	17	0.85 (0.52–1.40)	25	1.24 (0.82–1.87)
Liver malignancy control cohort	6	1	3	1
Liver malignancy PBC cohort	2	3.15 (0.63–15.62)	5	19.91 (4.74–83.63)
MI control cohort	66	1	126	1
MI PBC cohort	4	0.57 (0.21–1.58)	14	1.54 (0.89–2.68)

Analyses restricted according to UDCA treatment.

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Abstract 388 Analysis of predictors of hepatocellular carcinoma (HCC), hepatic decompensation (HD) and mortality

Complication	Asian (%)	Non-Asian (%)	p Value	SVR (%)	No SVR (%)	p Value	%/year
HCC	4/21 (19)	3/144 (2)	0.0054	1/57 (2)	6/108 (6)	0.42	1.02
HD	1/21 (5)	12/144 (8)	1.00	2/57 (4)	11/108 (10)	0.22	1.89
Death	1/21 (5)	6/144 (4)	1.00	1/57 (2)	6/108 (6)	0.42	1.02
All	4/21 (19)	16/144 (11)	0.29	4/57 (7)	16/108 (15)	0.21	2.90

Asian: of East Asian origin.

388 THE RISK OF HEPATOCELLULAR CARCINOMA AND DECOMPENSATION FOLLOWING HEPATITIS C TREATMENT WITH INTERFERON-BASED THERAPY

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Introduction: Patients with advanced hepatic fibrosis due to hepatitis C virus (HCV) are at high risk of hepatocellular carcinoma (HCC) and hepatic decompensation (HD).[1–3] We evaluate their incidence following interferon therapy in patients with F3/4 fibrosis, and study the effect of SVR.
Aims & Methods: A cohort of patients with F3-4 fibrosis (METAVIR) treated with IFN therapy from 1995 to 2006 was identified from the HCV databases at three centres in WA. All patients had compensated (Child's A) liver disease. The incidences of HD, diagnosis of HCC and mortality were recorded. Frequency of HCC screening with U/S and AFP were assessed. Statistical methods used were: χ^2 test, Fischer's exact test and Welch's unpaired *t* test.
Results: 165 patients (128 males and 37 females) were followed for a median of 50 months (0–177) Mean age was 47 years (SD 8.5). 45 had IFN monotherapy (SVR 22%), 34 had IFN/RBV combination therapy (SVR 41%) and 86 had PEG-IFN/RBV therapy (SVR 43%). Asian ethnicity was associated with development of HCC (p = 0.0054). Incidence of HCC was 1.02%/year overall (4.5%/year in Asians, 0.5%/year in non-Asians). There was a reduction in HCC and mortality following SVR (see table) but this was not statistically significant. There was no difference in development of complications between F3 (10/92, 11%) and F4 (10/73, 14%) patients. Overall, 129 patients had HCC screening of which 71% was sporadic, 27% was annual and 2% was 6 monthly. 63 are currently in a screening schedule.
Conclusion: HCV eradication in this high risk population may reduce the risk of HCC and mortality. Patients with F3 fibrosis are at similar risk to F4 for HCC and decompensation and require analogous screening. Asian patients are at greater risk of HCC from HCV-related cirrhosis. There is a need for standardised screening methods and follow-up in all patients.

1. NIH Consensus Statement on Management of Hepatitis C: 2002. *NIH Consens State Sci Statements* 2002;**19**:1–46.
2. **Hayashi K**, *et al.* Incidence of hepatocellular carcinoma in chronic hepatitis C after interferon therapy. *Hepatogastroenterology* 2002;**49**:508–12.
3. **Poynard T**, *et al.* Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C. *Gastroenterology* 2002;**122**:1303–13.

389 MANAGEMENT OF DEPRESSION IN PATIENTS TREATED WITH PEGYLATED INTERFERON AND RIBAVIRIN FOR HEPATITIS C

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Introduction: Depression is a common side effect of PEG-IFN/RBV therapy for hepatitis C. It is a major cause of treatment interruptions, reducing the chances of achieving viral eradication.[1] This study investigates the incidence, risk factors and outcome of patients with PEG-IFN associated depression.
Aims & Methods: Data were collected prospectively using a standardised data sheet on all patients treated with PEG IFN and RBV for hepatitis C. Patients with a history of depression before antiviral therapy were identified. Depressive side effects (DSEs, defined as symptoms necessitating IFN dose reduction, psychiatric consultation, initiation or change of antidepressant medication) were recorded. Predictors of DSEs, IFN dose reductions, psychiatric intervention and rate of sustained virological response (SVR) were recorded. Logistic regression models were used to examine predictors of SVR and DSEs.
Results: DSEs occurred in 30/160 patients (19%), and were independently associated with previous psychiatric history and younger age, but not with sex or treatment duration. Dose reductions and major SEs (suicide attempt or psychiatric admission) were more common with a prior psychiatric history. There was a trend for lower SVR in patients with a prior history of depression compared with those with no history (40 *v* 50%). However this was not significant. There was no difference in SVR between patients who developed DSEs and those that did not.
Conclusion: Patients with a preceding history of depression comprise a high risk, ''difficult to treat'' group with possible reduced SVR. Pre-emptive SSRI use in this group may be beneficial. Otherwise, development of de novo depression responds wells to SSRI therapy and does not affect SVR.

Abstract 389

	Previous psi history	No previous psi history	p Value	Mean age (SD)
No DSE	24/40 (60%)	106/120 (75%)	0.0002	47 (10.3)
DSE	16/40 (40%)	14/120 (12%)		41 (10.5)
Intervention				p = 0.009
SSRI	6 (15%)	5 (4%)	0.0293	
psi review	8 (20%)	8 (7%)	0.0285	
Major SE	3 (8%)	0 (0%)	0.0147	
Dose reduction	7 (18%)	5 (4%)	0.011	
SVR	16 (40%)	60 (50%)	NS	

1. **Rosenberg SD**, Goodman LA, Osher FC, *et al.* Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Public Health* 2001;**91**:31–7.

390 INTERFERON INDUCED THYROID DYSFUNCTION IN CHRONIC HEPATITIS C

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Introduction: Treatment of chronic hepatitis C with interferon is known to be associated with thyroid dysfunction in 5–14% of patients. We studied the incidence, types, outcome and risk factors predictive of thyroid dysfunction.
Aims & Methods: A retrospective analysis was performed on all patients treated with interferon alpha (IFN) or pegylated interferon alpha (PEG-IFN) $\pm$ ribavirin (RBV), who developed abnormal thyroid function tests (TFTs). These cases were compared with treatment-matched controls to identify factors predictive of thyroid dysfunction. Statistical methods consisted of: χ^2 test, Fischer's exact test, Welch's *t* test, and multivariate analysis.
Results: From a total of 511 patients, 45 cases with thyroid dysfunction were identified (8.8%). PEG-IFN was associated with significantly higher rates of abnormal TFT than IFN (14.1% *v* 6.0%, p = 0.0029). Female sex, Asian ethnicity and previous history of thyroid abnormality were predictors of developing TFT abnormality, with sex and ethnicity being independent predictors (table). There was no association with age, weight, autoantibodies, diabetes or SVR. Mean time to development of abnormal TFT was

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Abstract 390 Predictors of thyroid dysfunction

	Cases n (%)	Controls, n (%)	Univariate p value	Multivariate p value	Odds ratio (95% CI)
Total	45 (100)	45 (100)	–	–	–
Females	21 (47)	11 (24)	0.047	0.035	5.6 (1.1–7)
Asian	13 (29)	3 (7)	0.021	0.014	2.7 (1.4–22)
History of thyroid disease	6 (13)	0 (0)	0.026	NS	–

Asian: of East Asian origin.

21.4 weeks. Cytology was obtained in 13 patients: benign follicular pattern (8); thyroiditis (3); and normal (2). 24 patients had mild transient TFT changes, while 21 required treatment. Earlier onset of dysfunction was significantly associated with need for treatment (p = 0.05). 18 patients had persistent thyroid dysfunction by the end of follow-up.
Conclusion: (1) PEG-IFN is associated with a higher rate of thyroid dysfunction than IFN. (2) TFTs should be monitored during and after IFN-based therapy. (3) Females and Asians are the most susceptible. (4) The most common cytological finding is a benign follicular pattern.

391 MANAGEMENT OF TREATMENT FAILURES IN CHRONIC HEPATITIS C: DOES RETREATMENT SUCCEED?

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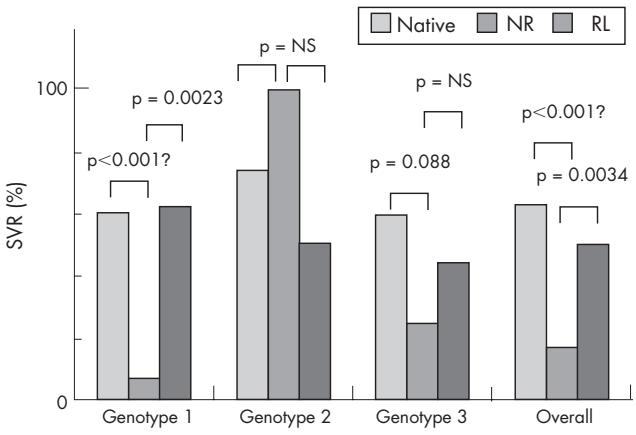
Introduction: A significant proportion of patients fail to achieve a sustained virological response (SVR) to treatment for hepatitis C. Re-treatment with PEG-IFN/RBV in patients that failed standard IFN may prove beneficial.
Aims & Methods: Patients treated with PEG-IFN/RBV who had failed previous IFN-based therapy were classified according to previous response. Relapsers (RLs): HCV RNA transiently undetectable on PCR; non-responders (NRs): HCV RNA never undetectable. Treatment episodes were analysed and logistic regression models used to examine predictors of SVR.
Results: 160 patients underwent PEG-IFN/RBV therapy (71 re-treated and 89 naïve). 71% were male and mean age was 45 years (SD 10.5). The SVR was significantly lower in re-treated NRs (16%) when compared with naïve patients (62%) and with RLs (50%). This difference remained in the subgroup analysis for genotype 1 (see chart). There was no difference in SVR between RLs and treatment naïve patients in all genotypes or in SVR rates according to type of previous failed treatment: 38% for IFN monotherapy, 27% for IFN/RBV therapy.
Conclusion: Success of re-treatment for hepatitis C with PEG-IFN/RBV depends on response to previous therapy. In relapsers, the chance of success is equal to naïve patients, while non-responders have very low rates of SVR, particularly for genotype 1 infection. These points should be taken into account when counselling patients prior to re-treatment.



Abstract 391 Sustained virological response by genotype and treatment history.

392 ADVANCED FIBROSIS DUE TO HEPATITIS C: IS ANTIVIRAL TREATMENT EFFECTIVE?

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Introduction: Cirrhotic patients with hepatitis C gain most benefit from viral eradication, as they are at high-risk of developing complications of end-stage liver disease. However tolerance and adherence to PEG-IFN/RBV therapy is reduced in this group. We evaluate treatment in these patients.
Aims & Methods: Data were collected prospectively, using a standardised data sheet, on all patients treated with PEG IFN and RBV for hepatitis C at Royal Perth Hospital between 2001 and 2005. Demographic, genotype, liver histology, treatment and outcome data were collected, with subgroup analysis according to METAVIR fibrosis stage. Optimal adherence rates (receiving >80% of optimal dose of IFN and RBV for >80% optimal duration) were analysed. Statistical methods consisted of the χ^2 test, Fischer's exact test and Welch's unpaired *t* test.
Results: 137 patients were identified: 41 with METAVIR stage F3/4 and 96 with F0/1/2. All had Child-Pugh class A compensated disease. Mean age for F3/4 patients was significantly higher than for F0/1/2 (p = 0.0041). There was no significant difference in genotype, SVR, dose reductions or haematological side effects between the groups (see table). These findings were maintained in the subgroup analyses of F0/1, 2, 3 and 4. However there was a trend towards lower optimal adherence rates in the F3/4 group compared with the F0/1/2 group (66 *v* 81%).
Conclusion: Adherence and tolerance to treatment may be reduced in patients with advanced fibrosis, who tend to be older. Achieving SVR in this group is an important challenge, and strategies to improve adherence should be explored.

Abstract 392 Treatment according to fibrosis stage

Fibrosis stage	F 0, 1, 2	F3, 4	p Value
Total number	96	41	
Males	66 (71%)	29 (71%)	NS
Age, mean (SD)	43 (10)	49 (8)	0.0041
SVR overall	42 (44%)	20 (49%)	NS
Genotype 1	18 (36%)	9 (47%)	NS
Non-genotype 1	24 (52%)	11 (50%)	NS
IFN dose reduction	32 (33%)	15 (36%)	NS
RBV dose reduction	28 (29%)	15 (36%)	NS
Neutropenia	16 (17%)	8 (20%)	NS
Anaemia	8 (8%)	5 (12%)	NS
Optimal adherence	81%	66%	NS

Neutropenia: WBC<0.8×10⁹/l; anaemia: Hb <100 g/l.

393 ABNORMAL LIVER FUNCTION TESTS AND DIABETES MELLITUS: A PREVALENCE STUDY

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Introduction: Chronic liver disease (CLD) is a major cause of morbidity and mortality in the UK. Up to 75% of people with type 2 diabetes have a degree of non-alcoholic fatty liver disease (NAFLD) at diagnosis.[1] Recent studies have shown that the risk of CLD and hepatocellular carcinoma is significantly increased in patients with diabetes.[2, 3] Diabetics are also at risk of other disorders associated with abnormal liver function tests (LFTs). Currently the diabetes annual review does not involve assessing liver disease risk.
Aims & Methods: This study aimed to determine the prevalence of abnormal LFTs in the population attending diabetic clinic in the secondary care setting of a large rural university hospital. Demographics, LFTs, HbA1C, lipid levels and body mass index (BMI) were recorded for all patients attending the hospital diabetic clinic between 1/9/05 and 31/12/05. Data were collected retrospectively from hospital records.
Results: During the study period 910 diabetics attended the clinic. 49% had type 1 and 51% had type 2 diabetes. In 55 (6%) patients both ALT and GGT were raised above the normal range. In 181 (19.9%) patients ALT, GGT or both were elevated (Group 1). This group was compared to patients with normal ALT and GGT (Group 2). Group 1 patients had significantly higher BMI and a more adverse lipid profile. The proportion of type II diabetics

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Abstract 393 All patients

	Group 1	Group 2	p Value
n (%)	181 (19.93)	727 (80.10)	
Age (mean (SD))	56.96 (16.11)	56.67 (17.5)	
BMI	31.14	29.16	<0.05
HbA1c	8.66	8.44	NS
TC/HDL	3.97	3.39	<0.05

was also significantly higher in Group 1 (43.6% *v* 39.7%, $p<0.05$). Subgroup analysis of the type II diabetics showed that the lipid profile was the only significant variable between the groups.
Conclusion: This study shows that 20% of patients with diabetes and 22% of type 2 diabetics had a raised ALT, GGT or both. This is higher than has been previously reported in the literature. Most of these patients have not had a formal hepatological assessment. Further work is needed to identify which patients are at risk of serious liver disease and need further hepatological evaluation. The resource implications to the NHS are likely to be considerable.

1. **Medina J**, Fernandez-Salazar LI, Garcia-Buey L, *et al.* Approach to the pathogenesis and treatment of nonalcoholic steatohepatitis. *Diabetes Care* 2004;**27**:2057–66.
2. **De Marco R**, Locatelli F, Zoppini G, *et al.* Cause-specific mortality in type 2 diabetes. The Verona Diabetes Study. *Diabetes Care* 1999;**22**:756–61.
3. **El-serag HB**, Tran T, Everhart JE. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. *Gastroenterology* 2004;**126**:460–8.

394 TIPSS IN TREATMENT OF BLEEDING GASTRIC VARICES: A LARGE SINGLE CENTRE EXPERIENCE

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Introduction: Transjugular intrahepatic portosystemic stent shunt (TIPSS) is an established management option for bleeding from gastric varices (GV). We have previously reported a better survival in patients with TIPSS for GV cf oesophageal varices (OV).[1] We report here a much larger, single centre series of patients who had TIPSS for management of bleeding GVs.
Aims & Methods: A retrospective study of patients who had TIPSS inserted for GV. Patients identified from a dedicated database.
Results: Over 14 years, 768 TIPSS have been inserted, of whom 81 (10.5%) were for bleeding gastric varices (males 43; mean age 51.6 (12.4) years). Underlying aetiologies were ALD (69%), viral (4%), and others (13%). Mean Child-Pugh (CP) score was 9.1 (2.5). TIPSS was done as an emergency procedure in 49 (60.4%) patients. Covered stents were used in 26% patients. Mean PPG pre-TIPSS insertion was 16.73 (6.9) and post-TIPSS was 6.07 (2.96) mmHg. TIPSS successfully achieved haemostasis in all but one patient. Ten (12.3%) patients had variceal rebleeding at a median of 7 days (4 days to 124 months). This was related to shunt modification in one and shunt dysfunction in 8 patients, which responded to shunt interventions. 61 deaths (40, liver related) and 5 transplants have occurred at a median duration of 21 months (1 day to 160 months). When compared with an age, sex and alcoholic aetiology matched group of patients with OVs, the GV patients were found to have a significantly lower CP score, a lower pre TIPSS PPG (16.7 (6.9) *v* 21.8 (7.1), $p<0.001$) and better survival (survival at 6, 12 and 24 months was 68, 61 and 51% and 53, 45 and 36% respectively, $p=0.02$, by log rank statistic) but there was no significant difference in rate of variceal rebleeding. Dividing patients with GVs into two groups according to pre TIPSS PPG (PPG $\leqslant 12$ and PPG >12 mm Hg), we found that the improved survival of the GV group cf OV group was mainly confined to those with pre-TIPSS PPG >12 mm Hg.
Conclusion: TIPSS is highly effective treatment for bleeding gastric varices with initial haemostasis in almost all patients and very low rebleeding rates. Rebleeding almost invariably is related to shunt insufficiency and responds well to shunt intervention. In this larger cohort of patients we have confirmed the finding that higher PPG at the time of TIPSS insertion may predict a group with better prognosis.

1. **Tripathi D**, Therapondos G, Jackson E, *et al.* The role of the transjugular intrahepatic portosystemic stent shunt (TIPSS) in the management of bleeding gastric varices: clinical and haemodynamic correlations. *Gut* 2002;**51**:270–4.

