Abstracts

Surgical Section in association with the Association of Coloproctology (ACPGBI) and IBD Section joint symposium

001 CLINICAL AND MOLECULAR CHARACTERISTICS OF ISOLATED COLONIC CROHN’S DISEASE


Background: Clinical, serological, and molecular data support the existence of discrete subsets of Crohn’s disease (CD) defined by location of disease. Little is known about the epidemiology and natural history of isolated CD of the colon (Montreal Classification L2) because most studies have not accurately distinguished L2 from L3 disease (ileo-colonic).

Aims: (1) To describe the clinical features and natural history of isolated colonic CD in a rigorously characterised patient cohort. (2) To confirm the association with HLA-DRB1*0103, reported in smaller cohorts, and to investigate its role in predicting disease course and need for surgery.

Methods: Patients with L2 disease were identified from a database of 1318 CD patients. Only patients with a normal small bowel enema (70%), ileoscopy alone (30%), or both (20%) were included. No patients had capsule enteroscopy. HLA typing was performed using PCR-SSP.

Results: 136 (10.3%) patients were classified with L2 disease after a median follow up of 10.8 years (range 1.4–39.8). The mean age at diagnosis was 37.0 years. L2 disease was more common in women (74.3% vs 61.0%; p = 0.001; RR = 1.7) and in never smokers (52.2% v 41.3%; p = 0.007; RR = 1.5). 29.4% and 14.0% reported a family history (1st or 2nd degree) of CD and UC respectively. Strictureing colonic disease was noted in 10% of patients. 12% of the entire cohort received ≥1 Infliximab infusion and 19% underwent colonic resection for severe disease (cumulative risk at 2 years, 10.6%; 5 years, 17.1%; 10 years, 32.8%). We confirmed the association with DRB1*0103 (14.7% cases v 2.7% controls; p = 5.5 x 10^-9; RR = 3.2) and report the novel association of this allele with time to first surgical event (Log Rank p = 0.002) and time to first “severity event” (resection/diversion ileostomy/Infliximab) (p = 0.001).

Conclusions: This study reports the clinical manifestations of isolated colonic CD. We confirm the association with HLA-DRB1*0103 and further demonstrate that this allele may predict disease course.

002 ANALYSIS OF CCL20 VARIANTS IN IBD PROVIDES FURTHER EVIDENCE FOR GENETIC HETEROGENEITY IN DISEASE SUSCEPTIBILITY


Introduction: Recent data have suggested that variants of the CCL20 gene are associated with susceptibility to ulcerative colitis (UC). 1 In a South Korean population, the 1706G→A polymorphism in the CCL20 promoter was strongly associated with susceptibility to UC (p = 0.0001). 1 These data have yet to be replicated in other populations. The CCL20 gene is located on chromosome 2q36.3 in a short haplotype block containing no other genes (see http://www.hapmap.org). The protein is a key immunological signal, fundamental to the pathogenesis of inflammatory bowel disease (IBD). We have assessed the contribution of the 1706G→A polymorphism in determining susceptibility and disease phenotype in UC and Crohn’s disease (CD).

Methods: 523 UC, 442 CD, and 351 healthy controls (HC) were studied. The Scottish IBD population was 100% white with a mean age of diagnosis of 28.1 years. Genotyping for the 1706G→A variant was carried out using the Taqman system for allelic discrimination.

Results: In all Scottish IBD cases there was a non-significant increase in the allelic frequency and carriage rate of the variant A allele compared with HC (see table). Genotype analysis reveals borderline increased homozygosity in Scottish IBD compared with HC (p = 0.049, RR 1.37).

Conclusions: The weak effect in the Scottish population contrasts strongly with the strong effect in the South Korean population. Heterogeneity between Eastern and Northern European populations is the most plausible explanation, paralleling the experience of NOD2/CARD15 in CD. 2 Direct sequencing has been performed and the contribution of further SNPs is currently under study in both the Scottish population and in complementary Scandinavian and Japanese studies.


003 INTENSIVE GRANULOCYTE AND MONOCYTE APHERESIS Versus INTRAVENOUS PREDNISOLONE IN PATIENTS WITH SEVERE ULCERATIVE COLITIS: A MULTICENTRE RANDOMISED CONTROLLED STUDY

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Background: Recently several uncontrolled studies have reported on the efficacy of adsorptive depletion of peripheral blood granulocytes and monocytes/macrophages (GMA) in patients with moderate or severe ulcerative colitis (UC). This study compared the efficacy and safety of intensive GMA with intensive intravenous (IV) prednisolone (PSL) in patients with severe UC.

Methods: Sixty six patients with clinical activity index CAI 10–18 were randomly assigned to intensive GMA with the Adacolumn, at two sessions/week in the first 3 weeks and then one session/week for up to 10 sessions (n = 33) or IV PSL, 40–60 mg/day for 5–10 days. Up to 65% of granulocytes and monocytes/macrophages and a small fraction of lymphocytes (FcγR and complement receptors bearing leucocytes) adhere to the column leucocytopheresis carriers. No patient received immunomodulators. Efficacy was assessed at weeks 2, 6, 12.

Results: Four patients in the PSL group withdrew within the first 5 days, while all 33 patients in the GMA group completed their treatment course. At weeks 2, 6, and 12, the remission (CAI = or <4) rates (%) in the GMA group were 9.1, 54.5, 75.8, respectively. The corresponding values in the PSL group were 21.2, 45.5, and 39.4. In the GMA group, flushing and light-headedness were observed in four patients versus typical steroid side effects in 43% of the PSL group.

Conclusions: In this study, GMA appeared to be safe and induce sustainable remission in the majority of the treated patients compared with PSL. The results support the view that granulocytes and monocytes/macrophages, which in patients with UC are elevated with activation behaviour and increased survival time contribute to the exacerbation and perpetuation of UC.

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[004] FACTORS ASSOCIATED WITH EARLY MORTALITY IN DECOMPENSATED ALCOHOLIC LIVER DISEASE: THE EFFECT OF CORTICOSTEROIDS

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Background: Determinants of mortality in severe alcoholic liver disease (ALD) are incompletely characterised and the benefits of corticosteroids remain uncertain.

Aim: Assessment of factors associated with short term survival in patients with first presentation of decompensated ALD (defined as Child grade B or C).

Methods: Retrospective analysis of 227 patients (150 men, median age 50 (range 28-77) years) presenting consecutively between 1/4/98 and 31/3/05. Townsend and Jarman indices of social deprivation derived from postcodes in the 155 Sheffield residents.

Results: Median of initial hospital stay was 14 (range 0-93) days, during which 37 patients (16%) died. Overall survival 28 and 84 days after admission was 89% and 78%, respectively. In 92 patients with Maddrey Discriminant Function >32 on day 1 (admission) or day 7, 28 day survival was higher in patients receiving corticosteroids (n=27) than in those (n=65) who did not. (89 (SD 6%) v 69 (SD 6%)). After 84 days these differences were not significant (70 (SD 9%) v 57 (SD 7%)). Using Cox regression analysis, MELD, Glasgow scores and Maddrey scores on day 1 were all found to be highly predictive of 28 and 84 day survival (p = 0.00-0.01).

Conclusions: Corticosteroid treatment was not a significant covariate with these scores. However, together with MELD and with Maddrey score, at day 7, corticosteroid treatment was an independent predictor (p<0.05) of survival at 28 days, although not at 84 days. A similar interaction with Glasgow score at day 7 was almost significant (p = 0.055).

Age, gender, presence of infection or gastrointestinal bleeding, serum sodium, serum AST, and Townsend and Jarman social deprivation scores were not uniformly significant predictors of 28 or 84 day mortality.

[005] HEPATIC INFLAMMATION INCREASES PORTAL PRESSURE THROUGH INHIBITION OF ENOS ACTIVITY: POTENTIAL MECHANISMS

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Background: Previously we have described an acute and sustained reduction of portal pressure in alcoholic hepatitis (AH) patients following anti-TNF antibody therapy. Animal data suggest inflammation can modulate eNOS activity by reducing the hepatic metabolism of an endogenous inhibitor, ADMA.

Aims: (1) To demonstrate reduced eNOS activity in AH compared to cirrhosis alone. (2) To assess hepatic tissue ADMA, and NOSTRIN (NOS trans-inhibiting protein) and Caveolin-1 (other mediators believed to translocate eNOS to intracellular sites away from interaction with its substrate, arginine) and increased Caveolin-1 (an eNOS inhibitor described in animal cirrhotic models).

Our findings suggest that hepatic inflammation in AH exacerbates portal hypertension through multiple and complex regulators of hepatic eNOS, which could serve as targets for future therapy. To address causal relationships of these eNOS regulators with inflammation requires studies in appropriate models.

[006] AN ASSESSMENT OF CARDIOVASCULAR MORBIDITY AND MORTALITY FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION

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Background: Cardiovascular (CV) disease is a major cause of morbidity and mortality in the first year post OLT and, in the limited studies performed to date, it accounts for between 30 and 70% of major clinical events.

Aims: The American College of Cardiology (ACC) has issued guidelines aimed at identifying patients at risk of cardiac disease. The aim of this study was to (1) document the prevalence of CV risk factors pretransplantation in OLT recipients and (2) the incidence of CV events following OLT. We also evaluated the use of ACC clinical predictors as a guide to identifying patients in a high risk group.

Methods: Single centre retrospective observational study. We studied 110 consecutive patients who underwent OLT from January 1998 to December 2002. Only patients with chronic liver disease who were undergoing elective OLT were included. Cardiac risk factors were identified at transplant assessment and patients were followed for 6/12 post OLT. The incidence of CV events or cardiovascular death was recorded. Predictors of CV risk as defined by ACC guidelines; two or more of the following (obesity, hypertension, smoking, elevated total cholesterol, family history of premature CV disease, age >50 years) or one of the following (previous MI or CVA, abnormal echocardiogram, evidence of an arrhythmia, LBBB, ST, or 1 wave changes on ECG). A cardiac event was defined as CV death, non-fatal myocardial infarction, hospitalisation for myocardial ischaemia or cardiac failure, stroke or transient ischaemic attack, or coronary revascularisation.

Results: Ninety three patients (56 males and 37 females) were studied in total. Seven patients were excluded (three transplanted for acute liver failure and four retransplants). Indications for transplant were ALD 22 patients (23.7%), PBC 20 patients (21.5%), HCC 12 patients (12.9%), PSC 11 patients (11.8%), cirrhotic cirrhosis 11 patients (11.8%), Hepatitis C seven patients (7.5%), CAH three patients (3.2%), and other causes such as haemochromatosis, Wilson’s disease, and Caroli’s syndrome accounted for the remaining seven patients (7.5%). The mean age at transplant was 54.8 years. 21.5% of patients were smokers, 20.4% had a diagnosis of DM and 10.8% of patients had documented hypertension. Mean BMI was 26.6 with 28% of patients classified as obese with a BMI>30. During the 6/12 follow up period seven patients died (6.3%), with two deaths attributable to CV events. Non-fatal CV events occurred in 10 patients (10.8%) (three had MI, one CCF, four documented arrhythmias, one new onset angina, and one CVA). Preoperatively 38.7% of patients were deemed to be at high risk of CV events with only 50% of total CV events occurring in this group.

Conclusions: 12.9% of our patients had a CV event within six months of OLT. The American College of Cardiology clinical predictors of CV risk did not identify the group of patients who are at increased risk of CV events post OLT, with half the patients being in the low risk group.

[007] HOW GOOD ARE WE AT MINIMISING CARDIOVASCULAR RISK FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION?

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Introduction: Cardiovascular complications are a major cause of late morbidity and mortality following liver transplantation. Treatable risk factors are possibly overlooked during long term follow up. In Newcastle, 40 orthotopic liver transplants (OLT) are undertaken every year but no formal strategy exists to minimise post-transplant cardiovascular risk.

Aim: To assess the prevalence of pre- and post-transplant risk factors for cardiovascular disease in a cohort of patients who underwent OLT between 1997 and 1999 and who were randomised to either tacrolimus or cyclosporin as part of the TMC study.

Methods: Retrospective review of patients’ hospital records.

Results: Forty three patients (18 female, 10 smokers, median age at OLT=57 years) were included over a median follow up time of 72 months.
Indication for transplant was alcoholic liver disease (17), autoimmune liver diseases (13), cryptogenic cirrhosis (4), viral hepatitis (2), fulminant liver failure (2), tumours (2), others (3). Two patients had ischaemic heart disease before transplant, eight (19%) suffered a cardiovascular event post-transplant. Six patients died, none from cardiovascular complications. 84% patients gained weight with 28% being obese (body mass index >30 kg/m²) by three years. Only 56% patients had a pretransplant cholesterol checked and of these 21% were above 5 mmol/l. 63% developed hypercholesterolaemia after transplantation but only 20% were treated by statins. Eleven patients developed new onset or a progression of diabetes. Nine (75%) of all diabetics had blood pressure recordings persistently outside national target ranges despite seven being on antihypertensive treatment and four (33%) developed cardiovascular complications. Neither weight gain nor diabetes were associated with choice of immunosuppressant. Twenty seven (63%) patients developed hypertension requiring drug therapy post OLT.

Conclusion: Liver transplant patients have a one in five chance of suffering a significant cardiovascular complication in the first six years. Several of the risk factors are undertreated or underrecognised. A formal long term programme of assessment, risk stratification, and appropriate therapy should be mandatory for all liver transplant patients in the UK.

**MANAGEMENT OF BLEEDING ECSTATIC VARICES: THE EDINBURGH EXPERIENCE**

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Introduction: Bleeding from ecstatic varices is uncommon but can be difficult to manage. We report our experience of uncontrolled bleeding from ecstatic varices managed by insertion of TIPSS.

Methods: Patients in whom TIPSS was inserted for ecstatic varices were selected from a TIPSS dedicated database.

Results: Over 14 years, 732 TIPSS have been inserted. TIPSS was inserted for bleeding ecstatic varices in 24 (11%) patients. Mean age (SD) at TIPSS insertion was 56.6 (10.6) years. Mean (SD) Child Pugh score was 7.6 (1.84); A/B/C (%): 9/59/32. Aetiology of liver disease: (alcoholic 15, cryptogenic 3, viral 2, others 4). Site of bleeding was rectal 11, stoma 7, duodenal 3, caput medusae 1, falciform ligament varix 1, and intraprostatic varix 1. TIPSS was successful in 23/24 (96%). Complete data available on 20 patients. Portal pressure gradient (PPG) fell from 19 (6.34) to 7.47 (3.84) mmHg. Covered stents were used in four patients. Embolisation of varices was performed in four at the initial procedure. TIPSS insertion was initially effective in controlling bleeding in 18 (90%) patients. In four (covered stents 2, uncovered stents 2) of these patients bleeding recurred at 13 to 202 days after TIPSS insertion. This necessitated parallel stent insertion for occluded stents in two, shunt extension for shunt insufficiency in one, thrombin injection into the stomal varix in two patients and embolisation of varices in one. These measures effectively controlled rebleeding. Eighteen were discharged from hospital without rebleeding and none had surgery. Twelve have been followed for at least 5 years and none have had further rebleeding. Our aims were twofold: (1) to prevent dose reduction of ribavirin and thus increase the SVR rates. Dose reduction is required in up to 45% of patients. Erythropoietin (Epo) treatment reduces ribavirin induced anaemia and therefore should otherwise be indicated and (2) to determine the cost of such intervention and the potential cost effectiveness.

**INVESTIGATING THE ROLE OF VASCULAR ENDOTHELIAL GROWTH FACTOR SIGNALING IN CEREBRAL ODEMA DUE TO EXPERIMENTAL ACUTE LIVER FAILURE**

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Introduction: Cerebral oedema remains a major cause of mortality in patients with acute liver failure (ALF). Vascular endothelial growth factor (VEGF) mediated increases in endothelial permeability have been shown to cause cerebral oedema around neoplasms, strokes, and in acute lead poisoning. The effects of VEGF on permeability are mediated by the VEGF receptor Flk and the Src family kinases, Src and Yes (Wei et al, J Clin Invest 2004). We examined whether these pathways might also contribute to cerebral oedema in a murine model of experimental acute liver failure. Methods: ALF was induced by ip injection of oxazomethane 100 μg/kg. Mice were either Balb/c, Tie2-GFP, VEGF-GFP transgenic, or Yes or Fyn knockout strains. Animals were actively maintained in isothermic conditions and ip dextrose used against hypoglycaemia and dehydration. Plasma VEGF levels were measured by EUSA. Size selective BBB permeability was assessed using tracer dyes of varying molecular weight. Brains were harvested for immunohistochemistry, confocal microscopy, and quantitative PCR of VEGF, Flk and flit mRNA. Histological specimens and protein lysates for immunoblotting were also prepared from livers and brains at set time points.

Results: All mice developed severe hepatic necrosis on histology. Encephalopathy progressed through to coma and death. Plasma VEGF levels were undetectable in normal mice but rose significantly after liver failure reaching a mean of 172 pg/ml (SD 45) by Grade III/IV (p<0.001), VEGF-GFP transgenic mice with advanced ALF demonstrated enhanced fluorescence of astrocytes in the cerebral cortex.

Discussion: Both cerebral and circulating levels of VEGF are significantly raised following oxazomethane induced liver failure in mice. We are currently examining the effects of genetic and pharmacological inhibitors of VEGF signalling pathways on the pathogenesis of cerebral oedema due to acute liver failure in this model.

**CAN ERYTHROPOIETIN TREATMENT DURING ANTIVIRAL DRUG TREATMENT FOR HEPATITIS C BE COST EFFECTIVE?**

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Introduction: Sustained viral response (SVR) of hepatitis C to antiviral drug treatment with ribavirin and PEG interferon is dose dependent. Dose reduction is required in up to 45% of patients. Erythropoietin (Epo) treatment reduces ribavirin induced anaemia and therefore should reduce the need for dose reduction and thus increase the SVR rates.

Aims: Our aims were twofold: (1) to prevent dose reduction of ribavirin by intervening with Epo therapy when a ribavirin dose reduction would otherwise be indicated and (2) to determine the cost of such intervention and the potential cost effectiveness.
Methods: Twenty-three patients with chronic hepatitis C (9 with genotype 1, 14 genotypes 2/3) commenced treatment with ribavirin and peg-interferon (in keeping with manufacturer's guidelines) between June 2000 and April 2004. Fifty patients with genotype 1 and 64/14 genotypes 2 and 3, all but one within eight weeks of beginning antiviral therapy. Genotype 1 patients required higher doses of Entonox, with 6/7 needing dose increases, and three needing doses in excess of 7500 IU twice weekly. Genotype 2 and 3 patients, a dose of 2000 IU twice weekly was sufficient in 4/6. Ribavirin dose was reduced due to anaemia in two (9%) patients. 2. Costs: The cost of full dose peg-interferon and ribavirin is £11,500 for genotype 1 and £5500 for genotypes 2 and 3. The mean additional cost of Entonox was £4700 for genotype 1 and £864 for genotypes 2 and 3.

Conclusions: Entonox treatment sustained 91% of patients at initial ribavirin dose. This intervention increased the drug costs by 40.9% for genotype 1 and 17.3% for genotypes 2 and 3. To achieve cost effectiveness, Epo would thus need to increase the SVR by 40.9% for genotype 1 and by 17.3% for genotypes 2 and 3. Using previous trial data this would mean increasing the SVR from 42% to 59.2% for genotype 1 and from 80% to 93.8% for genotypes 2 and 3.