395 CHRONIC RENAL FAILURE POST LIVER TRANSPLANT: PREVALENCE AND RATE OF DECLINE

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Introduction: Chronic renal dysfunction is a recognised cause of morbidity and mortality after liver transplantation. However, the definition of chronic renal dysfunction varies widely and its true prevalence and clinical significance is underestimated.
Aims & Methods: Our aim was to assess the prevalence of chronic kidney disease at 5 years post elective liver transplantation, and to determine the rate of decline in renal function. A single-centre retrospective study of 135 consecutive patients who received 148 liver transplants between 1 January 1996 and 31 December 2000. 106 patients survived for the 5-year follow-up period. Estimated glomerular filtration rate (GFR) was calculated using the MDRD6 equation. As per the National Kidney Foundation a GFR of $\geqslant 90$, 60–89, <60 and <15 was used to define normal renal function, mildly reduced GFR, chronic kidney disease (CKD) and kidney failure respectively. Values were expressed as mean and standard deviation, and median and interquartile range as appropriate.
Results: The mean age at time of transplantation was 50.1 (10.9) years (M:F = 1:1.1). 97% were of European ethnic origin. Indications for transplantation were primary biliary cirrhosis (33%), alcoholic liver disease (22%), hepatitis C (10%) and others (35%). Pre-transplantation 38% had a reduced GFR and 7% met the criteria for CKD. Postoperatively, 60%, 74%, 81% and 80% had some degree of renal impairment and 15%, 27%, 26% and 28% had CKD at 1, 6, 12 and 60 months respectively. The mean GFR at 5 years was 44 (12) in those with CKD and 81 (16) in those without. Notably, the median serum creatinine at 5 years in the former was only marginally elevated at 135 (125–157). Two patients (2%) developed kidney failure and required dialysis during the follow-up period. Mean GFR at 5 years was 31 ml/min/1.73 m^2 less than the preoperative level. The fastest rate of decline was observed during the peri-operative period. Thereafter, GFR stabilised. Although there was no significant difference in the mean GFR at 1 and 5 years of the group as a whole ($p=0.46$), 46% demonstrated a deterioration in renal function at a rate greater than that expected with age. Of this cohort 86% had a reduced GFR, 37% had CKD and 2% had kidney failure at 5 years. The mean rate of decline was 4.5+/−2.7 ml/min/1.73 m^2/year. Therefore, the predicted prevalence of kidney failure (or dialysis) at 10 and 15 years post-transplantation is 5% and 18% respectively.
Conclusion: Chronic renal dysfunction is an important complication after liver transplantation. More than a quarter of patients at 5 years fulfil the criteria for CKD. In those who demonstrate progressive impairment, the mean rate of decline is comparable with the rate observed in non-transplant patients with CKD. Further research is required to identify modifiable risk factors for both prevalence and rate of decline.

396 MINIMAL HEPATIC ENCEPHALOPATHY AFTER TIPS INSERTION IS ASSOCIATED WITH A REDUCED QUALITY OF LIFE

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Introduction: One of the main drawbacks of TIPS is the development of hepatic encephalopathy (HE). The diagnosis of HE is typically clinical yet this is insensitive; the development of psychometric testing has allowed the detection of subtler degrees of neuropsychiatric impairment—subclinical or ''minimal'' HE. However, the morbidity associated with minimal HE and the extent to which this affects quality of life (QOL) is unclear.
Aims & Methods: We aimed to determine the incidence of minimal HE after TIPS insertion and the impact this had on perceived health status and QOL. From our database of patients in whom TIPS has been inserted in the last decade (n = 197), those still attending (n = 59) were invited to attend for psychometric testing. A test battery for the detection of minimal HE, the psychometric hepatic encephalopathy score (PHES), was derived from six paper and pencil tests. Computerised psychometry (CDR) was also undertaken within one week of the paper and pencil tests by the same operator (HM). Blood was collected at the time of testing for Child-Pugh and MELD score and whole blood ammonia. These patients were asked to complete 2 health profile questionnaires—the Short Form 36 (SF-36) and the chronic liver disease questionnaire (CLDQ).
Results: PHES were available in 35/59 (59%) patients. Testing was undertaken at a mean length of 81 months (range 3–123) after TIPS insertion. PHES was abnormal (score −5 to −18) in 17 patients (49%); some (n = 6) had no clinically evident HE during FU. PHES was normal (−4 to 2) in 18 patients. The CDR score was significantly lower in those with abnormal PHE scores ($p<0.01$) and was in the normal range (−3 to +5) in

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only 14 of the 36 tests performed (39%). QOL questionnaires were completed by 19/35 (54%) of those who underwent psychometric testing. In both the SF-36 and CLDQ questionnaires, the total scores for patients with abnormal psychometric test results were significantly lower than that for patients with normal psychometric test results ($p<0.05$). This difference was significant in the domains covering physical health in the SF-36 questionnaire and in the domains of fatigue, systemic symptoms and activity in the CLDQ.
Conclusion: Abnormal PHE scores are seen in around half of all patients after TIPS insertion. This subclinical abnormality represents psychomotor slowing along with impairment of visual perception and attention, that is, minimal HE. Additionally, this results in a globally diminished functional level, with impairments in dimensions of physical and mental health. Minimal HE is associated with a reduced perceived and actual QOL.

397 CORRELATION OF CORONARY ARTERY CALCIFICATION SCORES WITH FEATURES OF THE METABOLIC SYNDROME IN PATIENTS UNDERGOING ASSESSMENT FOR ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: An increased incidence of cardiovascular events is seen in patients with end stage liver disease; with the underlying mechanisms currently not fully understood. As non-alcoholic fatty liver disease (NAFLD) is increasing in prevalence, with more of these patients progressing to end stage liver disease, we aimed to assess the relationship between the presence of features of the metabolic syndrome (MS) and coronary artery calcification (CAC) score, a well-validated, non-invasive assessment tool used in the detection of subclinical coronary artery disease. We also examined if any relationship exists between insulin resistance (as assessed by HOMA-IR index), features of the MS and CAC scores in an unselected cohort of patients being assessed for liver transplantation.
Aims & Methods: Single centre prospective observational study. We recruited patients who were undergoing assessment for orthotopic liver transplantation (OLT) from April 2005–May 2006. All patients underwent CT scanning of the thorax to allow CAC scores to be generated and correlated this with the number of features of metabolic syndrome as classified by ATP III criteria and the HOMA-IR index, calculated by obtaining simultaneous fasting glucose and insulin, to assess insulin resistance (IR).
Results: Fifty two patients underwent cardiac CT scanning (38 males: 14 females) with a median age of 54 years (range 24–69). The median CAC score was 102 (range 0–3533). Features of the MS were common in this unselected cohort of OLT candidates with 27.45%, 41.18%, 23.53% and 7.84% of patients having no, one, two and three features respectively. Insulin resistance was almost universal with 19.61% having moderate and 70.59% severe insulin resistance defined by HOMA-IR index as HOMA-IR>2 and HOMA-IR>3 respectively. CAC scores identified patients as within the high risk group in 23.53%. Looking at the relation between these 3 risk factors for cardiovascular events we identified a significant ($p=0.038$) albeit weak correlation ($r=0.291$) between the number of features of the MS and the CAC score and a significant ($p=0.047$) relation between features of the MS and HOMA ($r=0.28$). No relationship was however found between the CAC score and HOMA.
Conclusion: The relationship between the MS, IR and coronary artery disease may be important in determining cardiovascular risk in OLT candidates. Further evaluation of these risk factors for cardiovascular disease is important and should be addressed in prospective studies. The significance of the high prevalence and severity of insulin resistance in patients with advanced liver disease is worthy of further study in view of our current understanding of the pathogenesis of NAFLD.

398 LIVER DISEASE AND KHAT CHEWING IN YOUNG SOMALIAN MEN

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Introduction: Historically, port workers from Somalia have settled in Bristol since the last century. Following conflict in East Africa the local population has increased to around 700–1000. Cryptogenic liver disease within the Somalian population has been recognised by liver units around the UK, but publications are rare. An unusual form of autoimmune hepatitis in young Somalian men has recently been described.[1] Khat chewing is highly prevalent within the male Somalian culture; in contrast women rarely partake. The leaves of the Khat shrub (Catha edulis) contain an active amphetamine-like stimulant cathinone. Animals fed Khat leaves develop an acute hepatitis[2] and long-term feeding is associated with fibrotic liver disease.[3]
Aims & Methods: To determine the prevalence of liver disease in Somalians presenting to a teaching hospital in Bristol, UK between 1999 and 2006. All cases were identified using departmental and histopathology databases. In all but one an accurate record of khat ingestion was documented in the notes.
Results: Seven Somalian men (no women) were identified (median age 33, range 28–41 years). All presented with a predominant hepatitic derangement in LFTs. In 6 there was a clear history of regular khat chewing and a collateral history of a possible habit in the remaining 1. All subjects denied ever drinking alcohol. No other aetiological factors for liver disease were identified (ie neg viral serology, copper studies, etc). Six patients had liver biopsies with features consistent with a chronic hepatitis. Two also had established cirrhosis. Three patients were seropositive with raised SMA titres (table). In 2 of these immunosuppression therapy failed. In 4 patients (patients 1, 5, 6, 7) the liver disease recovered or stabilised following cessation of khat and immunosuppression has not been required.
Conclusion: There appears to be a high prevalence of ''cryptogenic'' liver disease in Somalian men; a population known to frequently ingest a potential hepatotoxin in khat. Khat-induced liver disease appears to mimick autoimmune hepatitis and this may explain the poor response to immunosupression previously described.[1] Supporting this supposition is the lack of liver disease in women. The precise hepatotoxin(s) in Khat (or contaminants during transportation) remains unclear and warrants further study.

1. **D'Souza**, *et al. Liv Int* 2005;**25**:325–30.
2. **Al-Mamry**, *et al. Phytother Res* 2002;**16**:127–32.
3. **Al-Habori**, *et al. J Ethnopharmacol* 2002;**83**:209–17.

399 THE LONG-TERM PROGNOSIS OF BLEEDING OESOPHAGEAL VARICES: A 14-YEAR FOLLOW-UP STUDY

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Introduction: Variceal bleeding has long been identified as a significant cause of morbidity and mortality among cirrhotic patients. Although there have been several reports on short-term prognosis following variceal bleeding less is known about the long-term survival. Knowing more about the natural history of variceal bleeding allows us to make informed

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Patient	Age	Khat	Onset	AI	H.A.I /18	Fibrosis/6	Outcome	Comments	
1	41	++	Acute	SMA 1/40	5		Resolved	Khat	Stopped
2	41	+	Acute	Neg	Declined	Biopsy		Lost f-up	
3	33	+	Subacute	SMA 1/80	9	0	OLT*		
4	28	Possible	Chronic	SMA1/160	7	6	Died*	Variceal	Bleed
5	33	++	Chronic	Neg	7	6	Stable	Khat	Stopped
6	39	++	Acute	Neg	4	0	Resolved	Khat	Stopped
7	28	++	Chronic	Neg	6	3	Resolved	Khat	Stopped

*Failed immunosuppression.

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decisions about subsequent management including secondary variceal prophylaxis and hepatoma screening.
Aims & Methods: Details of all patients admitted to our Gastrointestinal Bleeding Unit over the past 14 years were recorded in a database. Patients whose primary cause of bleeding was oesophageal varices were identified and survival was evaluated at 30 days, 6 months and 5 years. Overall survival was analysed using Kaplan Meier survival curves. Only the first admission to our unit was analysed in survival data. Survival was evaluated dependent on year of admission, gender, age, alcohol intake and rebleeding during admission.
Results: There were 288 patients admitted with variceal bleeding on a total of 434 bleeding related admissions. Males accounted for 66.7% and mean age was 55.2 years. The mean duration of stay in the HDU per admission was 8.1 days and the mean transfusion requirement was 3.9 units of blood. Median follow-up was 11 months (range 0–165). Overall mortality was 23% at 30 days, 34% at 6 months and 67.7% at 5 years. There was no statistically significant difference in survival time dependent on gender or weekly alcohol consumption. Age significantly affected survival ($p<0.01$) with a 2.5% increase in risk of death per year of age. Patients who had rebleeding from varices during their admission had a significant reduction in survival, median 14 months versus 66 months if no rebleeding ($p<0.01$).
Conclusion: We have demonstrated that increasing age and rebleeding have an adverse influence on survival. Although we have previously shown that alcohol history had an adverse effect on short-term mortality, we did not find a significant influence on long-term survival. There is a 34% mortality at six months, however a significant number of patients who survive the acute bleeding episode live for many years and therefore when discussing therapeutic strategies during the acute presentation this should be taken into consideration. Given the large numbers surviving we need to make provision for secondary prophylaxis against variceal haemorrhage and hepatoma screening in those where it is indicated.

400 NON-TRANSPLANT SURGERY FOR DOMINANT STRICTURE IN PRIMARY SCLEROSING CHOLANGITIS: REVISITED

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disorder characterised by strictures and dilatations of the biliary tree. A dominant stricture in common bile duct and/or right hepatic duct or left hepatic duct has been reported in upto 45% patients.[1] It is complicated by cholangiocarcinoma (CC) in 10% to 20% of cases, and is more common in large duct disease. Treatment options include repeated stenting of strictures, surgical excision and liver transplant.[2]
Aims & Methods: The aim of this study was to assess the outcome of patients with histologically proven non-cirrhotic PSC, who under went surgical excision of extrahepatic dominant strictures (EHDS. A retrospective case note review of 130 patients with PSC presenting to the Freeman Hospital Liver unit between April 2000 and March 2005 identified 13 pts as having EHDS due to PSC. 11 patients underwent surgery. Pre-op presentation, pre and post-op liver function (LFT), post-op complications and follow-up to date were evaluated.
Results: Of the 11 patients, six underwent segment 4B resection and a Hepp-Couinard hepaticojejunostomy (HJ) with total excision of the EHBD. Four patients underwent left hepatectomy, total excision of the EHBD and right duct HJ for disease involving the confluence and one patient underwent a pylorus preserving whipples resection plus total excision of the EHBD. Mean age was 65 years (range =33–70). All patients had life threatening recurrent cholangitis prior to surgery. In nine patients LFT stabilised post operatively. No perioperative mortality occurred. Median follow-up was 42.45 months (range 5–78). Two patients had CC on histological assessment of the stricture, both died with metastatic CC, one at 6 months and one at 3 years. All of the remaining nine patients have not progressed to cirrhosis or required OLT. Four patients have developed minor episodes of cholangitis postoperatively—1 anastomotic stricture, 1 dysfunctional Roux and 1 intrahepatic disease progression.
Conclusion: Although patients with EHDS PSC make up the minority of patients presenting with PSC; evidence suggests that it is more aggressive and carries a higher risk of CC as was the case in our small cohort of patients. From our data it would appear that surgery in this highly selected group of non-cirrhotic PSC patients may have some benefit.

1. **Bjornnson E**, Lindqvist-Ottosson J, Asztely M, *et al.* Dominant strictures in patients with primary sclerosing cholangitis. *Am J Gastroenterol* 2004;**99**:502–8.
2. **Ahrendt SA**, Pitt HA, Kalloo AN, *et al.* Primary sclerosing cholangitis: resect, dilate, or transplant? *Ann Surg* 1998;**227**:412–23.

401 PORTAL BILIOPATHY: A MULTIDISCIPLINARY APPROACH TO MANAGEMENT

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Introduction: Portal vein thrombosis frequently results in the formation of a portal cavernoma, when bridging collateral veins dilate to bypass the obstruction and shunt portal venous blood to the liver. Biliary obstruction as a consequence of portal cavernoma, portal biliopathy, develops when the thin walled epi- and para-choledochal venous plexuses dilate and compress the bile duct and gallbladder. Although biliary changes can be identified on imaging in the majority of cases of portal cavernoma, portal biliopathy is an uncommon cause of symptomatic biliary disease in the Western world.
Aims & Methods: We reviewed all patients presenting to the Liver Unit in Birmingham with symptomatic portal biliopathy between 1992 and 2005 and report the presentation, investigation, management and outcome of these complex patients.
Results: Thirteen patients (median age at presentation 34 (range 23–61 years)) with median follow-up of 2 years (range 1–18 years) were identified. Jaundice, associated with typical biliary pain in 5 cases, was the presenting feature in all cases. Intrahepatic biliary dilatation with multiple intra- and extrahepatic strictures were present in all cases. In addition gallbladder stones (n=11) and bile duct stones or sludge (n=10) were commonly present. Biliary symptoms were successfully treated by biliary decompression in six cases (metallic stent 3, plastic stent 1, combined procedure 1, sphincterotomy 1) and portal decompression in three cases (TIPS 2, Meso-caval shunt 1). Biliary obstruction could not be relieved endoscopically or by portal decompression in one case who was accepted for combined liver and small bowel transplantation. Three patients had spontaneous resolution of symptoms without recurrence over the follow-up period. All patients had endoscopic evidence of oesophageal varices and 10 (77%) experienced a total of 18 episodes of gastrointestinal bleeding. There were two deaths over the follow-up period, each resulting from complications following variceal haemorrhage.
Conclusion: Portal biliopathy is an uncommon cause of biliary obstruction. Endoscopic management (sphincterectomy and stone extraction or stent insertion) is effective initial therapy for patients whose symptoms do not resolve spontaneously. In the case of persistent biliary obstruction porto-systemic shunting (TIPS or surgical) should be considered however the extent of vascular thrombosis precludes this in most cases. Liver or multivisceral transplantation should be considered for patients who are unsuitable or are resistant to these therapies.

402 LINEAR ENDOSCOPIC ULTRASOUND (EUS) ASSESSMENT AND EUS-FINE NEEDLE ASPIRATION OF HILAR LESIONS

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Introduction: Optimal management of hilar cholangiocarcinoma requires good imaging of the tumour mass, its relationship to vascular structures and a tissue diagnosis. Endoscopic ultrasound (EUS) and EUS-fine needle aspiration (FNA) offers the potential of gaining staging information and a tissue diagnosis in the same sitting. Previous studies[1–3] have reported sensitivities of 25–83%. We report our experience of EUS assessement and EUS-FNA of hilar lesions.
Aims & Methods: All patients who underwent Linear EUS assessment followed by EUS- FNA for hilar lesions between April 2004 to April 2006 were identified.All these patients had a provisional diagnosis of a hilar cholangiocarcinoma on prior cross-sectional imaging. The final diagnosis was determined by surgical pathology, cytology or follow-up.
Results: Fifteen patients underwent 17 procedures for hilar lesions during the study period. There were 7 males and 8 females with a mean age of 69.9 years (range 40–79). All but one patient (who had a hilar node) had a suspected hilar stricture. All patients had prior radiological imaging (CT and or MRI). Two patients had repeat procedures. Good images were obtained in all cases. The lesion was able to be identified and an assessment of operability made. Positioning for EUS-FNA was often awkward and restricted the number of passes made mean 2.06 (range 1–3). There were no complications. An inadequate specimen was obtained in 9 procedures. The cytological diagnosis was adenocarcinoma (4) and

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benign (3). Six patients had definite diagnosis of adenocarcinoma on biliary brushings (3) and surgical pathology (3). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of EUS-FNA were 33%, 100%, 100%, 38.5%, 53% respectively.
Conclusion: EUS assessment provided useful staging information of hilar lesions. However the performance of EUS-FNA was technically difficult and the sensitivity poor. This was predominantly due to the high proportion of inadequate specimens.

1. **Fritscher-Ravens A**, Broering DC, Knoefel WT, *et al.* EUS-guided fineneedle aspiration of suspected hilar cholangiocarcinoma in potentially operable patients with negative brush cytology. *Am J Gastroenterol* 2004;**99**:45–51.
2. **DeWitt J**, Misra L, Le Blanc J, *et al.* EUS-guided FNA of proximal biliary strictures after negative ERCP brush cytology results. *Gastrointest Endosc* 2006;**64**:325–33.
3. **Rosch T**, Holfrichter K, Frimberger E, *et al.* ERCP or EUS for tissue diagnosis of biliary strictures? A prospective comparative study. *Gastrointest Endosc* 2004;**60**:390–6.

403 PREDICTION OF OUTCOME AND COMPLICATIONS AFTER LIVER TRANSPLANTATION USING EARLY NON-INVASIVE INDOCYANINE GREEN CLEARANCE: COMPARISON WITH CONVENTIONAL MARKERS OF GRAFT FUNCTION

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Introduction: Invasive measurement of graft function by indocyanine green clearance (ICG Cl) has been shown to predict outcome after liver transplantation. Non-invasive measurement is now possible with the LiMON device. We report our experience of ICG Cl determination in this way, assessing its potential for early prediction of adverse post operative events making comparison with other parameters in a cohort of patients undergoing liver transplantation (LT).
Aims & Methods: ICG PDR was measured by LiMON in 93 patients at a median of 1 day (interquartile range 0–1) after LT. Clinical and laboratory markers of graft and extra-hepatic organ function were recorded at the time of ICG measurement. Primary outcome measures were 28 day (28DS), 90 day graft survival (90DS) and postoperative complications (renal failure (RF) and need for haemofiltration (HF)). Predictive accuracy was assessed by area under receiver operator characteristic curves (AUC).
Results: Sixty eight patients underwent elective LT for chronic liver disease (CLD) and 25 emergency LT for acute liver failure (ALF). Significant differences were present in relation to 28DS in both lactate and ICG Cl (lactate: 1.8 mmol/l (1.3–3.7) survivors *v* 4.45 mmol (1.8–16) in non survivors ($p=0.01$); ICG PDR :17% (11.7–24.2) *v* 10.8 (5.8–18.5), $p=0.04$). Similar findings were present in relation to 90DS. AST, Bilirubin and INR showed no significant differences. AUC for the prediction of 28DS and 90DS were 0.72 for lactate and 0.68 for ICG Cl. In ALF patients ICG Cl predicted 28DS more accurately than lactate. In CLD patients, ICG Cl did not predict 28DS but performed as well as lactate when predicting 90DS. Significant differences were present in relation to development of RF in ICG Cl, creatinine (Cr) and urine output (U/O) (ICG Cl 13.5% (8.9–19.5) with RF *v* 21.5% without (15–30.1), $p<0.001$; Cr 138 μmol/l (99–203) *v* 88 (76–110), $p<0.001$, U/O 200 ml/day (0–1023) *v* 1180 (912–2120), $p<0.001$). Overall, AUCs for Cr were 0.8, U/O 0.8 and ICG Cl 0.78 for prediction for HF. In ALF patients, Cr, U/O, ICG Cl and bilirubin predicted the need for HF at day 7, but only ICG Cl and U/O accurately predicted need for HF in the CLD group.
Conclusion: Early ICG Cl measured non-invasively predicted graft survival in patients undergoing emergency and elective LT. However, it did not appear to be superior to existing conventional measures. In those transplanted for CLD, a low ICG Cl was associated with a subsequent need for HF suggesting an association of graft dysfunction with renal failure.

404 PRELIMINARY DATA OF THE ROLE OF CHEMOEMBOLISATION FOLLOWED BY RADIOFREQUENCY ABLATION IN THE TREATMENT OF MULTIPLE OR LARGE HEPATOCELLULAR CARCINOMA

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Introduction: Hepatocellular carcinoma (HCC) is the 4th commonest cause of cancer in the world with increasing UK incidence due Hepatitis C and alcohol/non-alcoholic steatohepatitis related cirrhosis. Although surgery or radio-frequency ablation (RFA) can be effective for small tumours, once the size is >3 cm effective therapies are limited. Chemoembolisation is often used as palliative therapy for larger or multiple tumours, but there are very limited data on combined chemoembolisation and RFA as therapy for this patient group.
Aims & Methods: The aim of our audit was to assess the impact and outcome of combined chemoembolisation and RFA in our centre in the management of patients with HCC >3 cm or multiple tumours. A retrospective case note analysis was performed of patients diagnosed with HCC over a 6-year time period (January 2000–6). Patients treated with chemoembolisation followed by RFA (combined therapy) were identified and outcome assessed.
Results: Fifty two patients were diagnosed with HCC over the study period. Aetiology was alcoholic liver disease (ALD) in 46% and 73% patients had Childs C disease. 33% had a single HCC (mean diameter 5.89 (2.57) cm). The overall one-year survival was 35%. 12 patients were treated with chemoembolisation followed by RFA (11 male; mean age 59.2 (10.6)). Aetiology included: ALD in 6 patients, haemochromatosis in 2, cryptogenic cirrhosis in 2, hepatitis C in 1 and primary biliary cirrhosis in 1. The Child-Pugh grades were: 8 grade A and 4 grade B with 42% having a raised AFP at diagnosis. 50% patients had a single HCC (median diameter 6 cm, range 3.5 cm–20 cm). None had extra-hepatic metastasis on CT +/− MR imaging. 50% were Barcelona Clinic Liver Cancer (BCLC) stage A, 17% stage B and 33% stage C. The median no of chemoembolisation sessions was 2 (range 1–5), followed by a median no of 2 (range 1–6) RFA sessions. The only complication encountered was a pyrexia with abnormal LFTs post-procedure in one patient which settled after antibiotic therapy. The median follow-up was 29 (range 9–78) months. Following combination therapy, 75% of patients had complete radiological resolution of their HCC based on imaging at a median of 6 (range 2–25) months. 25% had a recurrence of ablated HCC and 42% had new HCCs diagnosed on follow-up imaging. Overall one and two-year survival for those treated with combination therapy was 58%, and 50% respectively. The median survival for patients graded BCLC stage A, B and C was 33, 20 and 10 months.
Conclusion: Chemoembolisation followed by RFA therapy results in good radiological tumour resolution in patients with >3 cm or multiple HCC without metastatic disease. However recurrence and new HCC occurs frequently on follow-up. This combination therapy requires further study to clarify its exact role in the management of HCC.

405 BEDSIDE DIAGNOSIS OF SPONTANEOUS BACTERIAL PERITONITIS USING URINE DIPSTICKS

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Introduction: Spontaneous bacterial peritonitis (SBP) affects up to one third of cirrhotic patients and has a high mortality. Diagnosis of SBP is traditionally based upon finding more than 250/mm^3 polymorphonuclear (PMN) cells in ascitic fluid (AF) and on AF culture, both of which are labour intensive and expensive techniques. Leucocyte esterase reagent strips can rapidly detect leucocytes in physiological fluids. They are used for the diagnosis of urinary tract infections, meningitis, empyema and peritonitis associated with chronic ambulatory dialysis.
Aims & Methods: The purpose of this study was to assess the usefulness of leucocyte esterase reagent strips for the rapid exclusion of SBP at the bedside. All cirrhotic patients admitted acutely or electively for paracentesis between December 2005 and August 2006 underwent testing of AF using

Abstract 405 Mean polymorphonuclear (PMN) count for each Combur9 result

Combur9 result	0 (n = 128)	1 (n = 22)	2 (n = 10)	3 (n = 2)
PMN/mm^3 (mean + range)	17.9 (<1–200)	47.5 (<1–698)	1546 (<1–14400)	3450 (2100–4800)

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the 4-grade colorimetric scale of the Combur9 urine dipstick (read at 120s: grade 0, 1, 2 and 3). Results were compared with standard cell count and culture of AF in blood culture bottles. SBP and bacterascites were defined according to the International Ascites Club criteria.[1]

Results: 183 AF samples were obtained in 59 patients. 21 samples were excluded: 13 were not received by the laboratory, 3 were clotted and the dipstick could not be read in 5 patients due to hyperbilirubinaemia. 24% of tests were performed in elective admissions. Mean patient age was 56 years, 60% male. Cirrhosis was most frequently due to alcohol (76%), mean MELD 16. SBP was diagnosed in 3 cases; bacterascites in 10 cases. When we considered a positive reagent strip result of 3, sensitivity was 33% (2 of 6), specificity 100% (156 of 156), positive predictive value (PPV) 100% and negative predictive value (NPV) 98%. When we considered positive a reagent strip result of 2 or more, sensitivity was 83% (5 of 6), specificity was 96% (150 of 156), PPV 42% and NPV 99%.

Conclusion: Leucocyte esterase reagent strips are a reliable bedside test for the exclusion of SBP. A negative result (0 or 1) may be useful as a cheap alternative screening test to exclude SBP and result in significant cost savings for the NHS by preventing the need for further microbial analysis. A result of 2 or more should be an indication for empirical antibiotics and confirmation of the result with standard cell count and ascitic fluid culture.

1. **Moore KP**, *et al. Hepatology* 2003;**38**:258–66.

406 ACUTE RENAL FAILURE IN CIRRHOSIS: IS IT AS BAD AS WE THINK?

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Introduction: Acute renal failure (ARF) is associated with a mortality of 50–60% in critically ill patients admitted to the intensive care unit (ICU). Prerenal causes and acute tubular necrosis (ATN) account for more than 85% of cases and are potentially reversible. ARF frequently complicates cirrhosis, is often attributed to hepatorenal syndrome (HRS), which may preclude aggressive treatment with its mortality up to 90%.

Aims & Methods: The aim of this study was to identify factors that may predispose to or precipitate ARF in cirrhosis, and determine outcome and mortality. A retrospective review of cirrhotic patients admitted with or developing renal impairment (defined as serum creatinine >130 μmol/l or oliguria <500 ml/24 h) from October 1999–April 2004. Patients with bleeding gastro-oesophageal varices were excluded. Demographic details, cause of ARF, potential early warning features, management and outcome were recorded.

Results: Eighty patients, median age 52 years (25–84), 46 male, median MELD 26 (7–43). Alcohol was causal in 88.8%. ARF occurred in 41/80 (51.3%) on admission, or a median of 6 days after admission (1–34). Median serum creatinine at onset of renal impairment 172 μmol/l (60–589). An identifiable precipitant was found in 62/80 (77.5%) and were concurrent in 51%; nephrotoxic drugs 50%, sepsis 45% (culture positive 27/36), recent paracentesis (preceding month) 28.8%, fluid loss 26.3%, and spontaneous bacterial peritonitis 13.3%. HRS occurred in 17.5%. No parenchymal renal disease or obstructive uropathy was seen. 54% were hyponatraemic (serum sodium <130 μmol/l) at onset of ARF. ARF was heralded by a fall in median mean arterial pressure (MAP) of 14.1 mm Hg from admission ($p<0.001$, CI 6.8–19.7). 71.2% received volume expansion, 91.1% terlipressin, 79.7% salt poor albumin, 93.4% antibiotics, 7.5% MARS/renal support. MAP did not rise significantly 24 h after initiation of treatment ($p=0.56$). 28 day mortality was 61%. HRS patients had higher MELD scores than non-HRS patients (30 *v* 25; $p=0.0152$) but 28 day mortality was not significantly different (64.3% *v* 60.6% respectively, $p=0.797$).

Conclusion: ARF in cirrhosis is rarely due to HRS but is most commonly prerenal in origin and multifactorial. Potential early warning features include hyponatraemia and a falling MAP. Current treatment regimes may not be aggressive enough to reverse renal hypoperfusion. Despite this mortality for our cirrhotic cohort was similar to non-cirrhotic patients admitted to ITU with ARF. Development of ARF in a cirrhotic patient should not preclude aggressive treatment.

407 HOSPITAL READMISSION WITH DECOMPENSATED ALCOHOLIC LIVER DISEASE: DETERMINANTS, EARLY OUTCOME AND ACCURACY OF PROGNOSTIC SCORES

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Introduction: We have previously reported (McFarlane. *Gut* 2006;**55**:A2; Kerss, *Gut* 2006:A42) on early outcome and on accuracy of Maddrey, MELD, Child and Glasgow prognostic scores in patients presenting with first episode of decompensated alcoholic liver disease (ALD) (defined as Childs grade B or C). There are limited data regarding subsequent hospital admissions in such patients.

Aims & Methods: To evaluate determinants and early outcome of readmission in patients with decompensated ALD and to assess reliability of prognostic scores. Of 249 patients admitted to the Royal Hallamshire Hospital (RHH) with first episode of decompensated ALD, 37 died and 212 were discharged. We reviewed records of these 212 patients. We documented first readmissions with decompensated ALD to either RHH or Northern General Hospital (the other Sheffield acute hospital) For RHH readmissions, we reviewed case notes and calculated prognostic scores on readmission. We also evaluated drinking behaviour following initial discharge (graded as 1: abstinent, to 4: no reduction of intake).

Results: Ninety nine patients were initially readmitted with decompensated ALD to RHH and 19 initially to NGH (of whom 7 were subsequently admitted to RHH). We excluded 4 other patients with coincidental advanced malignancy (2 hepatoma, 1 pancreas, 1 lung). Readmission rates with decompensated ALD after 6, 12 and 24 months were (mean (SE)) 39 (3)%, 48 (5)% and 59 (6)% respectively. By multivariate analysis, readmission was associated with drinking behaviour after initial discharge ($p<0.01$) but not with gender, age or severity of liver dysfunction during initial admission. Following readmission to RHH, 28- and 84-day mortality rates were 7 (2)% and 20 (4)% respectively, similar to those following initial admission. As, following initial admission, gender, age, and presence of bleeding or infection did not predict mortality in multivariate analysis. Mortality was significantly associated with readmission Maddrey, MELD and Glasgow scores, and (for 84 day mortality only) Child score. The table shows (after excluding 35 patients given corticosteroids) areas under ROC curves (AUROC) and % accuracy of admission scores for prediction of 28-day mortality. Values for Child score were lower ($p<0.05$) for admission 2 than for admission 1; other differences were not significant.

Conclusion: The major determinant of hospital readmission with decompensated ALD is continued heavy drinking. The early outcome and prognostic value of the Maddrey, MELD and Glasgow scores are similar to those following initial admission.

408 AN AUDIT OF THE MANAGEMENT OF OSTEOPOROSIS ASSOCIATED WITH CHRONIC LIVER DISEASE

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Introduction: Chronic liver disease and alcohol consumption are important risk factors for the development of osteoporosis. Moreover heavy alcohol users are at increased risk of osteoporosis irrespective of the presence of cirrhosis. All patients with cirrhosis or severe cholestasis (bilirubin >3× normal for >6 months) should be assessed and treated for osteoporosis (Collier JD, *et al.* BSG Guidelines. *Gut* 2002;**50**(Suppl I):i1–i9).

Aims & Methods: We audited outpatients with a clinical or histological diagnosis of cirrhosis and compared the assessment of three subgroups according to aetiology: alcoholic cirrhosis (ALD), primary biliary cirrhosis (PBC) and autoimmune hepatitis (AIH) to see if they were being assessed for

Abstract 407

SCORE (cut-off point)	Admission 1 AUROC	Admission 1 accuracy (%)	Admission 2 AUROC	Admission 2 accuracy (%)
MELD (17)	0.79+0.05	84	0.77+0.06	90
Maddrey (40)	0.81+0.05	79	0.77+0.07	85
Glasgow (9)	0.80+0.04	87	0.71+0.12	95
Child (12)	0.78+0.05	81	0.64+0.09*	73*

*$p<0.05$ compared with values on admission 1.

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Abstract 408 Demographics and risk factors for osteoporosis

	ALD 30	PBC 12	AIH 12	Total 54
Male	20 (66.6%)	2 (16.6%)	1 (8.3%)	23 (42.6%)
Female	10 (33.3%)	10 (83.3%)	11 (91.6%)	31 (57.4%)
Child-Pugh A	15 (50%)	10 (83.3%)	7 (58.3%)	32 (59.2%)
Child-Pugh B	11 (36.6%)	2 (16.6%)	4 (33.3%)	17 (31.4%)
Child-Pugh C	4 (13.3%)	0	1 (8.3%)	5 (9.2%)
Smokers	20 (66.6%)	0	1 (8.3%)	21 (38.9%)
Long-term steroids	0	3 (25%)	11 (91.6%)	14 (25.9%)
Previous fractures	2 vertebral	4 vert: 1 NOF	0	7 (13%)
Post menopausal (% females)	6 (60%)	10 (100%)	9 (81.8%)	25 (80.6%)
DEXA scan done	1 (3.3%)	11 (91.6%)	4 (33.3%)	16 (29.6%)
Normal BMD T score >-1	–	2	3	5 (35.7%)
Osteopaenia T -1 to -2.5	1	5	1	7 (50%)
Osteoporosis T score <-2.5	–	2	0	2 (14.2%)
Calcium 1 g + Vitamin D3	5 (16.6%)	9 (75%)	8 (66.6%)	22 (40.7%)
Bisphosphonates	1 (3.3%)	4 (33.3%)	5 (41.7%)	10 (18.5%)

osteoporosis according to BSG guidelines. An electronic search of clinic letters for the word ''cirrhosis'' was performed, then notes used to identify those with a clinical and/or histological diagnosis of liver cirrhosis and the likely aetiology.
Results: The demographics, risk factors, DEXA scan results and prescription of calcium/vitamin D3 and bisphosphonates are presented in the table.
Conclusion: Patients with chronic liver disease from all causes are at risk of developing reduced bone mineral density and osteoporosis. There is also a significant pre existing vertebral fracture rate within this population. Bone mineral density did not correlate with severity of liver disease as measured by Child-Pugh score. Assessment of bone mineral density by DEXA scanning leads to a change in management by initiating a bisphosphoante in 21.4% of patients with chronic liver disease. However although 91.6% of patients with PBC are being assessed according to the BSG guidelines, only a small proportion of those with ALD are being assessed. This audit highlights that those with alcoholic cirrhosis should be a target group for improved assessment of bone health.