03 PRIMARY SCLEROSING CHOLANGITIS: EDINBURGH LIVER TRANSPLANT EXPERIENCE 1992–2005

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic progressive cholestatic liver disease of unknown aetiology. It is characterised by inflammation, strictureting, and fibrosis of the biliary tree. 70–80% of patients have concomitant inflammatory bowel disease, usually ulcerative colitis (UC). The medium survival is 12 years from diagnosis. Liver transplantation is performed in patients with end stage liver disease and has a reported five year survival of 85%.

Methods: Fifty five patients (37M) that underwent liver transplantation for PSC were identified. Demographic data, disease characteristics, treatment interventions, and survival post-transplant were collected. Kaplan–Meier analysis, the log rank test, and multiple logistic regression was used to identify independent factors associated with disease recurrence.

Results: Sixty one liver transplants were conducted for 55 patients in the study period. The median follow up time was 4.89 years during which seven patients died. Patient and graft survival at 1, 5, and 10 years was 94%, 86%, 79% and 89%, 82%, 74% respectively. 12 patients had PSC recurrence. The five year survival rate of 86%. PSC recurrence developed in 21.8% of seven patients died. Patient and graft survival at 1, 5, and 10 years was 94%, 86%, 79% and 89%, 82%, 74% respectively. 12 patients had PSC recurrence rates at 1, 5, and 10 years were 2%, 34%, and 45% respectively. Multivariate analysis identified pretransplant therapy of cyclical antibiotics (p = 0.04) and pre-OLT UC (p = 0.03) as independent predictors of recurrence. 77% of patients had concomitant inflammatory bowel disease, usually ulcerative colitis (UC). The medium survival is 12 years from diagnosis. Liver transplantation is performed in patients with end stage liver disease and has a reported five year survival of 85%.

Conclusions: Liver transplantation sustained 91% of patients at optimal ribavirin dose. This intervention increased the drug costs by 40.9% for genotype 1 and 17.3% for genotypes 2 and 3. To achieve cost effectiveness, Epo would thus need to increase the SVR by 40.9% for genotype 1 and by 17.3% for genotypes 2 and 3. Using previous trial data this would mean increasing the SVR from 42% to 59.2% for genotype 1 and from 80% to 93.8% for genotypes 2 and 3.

04 ENTONOX IS SUPERIOR TO INTRAVENOUS SEDATION: PROOF FROM RANDOMISED CONTROLLED TRIAL

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Introduction: Intravenous sedation for colonoscopy is associated with respiratory complications, delayed recovery, and prolonged layover. We aimed to determine whether inhaled Entonox (50% nitrous oxide: 50% oxygen) provides adequate analgesia compared to midazolam/fentanyl, and its impact on psychomotor recovery and patient satisfaction.

Methods: All patients undergoing elective colonoscopy except those with history of surgical resection were included in the study. Randomisation was stratified by endoscopist grade with adequate allocation concealment. Patients completed anxiety score (HAD questionnaire), baseline letter cancellation test and pain score on visual analogue scale. Post-procedure patients completed letter cancellation tests and marked pain assessments on visual analogue scale. Secondary endpoints were completion rates, nurse and patient satisfaction, and complication rates.

Results: One hundred patients were randomised to receive Entonox (n = 50) or intravenous midazolam and fentanyl (n = 50). None of entonox patients required rescue medication. Intravenous midazolam and fentanyl patients reported significantly lesser pain (mean score 26 ± 40, p < 0.003), with similar pre-procedure anxiety scores in both groups (HAD score, p = 0.1). Though pre-colonoscopy letter cancellation tests were similar, Entonox group patients scored significantly better than the intravenous group (p = 0.001). The discharge time was significantly lesser (p = 0.004) for the entonox patients (mean 26 minutes) than intravenous group (mean 40 minutes). Patient satisfaction was higher in entonox group (median 98) than intravenous group (median 80; p = 0.001).

Conclusion: Entonox is more effective than midazolam with fentanyl in colonoscopy and has greater patient satisfaction, early psychomotor recovery, and facilitates early discharge. This has significant implications with introduction of screening programmes and non-medical colonoscopists.

05 A COMPARATIVE, RANDOMISED, COMPARISON OF ADRENALINE INJECTION IN COMBINATION WITH DETACHABLE SNARE VERSUS ADRENALINE INJECTION ALONE IN THE PREVENTION OF POST-POLYPECTOMY BLEEDING IN LARGE COLONIC POLYPS

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Background and Aims: Our study sought to compare the efficacy of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of post-polypectomy bleeding in large colonic polyps. To the best of our knowledge, this is the only prospective, randomised study in this issue.

Methods: At the time of colonoscopy patients with at least one colonic polyp ≥2 cm, were randomised to receive treatment with either injection of 1:10.000 solution of adrenaline and the position of a detachable snare followed by conventional snare polypectomy (group A) or injection of adrenaline followed by conventional snare polypectomy (group B). 152 consecutive patients were randomly assigned to one of the above groups. 77 patients (35 males, 42 females, mean age 61 years) were assigned to group A and 75 (38 males, 37 females, mean age 64 years) to group B. Early (<12 hours) and late (>12 hours–30 days) bleeding complications were assessed.

Results: Overall bleeding complications occurred in 9/152 (5.9%) of the patients. There was one case of late bleeding in group A (1.2%), and 8 in group B (10.6%) (p = 0.03). Late bleeding was more frequent than early bleeding in group B (7/15 vs 1). Multivariate stepwise logistic regression analysis revealed that among sex, age, polyp size, and the use of detachable snare, the latter was independently and significantly associated with the presence of a post-polypectomy bleeding episode (χ2 = 6.7, p < 0.01). The use of detachable snare is more likely to result in a lower possibility of a bleeding episode.

Conclusions: Our data suggest that the use of adrenaline injection in combination with detachable may significantly decrease the number of post-polypectomy bleeding episodes in patients with large colonic polyps.

06 A COMPARISON OF MIDAZOLAM PLUS FENTANYL OR PETHIDINE AS SEDATION FOR COLONOSCOPY

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Introduction: Pethidine (meperidine) and fentanyl are commonly used in sedation for colonoscopy. Fentanyl is an analogue of pethidine, but is more potent, has fewer adverse effects and requires reversal less often. It is hypothesised that these properties would allow the use of smaller doses.
of midazolam, increasing safety and reducing recovery time, without a significant impact on sedation, analgesia, and patient satisfaction.

**Methods:** Patients were randomised to receive either midazolam with pethidine (MP) or midazolam with fentanyl (MF) in a predetermined incremental dose regime. Patients indicated their anticipated level of pain before the endoscopy and their recollection of pain afterwards using a visual analogue scale (VAS). They completed a questionnaire after the endoscopy and 24 hours later. The colonoscopist and a designated endoscopy nurse, both of whom were blinded to the sedation given, also completed a VAS for their estimation of patient discomfort.

**Results:** 168 patients were analysed (97 female). Patients received a mean dose of 2.62 mg midazolam with pethidine 123.52 µg (MP; n = 83) or 4.88 mg midazolam with 53.53 µg pethidine (MP; n = 85). There were no significant differences between the two groups in terms of procedure time or completion rates. Mean recovery time was shorter with MF (12.59 ± 31.65 minutes, p < 0.00005). Whilst patients’ pre-endoscopy VAS scores did not differ between the two groups, post-endoscopy VAS scores were higher with MF (28.08 ± 15.02, p < 0.0005). Recall of consent was near total (MP 99%, MF 100%) but the MF group had greater recall of events both peri- (87% vs 71%, p < 0.01) and post-endoscopy (92% vs 72%, p < 0.001). In addition, patient recall of any pain during the procedure was higher with MF (65% vs 45%, p < 0.01). The number of patients requiring step-up doses was significantly higher for MF (25 vs 6, p < 0.001).

**Conclusion:** Using a combination of fentanyl and low dose midazolam significantly reduces the recovery time following colonoscopy when compared to pethidine and midazolam, but this effect is achieved at the expense of increased patient discomfort.

### THE BSG DRAFT SAFETY AND QUALITY INDICATORS FOR COLONOSCOPY: ARE THEY ACHIEVABLE?

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**Introduction:** The British Society of Gastroenterology has produced draft standards for safety and quality measures for endoscopy. We explored whether those for colonoscopy are achievable.

**Method:** Our endoscopy nurses performed a prospective audit of 415 consecutive colonoscopies performed from July–September 2005 inclusive. Data collected included planned extent of examination, actual extent of examination (intention to treat: ITT), endoscopist performing (trainee and supervisor where appropriate), polyp detection rate and polyp removal and retrieval rate, and complication rate. Although not part of the BSG indicators, we also recorded time to reach caecum and withdraw the colonoscope and whether the magnetic imaging system (Scopeguide) was used.

**Results:** Fourteen independent colonoscopists (performing 10–105 colonoscopies individually) and five trainees colonosced over the study period.

A trainee commencing the procedure had no effect on completion rate (89.4% without, 90% with trainee). Time to reach caecum varied from a mean 8.6 ± 21.2 minutes for (surgeons) and 13.2 ± 20.2 minutes (for medical consultants) and was related only to the presence of a trainee on endoscopy lists. Trainees lengthened intubation time from a mean 14 to 23.6 minutes and there was a slight reduction in the number of polyps detected (31.3% procedures to 28.6%). Extubation time varied from 2.3 ± 11.9 minutes (surgical) and 4.6 ± 11 minutes (medical) and was significantly correlated to polyp detection rate (r = 0.64). There was a slightly lower completion rate using the Scopeguide than procedures without (89 ± 90.8%). No perforations, significant bleeding or need for sedation reversal was recorded.