409 HAEMATOLOGICAL MALIGNANCIES PRESENTING WITH ACUTE LIVER FAILURE: A SINGLE CENTRE EXPERIENCE

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Introduction: Acute liver failure (ALF) is a condition with a high mortality rate. Early recognition and identification of the underlying cause is crucial in instituting medical treatment and assessing the need for liver transplantation. Previous experience of the management of ALF secondary to haematological malignancy is limited, with one published UK case series.[1]
Aims & Methods: Review our experience of ALF secondary to haematological malignancies. All patients admitted to the liver unit with ALF secondary to a haematological malignancy between 1996 and 2006 were identified. A retrospective review was made of case notes and database.
Results: Of 752 cases of ALF, 6 were associated with haematological malignancy. The underlying malignancies were NK-cell leukaemia (1), adult T lymphocytic leukaemia (1) and lymphoma (4). Median age was 45 (range 18–66). One patient was previously diagnosed with Hodgkin's disease and was subsequently transplanted for sero-negative hepatitis. Features common to all patients were a prodromal illness (median duration of 5 weeks; range 2–6) and jaundice (median bilirubin 208 μmol/l; range 112–238). 5/6 had palpable hepatomegaly, but only 2/6 had evidence of peripheral lymphadenopathy. Transjugular liver biopsy was performed in two patients and confirmed the diagnosis in both cases. In the remaining cases the diagnosis was made following lymph node biopsy (1), bone marrow examination (2) or postmortem (1). Encephalopathy developed in 4 patients following admission. Median time from jaundice to encephalopathy was 12 days; range 1–22. Four patients were managed on ITU and required haemofiltration. One patient was transplanted but died soon after the procedure, one patient underwent a course of chemotherapy and one patient was commenced on steroids and immunoglobulins. All six patients died soon after admission with a median survival of 8 days (range 3–26).
Conclusion: ALF secondary to a haematological malignancy is rare (<1% of referrals) but should be considered in all ALF patients presenting with a prodromal illness, jaundice, early lactic acidosis and hepatomegaly. Liver biopsy should be considered in these cases but the benefit of chemotherapy/transplantation in this setting is unclear.

1. Rowbotham D, Wendon J, Williams R Acute liver failure secondary to hepatic infiltration: a single centre experience of 18 cases. *Gut* 1998;**42**:576–80.

410 THE ROLE OF SMALL INTESTINAL BACTERIA IN DISEASE INITIATION AND PROGRESSION OF NON-ALCOHOLIC AND ALCOHOLIC STEATOHEPATITIS

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Introduction: Non-alcoholic steatohepatitis (NASH) is part of a spectrum of disorders related to fat deposition in the liver ranging from simple steatosis through steatohepatitis to fibrosis and cirrhosis. It is unclear what triggers disease progression from simple fatty liver to steatohepatitis. It has been proposed that overgrowth of bacteria normally residing in the small intestine contribute to the development of NASH.[1–3]
Aims & Methods: The aims of this study were to investigate if bacteria, normally resident in the small intestine, can be detected in the peripheral circulation of patients with NASH and alcohol-related steatohepatitis (ASH) and to investigate the impact this has on systemic cytokine expression in these patients. 12 patients with NASH, 12 with ASH and 12 control patients were studied. Venous blood samples were collected from each subject for blood culture, real-time PCR measurement of eubacterial DNA and cytokine expression and immunohistochemical measurement of anti-gastric autoantibodies. In vitro blood culturing and measurement of eubacterial DNA assessed bacterial translocation, measurement of anti-gastric autoantibodies was used to determine the extent of small bowel mucosal inflammation. Systemic immune response was studied by measurement of IL-1α, IL-10 and TNFα mRNA by real-time PCR.
Results: Escherichia coli was cultured in peripheral blood from one patient in the ASH cohort. Increased expression of eubacterial DNA was detected in 42% of NASH patients and 33% ASH patients, no significant difference was detected between the groups. Anti-gastrin autoantibodies were not detected in either group. There was no significant difference in cytokine expression between the two groups though levels of IL-1α and IL-10 mRNA were higher in ASH patients and TNFα expression increased in those with NASH.
Conclusion: Detection of eubacterial DNA in peripheral blood of NASH and ASH patients indicates that bacteria are translocating from the gut lumen to the systemic circulation. Bacteraemia occurs at levels below the detection limit of traditional blood culturing techniques. Bacterial translocation triggers alterations in systemic cytokine expression within both cohorts.

1. **Diehl AM**, Li ZP, Lin HZ, *et al.* Cytokines and the pathogenesis of non-alcoholic steatohepatitis. *Gut* 2005;**54**:303–6.
2. **Tilg H**, Diehl AM. Cytokines in alcoholic and non-alcoholic steatohepatitis. *N Engl J Med* 2000;**343**:1467–76.
3. **Wigg AJ**, Roberts-Thomson IC, Dymock RB, *et al.* The role of small intestinal bacterial overgrowth, intestinal permeability, endotoxaemia, and tumour necrosis factor? in the pathogenesis of non-alcoholic steatohepatitis. *Gut* 2001;**48**:206–11.

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411 EXTRACTION OF RNA FROM FORMALIN-FIXED, PARAFFIN-EMBEDDED ARCHIVAL HEPATOCELLULAR CARCINOMA

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Introduction: Most archival tissue is formalin fixed and paraffin embedded (FFPE) prior to histological examination. This process preserves the architecture of the tissues to allow accurate pathological diagnosis, but also degrades nucleic acids within these tissues. We have modified a pre-existing phenol-chloroform extraction method, and applied it to various FFPE samples of hepatocellular carcinoma (HCC) to assess the efficiency and reproducibility of this method.
Aims & Methods: Ninety nine cases of HCC were identified from our archive over an 18 year time period. Expert histopathological review then defined for each case an example of HCC and non-HCC. 10×5 μm section were then taken for each sample and extracted using a modified phenol-chloroform technique. The quality of the RNA was assessed objectively using a Nanodrop ND-1000 spectrophotometer, subjectively with an Agilent 2100 bioanalyser, and functionally using both real-time polymerase chain reactions (RT-PCR) and Agilent whole human genome gene array chips.
Results: All 99 cases (198 specimens) yielded significant amounts of RNA. The mean extracted RNA for all 198 cases was 1349 ng/ul. No statistically significant difference was noted when samples were stratified for age, aetiology or presence of tumour. When the nucleic acids were assessed using the Agilent Bioanalyser 34% of samples had gave excellent quality RNA with little or no degraded RNA present, 30% yielded RNA of good quality with a significant amount of degraded RNA present, and 36% of samples were composed of mainly degraded RNA. Functional analysis using RT-PCR showed that the majority of samples could be used in PCR experiments and over 1/3 of the samples were of sufficient quality to be used in gene array experiments.
Conclusion: Our nucleic acid extraction technique can reproducibly extract RNA from FFPE specimens up to 18 years old, with little variability in quality of RNA. The aetiology of the liver disease does not affect the extractions, and the RNA can be used in a variety of molecular pathology applications.

412 ALCOHOL AWARENESS IN MEDICAL UNDERGRADUATES

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Introduction: It has been shown that university students in general are poor at estimating the alcohol content in popular alcoholic beverages. However no data exist in relation to medical students specifically to determine the extent to which they, as future doctors, understand the alcohol content in alcoholic beverages.
Aims & Methods: To determine the awareness of alcohol consumption and the extent of teaching medical students consider they have received to see if this correlates with their confidence in taking a full alcohol history. To analyse medical students' knowledge of ''units'' and its definition. A questionnaire concerning demographic details, perceived safe drinking levels, teaching amount, and general alcohol knowledge was administered to all undergraduate medical students (years 1–5) at Cardiff University. To assess the student's knowledge, a point allocation system was designed. For each question correctly answered, the student was allocated one point. The AUDIT questionnaire was also included in these questions as a way of measuring alcohol consumption over the past year.
Results: There were approximately 1500 questionnaires distributed and 607 questionnaires were completed (40.5%). The mean AUDIT score for medical students for all five years was 11.36 with the male and female mean scores being (11.98) and (10.81) respectively. Fifth year students (7.86) drink less than any other year. The third year (13.48) had the highest AUDIT score. 45% of drinkers with scores above 20 were female. Over 16% had reported alcohol related injuries in the last year. The mean score for the level of alcohol knowledge was 5.13 out of a possible 11. However the scores did tend to increase progressively from year to year. With regards to maximum weekly intake of alcohol, 111 (18.3%) overestimated the levels recommended for men and 153 (25.2%) overestimated those for women. 313 (51.57%) had been taught how to take a full alcohol history while only 281 (46.29%) had the confidence to take a history. 123 fifth year students compared with just 15 first year students, were confident in their history taking abilities. Also there was a clear correlation between the years and the knowledge of the definition of a unit of alcohol. Less than 20% identified the correct number of alcohol units in Strongbow, Kronenburg and Wine.
Conclusion: Alcohol-related knowledge needs improving amongst medical students, especially when converting drinks to units as this is imperative if alcohol knowledge can be applied to real life situations and patients. It is important for the medical schools to design their own policies regarding ways to increase alcohol awareness.

413 MINIMALLY-ELEVATED LIVER FUNCTION TESTS: ARE WE SEEING OR DOING ENOUGH?

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Introduction: A rising burden of liver disease and increased deaths from cirrhosis are well documented in the UK. Asymptomatic minimally deranged liver function tests (LFTs) have been associated with significant liver disease.
Aims & Methods: We set out to identify what proportion of patients with an alanine aminotransaminase (ALT) in the range 40–90 IU/l were referred to either a gastroenterologist or hepatologist in Newcastle, from 1 January to 31 December 2003. We wanted to determine how fully investigated the patients were in primary care before referral and the outcome after being seen in secondary care. All LFTs in Newcastle are analysed in the Freeman biochemistry department. The pathology computer was interrogated to identify all patients with an ALT in the selected range and matched with the consultant gastroenterologists and hepatologists in the city. A retrospective case note review was undertaken.
Results: After correction for repeated sampling 5489 patients had an ALT between 40–90. Of these only 331 (6%) were referred to secondary care. 309 (93%) case notes were available for review, 190 (62%) were males, median age of the whole group was 52 (range 17–92) years. Of these patients 184 (60%) were referred from primary care for investigation of the abnormal LFTs, 19 (6%) had pre–existing liver disease, 17 (6%) were referred from within secondary care, 72 (23%) referred for other GI symptoms but LFTs not investigated, 17 (6%) for other GI symptoms but had their LFTs investigated. Of these 4 had coeliac disease. In primary care only 58% of patients had LFTs repeated before referral—median time between tests 8.5 weeks. Only 40% of patients had viral hepatitis serology, 23% autoantibody studies and 23% an ultrasound scan before referral. All patients had a ''liver screen'' at initial outpatient appointment. At clinic 27% had normal ALT <40. 28% underwent liver biopsy at a median 24 weeks from initial clinic appointment. This did influence management, patients with NASH were reviewed more frequently than those with NAFLD (5.5 *v* 3). However, only 25% of patients with simple steatosis on biopsy were discharged. Overall significant liver disease was found in 58% patients—29% NAFLD, 7% cirrhosis, 5.5% NASH, 5% alcoholic liver disease, 4% viral hepatitis.
Conclusion: Only a minority (6%) of patients with minimally abnormal ALT were referred to secondary care. The majority that were had little investigative work up prior to referral. Within those referred there was a significant incidence of cirrhosis and liver fibrosis. Clearer guidelines for referral within primary care, streamlining of referral pathways and sensitive screening tools for assessing fibrosis in fatty liver disease would greatly ease the assessment process.

414 SINGLE NUCLEOTIDE POLYMORPHISM OF THE SRB1 GENE AND SUSCEPTIBILITY TO HCV INFECTION

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Introduction: We have recently described a population of injection drug users who remain uninfected by hepatitis C virus (HCV) despite their long history of drug use and repeated sharing of injecting equipment. These individuals test negative for both HCV antibody and HCV RNA and we have termed them exposed but uninfected (EU). The absence of infection despite exposure raises the possibility that they have an innate resistance to infection. Alterations in receptors mediating viral entry can confer resistance, as described with CCR5 mutations in HIV infection. The scavenger receptor class B1 (SRB1) molecule is a lipid receptor recently shown to be an important HCV receptor. We aimed to examine if a functional polymorphism of the SRB1 receptor, which alters lipid metabolism, could have an impact on susceptibility to HCV infection.

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Abstract 414 Results of SRB1 genotype

Patient groups	Homozygous (GG)	Heterozygous (GA)	Homozygous (AA)
Exposed uninfected	28 (80%)	6 (17%)	1 (3%)
Chronic HCV	46 (79%)	11 (19%)	1 (2%)
Resolved HCV	34 (79%)	9 (21%)	0 (0%)

Aims & Methods: Genomic DNA was extracted from whole blood by salt precipitation. We studied three cohorts of subjects: (1) resolved HCV infection (HCV Ab +ve but HCV RNA –ve, n = 43), (2) chronic HCV infection (HCV Ab+ve and HCV RNA +ve, n = 58) and (3) exposed uninfecteds (HCV Ab and HCV RNA –ve, n = 35). Genotyping was done commercially (K Biosciences) to detect a G/A polymorphism at the 4th nucleotide position on exon 1 of the SRB1 gene (chromosome 12q24.32) which results in a change in amino acid from glycine to serine.
Results: The overall frequency of GG, GA, AA alleles was 79%, 19% and 1.5% respectively. There were no significant differences between groups.
Conclusion: Our data show no difference in the frequency of this single nucleotide polymorphism among individuals exhibiting resistance to HCV from those who are susceptible. Although this study does not support a role for this previously defined SRB1 polymorphism and the phenomenon of HCV resistance, other parts of the SRB1 genome remain to be studied.

415 PERCUTANEOUS LIVER BIOPSIES: DOES SIZE MATTER?

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Introduction: Percutaneous liver biopsy is associated with morbidity >5% and mortality of 0.01–0.1%. The number of passes taken increases the incidence of complications. There is a general consensus among pathologists that a sample should contain a minimum of 6 portal tracts with a greater number needed for staging of hepatitis C. However the operator taking the biopsy cannot use this criterion as a guide for adequacy of the sample.
Aims & Methods: The aim of this audit was to determine if there was any relationship between the length of sample obtained, number of portal tracts, whether sample was deemed adequate by pathologist and whether a definitive diagnosis was made. A large, single centre, retrospective audit of all the day case percutaneous liver biopsies between January 2000 and December 2005 was performed obtaining information from hospital databases and case notes. Biopsies carried out for grading of viral hepatitis and targeted lesions were excluded from the analysis of whether a definitive diagnosis was made.
Results: There were 640 biopsies (using needle gauge 14, 16 and occasionally 18) on 608 patients (238 females:370 males), median age at first biopsy 47 (range 17–84). 255 biopsies were performed for viral hepatitis grading. Number of portal tracts were recorded in 310 reports.
Conclusion: As cores of over 10 mm in length give a 80% chance of making a definitive diagnosis, >90% likelihood of the pathologist being happy with the sample sent and a >85% likelihood of there being 6 or more portal tracts within the sample, we would suggest, with the exclusion of hepatitis C staging, if the sample obtained is over 10 mm there is no need for a further pass. This avoids the increased risks of morbidity and mortality to the patient of a second or subsequent pass. If the sample obtained is less than 5 mm, a second pass is likely to be required for diagnosis to be made.

416 TREATMENT OF AUTOIMMUNE HEPATITIS WITH MYCOPHENOLATE MOEFITIL

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Introduction: Mycphenolate moefitil (MMP) use in autoimmune hepatitis (AIH) has been associated with a reduction in steroid requirements and improvement in liver histology but data are limited.[1 2]
Aims & Methods: Retrospective review of 20 patients with AIH treated with MMP after either failure to respond to, or intolerance of azathiprine (AZA).
Results: Seventeen patients were female; age at AIH diagnosis was (mean (range)) 44 (13–73) years. AIH score by International Group Criteria at diagnosis was 15 (10–19). 10 patients were switched to MMP (starting at 500 mg bd) because of failure to achieve histological remission after a mean of 125 months on AZA. 10 were switched to MMP after a mean of 26 months on AZA because of intolerance (5 N&V, 5 neutropenia). Two patients had to discontinue MMF after 3 months: 1 had severe deterioration of LFTs, the other was found to have a malignancy. No patients stopped MMF due to side effects or haematological problems. In the 10 patients given MMP because of failure to respond to AZA, the steroid dose (to maintain normal transaminases) fell in 5, but only 1 patient was able to discontinue steroids. 6 out of the 10 had repeated biochemical relapses; relapse frequency was similar on MMP and on AZA. The mean serum AST fell after 3 months of MMP (67 *v* 53) and after 2 years was 29. 3 patients were biopsied after 2 years, 2 showed improvement in necro-imflammatory and fibrosis scores whilst one showed no change. Of the 10 patients on MMP because of AZA intolerance, steroid dose fell in 9 and were stopped in 5. The mean dose fell from 19 mg, 3 months before MMP, to 9.5 mg and 5 mg at 3 and 12 months respectively. 2 patients had 1 relapse each over 4 years on MMP, these were easily controlled with steroids. The average AST fell from 142 to 39, 3 months before and after MMP. The average AST at 2 years was 29. Of the 3 patients biopsied on MMP after 2 years, 2 showed histological improvement, the third had worsening inflammation.
Conclusion: These data support the use of MMP as a second-line agent for treatment of AIH. In patients who are intolerant of AZA, MMP is well tolerated and is associated with reduced steroid requirements and a low relapse rate. In patients who fail to respond to AZA, MMP had no clear effect on relapse rate but did lower serum transaminases and allow a mean steroid dose to fall in 50% of patients. These results are in keeping with recent studies, although do suggest that patients who fail to respond to AZA may not respond to MMP and are often steroid dependant.

1. **Devlin SM**, Swain MG, Urbanski SJ, *et al.* Mycophenalate Moefitil for the treatment of autoimmune hepatitis in patients refractory to standard therapy. *Can J Gastroenterol* 2004;**18**:321–6.
2. **Richardson P**, James P, Ryder S. Mycophenalate Mofetil for maintenance remission in autoimmune hepatitis in patients resistant to or intollerent of azathioprine. *J Hepatol* 2000;**30**:371.

Abstract 415 Size of biopsy related to number of portal tracts and adequacy

Size of largest core	Definitive diagnosis	Deemed adequate by pathologist	≥6 portal tracts
1–5 mm	12 of 19 (63%)	9 of 44 (20%)	8 of 25 (32%)
6–10 mm	70 of 96 (73%)	139 of 188 (74%)	70 of 97 (72%)
11–15 mm	133 of 160 (83%)	233 of 260 (90%)	118 of 138 (85%)
16–20 mm	45 of 58 (77%)	94 of 103 (91%)	45 of 52 (87%)
>20 mm	9 of 10 (90%)	16 of 17 (94%)	7 of 7 (100%)

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Nutrition posters

417 ACID-BASE PROBLEMS DURING HOME PARENTERAL NUTRITION

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Introduction: The home parenteral nutrition (HPN) literature relates to D-lactic acidosis in patients with intestinal failure and large bowel in continuation. Hypokalaemic alkalosis is also recognised. There are few reports of other causes of acid-base disturbance (ABD) in adults. We wish to report our experience of severe hyperchloraemic metabolic acidosis and hypochloraemic metabolic alkalosis during HPN.
Aims & Methods: All 39 HPN patients from 1989–2006 were retrospectively audited for underlying condition, bowel anatomy, use of proton pump inhibitors, renal function, bicarbonate and chloride levels, D lactate and anion gap Na − (Cl +HCO3).
Results: Five patients had severe ABD and 5 others subclinical ABD. The latter 5 patients were chronically acidotic with high chloride and borderline bicarbonate levels and had normal renal function. In those who had severe ABD, 3 patients had evidence of severe hyperchloraemic acidosis with a normal anion gap excluding lactic acidosis. D-lactic acid levels were normal. Patient 1 (radiation enteritis, colon in line) developed a severe metabolic acidosis with pH 6.87, base excess −25.7, HCO_3 of 4 and pCO_2 2.8, lactate 0.7, Cl^- 126 and required haemofiltration. Patient 2 (Crohn's disease, jejunostomy) developed metabolic acidosis with gram negative sepsis, pH 6.91, base excess −22.9, HCO_3 5.4, Cl^- 109, Mg 0.25. Both patients had renal impairment and required intensive care with large amounts of bicarbonate supplementation. Only 4 acidotic patients were not on a proton pump inhibitor. Withdrawal of PPI improved acidosis. Two of our patients, 1 with an ileal conduit and colostomy, developed severe hypochloraemic alkalosis requiring intensive potassium and magnesium replacement. Both presented with severe cramps and paraesthesia, one with pH 7.55, Cl^- 85, HCO_3 36, the other with pH 7.55, Cl^- 75, HCO_3 30.3.
Conclusion: Acid-base disturbance is an underreported complication of HPN. Intercurrent sepsis and dehydration, particularly with renal impairment predisposes to overwhelming acidosis to which proton pump inhibitors may contribute. We now routinely measure chloride and bicarbonate in the regular follow-up of our HPN patients.

418 CLINICAL OUTCOMES CAN BE IMPROVED BY INCREASING PATIENT KNOWLEDGE WITH AN INFORMATION BOOKLET

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Introduction: Chronic intestinal failure (CIF) occurs when the function of most of the small intestine is lost either though extensive resection or as a result of severe chronic conditions such as radiation enteritis. Patients are advised to adhere to appropriate dietary advice to avoid diarrhoea or unmanageable output from a stoma/fistula, dehydration and oxalate kidney stones. By manipulating the diet patients can maintain or improve nutritional status thus avoiding or reducing dependency on home parenteral nutrition (HPN) or fluids.[1] This study aimed to assess the effectiveness of an information booklet on patients' knowledge of the CIF regimen and clinical outcomes.
Aims & Methods: Outpatients completed a 3-day food and gastrointestinal output diary plus a questionnaire to assess their knowledge of the CIF regime. Height, weight, body mass index (BMI), triceps skinfold thickness and mid-arm muscle circumference were measured. The ED-5Q was used to assess quality of life which generates an index and a visual analogue scale (VAS). The volume and content of HPN was recorded. Patients were provided with the booklet and given individually tailored advice by a dietician and reassessed at their next appointment. Paired *t* tests were used to compare data.
Results: Forty eight patients completed (31 female, 17 male, mean age 56.1 (13.4) years). 25 had Crohn's, 12 mesenteric infarct, 3 radiation enteritis, 5 surgical resections and 3 others. 33 received HPN, 4 intravenous fluids, 2 subcutaneous fluids and 4 oral nutritional supplements. There was a significant improvement in patients' knowledge,oral energy and fat intake, BMI and a reduction in parenteral energy, volume and frequency. There was no increase in gastrointestinal output resulting from an increase in oral intake. In HPN patients there was an improvement in ED-5D index ($p=0.007$) and VAS ($p=0.001$).
Conclusion: The study shows positive effects of education in stable CIF patients resulting in clinical benefits including the reduction of HPN.

1. **Jeppensen PB**, Mortensen PB. Dietary treatment of patients with a short bowel. In: Nightingale J (ed). *Intestinal failure*. London: Greenwich Medical Media Ltd, 2001:393–404.

419 ASSESSING THE SCREENING TESTS FOR MALNUTRITION

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Introduction: Assessment of nutritional status should be integrated into clinical practice. We assess several biochemical and diagnostic tests for assessment of nutritional status. Malnutrition is frequently observed in hospitals and is often under-diagnosed. It is associated with a higher morbidity and economic burden.
Aims & Methods: In this study we assessed the nutrition of 200 patients (114 F: 86M) on emergency admission to hospital—72% were above the age of 65. Biochemical markers together with mid-upper arm circumference (MUAC), triceps skinfold thickness and BMI measurements were performed in all patients. Investigators had performed more than 200 measurements using the Herbendens callipers for triceps skinfold thickness before starting the study. Malnutrition universal screening test developed by BAPEN and quality of life data using the SF36 was also performed on admission.
Results: Biochemical markers were not good indicators of malnutrition until patients were severely malnourished. Triceps skinfold thickness, BMI (using hoist in immobile patients) and MUAC were available for all 200 patients. Data on MUST and SF36 were available for 95% of patients. 66% of patients were malnourished. Poor quality of life data assessed by the SF36 questionnaire, age (>75), comorbidity, a dignosis of cancer, length of stay and patients unable to feed themselves independently were associated with severe malnutrition ($p<0.01$). BMI seemed to underestimate the presence of malnutrition and measurement of height and weight were difficult to measure in elderly immobile patients due to the need of a hoist and intensive nursing care. There was a close relation between BMI and MUAC. Triceps skinfold thickness and MUST were more sensitive markers of malnutrition and predicted quality of life and length of stay.
Conclusion: Malnutrition is prevalent in hospitalised medical and surgical patients. Nutritional assessment should be part of routine clinical practice and aggressive nutritional intervention of malnourished patients should be initiated.

Abstract 418

Variable	Before (mean (SD))	After (mean (SD))	p Value
Knowledge score	64.5 (27)%	80.7 (14.8)%	<0.001
Oral energy	2130 (895) kcal	2342 (983) kcal	0.04
Oral fat	93 (42) g	110 (52) g	0.003
BMI	22.3 (2.9)	22.8 (2.6)	0.02
Parenteral energy	881 (521) kcal	802 (546) kcal	0.02
Parenteral volume	2311 (880) ml	2198 (950) ml	0.02
Parenteral frequency	6.3 (1.3) days	5.9 (1.5) days	0.003

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420 THE NASAL BRIDLE—ITS PLACE WITHIN AN INTEGRATED NUTRITION SERVICE: A PROSPECTIVE AUDIT OF ONE YEAR'S DATA

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Introduction: The use of a nasal bridle to secure a nasogastric feeding tube was first described in 1980 and has subsequently been demonstrated to be safe and effective. The device was introduced as an integral part of the nutrition service on 1 August 2005 and this abstract presents one year of prospective data. We also compared our 30-day mortality data for PEG insertion after the introduction of nasal bridles to three previous audits.
Aims & Methods: Patient demographic data, indication for nutritional support, duration of feeding with a bridled NG tube and outcome was prospectively collected. We also collected prospective data on PEG placement including indication and 30-day mortality.
Results: Between 1 August 2005 and 31 August 2006 96 patients had a nasogastric tube secured with a nasal bridle. Indications included: CVA (34%), dementia (14%), sepsis (5%), post-op support (9%) and alcoholic liver disease (6%). Patients have had tubes secured for between 1 and 292 days (median time 16 days). 19% patients were discharged with the device in situ, 4% went on to have a PEG inserted when fit for the procedure and 30% died with secure NG tube feeding in place. The percentage of prescribed nutrition given prior to securing NG tube averaged 20%. This increased to 98% post bridle insertion. Since the use of nasal bridles, 30 day mortality for PEG insertion has decreased from 16% to 6%.
Conclusion: Nasal bridles are a safe and effective method of securing a nasogastric tube and can be maintained in both hospital and community settings. They provide an alternative to PEG feeding especially in patients with acute CVA. Patients can be guaranteed nutritional support whilst allowing a period for assessment, stabilisation and recovery prior to further intervention. An effective form of non-oral nutritional support allows PEG tubes to be placed in appropriate, stable patients with an associated reduction in 30 day mortality. These devices also assist the delivery of reliable enteral nutritional support in patients in whom PEG is not indicated (sepsis, postoperative, etc) and we are now able to support an increased number of malnourished patients appropriately.

421 PEXACT DIRECT-PUNCTURE PEG PLACEMENT: OUR FIRST 12 MONTHS' EXPERIENCE

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Introduction: Endoscopic gastrostomy placement is usually performed using a ''pull-through'' technique. In patients with oro-pharyngeal carcinoma, pulling the PEG bumper past the tumour may risk seeding of malignancy to the PEG site. A ''direct puncture'' technique is therefore preferred for such patients. Radiological insertion provides one option, but the tubes inserted are often small in calibre and tube dysfunction is relatively common. The Pexact (Fresenius) gastrostomy system uses an ingenious gastropexy suturing device and a 16Fr trocar with a peel away sheath. This allows a 15Fr balloon-retained gastrostomy to be inserted directly through the abdominal wall under endoscopic control. Since September 2004, we have used this technique for all oro-pharyngeal cancer patients referred from our regional Maxillo-Facial Unit for pre-operative PEG placement.
Aims & Methods: We wished to audit the results for our first year using this new technique. Case notes were reviewed for all patients referred for Pexact PEG placement during the period September 2004 to October 2005. Information relating to technical success of PEG placement, complications and mortality were obtained.
Results: Eighty nine patients were referred during this period. Procedures were performed under conscious sedation using midazolam and fentanyl. Pexact PEG placement was achieved in all cases. Minor haemorrhage (oozing) from the puncture site in one patient was the only immediate operative complication. This did not require specific treatment. Tube displacement during the first 30 days occurred in 7 patients (7.9%). 5 of these had a new gastrostomy tube placed at the bedside without difficulty; one required endoscopic replacement and one tube was replaced radiologically. None of these patients developed peritonitis. Tube blockage was recorded in one patient and leakage from the PEG site in two. No significant PEG-site infections were recorded. The overall 30-day complication rate was 12.3%. No patients died within 30 days of PEG placement. 90-day mortality was 10%, all due to disease progression or complications of maxillo-facial surgery. A PEG complication contributed to the death of one patient who died on day 92. She developed peritonitis while being treated for pneumonia on the intensive care unit and was found to have a partially displaced PEG at laparotomy.
Conclusion: Pexact provides a reliable direct-puncture method for PEG placement. Serious complications appear rare but early tube displacement is a significant problem. Minor complication rates are comparable to the standard pull-through technique, although PEG-site infection appears less common.

422 MRSA IN GASTROSTOMY SITES: PREVALENCE, ROUTE OF TRANSMISSION AND RELATION TO CLINICAL INFECTION AND SYMPTOMS

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Introduction: Localised gastrostomy site infections are a recognised complication of gastrostomy (PEG) insertion and occur in 15% of cases. In a previous study at St Georges Hospital, a high prevalence of MRSA gastrostomy site infections was noted, particularly in those already colonised prior to insertion.
Aims & Methods: A prospective study of 50 patients referred for PEG placement was carried out to assess prevalence of MRSA in patients referred for PEG tube placement; incidence and potential route of MRSA colonisation at PEG sites post procedure; relation of clinical evidence of infection to presence of MRSA; relation of pain at stoma site to presence of MRSA/infection. Full MRSA screening prior to insertion was requested. A bio-occlusive dressing was placed over the site for 24 h post insertion. Visual, microbiological and pain assessments of the site were made at 24 h, after which the dressing was removed and at 7 days.
Results: 30/50 (60%) patients were male. Median age 74 years (range 23–94 years). 46 (92%) had an MRSA screen sent prior to PEG insertion. 15 (32%) were MRSA positive in one or more sites prior to insertion. Information was available for 34 patients at 24 h and 31 patients at 7 days. 8/34 (24%) patients had MRSA identified in the PEG site within 24 h, 7 of which had also been positive at initial screening. 9/31 (29%) patients had MRSA identified in the PEG site within 7 days, 4 of which had also been positive on initial screening. 4/34 (12%) patients had PEG site infection at 24 h, 3 of which were colonised with MRSA ($p<0.05$). 3/4 (75%) of these reported moderate or severe pain, compared with 4/30 (13%) of those with no infection. 12/30 (40%) of patients had a PEG site infection at 7 days, 5 of which were colonised with MRSA. 6 (50%) of these reported moderate or severe pain compared with 0 with no infection ($p<0.005$).
Conclusion: Patients colonised with MRSA are likely to develop MRSA within their PEG site. Although the numbers are small, it is interesting that 3/10 patients who developed MRSA within their PEG site at 24 h only had positive swabs from their nose or sputum at the initial screening, thus raising the possibility that initial spread may occur via the gastroscope. This study has not been able to demonstrate that MRSA alone is responsible for PEG site infections, raising the possibility of other potential pathogens being transmitted via the PEG from the oropharynx. However, it should also be noted that 6/15 patients with evidence of MRSA within 7 days had not been previously positive, a serious concern relating to infection control.

Abstract 422

	24 h no infection (n = 30)	24 h infection (n = 4)	7 days no infection (n = 19)	7 days infection (n = 12)
Pain nil to mild	25 (83%)	1 (25%)	19 (100%)	6 (50%)
Pain moderate to severe	5 (17%)	3 (75%)	0	6 (50%)
MRSA	5 (17%)	3 (75%)	4 (21%)	5 (42%)

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Abstract 423 Vitamin D levels (number of patients + deficiency category)

Condition	n	Median Vit D level (nmol/l)	Severe <25	Mild–moderate 25–50	Sufficient >50
All	150	41	39	51	60
ALD	23	25	11	6	6
Liver other	13	30	4	6	3
IBS	32	58	4	10	18
IBD	33	43	6	14	13
Other	20	63	3	5	12
EPI	29	33	11	10	8

Vitamin D level by disease groups.

423 VITAMIN D LEVELS IN PATIENTS PRESENTING TO A GASTROENTEROLOGY CLINIC

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Introduction: Vitamin D deficiency is associated with non-specific symptoms, carries long-term risk to bone health, and certain groups are at higher risk (alcohol excess, old age, Asians). The prevalence among patients attending gastroenterology clinics is unclear; this prompted our pilot study.
Aims & Methods: Patients (n = 150); n = 121 randomly chosen: alcoholic liver disease (ALD) (23), inflammatory bowel disease (IBD) (33), irritable bowel syndrome (IBS) (32), other liver disease (13), other diagnosis (20); n = 29 with exocrine pancreatic insufficiency (EPI). Use of OTC supplements was checked and those on vitamin preparations excluded. Measurements: Vitamin D [1,25-(OH)2 Vitamin D3], calcium profile, magnesium, ferritin, B12, folate. Demography: 75 females; 10 Asian. Median age 54 (18–86) years. 75 patients were female, 10 Asian, median age 54.34 years (17.88 to 85.72 years).
Results: (1) Only 40% had normal levels. (2) Severe deficiency was most frequent in ALD (48%), EPI (38%), other liver disease (31%) and IBD (18%) (26% overall). Mild–moderate deficiency occurred in similar frequency ALD (26%), EPI (35%), other liver disease (46%) and IBD (42%) but in IOBS (46%). (3) Severe/moderate deficiency occurred significantly more often in females ($p = 0.0266$), Asians ($p = 0.0358$) but was unrelated to age ($p = 0.6047$) (Fisher's exact test). (4) 12%, 14% & 14% of 121 tested were deficient in folate, Vit B12 and iron (often associated with normocytosis). (5) No patient had toxic Vit D levels.
Conclusion: (1) Vitamin D deficiency is common in patients attending gastroenterology clinics, is almost always subclinical and its long-term significance is unknown. (2) Increasing awareness has allowed us to recognise the condition more often.