**Discussion:** The BSG safety and quality measures are achievable. There was difficulty defining an adenoma without histology. Our nurses recorded polyp detection rate. This resulted in a higher detection rate than the BSG standard but may have resulted in a lower polyp retrieval rate (experienced endoscopists may have left definite metaplastic polyps). Individuals maintaining their own records would be able to record histology and hence determine whether they were achieving BSG standards. Rapid withdrawal of the scope appeared to result in lower polyp detection rate and this information has been fed back to individual endoscopists within the unit.

### NON-MEDICAL COLONOSCOPIST ARE SAFE AND EFFECTIVE: RESULTS FROM RANDOMISED CONTROLLED TRIAL

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**Introduction:** There is an increasing demand for colonoscopy, especially with introduction of screening programmes. Though it is performed by doctors and nurses, there is an acute shortage of trained colonoscopists. Non-medical personnel were therefore trained to perform colonoscopy. The aim of this study was to prospectively compare the outcome and efficacy of non-medical colonoscopists (NMC), with both medical (MEC) and nurse colonoscopists (NC).

**Methods:** This study was drawn from a randomised controlled trial of sedation for colonoscopy. Randomisation was stratified by endoscopist grade: MEC or NMC or NC. Patients undergoing elective colonoscopy completed anxiety questionnaires, and baseline letter cancellation test and pain score on visual analogue scale (VAS). Post-procedure all patients marked assessment of pain and satisfaction on VAS and completed letter cancellation test. Secondary outcome variables included completion rates, nurse satisfaction and rate of complications.

**Results:** Out of 110 patients, 40 were randomised to MEC and NC group each and 30 patients to the NMC group. Demographic characteristics of all groups were similar. Completion rate was 95%, 97.5%, and 91% in MEC, NC, and NMC groups respectively (p = 0.3). There was no statistically significant difference between the groups in terms of median pain scores (p = 0.1), patient satisfaction (p = 0.8), nurse satisfaction (p = 0.6), and time to discharge (p = 0.08). No complications occurred.

**Conclusion:** This first prospective randomised controlled trial on non-medical colonoscopy has shown that NMC is safe, feasible, and therapeutic as well as diagnostic procedures can be performed with comparable completion rates and patient satisfaction. We conclude that this is a viable and effective option that complements and reduces clinician’s workload.

### THE USE OF HUMAN THROMBIN FOR THE TREATMENT OF GASTRIC AND ECTOPIC VARICES

N. C. McAvoy, P. C. Hayes. Scottish Liver Transplant Unit, Royal Infirmary of Edinburgh, UK

**Background:** Gastric and ectopic varices occur in approximately 20% of all patients with portal hypertension. Although less likely to bleed than oesophageal varices, they are still associated with high morbidity and mortality. Numerous therapeutic modalities exist for the treatment of non-oesophageal ectopic varices but there is no consensus on best treatment.

**Aim:** The aim of this study was to evaluate the use of human thrombin in the treatment of gastric and ectopic varices.

**Method:** Single centre retrospective observational study. We identified 37 patients who had human thrombin from the Scottish National Blood Transfusion Service from January 1999–October 2005 to treat gastric and ectopic varices. The volume of thrombin used and the incidence of complications were recorded, as was the incidence of rebleeding.

**Results:** Thirty seven patients were included (28 males; 9 females). Mean age of 53.2 years (range 18–83). Underlying diagnosis ALD 15; splenic vein thrombosis, 6; PBC, 2; cryptogenic cirrhosis, 6; CAH, 2;
be an important contributor to post-ERCP pancreatitis (PEP). Our aim was to examine if primary deep biliary cannulation with a guidewire is associated with a reduced rate of PEP as compared to contrast assisted cannulation.

**Methods:** From August 2003 to September 2005 all patients with an intact papilla referred for ERCP were eligible for inclusion. Exclusion criteria included pancreatic or ampullary cancer. Eligible patients were randomised to undergo sphincterotomy or guide wire cannulation of the CBD with either contrast injection or guide wire. The trainee attempted initially for 300 s. If unsuccessful, the consultant attempted for 300 s with the same technique. Cannulation failure with the first technique was followed by an attempt with the alternate technique in the same fashion. Cannulation time was recorded. 24 hour and 30 day complication rates were assessed by phone interview and by a 24 hour serum amylase and lipase level.

**Results:** 297 eligible cases from 1152 ERCPs were prospectively enrolled. Ten patients were excluded. Overall technical success was achieved in 280/287 cases (98.0%). 221/287 (77.0%) patients had a successful cannulation without contrast injection: 118/143 (82.5%) wire and 103/144 (71.5%) contrast (p = 0.027). Of the 7 patients who failed initial cannulation, 7/19 (36.8%) from the wire group and 23/42 (58.4%) from the contrast group were successfully cannulated with the alternate technique after crossover. Pancreatitis occurred in 17/287 (5.9%); 10 wire, 7 contrast (p = 0.047). Mean number of papilla attempts was 6.52 in the patients who developed PEP compared with 4.34 in those patients that did not develop PEP (p = 0.027).

**Conclusions:** Cannulation success rate is significantly higher with guidewire technique compared with contrast injection but the frequency of post-ERCP pancreatitis does not differ according to cannulation technique. Repeated attempts to cannulate the papilla significantly increases the risk of developing post-ERCP pancreatitis.

**022 RISK FACTORS FOR POST-ERCP COMPLICATION: RESULTS OF A LARGE SCALE PROSPECTIVE MULTICENTRE STUDY**

E. J. Williams. The Steering Committee. BSG Audit of ERCP, 3 St Andrews Place, London, UK

**Aims:** To identify risk factors for ERCP complication.

**Method:** Prospective multicentre study based in five English regions. Data were collected at the time of ERCP, and 30 days post procedure. Events were defined using consensus criteria.

**Results:** Sixty six centres participated for a mean period of 195 days. Data were collected on 5264 ERCPs. Overall 266 (5.1%) of ERCPs resulted in >1 complication: pancreatitis in 79 (1.5%); cholangitis in 59 (1.1%); haemorrhage in 46 (0.9%); perforation in 22 (0.4%); and miscellaneous in 74 (1.4%). Univariate analysis identified the following significant (p < 0.1) associations: (1) for overall complication: precut; cannulation attempt >1 and suspected sphincter of Oddi dysfunction (SOD); (2) for pancreatitis: pancreatic sphincterotomy; cannulation attempt >1; pancreatic duct injection >1; female sex; previous post ERCP pancreatitis; suspected SOD; younger age, and lower bilirubin levels; (3) for haemorrhage following sphincterotomy: use of pure cutting current for entire procedure; visible bleeding at time of procedure; lower platelet count and concurrent haemodialysis; (4) for perforation: suspected malignancy and use of precut. Variables significant in univariate analysis were selected for entry into a multiple regression. Significant factors from multiple regression were subjected to multilevel analysis to account for the hierarchical nature of the dataset (see table).

**Conclusion:** Although overall complication rates compare favourably with other large studies, certain patient factors (SOD, female sex, younger age) and procedure factors (difficult cannulation, precut) increase risk.

### Abstract 20

**Group analysed** Successful cannulation: % (n/N) Univariate p value

<table>
<thead>
<tr>
<th>Group analysed</th>
<th>Successful cannulation</th>
<th>Univariate p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First ever ERCP (all)</td>
<td>83.6% (2687/3214)</td>
<td>-</td>
</tr>
<tr>
<td>CBD-PD intended</td>
<td>71.6% (174/2343)</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Prev Billiorith</td>
<td>43.3% (133/30)</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Prev Whipples</td>
<td>20% (2/10)</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>Accessory duct attempted</td>
<td>0% (0/3)</td>
<td>p = 0.04</td>
</tr>
</tbody>
</table>

**Conclusion:** Cannulation rates achieved by individual endoscopists vary significantly, though defining operator and institutional factors that are predictive of competence remains difficult. Previous gastric surgery makes successful cannulation less likely, but these cases account <1% of the ERCPs undertaken.

### Abstract 22

<table>
<thead>
<tr>
<th>Overall complication</th>
<th>p Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complication</td>
<td>0.09</td>
<td>1.32 (0.95 to 1.83)</td>
</tr>
<tr>
<td>Precut</td>
<td>0.03</td>
<td>1.55 (1.04 to 2.32)</td>
</tr>
<tr>
<td>Suspected SOD</td>
<td>0.12</td>
<td>1.97 (0.84 to 4.64)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0.0001</td>
<td>3.14 (1.74 to 5.67)</td>
</tr>
<tr>
<td>Female sex</td>
<td>&lt; 0.001</td>
<td>2.23 (1.42 to 3.49)</td>
</tr>
<tr>
<td>Age (per 5 year decrease)</td>
<td>&lt;0.002</td>
<td>1.09 (1.03 to 1.15)</td>
</tr>
</tbody>
</table>

**Aim:** Inadvertent contrast injection of the pancreatic duct is believed to be an important contributor to post-ERCP pancreatitis (PEP). Our aim was to determine if patients with accidental contrast injection of the pancreatic duct are at increased risk of developing PEP.

**Methods:** A 6 month prospective study based in five English regions. A total of 66 trainees (56% female) working in 66 hospitals.

**Results:** In total, 2824 patients were included in the study. There were 1715 patients with accidental contrast injection of the pancreatic duct compared with 1109 with normal injection. Overall technical success was achieved in 280/287 cases (98.0%). 221/287 (77.0%) patients had a successful cannulation without contrast injection: 118/143 (82.5%) wire and 103/144 (71.5%) contrast (p = 0.027). Of the 7 patients who failed initial cannulation, 7/19 (36.8%) from the wire group and 23/42 (58.4%) from the contrast group were successfully cannulated with the alternate technique after crossover. Pancreatitis occurred in 17/287 (5.9%); 10 wire, 7 contrast (p = 0.047). Mean number of papilla attempts was 6.52 in the patients who developed PEP compared with 4.34 in those patients that did not develop PEP (p = 0.027).