424 REFERRAL FOR INTESTINAL TRANSPLANTATION: AN AUDIT OF INTESTINAL FAILURE PATIENTS

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Introduction: Survival after intestinal transplantation is improving. It is considered an alternative to home parenteral nutrition (HPN) in patients with intestinal failure (IF) who have complications associated with HPN. US guidelines for referral for intestinal transplantation have been published.
Aims & Methods: The aims of this study were to review numbers of HPN patients at a single UK tertiary referral centre eligible for consideration of intestinal transplantation, to assess the proportion of eligible patients who had been referred, and to compare details with patients who had undergone intestinal transplantation. Case records of patients receiving HPN on 31/12/2005 were reviewed. Patients were considered eligible for referral if they fulfilled 1 or more of the following criteria: advanced PN-associated liver disease (PNALD); thrombosis of 2 or more major veins; frequent CVC related sepsis; frequent severe dehydration; patient request. Case records of patients with intestinal failure who had undergone intestinal transplantation at a single UK transplant centre were reviewed.
Results: Records of 123 patients receiving HPN were reviewed (median age 51 years (range 19–80)). 33 patients (27%) fulfilled 1 or more criteria for referral (median age 47 years (range 24–76)). Of these only 7 (21%) had been referred (median age 39 (range 24–50)). Number of patients fulfilling each criterion and % referred was: advanced PNALD 2 (100%); multiple venous thrombosis 16 (19%); CVC sepsis 16 (12%); frequent dehydration 1 (100%); patient request 1 (100%). Of those not referred, referral was precluded by perceived comorbidity in 23% and psychosocial/compliance issues in 19%; alternate management strategies were employed in 23% and referral was not considered warranted in 31%. Other reasons were recorded in 4%. Records of 4 patients who had undergone intestinal transplantation were available for review (median age 30 (range 22–44)). Indications for transplantation were: multiple venous thrombosis and frequent CVC sepsis; advanced PNALD and recurrent CVC sepsis; frequent CVC sepsis; advanced desmoid disease.
Conclusion: Over a quarter of HPN patients fulfil criteria for consideration of intestinal transplantation. At present adult patients are only referred once complications are life threatening. Patients with CVC sepsis are rarely considered for transplantation. Similarly, patients with venous thromboses are only referred once access is very limited. Earlier referral may improve transplantation outcomes in this group but this must be balanced against favourable survival in patients receiving HPN. Close liaison with transplant centres is essential to ensure appropriate and optimally timed referral.

425 FALL IN PEG INSERTION RATE IN NORTHERN ENGLAND FOLLOWING NCEPOD

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Introduction: The major concerns highlighted by the NCEPOD (National Confidential Enquiry in Patient Outcome and Death) report, 2004, on percutaneous endoscopic gastrostomy (PEG) related deaths in UK were (a) inadequate preoperative assessment by a multidisciplinary team, (b) selection of very high-risk patients and (c) concomitant use of sedation and throat spray during the procedure.[1] We have previously, under the auspices of the Northern Nutritional Network, performed a prospective three month audit of PEG insertion in the Northern region.[2]
Aims & Methods: In order to study changes in PEG insertion practices following NCEPOD we decided to undertake a further prospective audit over exactly the same period of the year as the previous one. A standard audit proforma identical to the one used in the previous audit was completed in all centres affiliated to Northern Nutritional Network for all the PEGs done from December 2005 to February 2006.
Results: Of the 17 centres results were available prospectively from 15 and retrospectively from 2. There was a substantial fall in the number of PEGs done in the whole region as compared to the last audit (102 *v* 157). Also, a greater proportion of patients were assessed formally by a multidisciplinary PEG team preoperatively as compared to the last time (60% *v* 40%).As in the last audit, majority of PEGs were inserted for neurological causes (49%) or obstructing lesions (16%). Fewer PEGs were inserted for non-specific dysphagia or dementia 4 (4.5%) *v* 16 (10%). The success rate was marginally better 96% as opposed to 93% in last audit. None of the patients received both sedation and throat spray. Incidence of all complications 25 (33%) and chest infection 7 (8.5%) within 28 days was marginally higher than in last audit 32 (20%) and 8 (5%) respectively. Nevertheless there was a substantial fall in mortality at 28 days, that is 7 (6.8%) *v* 25 (15.8%). Mortality at 7 days was similar in the two audits at 3 (3.4%) and 4 (4.4%). There was an increase in the percentage of patients followed up by a dedicated PEG service 68 (78%) *v* 74 (47%).
Conclusion: Following the NCEPOD report there has been a substantial fall in the PEG insertion rate in the Northern Region with more frequent involvement of a multidisciplinary team in preoperative assessment of patients. This is reflected in better outcome in terms of 28-day mortality and follow-up by a dedicated PEG service.

1. Scoping our practice: NCEPOD Report 2004. Available at http://www.ncepod.org.uk.
2. Prospective three month audit of gastrostomy insertion in Northern Region. Poster Presentation at BAPEN 2005.

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426 A ONE-YEAR RETROSPECTIVE AUDIT OF NASO-JEJUNAL TUBE PLACEMENT COMPARING ENDOSCOPICALLY-PLACED VERSUS RADIOLOGICALLY-PLACED TUBES: DO THOSE PLACED WITH IMAGING AT THE TIME OF INSERTION LAST LONGER?

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Introduction: Naso-jejunal (NJ) tubes are currently being placed at our unit for patients requiring post-pyloric feeding. Tubes are placed either using an endoscopic technique with a follow-up abdominal *x* ray (AXR) prior to feeding versus radiological insertion using imaging to guide the tube into the jejunum.
Aims & Methods: We aimed to assess the safety and efficacy of our practice in NJ tube placement and to see if radiologically inserted tubes last longer.
Results: Over a 12-month period there were 75 NJ tubes placed, endoscopically (E), n = 45, and radiologically (R), n = 30. In the E group (27 M, 18 F), in the R group, (13 M, 17 F). In the E group, mean age was 64 years, in R group, mean age was 65 years. In the E group, most patients were from intensive care (ITU, 80%) with majority of R group from wards (73%). Main indications in each group were: E group, acute pancreatitis, n = 20; gastroparesis, n = 16; compared to R group, failed naso-gastric feeding with persistent vomiting, n = 8; gastric outlet obstruction, n = 5. The position of the tip of the NJ tube was judged at either AXR in E group or at time of imaging in R group. In E group, the tip was found to be in the jejunum in 40% and 2nd or 3rd part of duodenum in 60%, in R group tip was in jejunum in 100%. The mean duration of each tube was E group n = 5.2 days and in R group n = 6.5 days. 21/45 (47%) in E group lasted <3 days with 10/30 (33%) in R group lasting <3 days. Minor complications were found in both groups and included E group overall 80%, dislodgement, n = 19; blockage, n = 11; and GI dysfunction, n = 6 and in R group overall 70%, dislodgement, n = 17; blockage, n = 4; and GI dysfunction, n = 0. In E group, 53% required more than one NJ tube to be placed for feeding whereas in R group only 23% required more than one tube. Of those who failed NJ feeding and required parenteral nutrition (PN), E group n = 26% and R group n = 13%. The number of patients who regained oral intake at end of feeding was 67% in E group versus 87% in R group. Overall mortality whilst in hospital was 35% in E group versus 13% in R group.
Conclusion: Radiologically-inserted NJ tubes are more effective at getting into the jejunum (100% *v* 40%) but do not appear to last significantly longer than endoscopically placed tubes 6.5 days *v* 5.2 days. There is a trend towards less complications in radiological tubes and less need for multiple tubes being placed. Our unit is going to assess the effect of using radiological screening at the time of endoscopic placement to see if we can improve the duration of these tubes. We will also improve our current techniques to secure tubes, improve flushing techniques to prevent blockage and improve education of staff in care of these tubes.

427 PEG ASSESSMENT TEAM IMPROVES CONTINUITY OF CARE FOR PATIENTS REQUIRING ENTERAL NUTRITION IN A DISTRICT GENERAL HOSPITAL

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Introduction: Percutaneous endoscopic gastrostomy (PEG) has been the procedure of choice for patients requiring long-term enteral nutritional support for over 25 years. However the 2004 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) ''Scoping our practice'' identified concerns regarding the appropriateness of referrals and highlighted a 6% 30-day mortality associated with PEG placement. In response to NCEPOD, a PEG assessment team was formed in 2005 comprising a consultant gastroenterologist, specialist nurse, nutrition team dietician and the speech and language therapy team.
Aims & Methods: A comparison was made of patients referred for PEG in the 14 month period before and after the introduction of the PEG team. The results were compared for indications, appropriateness and outcome as well as satisfaction of patients, relatives and ward staff.
Results: See table. There was no significant difference between the groups as regard to age, sex and indications. Pre-PEG team 41 patients; age range 17–90; mean 64 years; male, 22; female, 19. Post-PEG team 70 patients; age range 27–90; mean 65.8 years; male, 38; female, 32 (paired *t* test NS). The introduction of the PEG team has led to very positive feedback from patients, relatives and ward staff. Referrals have increased but the proportion of procedures has decreased due to more patients being deemed inappropriate (adequate nutritional intake, unfit for procedure, etc) More patients were referred directly for RIG insertion (usually patients with previous abdominal surgery).
Conclusion: The introduction of a dedicated PEG team has improved the assessment of patients, improved identification of those deemed inappropriate for PEG and has resulted in a reduction in PEG-associated mortality. The PEG team now arranges appropriate nutritional support for all referrals (including RIGs). We recommend the formation of similar PEG teams in every hospital.

Abstract 427

	Pre-team	Post-team
Referrals	41	70
PEGs placed	27 (66%)	36 (51%)
30-day mortality post PEG	3 (11%)	1 (2.8%)
PEGs declined	14 (34%)	34 (39%)
Unfit/futile*	8	11
Refer for RIG†/surgery	2	8
Adequate nutrition	4	10
Declined by patient‡	0	5

*Futile: severe end stage dementia or poor prognosis. †RIG: radiologically inserted gastrostomy. ‡Declined by patients after full discussion with the PEG team.

428 EXPERIENCE FROM THE NUTRITIONAL SUPPORT TEAM AT BELFAST CITY HOSPITAL

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Introduction: The Belfast City Hospital (BCH) nutrition team started in June 2001. Its members consist of a consultant chemical pathologist, clinical pharmacist, dietician, and a nutrition nurse. Since its emergence the team has been involved in managing parental nutrition (PN) in 497 patients.
Aims & Methods: Retrospective information was obtained from records of 497 patients. Data included numbers of patients per year, department usage, duration, and central venous catheter (CVC) infection rates.
Results: Statistics are available from May 2001 to June 2006 (table 1). In this period 497 patients received PN. The initial year had results for 7 months therefore modified figures were calculated to estimate 12 month results. This is also relevant to 2006 in which only 6 month results were available. Modified results were also calculated for this final year (table 2).

Abstract 428 Table 1 Frequency of usage of parenteral nutrition

	2001 (7/12)	2002	2003	2004	2005	2006	
HDU/ICU	22	40	41	30	35	7	
Haematology	14	13	12	23	8	7	
Renal	1	4	2	4	4	2	
Surgical	23	40	40	46	23	46	
Medicine	1	2	1	4	2	3	
Oncology	2	9	8	6	5	12	
Total	63	108	104	113	77	77	542

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Abstract 428 Table 2 Frequency of usage of parenteral nutrition (modified)

	2001 (modified)	2002	2003	2004	2005	2006	
HDU/ICU	37	40	41	30	35	7	
Haematology	24	13	12	23	8	7	
Renal	2	4	2	4	4	2	
Surgical	39	40	40	46	23	46	
Medicine	2	2	1	4	2	3	
Oncology	3	9	8	6	5	12	
Total	107	108	104	113	77	77	586

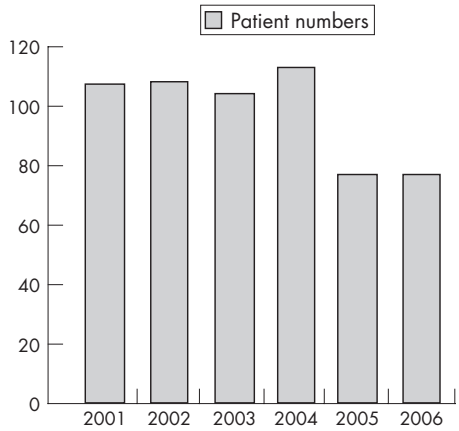
Abstract 428 Table 3 Percentage of patients receiving parenteral nutrition >5 days

Year	% pts
2001	56
2002	59
2003	59
2004	58
2005	52
2006	71

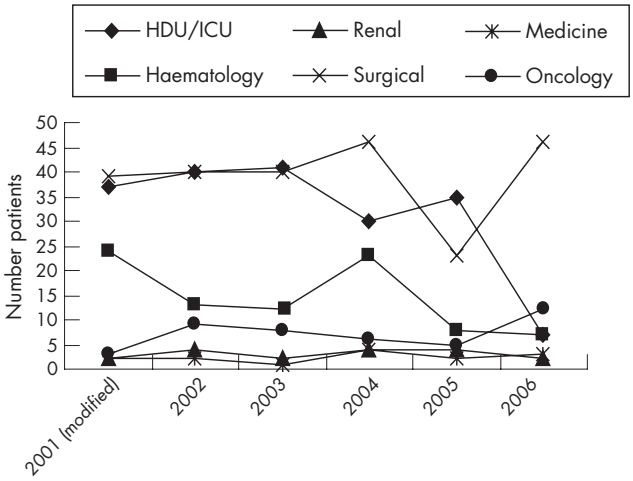
Abstract 428 Table 4 Frequency of CVC sepsis between September 2005–August 2006

	Number	% pts
Total	79	
Positive tip	29	36.7
Positive tip and BC	9	11.4

The modified results show a decrease in the usage of PN over this 6-year period (chart 1). The departmental results also show a decline in the usage of PN in the intensive care unit (ICU) and the haematology department (chart 2). The percentage of patients receiving PN for duration greater than 5 days has remained consistent except for the final year of analysis in which it increased to 71% (table 3). CVC infection rates were accurately recorded over a 12-month period from September 2005 to August 2006 (table 4). 79 patients received PN during this period. 37% of these patients had positive organism growth on CVC tips. However only 11% of the total patients appeared to be symptomatic, that is pyrexia, positive peripheral blood culture, positive central blood culture and positive organism growth on CVC tip.



Abstract 428 Figure 1 TPN usage.



Abstract 428 Figure 2 TPN usage in each hospital department.

Conclusion: The role of the BCH nutrition team cannot be underestimated given the large numbers of patients receiving PN. Overall these data suggest that patient selection is improving as fewer patients are receiving PN and if they do receive PN it is for a longer duration. The CVC sepsis rates are below other institutes figures.

429 GASTROSTOMIES IN PATIENTS WITH DEMENTIA: KILL OR CURE?

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Introduction: Feeding gastrostomies (also abbreviated as PEG) is an established method of maintaining long term enteral nutrition in patients with swallowing difficulties arising mainly from strokes or cognitive impairment. Not many studies have been done to look at the short and particularly the long-term outlook of these patients with dementia after PEG insertion.

Aims & Methods: To review outcomes of patients with dementia who had a PEG inserted in a 600 bed district general hospital. METHODS: Records of such patients who had a PEG inserted between July 2000 and June 2003 were reviewed for 7 day, 1 month and 1 year mortality at our hospital. Nursing homes and carers were contacted to provide details where case notes could not be found.

Results: Sixty nine patients (48 males, 21 females) had a PEG inserted. The causes of the dementia were senile or vascular in aetiology. There were no procedure related deaths. Minor complications included wound related infection (2 patients), tube leak (1 patient) and tube dislodgement (1 patient) which were corrected. Nine patients died by day 7 (13%), a total of 20 were dead by 1 month (29%), 31 had succumbed by 3 months (45%) and 8 patients were alive at one year giving a 12 month mortality of 89%. All the deaths could be attributed to progression of the dementia and/or aspiration pneumonias and subsequent worsening of their condition. On a positive note, 3 of the 8 patients who were alive at 12 months had their PEG tube removed as their swallowing had returned.

Conclusion: Early and particularly late mortality are high as shown from this study. PEG tubes do not appear to improve mortality or quality of life in patients with dementia. Less invasive methods of feeding (nasogastric, thickened oral feeds or subcutaneous fluids) should be considered instead

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for these patients. Importantly, valuable endoscopy slots, resources and time could be used for more productive causes.

Small bowel posters

430 SPECIALIST FOLLOW-UP FOR PEOPLE WITH COELIAC DISEASE: A QUESTIONNAIRE STUDY

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Introduction: Regular follow-up is recommended for all patients with coeliac disease.[1] Studies have found regular follow-up is associated with better adherence to gluten free diet.[2] A significant proportion of patients fail to attend their appointments.[3]
Aims & Methods: This study aimed to explore why people do or do not attend clinic appointments and how this links with dietary adherence. Findings from a previous qualitative study were used to inform the design of a questionnaire which was sent by post to 304 patients diagnosed with coeliac disease. The questionnaire was piloted face to face with patients with coeliac disease in the waiting area of a gastroenterology clinic. The questionnaire was sent on two occasions to improve response rate. Questionnaires were sent to attenders and non-attenders on different coloured paper. Non-attenders were defined as those who had not attended a follow-up appointment during the preceding year and/or had failed to attend an appointment on 5 or more occasions.
Results: 185 responses were received from attenders (78%) and 29 from non-attenders (43%). 52% of attenders compared with 17% of non-attenders reported they got all the information they needed about coeliac disease at their appointments. 62% of attenders and 24% of non-attenders reported they got all the practical help and advice about living with a gluten-free diet they needed. A dedicated coeliac clinic where a specialist doctor and dietitian would be available was selected as a useful service by over 70% of attenders and non-attenders.
Conclusion: This study represents an attempt to study the needs of people with coeliac disease who fail to attend follow-up. The results are limited by small sample size but suggest that some non-attenders may not be having their needs for information and practical advice met in a way that enables them to adhere to gluten free diet. Further research is required to find how these needs can best be met to facilitate dietary adherence. A dedicated coeliac clinic is an approach to follow up which is preferred by many patients.[4]

1. **Pietzak MM**. Follow up of patients with celiac disease: achieving compliance with treatment. *Gastroenterology* 2005;**128**(Suppl 1):135–41.
2. **Butterworth JR**, Banfield LM, Iqbal TH, *et al*. Factors relating to compliance with a gluten-free diet in patients with coeliac disease: comparison of white Caucasian and South Asian patients. *Clin Nutr* 2004;**23**:1127–34.
3. **Murdock A**, Rodgers C, Lindsay H, *et al*. Why do patients not keep their appointments? Prospective study in a gastroenterology outpatient clinic. *J R Soc Med* 2002;**95**:284–6.
4. **Bebb JR**, Lawson T, Long RG. Long-term follow-up of coeliac disease—what do coeliac patients want? *Aliment Pharmacol Ther* 2006;**23**:827–31.

431 ADAPTING TO LIFE WITHOUT GLUTEN

E. K. Bridcut. *Nutrition and Dietetics, Wirral Hospital NHS Trust, Wirral, UK*

Introduction: The only treatment for coeliac disease is a gluten free diet.[1] Strict adherence to a gluten-free diet is difficult to maintain[1] and has been associated with reduced quality of life.[2] This study explored how people with coeliac disease manage, or fail to manage, a gluten-free diet and the role played by health professionals in this.
Aims & Methods: The aim of the study was to understand in greater depth how people with coeliac disease manage a gluten-free diet and how health professionals can improve dietary adherence. This was a qualitative study using grounded theory. Data collection and analysis were carried out concurrently. Initial analysis informed further data collection in an iterative fashion until an adequate degree of saturation was reached. Data comprised transcripts of semistructured interviews carried out in respondents' homes.
Results: Factors which helped or hindered adoption of a strict gluten-free diet were identified. These included experience of symptoms, beliefs about complications, social support, practical skills, information and attitude to gluten free diet. A key strategy employed in adapting to life without gluten was normalisation. In the context of coeliac disease normalisation means minimising the social consequences of gluten free diet in order to lead a normal life.
Conclusion: This study suggests that the goal of adaptation to a gluten-free diet, from a patient perspective, is the reconstruction of normal life, gluten-free. This echoes the findings of another recent qualitative study.[3] The factors identified as promoting successful adaptation could be used to plan interventions by health professionals aimed at improving dietary adherence.

1. **McGough N**, Cummings JH. Coeliac disease: a diverse clinical syndrome caused by intolerance of wheat, barley and rye. *Proc Nutr Soc* 2005;**64**:434–50.
2. **Hallert C**, Granno C, Grant C, *et al*. Quality of life of adult coeliac patients treated for 10 years. *Scand J Gastroenterol* 1998;**33**:933–8.
3. **Gregory S**. Living with chronic illness in the family setting. *Sociol Health Illn* 2005;**27**:372–92.

432 RESPONSE OF REDUCED BONE MINERAL DENSITY IN COELIAC DISEASE TO TREATMENT

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Introduction: Current BSG guidelines[1] recommend DEXA scanning for all newly diagnosed patients with coeliac disease (CD), though the need for this has been questioned.[2] It is not clear how best to manage reduced bone mineral density (BMD) in CD.
Aims & Methods: Our approach has been to treat osteopenia ($-1.0>T>-2.5$ SD) by adequate calcium/vitamin D supplementation within a gluten free (GF) diet, adding weekly bisphosphonate (alendronate or risedronate) if osteoporosis ($T \leqslant 2.5$ SD) is present. We report the effect of this approach as assessed by follow-up (2 year) DEXA scan. We studied 158 patients with biopsy-proved (villous atrophy and lymphocytosis) CD. BMD was recorded by DEXA at the L2-4 lumbar spine (LS) and neck of femur (NOF) at diagnosis (t0) and repeated after two years (t2) if osteopenia or osteoporosis was present.
Results: At diagnosis, 70 patients (44%) had normal BMD, 56 (35%) osteopenia at either site, and 32 (21%) osteoporosis. After two years' treatment (t2), there was significant improvement in BMD in patients with osteopenia and osteoporosis at both sites ($p<0.002$ for all). No patient with osteopenia developed osteoporosis.
Conclusion: GF diet with adequate calcium/vitamin D, plus bisphosphonate for osteoporosis, results in significant improvement in BMD. Follow-up DEXA does not appear to be needed. As only one fifth of CD patients have osteoporosis at diagnosis, risk factors should be identified to allow patient selection for initial DEXA.

1. **Scott EM**, *et al*. *Gut* 2000;**46**(Suppl 1):1–8.
2. **Lewis NR**, Scott BB. *Eur J Gastroenterol Hepatol* 2005;**17**:1065–70.

Abstract 432

	Patients (n)	Mean BMD t0	Mean BMD t2	Normal BMD t2	Osteopenia t2	Osteoporosis t2
LS osteopenia	50	1.033	1.069	12 (24%)	38 (76%)	0
NOF osteopenia	47	0.792	0.812	4 (9%)	43 (91%)	0
LS osteoporosis	27	0.792	0.876	0	16 (59%)	11 (41%)
NOF osteoporosis	14	0.616	0.700	1 (7%)	6 (43%)	7 (50%)

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433 IDENTIFICATION OF PATIENTS WITH IDIOPATHIC BILE ACID MALABSORPTION PRESENTING WITH CHRONIC DIARRHOEA

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Introduction: Bile acid malabsorption (BAM) is an important cause of chronic diarrhoea and is present in many patients without evidence of ileal disease.[1] Previous studies have been unable to distinguish patients with BAM based on their clinical presentation and investigations other than ^{75}SeHCAT retention.[2]

Aims & Methods: The aim of our study was to examine demographic, clinical and pathological variables in a cohort of patients with chronic diarrhoea who underwent ^{75}SeHCAT scanning, in order to diagnose BAM at an earlier stage obviating unnecessary investigations. Sixty three patients underwent a ^{75}SeHCAT test between January 2002 and September 2006. They were divided based on their 7 day ^{75}SeHCAT retention; 40 patients were positive ($\leqslant$15% retention) and 23 were negative (>15%). A diagnosis of primary BAM was considered when bile acid retention was $\leqslant$15% after exclusion of secondary causes (Group A). This group was compared with cases with a diagnosis of functional diarrhoea and normal ^{75}SeHCAT retention (Group B). The two groups were similarly investigated with blood tests, stool culture and endoscopy to exclude other causes of diarrhoea.

Results: Of the 40/63 cases with ^{75}SeHCAT result $\leqslant$15%, 18 had secondary BAM (9 terminal ileal resection, 3 cholecystectomy, 2 small bowel Crohn's disease, 2 collagenous colitis, 1 post infective enteritis and 1 prior radiotherapy). The remaining 22 patients were defined as having idiopathic BAM-Group A (median ^{75}SeHCAT retention 9%). Of the 23/63 cases with a negative result, 3 patients had other causes of diarrhoea (2 Crohn's disease, 1 bacterial overgrowth) and the remaining 20 patients were diagnosed with functional diarrhoea, Group B (median ^{75}SeHACT retention 18.9%). The female to male ratio in groups A and B was similar (2.5:1 *v* 2.3:1). Primary BAM patients presented at a later age (60 *v* 44 years, $p<0.05$) and had a longer duration of diarrhoea at presentation (24 *v* 15 months, $p<0.05$). No significant difference was noted in bowel frequency, haemoglobin, white cell count, platelet count and C-reactive protein between the two groups.

Conclusion: Our study indicates that patients with primary BAM were older and had diarrhoea for longer duration than patients with functional diarrhoea. Biochemical and haematological results could not distinguish between these groups. Our study demonstrates higher detection rate of primary BAM (22/63, 34.9%) by ^{75}SeHCAT scanning as compared to a previous study (6%).[3] This may be attributed to differences in patient selecton and preliminary workup prior to ^{75}SeHCAT scanning.

1. **Galatola G**, *et al. Eur J Gastroenterol Hepatol* 1992;**4**:533–7.
2. **Williams, et al**. *Gut* 1991;**32**:1004–6.
3. **McKaig, et al**. *Gut* 2002;**50**(Suppl II):A156.

434 NUTRIENT SUPPLEMENTS PREVENT DOWNREGULATION OF INTESTINAL DEFENSIN EXPRESSION DURING DIARRHOEAL DISEASE

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Introduction: We have previously demonstrated that alpha-defensin expression in small intestine is reduced in a tropical population compared to a European population.[1] This counterintuitive difference between two populations could be due to genetic or environmental factors. Intestinal infection is common in urban Africa, and other groups have shown that intestinal pathogens can downregulate defensin expression.[2, 3]

Aims & Methods: We studied expression of HD5 and HD6 during and one month after episodes of diarrhoea, in Zambian adults participating in a randomised controlled trial of a micronutrient supplement. In this trial, 500 adults were randomised to a multiple micronutrient supplement or placebo and followed up for 3.5 years. HD5 and HD6 mRNA were measured by real time quantitative RT-PCR in 53 pairs of biopsies obtained by endoscopy during and after diarrhoea.

Results: The full results are not yet known as the randomisation code will not be broken until December 2006, but interim analysis is available. In placebo recipients, HD5 mRNA was lower by 0.87 transcripts/microgram total RNA during diarrhoea, but in micronutrient recipients this reduction was abolished ($p=0.02$). Full results after breaking the code will be available by February 2007, and these data will also include analysis of asymptomatic infections.

Conclusion: These preliminary data suggest that diarrhoea-causing pathogens cause a downregulation of intestinal alpha-defensin expression, which may partly explain the lower defensin expression referred to above. The data also suggest that a multiple micronutrient intervention can protect against this effect.

1. **Dhaliwal W**, *et al.* Intestinal defensin gene expression in human populations. *Mol Immunol* 2003;**40**:469–75.
2. **Islam D**, *et al.* Downregulation of bactericidal peptides in enteric infections: a novel immune escape mechanism with bacterial DNA as a potential regulator. *Nat Med* 2001;**7**:180–5.
3. **Salman N**, *et al.* Enteric salmonella infection inhibits Paneth cell antimicrobial peptide expression. *Infect Immun* 2003;**71**:1109–15.

435 THE CHANGING PRESENTATION OF COELIAC DISEASE IN THE NORTH EAST OF ENGLAND: AN EPIDEMIOLOGICAL ANALYSIS OF FOUR YEARS

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Introduction: The clinical presentation of coeliac disease (CD) is reported to be changing with an increase in extraintestinal and atypical presentations in comparison to the traditional malabsorptive presentation (NIH Consensus Meeting 2004, USA).[1] The data on this phenomenon from the UK are limited, although larger centres have reported on this phenomenon.[2]

Aims & Methods: (1) To determine whether the clinical epidemiology of CD has changed in a closed population of the North East of England. (2) To study the positivity of anti-endomysial antibody (EmA) in these ''atypical'' presentations of CD compared to the ''classical'' presentation. A retrospective case notes review of all cases coded histologically as coeliac disease or subtotal/partial/total villous atrophy over a 4-year period from January 2001–December 2004 in the South of Durham (population 200 000) was carried out. The clinical symptoms, EmA positivity and Marsh Grading of the histology were compared.

Results: Ninety two patients were coded to have histology compatible with CD over the 4-year period giving a population prevalence of approx 1:2000. 76 case notes were available for review, and 6 paediatric cases were excluded from final analysis. 50 patients had total villous atrophy and 20 had various grades of partial villous atrophy on histology. Mean age at presentation was 53 years, and M: F ratio was 1:3. 27% patients had extraintestinal presentation (dermatitis herpetiformis 22%, pruritus 15%, foetal loss in 15% and osteoporosis 15%); 27% had neuropsychiatric presentations with anxiety being the commonest (56%). The classical manifestations of CD were present in only 46% patients with diarrhoea in 19% and abdominal pain in 25%. 51% of CD patients had anaemia according to the WHO definition, but it did not discriminate between the groups. Overall EmA positivity was 74%. 3 patients were diagnosed as CD on the basis of a HLA DQ2/DQ8 association despite equivocal EmA and histology.

Conclusion: The clinical epidemiology of CD in the North East of England is changing similar to that reported from the US. Atypical presentations are commoner than the classical presentation and there is a need to recognise the importance of coeliac screening in patients with osteoporosis and neuropsychiatric symptoms.

1. Proceedings of the NIH Consensus Conference on Coeliac Disease, June 28–30, 2004. *Gastroenterology* 2005;(Suppl 1):128.
2. **van Heel DA**, West J. Recent advances in coeliac disease. *Gut* 2006;**55**:1037–46.

436 ''HIDDEN'' LACTOSE IN DRUGS MAY CONTRIBUTE TO SYMPTOMS IN PATIENTS WITH GASTROINTESTINAL CONDITIONS AND COEXISTING LACTOSE SENSITIVITY

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Introduction: Lactose sensitivity is a common problem affecting up to 9% of the UK population. Primary adult hypolactasia (lactase non-persistence) has been shown to occur in 14.5% of patients with inflammatory bowel disease. Hypolactasia can also present with symptoms that mimic IBS. Lactose consumption above a patient's natural threshold may result in

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abdominal and systemic symptoms. Lactose is used as filler in a wide range of drugs including those used to treat GI disorders.
Aims & Methods: The aim of this study was to identify and quantify ''hidden'' lactose in drugs used for the treatment of a wide range of GI disorders, to assess whether this ''hidden'' lactose contributes significantly to symptoms in patients with coexisting lactose sensitivity and also to identify alternative ''lactose free'' preparations. Drugs used for the treatment of a wide range of GI disorders were identified via the British National Formulary and by reference to the Electronic Compendium of Medicine. Data were also obtained from Medicines Information, Great Ormond Street Hospital. A selection of drugs was analysed for lactose content by high performance liquid chromatography (HPLC).
Results: Drugs were identified that contained lactose. Some of these are Asacol MR, Colofac, Merbentyl, Deltacortil, Immodium, Codeine, Dulcolax and others. Those that were lactose free were Pentasa, Pantoprazole, Colpermin, Entocort CR and others. The range of lactose added to drugs used in the treatment of a wide range of GI disorders ranged from 3 mg Ranitic (Ranitidine) 150 mg tablet – 600 mg in Budenofalk (Budesonide) 3 mg tablet. The quantity of ''hidden'' lactose consumed by recommended guidelines ranged from 3 mg to over 2 g daily. We identified alternative, lactose-free preparations for all indications.
Conclusion: Our results clearly demonstrate that lactose is present in drugs prescribed for a wide range of GI disorders. Furthermore patients may take over 2 g/day of ''hidden'' lactose (equivalent to 42 ml of milk). The quantity of lactose present in drugs is not often listed on the label or manufacturer's leaflet. Many patients are on multiple drugs. It has been reported that most individuals tolerate 11.8 g of lactose per day (250 ml of milk). Our data show that a significant consumption of ''hidden'' lactose occurs with drug treatment in a wide range of GI disorders. The identification of patient's lactase non-persistence status and a dietary assessment of lactose consumed, including that from drug treatment, should now be undertaken. Lactose-free alternative drugs should be prescribed where appropriate.

437 MONOCLONAL ANTIBODIES RAISED AGAINST HIGH MOLECULAR WEIGHT GLUTENINS

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Introduction: High molecular weight glutenin subunits (HMW-GS) are coeliac-toxic in vivo, but are not assesed by commercially avaliable methods of gluten analysis. Instead the formula gliadin ×2 is used for total gluten content, which has been shown not to be justified.
Aims & Methods: We wished to developed reagents for use in assays for measurement of these proteins. Ideally such assays would comprise a single cocktail of anti-gliadin and anti-glutenin antibodies with appropriate standards. Recombinant 1Dx5 and 1Dy10, which are the principle dough forming HMW-GS, were isolated from transgenic yeast and maize and partially hydrolysed by pepsin and typsin. European standard gliadin was aquired. Murine monoclonal antibodies were raised against subunit 1Dy10 and characterised by ELISA and SDS-PAGE.
Results: Monoclonals raised against 1Dy10 cross-reacted fully with 1Dx5 subunits. ELISA revealed considerable cross-reactivity of the antibodies with European Standard Gliadin. Gel electrophoresis of the latter, followed by immunoblotting demonstrated that the cross-reaction was due to the presence of HMW-GS in the gliadin standard, but there was no cross-reaction with gliadin bands.
Conclusion: A single HMW-GS monoclonal antibody is sufficient to measure both of the important dough forming subunits 1Dy10 and 1Dx5. Such antibodies could be used in a cocktail ELISA system with combined gliadin and glutenin standards for which appropriate reference material will be required.

1. **Dewar DH**, Amato M, Ellis HJ, *et al*. Immunogenicity and in vivo toxicity of HMW glutenins in coeliac disease. *Eur J Gastroenterol Hepatol* 2006;**18**:483–91.

438 DOES TISSUE TRANSGLUTAMINASE SENSITIVITY INCREASE WITH THE SEVERITY OF VILLOUS ATROPHY IN COELIAC DISEASE?

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Introduction: Immunoglobulin (Ig)A anti-tissue transglutaminase antibody (TTG) has been shown to be both sensitive and specific for detecting cases of coeliac disease (CD). Some centres now recommend TTG as the first serological test when considering the diagnosis of CD. Previous investigators have shown that the sensitivity of endomysial antibody (EMA) is dependent on the degree of villous atrophy. We aimed to determine if TTG can predict the severity of villous atrophy in CD.
Aims & Methods: Consecutive adult patients diagnosed with CD were recruited prospectively over a 26 month period (January 2004 to April 2006). All patients had 4 biopsies taken from the second part of the duodenum. A blood sample was obtained from each patient and analysed for IgA-TTG, IgA-EMA and total IgA. The total IgA titre was measured on a Behring BN2 nephelometer. Human IgA-TTG antibodies were assayed on ELISA kits from Aesku with a titre of >15 U/ml being taken as positive. EMA were detected by immunofluorescence on primate oesophagus sections from Binding Site. Villous atrophy was graded according to the modified Marsh criteria: Marsh 3a: partial villous atrophy, 3b: subtotal villous atrophy and 3c: total villous atrophy. Statistical analysis was performed using the unpaired *t* test with a $p<0.05$ taken as significant.
Results: A total of 77 patients were diagnosed with new CD: 52 (68%) female, mean age 47.6, range 17–85. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for TTG was 90.9%, 90.1%, 28.6%, 99.6% respectively. There were 7 patients with CD who had a TTG value of <16 U/ml (TTG negative), of these, 4 had marsh 3a lesions and 3 had marsh 3b lesions. There were 10 patients with CD who were EMA negative, of these, 6 had marsh 3a lesions and 4 had marsh 3b lesions. The TTG titres found in CD patients with Marsh grades 3a and b were significantly lower than those with Marsh grade 3c: $p=0.016$, see table.
Conclusion: Given the lesser degree of intestinal damage associated with a lower TTG titre, multiple duodenal biopsies should be considered at endoscopy to avoid false negative biopsies.

439 MALIGNANCY AND MORTALITY IN PEOPLE WITH DERMATITIS HERPETIFORMIS: A POPULATION-BASED COHORT STUDY

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Introduction: Dermatitis herpetiformis forms part of the same spectrum of gluten-sensitive disease as coeliac disease. People with coeliac disease have modest increases in overall risk of mortality and malignancy though precise estimates of the mortality and malignancy risk experienced by people with dermatitis herpetiformis in comparison to the general population and to people with coeliac disease is not known. We performed a population-based cohort study by using the General Practice Research database to quantify the risks of mortality and malignancy in people with dermatitis herpetiformis compared with the general population.
Aims & Methods: We identified 641 people with dermatitis herpetiformis and 3205 age- and sex-matched control subjects. We used Cox regression to estimate the hazard ratios for malignancy and mortality in the dermatitis herpetiformis cohort compared with the general population.
Results: The mean age at diagnosis was 47 years and 535 were women. The overall hazard ratio for any malignancy was 1.19 (95% CI 0.85 to

Abstract 438 TTG titres found in CD patients with different Marsh grade duodenal biopsies

Marsh grade severity	3a	3b	3c
Number of patients	29	30	18
TTG value average (range) U/ml	176 (0–300)	151 (5–300)	264 (55–300)
Sensitivity of TTG (positive>15 U/ml)	86.2% (25/29)	90% (27/30)	100% (18/18)
Number of EMA positive patients	23	26	18
Sensitivity of EMA	79%	87%	100%

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1.67); for mortality was 0.98 (0.71 to 1.34); for gastrointestinal cancer was 1.72 (0.68 to 4.34); for breast cancer 0.64 (0.23 to 1.82); for lung cancer 0.97 (0.28 to 3.21); and for lymphoproliferative disease 1.03 (0.23 to 4.69).
Conclusion: There is no excess risk of mortality nor malignancy experienced by people with dermatitis herpetiformis.