**Conclusions:** Cannulation success rate is significantly higher with guidewire technique compared with contrast injection but the frequency of post-ERCP pancreatitis does not differ according to cannulation technique. Repeated attempts to cannulate the papilla significantly increases the risk of developing post-ERCP pancreatitis.
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023 SELF REPORTED EXPERIENCES OF 2059 PATIENTS UNDERGOING ERCP: RESULTS OF A MULTICENTRE SURVEY IN FIVE ENGLISH REGIONS

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Introduction and Methods: Professional bodies emphasise the importance of appropriate counselling of patients undergoing ERCP. However little has been published on patients’ experiences of this. In 2004 the BSG conducted a prospective multicentre survey of ERCP practice, which involved analysis of 5264 unselected ERCPs performed on 4561 patients. As part of this, patients were supplied with a (voluntary) questionnaire to complete one week post procedure.

Results: In total 2059/4561 patients (45%) completed a questionnaire following their first recorded procedure, at a mean of 11 days post ERCP (date of response unknown in 9.4%). Mean age of respondents was 64.6 years, and 128/2059 (6%) of respondents had undergone an urgent ERCP. ASA grade was <3 in 1829/2059 (89%); ASA unknown in n=60). A total of 1602/2059 (78%) recalled being given written information though only 986/1602 (62%) of these indicated that they received this >24 hours prior to ERCP. Although 1745/2059 (85%) were informed of complications, only 740/1745 (42%) recalled receiving this information in writing. No verbal explanation of the procedure was reported by 20/2059 (1%) of patients. The majority (1935/2059; 94%) of patients knew why their doctor had recommended an ERCP and 1815/2059 (88%) had been given a chance to ask questions before the procedure. Aftercare varied with 1076/2059 (52%) patients reporting that they were warned of specific symptoms to be aware of post ERCP and 876/2059 (43%) being given an information sheet post procedure. At the time of reply 1724/2059 (84%) of patients had had the result of their ERCP explained. The majority of patients (1968/2059; 96%) were “fairly” or “very” satisfied with the explanation they had been given, with 1908/2059 (95%) reporting the ERCP to be similar or very similar to what they had been led to expect.

Conclusion: Though based on a self-selecting sample, responses suggest that most ERCP patients are satisfactorily counselled pre- and post- ERCP.

024 IS THE TWO WEEK CANCER WAIT SAVING LIVES? A PROSPECTIVE FOLLOW UP OF PATIENTS DIAGNOSED WITH OESOPHAGEOGASTRIC AND PANCREATIC CANCER IN 2003

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Background: The NHS Cancer Plan, published by the government in September 2000 promised that patients with suspected cancer would be seen by a specialist within 14 days. It was claimed that cancer survival would be improved by immediate access to diagnostic services. Despite scepticism about this claim, few long term data are available comparing survival outcomes of patients referred through the two week wait route to those referred via traditional routes.

Aims: We examined the difference in survival between patients with oesophagogastric (OG) or pancreatic (Panc) cancer diagnosed in 2003 who were referred either via the TWR or the traditional route of referral.

Methods: Data were collected prospectively from all patients diagnosed with OG or Panc cancer from 1 January 1 to 31 December 2003.

Results: In 2003, we received 356 referrals via the TWR, of which 18 (5%) were diagnosed with an OG or Panc cancer, out of an overall total of 124 patients diagnosed. TWR patients were significantly younger at diagnosis (mean age 65 (SD 10.6) v 71 (SD 11.3), p = 0.04). Only 8/67 (12.5%) of oesophagogastric cancers: 23 squamous carcinoma; 7/31 (22.5%) of gastric cancers, and 3/26 (11.5%) of pancreatic cancers were referred via the TWR (<0.0001 for all diagnoses). Rates of surgery with curative intent were similar for oesophageal (37.5% TWR v 27%), gastric (0% TWR v 41% (p = 0.07)) and Panc cancer (33.3% TWR v 87%). Kaplan Meier survival analysis at a mean follow up of 311 days (range 0–856 days) indicates no difference in survival between the patient groups for each of oesophageal (adenocarcinoma/ squamous carcinoma), gastric, or pancreatic cancer (p=NS for all).

Conclusion: Only 5% of TWR referrals for suspected upper GI cancer turn out to have an OG or Panc cancer. Contrary to government expectations, survival of these patients is not improved despite faster diagnosis. Scarce NHS resources are not being optimally utilised in the fight to detect upper GI cancer earlier and improve overall survival.

025 DECLINING PREVALENCE OF CANCER IN TWO WEEK WAIT REFERRALS FOR SUSPECTED UPPER GASTROINTESTINAL MALIGNANCY


Background: The two week wait (TWW) referral initiative for suspected upper gastrointestinal (GI) cancer was introduced in July 2000. This standard now forms the gateway to a larger framework to diagnose and initiate treatment of cancer cases within a 62 day period. We aimed to examine the current referral pattern for suspected upper GI cancers to our institution in 2004.

Methods: We identified all TWW referrals for the year 2004 and examined their medical records. This list was correlated with a database of all cases of diagnosed upper GI cancers in our institution.

Results: In the year 2004, 321 patients (mean age 62.7 years, 57% female) were referred using the TWW route, out of which 12 cases (3.7%) were diagnosed with upper GI cancer. This constituted 16% (12/75) of all diagnosed cases of upper GI cancer in that year. In particular 288 endoscopies (11.4% of upper GI endoscopy activity) were performed of which nine (3.1%) showed cancer, 50 (17.4%) showed gastrointestinal pathology related to H pylori and 94 (32.6%) were normal.

Conclusion: The incidence of diagnosis of upper GI cancers remains similar with 65 cancers annually in 2001/02 and 75 cases in 2004.

026 NURSE LED VERSUS GP LED MANAGEMENT OF DYSPEPSIA FOLLOWING DIRECT ACCESS GASTROSCOPY

D. Chan1, S. Harris2, P. Roderick3, D. Brown3, P. Patel4. 1Southampton City PCT & PhD student Portsmouth University; 2Southampton University; 3Portsmouth University; 4Southampton General Hospital, UK

Background: Nurse Practitioners (NP) are now well established in undertaking roles traditionally carried out by doctors. However, whether NPs are as effective as doctors in managing patients is limited.

Aim: To compare the effect of systematic “nurse led” follow up to that of “GP led” follow up, after direct access gastroscopy (DAG), for dyspepsia.

Methods: We prospectively recruited dyspeptic patients undergoing DAG. Inclusion criteria were those with normal findings or grade I–II oesophagitis. They were randomised into follow up at two weeks with ‘GP led’ follow up, after direct access gastroscopy (DAG), for dyspepsia.

Results: Of 196 patients 175 were eligible (GP = 86, NP = 89) and 15 (GP = 7, NP = 8) were lost at month 6. The table below compared changes within and between the two groups at 0 and month 6.

Conclusion: This study shows that “nurse led” follow up is highly effective in improving patients’ general health and reducing dyspepsia, when compared with traditional GPs’ follow up; and there is scope for significant cost savings with reduced UHDs use.

www.gutjnl.com
Aim: The colorectal cancer screening programme is currently in its fifth year of trial at Coventry. Wallsgrave hospital is the major centre catering to this unique population of screened patients. Our primary aim was to see if there was a progressive decrease in emergency colorectal cancer admissions over this period. Our secondary aim was to see if it had any effect on Dukes staging, workload of emergency operations, and mortality of emergency cancer admissions.

Methods: A retrospective analysis of data of colorectal cancer admissions over a period of five years from 1999 to 2004 was done. The first year represented the prescreening year 1999 (PSY) which was taken as base line. Data for the next five years SY1-SY5 were recorded for the mode of admission, emergency surgery, mortality, Dukes staging with emphasis on the last three years.

Results: In PSY 29.4% of colorectal cancers were admitted as emergency. In SY3: 57, SY4: 37, SY5: 32 patients were admitted as an emergency showing a gradual decline. There was an appreciable decline in emergency colorectal cancer operations: PSY: 57, SY1:53, SY2:50, SY3:52, SY4:34, SY5:30. This had significant impact with a steep lowering of 30 day mortality (PSY 29, SY1-5: 15, 13, 5, 2, and 4 deaths), Majority cancers were poor prognosis Dukes staging: SY3-5B3%, C60%, SY4-B40%, C43%, SY5-B30%, C53%.

Conclusion: These unique data have shown that three years following the screening programme there has been a significant decline in the emergency colorectal cancer workload with an improvement in 30 day mortality. Unfortunately there has been a trend towards a worse Dukes staging. We feel the huge positive impact in such a short duration is because of increased awareness of the symptoms of colorectal cancer and change in attitude both in patients and referral pattern of general practitioners.