440 FRACTURE RISK IN PEOPLE WITH DERMATITIS HERPETIFORMIS: A POPULATION-BASED COHORT STUDY

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Introduction: Dermatitis herpetiformis forms part of the same spectrum of gluten-sensitive disease as coeliac disease. People with coeliac disease are a modest increased risk of fracture though precise estimates of the fracture risk experienced by people with dermatitis herpetiformis in comparison to the general population and to people with coeliac disease is not known. We performed a population-based cohort study by using the General Practice Research database to quantify the fracture risk in people with dermatitis herpetiformis compared with the general population.
Aims & Methods: We identified 641 people with dermatitis herpetiformis and 3205 age- and sex-matched control subjects. We used Cox regression to estimate the hazard ratios for any fracture, hip fracture, and ulna or radius fracture in the dermatitis herpetiformis cohort compared with the general population.
Results: The mean age at diagnosis was 47 years and 535 were women. The overall hazard ratio for any fracture was 1.10 (95% CI 0.80 to 1.50); for hip fracture was 1.35 (95% CI 0.55 to 3.31); and for ulna or radius fracture was 1.79 (95% CI 0.84 to 3.81).
Conclusion: There is no excess fracture risk experienced by people with dermatitis herpetiformis. Screening and surveillance of people with dermatitis herpetiformis for decreased bone mineral density is not warranted.

441 CAPSULE ENDOSCOPY FOR OBSCURE GASTROINTESTINAL BLEEDING: ANALYSIS OF FACTORS FOR A POSITIVE YIELD

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Introduction: Capsule endoscopy (CE) is now an established investigation in patients with obscure gastrointestinal bleeding (OGB). In carefully selected patients (who have had negative standard tests) the diagnostic yield has been reported to range from 45–80%. However, there is uncertainty as to which clinical factors predict the ability of CE to detect pathology.
Aims & Methods: We evaluated which clinical factors were predictive of a higher diagnostic yield in patients who underwent CE for OGB. OGB patients referred for CE in routine practice over 52 months were studied (n = 159). Case notes were reviewed for type of OGB (occult/overt), age, sex, comorbidity, use of anticoagulants, non-steroidal anti-inflammatory drugs (NSAIDs), transfusion dependence, subsequent CE diagnosis and follow-up data.
Results: There were 88 females, mean age 42 years. The average follow-up was 17 months. The overall positive yield was 53%. The diagnostic yield was notably higher in overt bleeders: 66% when compared to the occult group 46% ($p<0.025$). The commonest finding in both groups was angiodysplasia (AD, n = 35). Other diagnosis obtained included gastric antral vascular ectasia (GAVE) (6), GAVE & AD (6), tumour (9), polyps (2), Crohn's disease (3), NSAIDs ulceration (3), peptic ulcer disease (3), varices (2), small bowel ulcers (4), dieulafoy (1) and miscellaneous (11). Significant independent factors predictive of a positive yield by univariate analysis included age >55 ($p<0.001$, OR 3.3, 95% CI 1.7 to 6.4), type of OGB ($p<0.025$, OR 2.2, 95% CI 1.1 to 4.3), presence of comorbidity (cardiac/cirrhosis/haematological/carcinoma) ($p<0.001$, OR 18.7, 95% CI 4.3 to 81.2) and requirement for regular blood transfusions ($p<0.025$). On multivariate analysis transfusion dependence ($p = 0.005$) and comorbidity ($p<0.0001$) remained significant. Management was altered in 42% and 23% in the overt bleeders and anaemia group respectively ($p<0.025$). This was in the form of endoscopic treatment of angioectasia: heater probe (16), variceal glueing (1), polypectomy (n = 1), surgery (12) and drug therapy (11: helicobacter eradication/proton pump inhibitors (2), thalidomide (n = 3), beta blockers (1), azathioprine (1)/withdrawal of NSAIDs (4)) and initiation of a gluten-free diet (1).
Conclusion: For patients with OGB who undergo CE, transfusion dependence and co-morbidity are significant predictors of a positive diagnostic yield. Further CE studies are required to validate these criteria, ensuring efficient use of the CE service.

442 ANAEMIA AND OSTEOPOROSIS IN ADULT COELIAC DISEASE

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Introduction: Anaemia is now the commonest presenting feature of coeliac disease in primary care[1] but wide variation is reported in the prevalence of osteoporosis associated with coeliac disease in primary and secondary care studies. 47% of adults with coeliac disease in secondary care were found to have osteoporosis[2] compared to 12% of cases in a community based study of endomysial antibody positive subjects.[3] The aims of this study were to compare the prevalence of osteoporosis in coeliac disease with anaemic status and with symptoms at diagnosis in a large secondary care cohort of patients.
Aims & Methods: 144 adult cases of biopsy proven coeliac disease were assessed according to symptoms at presentation, age at diagnosis, red cell indices and iron studies, Marsh grade of small bowel histology and bone densitometry results. Anaemia was diagnosed in males Hb <13 g/dl and females Hb <11 g/dl; serum ferritin levels <15 ug/l were considered compatible with iron deficiency. Bone density was analysed according to nationally accepted Z scores with osteopenia diagnosed with Z score 1 to 2.5 and osteoporosis <2.5 below age-matched controls.
Results: Seventy eight patients were anaemic at diagnosis (54%) and 66 non-anaemic (46%) cases. Peak age of presentation was 60–69 years with 42% of new cases of coeliac disease diagnosed older than 60 years. Frequencies of principle presenting features were: diarrhoea (36%), anaemia (33%), irritable bowel syndrome (8%) and weight loss (6%). Osteopenia was present in 38% and osteoporosis in 47% of patients with only 15% showing normal bone densitometry. Abnormal bone densitometry was found in 96% of patients older than 50 years but also in 43% of patients younger than 50 years ($p<0.005$). No significant difference in bone densitometry was found between anaemic and non-anaemic groups but patients presenting with diarrhoea or steatorrhoea showed a significantly higher prevalence of osteopenia and osteoporosis compared to other patient groups ($p<0.05$).
Conclusion: Diarrhoea and anaemia are the commonest presenting feature of coeliac disease in secondary care but patients presenting with diarrhoea (classical cases) have a significantly higher prevalence of osteopenia and osteoporosis compared to cases presenting with iron deficiency anaemia (subclinical cases). Varying length of small bowel involvement is recognised in coeliac disease and patients presenting with diarrhoea may have a longer length of small bowel involvement with greater intestinal calcium malabsorption. Abnormal bone densitometry is present in the majority of older coeliac patients in secondary care but should be considered in patients of any age presenting with diarrhoea.

1. **Hin H**, *et al. BMJ* 1999;**318**:164–7.
2. **MacFarlane XA**, *et al. Gut* 1995;**36**:710–14.
3. **West J**, *et al. Gut* 2003;**52**:960–5.

443 PERSISTENT DIARRHOEA DUE TO BACTERIAL OVERGROWTH IN PATIENTS WITH MIDGUT CARCINOID TUMOURS

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Introduction: Midgut carcinoid tumours may present clinically either with ''carcinoid syndrome'' or with symptoms related to peritumoural mesenteric fibrosis. The latter may predispose to small intestinal bacterial overgrowth, which results in increased diarrhoea and malabsorption.
Aims & Methods: To evaluate whether persistent and non-responding to treatment diarrhoea, in a series of patients with midgut carcinoid tumours was associated with bacterial overgrowth. 15 with metastatic midgut carcinoid tumours and mesenteric fibrosis (mean age 61.1 years, range 23–78 years) were included in our study. All had persistent diarrhoea (more than 6 times per day) despite treatment with high doses of long-acting somatostatin analogues, antimotility agents, or pancreatic enzymes supplements. They underwent the non-invasive, non-radioactive ''Hydrogen Breath Test''. None of them had any antibiotics for at least one month prior to the test.

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Results: In five out of 15 patients (33%), the test was positive. Four out of 5 had had small bowel resection to remove the primary lesion, while 2 out of 5 had several episodes of subacute bowel obstruction, treated conservatively. Three of these patients had reported weight loss (despite no tumour progression) and had low serum albumin levels, while in one of them serum B12 levels were also low. Four out of 10 of those with negative breath test had had small bowel surgery, 1 had episodes of subacute bowel obstruction, while none of them reported weight loss, or biochemical evidence of malabsorption. All patients with positive test received oral ciprofloxacin 500 mg bd for 7 days every month since the date of test, resulting in significant control of their symptoms (decrease of diarrhea, cessation of malabsorption). No antibiotic-related adverse effects were reported. Mean follow-up of these patients is 6.9 months (range 3–9.5 months).

Conclusion: (1) Small intestinal bacterial overgrowth may be a cause of diarrhoea resistant to treatment in patients with midgut carcinoid tumours and mesenteric fibrosis. (2) Hydrogen breath test is non-invasive and helpful test for its diagnosis. (3) Short course of oral ciprofloxacin seems effective treatment for this situation.

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HOMA of the relationships between IS and typical correlates, such as obesity, insulin secretion and glucose tolerance.[2] Under these conditions, the mathematical modelling approach based on 24 h circadian rhythm of glucose and insulin suggested by Nobili has a different meaning to "stressing" glucose homeostasis during an oral glucose test. This test is more physiological and reflects the effects of insulin throughout the day. Also, measuring insulin secretion would add importantly to the understanding of the process, but the test remains extremely cumbersome and unsuitable for clinical studies.

The differential impact of basal and post-load insulin resistance on liver fibrosis might reflect the intrinsic difference in the physiological meaning between HOMA-R and OGIS, although the complex interplay between insulin resistance and liver damage is still unknown. In chronic hepatitis C (CHC), insulin resistance may be attributed both to host factors and to a possible interference of hepatitis C virus with intrahepatic insulin signalling. In genotype-1 CHC, we and others[3] failed to identify an independent association of HOMA-R with liver fibrosis. On the contrary, this association was found in genotype-3 CHC patients, with rare or no components of the metabolic syndrome, where the low degree of insulin resistance might reflect a virus-related hepatic insulin resistance, quantitatively measured by HOMA-R.

In the analysis, we introduced both HOMA-R and OGIS into the model without evidence of collinearity. This is further evidence suggesting that the two surrogate indices, although statistically correlated with each other and both with the clamp, clearly measure two different processes.

Insulin sensitivity has a gaussian distribution in the general population. As such, for each method a population reference is needed, derived from subjects with similar characteristics (ethnicity, BMI, etc). Although investigators commonly use cut-offs published in large studies, none of them can be taken for granted. The cut-offs of HOMA-R and OGIS we used are derived from our personal experience (HOMA-R) or from the large experience of the group that described OGIS. We apologise for a mistake in the reference of the HOMA-R cut-off of 2.7. The correct reference study for HOMA-R in our setting was reported elsewhere.[4]

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REFERENCES

1. **Pacini G,** Mari A. Methods for clinical assessment of insulin sensitivity and beta-cell function. *Best Pract Res Clin Endocrinol Metab* 2003;**17**:305–22.
2. **Mari A,** Pacini G, Brazzale AR, *et al*. Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. *Diabetologia* 2005;**48**:748–51.
3. **Camma C,** Bruno S, Di Marco V, *et al*. Insulin resistance is associated with steatosis in nondiabetic patients with genotype 1 chronic hepatitis C. *Hepatology* 2006;**43**:64–71.
4. **Marchesini G,** Pagotto U, Bugianesi E, *et al*. Low ghrelin concentrations in non-alcoholic fatty liver disease are related to insulin resistance. *J Clin Endocrinol Metab* 2003;**88**:5674–9.

Is ileocaecal Crohn's disease L1 or L3 according to the Montreal classification?

In a recent issue of the journal, Satsangi *et al* reviewed the key issues that have emerged from discussions of the Montreal Working Party (*Gut* 2006;**55**:749–53). One problem that I have encountered in my clinical practice is to define ileocaecal Crohn's disease according to the Montreal classification. In both articles on the Montreal classification, terminal ileum involvement is L1, colonic disease is L2, and ileocolonic involvement is L3.[1] Should we consider ileocaecal Crohn's disease as L1 or L3 according to the Montreal classification?

I decided to interview 27 French and international experts in the field of inflammatory bowel disease via email asking them "What is ileocaecal Crohn's disease according to the Montreal classification?" Fifteen out of 27 (55.6%) colleagues classified ileocaecal Crohn's disease as L1, while the 12 remaining experts (44.4%) responded L3.

What can explain such discrepancy between the experts? Most experts who answered L1 argued that the caecum is the end of the small intestine and that caecal involvement is not sufficient to be considered as colonic disease, while those who classified ileocaecal Crohn's disease as L3 explained that the caecum is an integral part of the colon.

I think we forget that the Montreal classification is based on the same definitions as the original Vienna classification, as it is a revised version of the Vienna classification.[1 2] Indeed, it is clearly stated in the original paper on the Vienna classification that the term "terminal ileum" covers disease limited to the lower third of the small bowel with or without spill-over into the caecum.[2] In this regard, the term "terminal ileum" used in both articles on the Montreal classification may be misleading.[1]

Recently, Offerlbauer-Ernst *et al* confirmed that discrepancies in the Vienna classification existed mainly for L1 and L3, and concluded that the presence of coexisting colonic lesions may lead to disagreement between observers.[3] The authors proposed an alternative, segment-wise description of Crohn's disease as ileal, right colonic, transverse colonic, left colonic or rectal disease.[3] This might result in an improvement of L1 and L3 interobserver agreement to 85%.[3]

In conclusion, because it is well established that diagnostic misclassification reduces the ability to detect linkage in inflammatory bowel disease genetic studies,[4] we should keep in mind that, similarly to the Vienna classification, L1 corresponds to pure ileal or ileocaecal Crohn's disease according to the Montreal classification.

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REFERENCES

1. **Silverberg MS,** Satsangi J, Ahmad T, *et al*. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. *Can J Gastroenterol* 2005;**19**(Suppl A):5–36.
2. **Gasche C,** Scholmerich J, Brynskov J, *et al*. A simple classification of Crohn's disease: report of the Working Party for the World Congresses of Gastroenterology, Vienna 1998. *Inflamm Bowel Dis* 2000;**6**:8–15.
3. **Oefferlbauer-Ernst A,** Miehsler W, Eckmullner O, *et al*. Impact of interobserver disagreement on phenotype–genotype associations in Crohn's disease. *Inflamm Bowel Dis* 2007;**13**:156–63.
4. **Silverberg MS,** Daly MJ, Moskovitz DN, *et al*. Diagnostic misclassification reduces the ability to detect linkage in inflammatory bowel disease genetic studies. *Gut* 2001;**49**:773–6.

CORRECTIONS

Osonnaya C, Osonnaya K, Abdi M, *et al*. Effect of Helicobacter pylori eradication on dyspepsia, quality of life and utilisation of health care resources in the Eastern England Helicobacter Pylori project: randomised control trial (*Gut* 2007;**56**(Suppl II):A16.

It has come to the editor's notice that the wording of this abstract closely resembles that of an article published in the *BMJ* (Lane J A, Murray L J, Noble S, *et al*. Impact of Helicobacter pylori eradication on dyspepsia, health resource use, and quality of life in the Bristol Helicobacter project: randomised controlled trial. *BMJ* 2006;**332**:199–204). We therefore wish to withdraw the abstract by Osonnaya et al.

We also wish to withdraw the following abstracts, which closely resemble previously published articles by other authors.

Osonnaya C, Osonnaya K, Swain P. Investigating the link between mast cell density and severity of Helicobacter pylori gastritis in the corpus and antrum. *Gut* 2005;**54(**Suppl II):A85. This abstract withdrawn at the request of Professor Swain.

Osonnaya C, Swain P C, Sanderson I R. Mast cell density in the antrum and corpus: increase in Helicobacter pylori gastritis. *Gut* 2003:**52(**Suppl V1):A153. This abstract withdrawn at the request of Professor Sanderson.

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P Abdulhannan, J W L Puntis. Iron deficiency anaemia and perianastomotic ulceration as a late complication of ileal resection in infancy (*Gut* 2007;**56**:1478–9). The first author's name for this letter was published incorrectly and should be Peshang Abdulhannan. Furthermore, the letter should have read "We were interested…" not "I was interested …".

Committee on Publication Ethics (COPE) – Seminar 2008

9.30am–4.30pm Friday 4 April 2008, Woburn House, London, UK

This year's seminar will focus on three key topics: (1) How does patient privacy legislation affect an editor's ability to publish? (2) What is publication? — the changing definitions of publication. (3) COPE's new Best Practice Guidelines. There will also be a short demonstration of an anti-plagiarism system as it is working in a publishing house.

Invited speakers will discuss legislation on privacy and data protection that editors need to be aware of; how editors should respond to more and more data being available online prior to formal peer-reviewed publication; and what happens to a publication after it appears in print.

The newly designed COPE website will be demonstrated, and there will be interactive workshops on common ethical and editorial dilemmas.

Editors, authors and all those interested in improving the standard of publication ethics are welcome.

The seminar will include invited talks:

- A Pandora's box of tissues—legislation in relation to tissues and cells
- The promise and perils of patient privacy
- Pre-publication or duplicate publication? How to decide
- What really happens to a publication after it appears in print
- Screening for plagiarism: the CrossCheck initiative

In addition:

- Discussion of COPE's new Best Practice Guidelines with experiences from journals who have piloted the audit
- COPE's new website unveiled
- Interactive workshops on the key topics of the seminar.
- Opportunities to network with other editors and share your experiences and challenges

The seminar is free for COPE members and £50.00 for non-members. Numbers are limited and early booking is advisable. For registration or more information please contact the COPE Administrator at cope@bmjgroup.com or call 020-7383-6602.

For more information on COPE visit www.publicationethics.org.uk/