**Abstract 26**

<table>
<thead>
<tr>
<th></th>
<th>GP (n = 79)</th>
<th>NP (n = 81)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>21−75 (SD 47.9)</td>
<td>21−81 (SD 49.4)</td>
<td></td>
</tr>
<tr>
<td>Male:female</td>
<td>35 (44%): 44 (56%)</td>
<td>43 (53%): 38 (47%)</td>
<td></td>
</tr>
<tr>
<td>Mean score (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF12 0 month</td>
<td>671.8 (159.40)</td>
<td>623.7 (197.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF12 6 month</td>
<td>631.3 (200.23)</td>
<td>763.0 (128.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLADYS 0 month</td>
<td>10.2 (2.96)</td>
<td>10.2 (2.96)</td>
<td></td>
</tr>
<tr>
<td>GLADYS 6 month</td>
<td>7.1 (3.14)</td>
<td>4.7 (2.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall UHDC 0 month</td>
<td>54.20 (46.89)</td>
<td>61.80 (45.17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall UHDC 6 month</td>
<td>75.20 (62.98)</td>
<td>35.50 (46.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No of months of full PPI 0 month</td>
<td>1.5 (1.95)</td>
<td>1.5 (1.98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No of months of full PPI 6 month</td>
<td>2.1 (2.70)</td>
<td>0.5 (1.64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No of months of half PPI 0 month</td>
<td>1.2 (1.97)</td>
<td>1.6 (2.30)</td>
<td></td>
</tr>
<tr>
<td>No of months of half PPI 6 month</td>
<td>1.6 (2.45)</td>
<td>1.5 (2.36)</td>
<td>0.712</td>
</tr>
<tr>
<td>No of months of no treatment 0 month</td>
<td>3.3 (2.15)</td>
<td>2.9 (2.13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No of months of no treatment 6 month</td>
<td>2.4 (2.70)</td>
<td>4.0 (2.50)</td>
<td></td>
</tr>
<tr>
<td>Follow up clinic attendance</td>
<td>41</td>
<td>79</td>
<td></td>
</tr>
</tbody>
</table>

**027 PROSPECTIVE AUDIT OF COLONOSCOPY QUALITY IN KENT & MEDWAY**

A. W. Harris, K. Arais, T. Rouse. Kent Cancer Network, Preston Hall, Kent, UK

**Background:** National standards exist for quality of diagnostic colonoscopy. IOG on colorectal cancer and BSG/JAG recommend >90% caecal intubation where indicated and that >100 cases are performed per annum. It is recognised however that there is a wide variation in the quality of colonoscopy: an earlier study found caecal intubation in only 57% of cases (Bowles et al, Gut 2004;53:277). This audit is intended to provide clinical data as a benchmark to improve our service.

**Methods:** The audit was approved by the Kent Endoscopy Board & Colorectal Cancer DOG. A letter was sent to all colonoscopists explaining the process. Data were collected prospectively in all seven endoscopy units in Kent & Medway between February and September 2005. After first four months results were sent to each colonoscopist; where total colonoscopy was achieved in >79% of cases retraining or stopping colonoscopy was recommended. After first six months coded results were presented to Kent Executive and Endoscopy Boards.

**Results:** Sixty colonoscopists participated in the audit: 34 (57%) achieved total colonoscopy in >90% of cases; 12 (20%) achieved total colonoscopy in 80−89% of cases, and seven (12%) in <79% of cases. Seven (11%) stopped performing colonoscopy during the course of this study. Only 23 of 63 (36%) colonoscopists are expected to perform >100 colonoscopies each year.

**Discussion:** This eight month prospective colonoscopy quality audit found that 57% of colonoscopists in Kent & Medway met the national standard for total colonoscopy. However only 36% are performing enough to meet the benchmark of >100 procedures each year. As a consequence of this audit, seven endoscopists stopped performing colonoscopy and seven who achieve total colonoscopy in >79% of cases are considering either stopping colonoscopy or retraining. These data are of particular interest in view of the forthcoming NCCSP where more rigorous colonoscopy quality criteria will be applied.

Acknowledgement: we thank the Trust Chief Executives for permission to share these results and the Modernisation Agency for funding.

**028 DOES SCREENING DECREASE EMERGENCY ADMISSIONS FOR COLORECTAL CANCER? A FIVE YEAR EXPERIENCE**

A. Menon, S. Pedamallu, L. S. Wong. University Hospital Coventry and Warwickshire, UK

**Aims:** To validate the requirement for colonoscopy against current guidelines for patients referred to the Cumberland Infirmary. (2) To improve access times for colonoscopic examinations in those patients meeting referral criteria.

**Methods:** The case notes and pathology reports of patients awaiting a follow up colonoscopic examination as of July 2004 were reviewed to ascertain the indications. The case for further examination was then reconsidered in light of guidance given in the current BSG Guidelines. If further colonoscopy was not indicated, the GP and patient were informed by letter and offered the opportunity to discuss this change.

**Results:** 250 sets of case notes were reviewed, 79 (31.6%) were deemed appropriate to continue with surveillance as planned in accordance with BSG guidelines. Seventy one (28.4%) did not meet criteria for repeat colonoscopy; 37 (14.8%) had their follow up period extended (their previous review interval having been inappropriately short). Four patients had died, 16 (6.4%) sets of case notes were missing, and
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030 SUPPRESSION OF COLONIC EPITHELIAL APOPTOSIS AND CRYPT HYPERPLASIA OCCURS IN BAK-NULL MICE
C. A. Duckworth, D. M. Pritchard. Division of Gastroenterology, University of Liverpool, UK

Background: Apoptosis is a tightly regulated process that plays an important role in gastrointestinal homeostasis. Anti-apoptotic members of the bcl-2 family such as bcl-2 and bcl-x have previously been shown to be important regulators of small intestinal and colonic apoptosis. Although we have previously shown that small intestinal and colonic apoptosis is slightly suppressed in bak-null mice, the importance of pro-apoptotic family members is less well understood. We hypothesise that other pro-apoptotic members of the bcl-2 family play important roles in regulating intestinal apoptosis and have therefore assessed mice in which the pro-apoptotic gene bak has been deleted.

Methods: H and E sections were prepared from formalin fixed small intestine and colon from 10–12 week old female bak−/− mice and their wild-type (C57BL/6) counterparts. Apoptosis was induced by a single 10 mg/kg intraperitoneal injection of the carcinogen azoxymethane (AOM). Cell number, apoptosis, and mitosis were assessed on a cell positional basis.

Results: The colonic crypts of bak−/− mice were significantly longer (1.6 fold) than C57BL/6 and increased colonic epithelial mitosis (twofold) was observed in bak−/− mice. Significantly fewer apoptotic cells (fivefold) were observed in the colonic region of bak−/− mice relative to C57BL/6. However, no significant differences were observed in small intestinal crypt or villus cell number or small intestinal apoptosis or mitosis between bak−/− and C57BL/6 mice. Colonic crypt apoptosis was significantly reduced in bak−/− mice 8 hours following AOM. Whereas mitosis was suppressed in C57BL/6 colon following AOM, persistent mitosis was observed in bak−/− colon following this treatment. No differences were observed in small intestinal apoptosis or mitosis following AOM.

Conclusions: (1) Bak−/− mice demonstrate an altered colonic phenotype with reduced apoptosis in the table region, increased epithelial mitosis and crypt hyperplasia. (2) AOM induced apoptosis is suppressed in the colonic crypts of bak−/− mice. (3) Bak expression has little effect upon small intestinal homeostasis.

031 INHIBITION OF VEGFR REDUCES POLYP BURDEN IN THE APCMIN/+ MOUSE MODEL OF INTESTINAL CANCER
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Introduction: AZD2171, a novel, orally active inhibitor of vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase activity was used to study the effect of blocking angiogenesis in multiple intestinal neoplasia (ApcMin/+ ) mice. ApcMin/+ mice develop numerous polyps due to activation of the adenomatous polyposis coli (APC) gene, as occurs in familial adenomatous polyposis (FAP) in humans.

Methods: Two studies were performed in which 5 mg/kg/day of AZD2171 or vehicle was administered daily by oral gavage to 6 week old or to 10 week old ApcMin/+ mice for 28 days after which the number and size of polyps in the small and large intestines were scored.

Results: In the first study, AZD2171 reduced polyp number in the small bowel and colon by 46% and 62%, respectively (p<0.05). Polyp diameter was also reduced by 39% in the small bowel (p<0.001) but was unchanged in the colon. Mean tumour burden (the product of number and volume) in the small intestine was thus reduced 85% (p<0.001). In a second study small bowel polyp number was not altered by AZD2171 but diameter was reduced by 24%, in turn decreasing polyp burden by 46% (p<0.05). AZD2171 had little effect on the nuclear localisation of β-catenin but reduced the number of cells expressing VEGFR-2 from 7.4 (SD 0.6) to 4.0 (SD 0.9) per villus (p<0.02).

Conclusion: AZD2171 significantly reduced the number and size of polyps, mainly in the earlier stages of polyp formation. VEGFR-2 signalling plays a key role in the development of intestinal adenomas.

032 TRANSGENIC MOUSE MODEL FOR P-CADHERIN EXPRESSION
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Background: Epithelial (E), neuronal (N), and placent (P) cadherin isoforms belong to a highly conserved superfamily of calcium dependent cellular adhesion molecules. They are involved in the development and maintenance of normal tissue function. p-cadherin upregulation in particular has been associated with the early stages of cancer in the gastrointestinal (GI) tract. p-cadherin has also been shown to have a proliferative effect on the GI tract.

Methods: Transgenic mouse models have provided great insights into the pathological role of specific cadherins in the intestine. Our hypothesis was to test if cadherins could have a proliferative effect in the GI tract. To study the mechanism of action of p-cadherin, an in vivo model was designed consisting of transgenic animals and a fatty acid binding promoter was used to force the expression of p-cadherin within a site of the GI tract where it is not normally expressed.

Results: Test crosses were set up between F1 and transgene positive animals to generate a homozygous mouse model stable for p-cadherin expression. A total of six animals (two animals from each genotype of wild type, heterozygous, and homozygous) were examined blindly. The pathology report determined that all organs samples were normal, with no sign of Crohn’s disease and no significant difference between the wild type, heterozygous, or homozygous animals.

Conclusion: It would appear that while p-cadherin upregulation may be necessary for a metaplastic or dysplastic phenotype in man, it may alone not be sufficient. Subtle changes of p-cadherin in mucosal biology will be discussed.

033 GASTRIN AND CCK2 PROCESSING IN NEUROENDOCRINE TUMOURS AND CELL LINES: THERAPEUTIC TARGETS

Background: Neuroendocrine tumours predominantly express type 2 somatostatin receptors and this has been used for imaging and therapeutic purposes. The presence of the CCK2 (gastrin) receptor has been demonstrated in some neuroendocrine tumours (NET). Gastrin is a known growth factor for tumours including neuroendocrine tumours in particular type I and type II gastric carcinoids.

Aim: To assess CCK2/gastrin receptor expression in patients with NETs and to determine precursor progastrin (ProG) and Gly-gastrin (Gly-G) expression within these tumours. To correlate this expression with immunoblotting for CCK2 using neuroendocrine cell lines and to observe localisation of fluorochrome labelled gastrin in these cell lines.

Methods: The following patients with neuroendocrine tumours were assessed by immunohistochemistry: 24 carcinoid and 12 pancreatic neuroendocrine tumours. For histology, formalin fixed resection specimens were used. The expression of CCK2 was determined by immunohistochemistry using a specific polyclonal antibody to the CCK2 receptor. Antibodies to ProG, Gly-G, and G were also used to assess expression of gastrin forms on tumour specimens. Sections were scored by two independent observers (0 to 3: 0=no staining, and 3=strong staining). Rat and human carcinoid cell line lysates were used to identify specific CCK2 bands by western blotting.

Results: Of the carcinoid tumours significant expression (score>2) was observed in 22/24 (91%) for CCK2; 19/24 (88%) expressed ProG; 16/24 (66%) Gly-G; and 5/24 (22%) G. For pancreatic neuroendocrine
tumours 12/12 (100%) expressed CCK2; 10/12 (83%) ProG; 6/12 (50%) Gly-G; and 4/12 (33%) expressed G. Immunoreactivity to CCK2 was detected in all neuroendocrine tumours and cell lines and the expression may be associated with the autocrine/paracrine proliferative effect. Targeting gastrin peptides at the CCK2 receptor may be worth exploring for potential therapy.

Paediatric-section symposium

034 TUMOUR NECROSIS FACTOR & PROMOTOR POLYMORPHISMS INFLUENCE DISEASE PHENOTYPE AND SEVERITY IN CHILDHOOD INFLAMMATORY BOWEL DISEASE

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Background and Aims: The incidence of childhood inflammatory bowel disease (IBD) in Scotland is rising and is among the highest worldwide. Tumour necrosis factor α (TNF-α) is thought to play a pivotal role in the pathogenesis of IBD. The TNF gene lies within the HLA class III region of chromosome 6, a region identified as containing an IBD susceptibility gene in genome wide scans. Our aims were to assess the contribution of the promoter polymorphisms -1031CC, -863A/C, -857C/T, and -806C/T with regard to disease susceptibility and phenotype in childhood IBD.

Methods: 277 patients (male/female 148/129, median age (SD) 11 (3.26) years at diagnosis) [174 Crohn’s disease (CD), 77 ulcerative colitis (UC), and 26 indeterminate colitis (IC)] and their parents were enrolled. Transmission disequilibrium testing (TDT) and case control analysis with 256 controls. Detailed genotype-phenotype analysis were performed. Haploview 3.2 was used for analysis.

Results: By case control analysis, associations were found between TNF -863A and susceptibility to UC/IC (p = 0.05) and between the CACCC haplotype and IC (p = 0.01, Odds ratio (OR) 4.6, CI 1.22 to 14.97). TDT analysis was negative. Analysis showed a protective effect of the CCCC haplotype with small bowel disease and ileal disea (p = 0.003, OR 0.24, CI 0.10 to 0.59 and p = 0.003, OR 0.31, CI 0.13 to 0.77), irrespective of NOD2 carriage. A positive association was found between granulomatous disease and the CACC haplotype (p = 0.05). Negative associations were found between the TCCC haplotype and mild disease (BMI<50th centile and inflammatory disease (p<0.05)), whereas restricting disease, raised CRP, albumin<35, and granuloma formation were negatively associated with the CACC haplotype (p<0.05).

Conclusion: These variant alleles of the TNF promoter polymorphisms have a significant effect on disease location, severity, and behaviour in the Scottish early onset CD population. The negative association of TNF -1031CC with small bowel disease (p = 0.009, OR 0.02, CI 0.00 to 0.38) may underlie the haplotypic association with milder disease phenotypes.

035 ASCA POSITIVITY INDEPENDENTLY PREDICTS ORAL CROHNS DISEASE IN A LARGE EARLY ONSET INFLAMMATORY BOWEL DISEASE POPULATION

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Introduction: Anti-sacccharomyces cerevisiae antibodies (ASCA) have been proposed to be useful in the diagnosis of Crohn’s disease (CD). ASCA status and its relationship with disease phenotype was determined in a cohort of Scottish early onset inflammatory bowel disease (IBD) patients.

Patients and Methods: ASCA status (IgA, IgG) was determined in 301 IBD patients (197 CD, 76 UC, 28 IC) using an ELISA kit. ASCA data from 78 healthy adult controls was also available. ASCA status was matched with phenotypic features of IBD at diagnosis.

Results: CD patients had a higher prevalence of ASCA antibodies compared to healthy controls (p < 0.05). ASCA status was associated with ileal disease in CD patients (p = 0.009, odds ratio (OR) 3.80 (1.93–7.50) and 41.6% p<0.0001, OR 8.56 (3.55–20.62) respectively). ASCA status predicted CD with sensitivity of 41.6% and specificity of 88.6%.

In CD patients univariate analysis demonstrated a positive ASCA was associated with ileal disease and ileal disease in CD patients (p = 0.0003, OR 8.56 (3.55–20.62) and p = 0.0001, OR 8.56 (3.55–20.62) respectively). ASCA status predicted CD with sensitivity of 41.6% and specificity of 88.6%.
**Methods:** During a retrospective case note review, establishing the incidence of CD in SE Scotland, patients were identified where there had been significant diagnostic delay or likely diagnostic failure. Significant diagnostic delay was defined as greater than 24 months from symptom presentation to definitive diagnosis. Failure was defined as positive serology without performance of a biopsy. CD was defined according to the revised ESPGHAN criteria.

**Results:** 141 patients matched the criteria. Symptom onset data were identifiable in 135. From these, 18 had a delay of over 24 months. Reasons for diagnostic delay: failed biopsy not repeated within 2 years (4), IgA deficiency (3), initial reassurance despite family concern (2), positive serology without initial biopsy (3), dietary manipulation by family (1), administration problems leading to delay in biopsy (1), inconclusive histopathology (1), language problems with no suitable translation (1), lost to follow up following positive serology (1), and failure to adequately investigate iron deficiency anaemia and growth delay (1). In addition, there were six failed diagnoses (positive serology, no biopsy).

**Conclusions:** From our review we recommend: (a) all children must have IgA measured along with serology; (b) all children with positive serology should be biopsied; (c) all biopsies should be endoscopic to ensure adequate samples are obtained and (d) four biopsies should be taken to ensure adequate sampling; (e) biopsies should be repeated without delay if initial biopsies inadequate; (f) good communication should be ensured in all patient contact; (g) CD must be considered in investigation of growth delay and iron deficiency anaemia in children.

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**Small bowel and nutrition free pippers**

**Abstract 39**

### PLASMA CITRULLINE CONCENTRATION: A SIMPLE, SENSITIVE, AND NON-INVASIVE METHOD TO MONITOR SMALL BOWEL ABSORPTIVE FUNCTION IN PATIENTS WITH CROHN’S DISEASE

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**Background and Aims:** Plasma citrulline concentration (PCC) has been suggested as a marker of remnant enterocyte mass in patients with short bowel. A significant correlation between dramatically reduced PCC and histology has been shown in patients with intestinal damage, but the potential of PCC to indicate the degree of intestinal impairment has not been assessed. The aim of this study was to evaluate citrulline as a marker of intestinal functional integrity in patients with Crohn’s disease (CD) and to determine whether citrulline plasma concentrations are influenced by inflammation.

**Methods:** Fifty-five patients were divided into eight groups according to diagnosis, small bowel length and degree of bowel inflammation: (1) CD with massive small bowel resection with <50 cm remaining bowel (n = 6); (2) CD with small bowel resection with 50–150 cm remaining bowel (n = 9); (3) CD with no bowel resection but active inflammation (n = 7); (4) CD with no resection and no active inflammation (n = 6); (5) mesenteric infarction (MI) with massive small bowel resection with <50 cm remaining (n = 6); (6) mesenteric infarction with small bowel resection leaving 50–150 cm; (7) active coeliac disease (n = 6); (8) healthy volunteers (n = 6). Post absorptive fasting plasma citrulline (in mmol/l) was measured using reverse phase high performance liquid chromatography (HPLC). All patients had standard laboratory markers performed and were scored according to the Crohn’s Disease Activity Index (CDAI). Five hour urine collections were carried out on each patient following sugar mix ingestion (5 g lactulose, 1 g L-rhamnose, 0.5 g D-xylose, and 0.2 g 3-O-methyl-D-glucose in 100 ml of demineralised water) after overnight fasting.

**Results:** Plasma citrulline concentration strongly correlated with small bowel length (p<0.0001) and carbohydrate absorption (p<0.0001). No correlation was found between plasma citrulline concentration and small bowel permeability, and there was no correlation with CRP, ESR, WBC, platelets, or albumin. Plasma citrulline was significantly higher (p<0.0004) in CD/MI patients with a remnant small bowel length of 50–150 cm (mean value 21.02 ±mol/l) compared to CD/MI patients with a small bowel length <30 cm (mean value 9.20 ±mol/l). No significant difference (p=0.734) was found between groups of patients with CRP >10 compared to those >10, nor between active and inactive CD patients in whom the intestinal length remained intact.

**Conclusion:** Citrulline plasma concentration is a simple, sensitive and reliable surrogate for small bowel absorptive capacity and is not influenced by intestinal inflammation.

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**COELIAC DISEASE: IS BIOPSY STILL REQUIRED FOR DIAGNOSIS AT ALL LEVELS OF IGA TISSUE TRANSGLUTAMINASE ANTIBODY?**

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**Aim:** To review raised TGA results in adults in order to assess at what level the positive predictive value (PPV) for coeliac disease is 1.00.

**Methods:** Adult subjects (age >15 years) with TGA results >3 times the upper limit of normal (ULN), (Cellkey kit, Sweden Diagnostics, Milton Keynes, UK) in the period April 2002 to December 2003 and with a small bowel biopsy (Bx) were included. For new diagnoses of coeliac disease, the result immediately prior to Bx was included; for subjects with a prior histological diagnosis of coeliac disease, the first TGA result in the review period was included. For patients with a normal Bx, the highest result was included. Two patients with normal Bx reports were excluded because of the long interval (17 and 24 months) between Bx and subsequently abnormal serology in the review period.

**Results:** After exclusions, there were results on 149 individual patients. All samples with values greater than 10 times the upper limit of normal were from subjects with coeliac disease (see table).

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**Conclusions:** These results show that for TGA results >10 times the ULN, the PPV for CD is 1.00 which suggests that small bowel biopsy should not continue to be mandatory for diagnosis when TGA is above this cut-off. At lower levels, as shown in the table, the PPV falls and biopsy is still required to confirm the diagnosis. Numerical values for kits differ but most kits correlate well1, 2 suggesting that a cut off of 10 times the upper limit of normal will give similar PPVs for most kits.


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**INTESTINAL DENDRITIC CELLS IN COELIAC DISEASE**

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**Background and Aims:** To identify the changes in dendritic cells (DC) that may underlie the dysregulated T-cell response to gluten in coeliac disease, we examined coeliac lamina propria DC in terms of phenotype, activation/maturation and cytokine production, and investigated the in vitro effects exerted on DC by the immunodominant (p57–68) and the supposed to activate the innate immune system.

**Methods:** DC were identified in LPMC isolated from untreated coeliac disease patients and controls by multicolor flow cytometry as an HLA-DR+ expression on DC and COX-2 levels in duodenal biopsies. A simple, sensitive and reliable surrogate for small bowel absorptive capacity and is not influenced by intestinal inflammation.

**Conclusions:** COELIAC DISEASE: IS BIOPSY STILL REQUIRED FOR DIAGNOSIS AT ALL LEVELS OF IGA TISSUE TRANSGLUTAMINASE ANTIBODY?**

**INTESTINAL DENDRITIC CELLS IN COELIAC DISEASE**

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**Background and Aims:** To identify the changes in dendritic cells (DC) that may underlie the dysregulated T-cell response to gluten in coeliac disease, we examined coeliac lamina propria DC in terms of phenotype, activation/maturation and cytokine production, and investigated the in vitro effects exerted on DC by the immunodominant (p57–68) and the non-immunodominant (p31–43) gliadin epitopes, the latter of which is supposed to activate the innate immune system.

**Methods:** DC were identified in LPMC isolated from untreated coeliac disease patients and controls by multicolor flow cytometry as an HLA-DR+ expression on DC and COX-2 levels in duodenal biopsies. A simple, sensitive and reliable surrogate for small bowel absorptive capacity and is not influenced by intestinal inflammation.

**Conclusion:** Citrulline plasma concentration is a simple, sensitive and reliable surrogate for small bowel absorptive capacity and is not influenced by intestinal inflammation.
**Methods:** In active coeliac disease, lamina propria DC are activated and express higher number of transcripts of pathologically relevant molecules, but not p31–43 or p57–68.

**Results:** A significantly higher number of plasmacytoid DC were found in patients with active coeliac disease and express higher number of transcripts of pathologically relevant molecules, but not p31–43 or p57–68.

**Conclusions:** The ileo-caecal valve has a predictable blood supply in the majority of patients. Preservation of the anterior caecal artery would ensure a vascularised ileo-caecal valve in right hemicolectomy.

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**Background:** Chronic sodium (Na) and water depletion is well recognised in colectomy patients with ileostomies. The withdrawal of indications for PE were iron deficiency anaemia (n = 48), overt bleeding (n = 25), suspected coeliac disease (n = 32), refractory coeliac disease (n = 17), assessment for Crohn’s disease (n = 10), and miscellaneous (n = 11). The procedure was performed in 136 patients with an average length of 70 cm of small bowel examined (range 30–130 cm). PE was unsuccessful in seven patients due to anatomical strictures or patient distress. The overall diagnostic yield was 29%. A standard endoscope could have reached 10% of the lesions. The diagnostic yield based on subgroup was 29% in iron deficiency anaemia, 64% in overt bleeders, 16% in suspected coeliac disease, 3% in refractory coeliac disease, 10% in Crohn’s disease, and 36% in the miscellaneous category. Overt bleeding when compared to all subgroups had a greater diagnostic yield (χ² < 0.001). Overt bleeding was also compared to individual subgroups: iron deficiency anaemia (p = 0.025), suspected coeliac disease (p = 0.001), refractory coeliac disease (p = 0.001), Crohn’s disease (p = 0.01), and miscellaneous (p = 0.2). Comparison of the diagnostic yield in patients who had CE followed by PE against CE naïve patients was 44% versus 46% respectively (p < 0.1). There were no cases where PE recognised a lesion that had not already been detected at CE.

**Conclusion:** Push enteroscopy has the greatest diagnostic yield in overt bleeders when compared to other referral indications. A negative PE would appear to exclude the need for a PE. PE should be used for therapeutic intervention following CE.

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**NITROGEN BALANCE AND UREA KINETICS IN ILEOSTOMY PATIENTS**

**Abstract 43**

**N intake** | Urinary N | Stool N | N balance
---|---|---|---
Ref HD | 157.9 (25.3) | 150.3 (17.5) | 16.8 (8.6) | -9.2 (20.0)
LPD | 94.7 (9.0)* | 101.5 (15.6)* | 16.1 (1.1)* | -22.9 (7.1)*
NSBR HD | 172.4 (36.6) | 141.8 (29.0) | 25.5 (6.9) | 5.1 (13.6)*
LPD | 109.8 (21.6)* | 108.8 (24.2)* | 21.5 (7.7) | -20.8 (19.9)*
SBD HD | 188.8 (63.8) | 116.6 (27.5) | 49.1 (41.1) | 23.2 (33.1)
LPD | 109.0 (41.1)* | 81.8 (21.2)* | 39.2 (26.8) | -12.0 (16.1)*

Paired t test: *p < 0.05, v HD (values in mean (SD) mgN/kg/day).
**CONCLUSIONS:** Although TNFα retained 18.1 (SD 4.5) larvae (p = 0.001), WT mice retained 1.5 (SD 1.0) larvae, while p55/75 KOs did not expel any larvae. The infection, as demonstrated by the host response to clear parasites. At day 20, naive WT mice retained 1.5 (SD 1.0) larvae, while p55/75 KOs retained 2.2 (p = 0.001). Functional TNFs was absolutely not required for these effects: infected p55/75 KO mice consumed 1.75 (SD 0.15) % of baseline, while rising to 108.5 (SD 1.7) % in naive WT mice (p = 0.001). The weight loss was attributed to breaches of PN CVC protocols.

**METHODS:** After the introduction of the nutrition team and PN CVC protocols in 1997, this fell to 6.6% (range of 0–15.1%) with no septic CVC lines in 1999. Before 1986 the mean sepsis rate was 30.5% patients/year but after the introduction of the nutrition team and PN CVC protocols in 1997, this fell to 6.6% (range of 0–15.1%). No long term reports of central venous catheter (CVC) sepsis rates have been reported from a district general hospital in the UK. We have already demonstrated that CVC sepsis rates in our home parenteral nutrition patients are comparable to those in large tertiary centres.

**AIM:** To assess CVC sepsis since the start of an adult inpatient parenteral nutrition (PN) service in a District General Hospital in 1986.

**METHODS:** Cumulative prospectively collected annual data of CVC sepsis rates from 1985 to 2003 at a single district general hospital in all clinical areas was assessed by a central venous catheter (CVC) sepsis rates have been reported from a district general hospital in the UK. We have already demonstrated that CVC sepsis rates in our home parenteral nutrition patients are comparable to those in large tertiary centres.

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Inflammatory bowel disease free papers

048 ARE ALL MESALAZINES EQUAL? A META-ANALYSIS OF PH7-DEPENDENT VERSUS CONTROLLED RELEASE MESALAZINE IN THE MAINTENANCE OF MEDICALLY INDUCED REMISSION OF INACTIVE CROHN’S DISEASE

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Background: Research indicates that the maintenance of quiescent Crohn’s disease with oral mesalazines is most frequently observed following surgical rather than medically induced remission. Studies assessing the effectiveness of mesalazine in treating patients with medically induced remission have yielded inconsistent results. It is possible that these inconsistencies arise from differences in the formulation of mesalazine administered.

Methods: A meta-analysis was undertaken to evaluate the efficacy of pH7 dependent and controlled release mesalazine in maintaining medically induced remission of Crohn’s disease. A MEDLINE literature search identified six relevant (two pH7 dependent, four controlled release) randomised controlled trials (RCTs), involving a total of 683 patients (191 pH7, 492 controlled release). The crude rate of symptomatic relapse (CDAI ≥ 150) or an increase in baseline from 60 to 100 points) for both treatment and control groups was extracted for each RCT using the intention-to-treat method. Mantel-Haenszel approach was used to derive a pooled estimate of odds ratio (OR) and the number needed to treat (NNT) calculated.

Results: Treatment with pH7 dependent mesalazine significantly reduced the risk of symptomatic relapse (pooled OR 0.299 to 0.809) but not with controlled release mesalazine (pooled OR 0.888; 95% CI 0.603 to 1.307) when compared with placebo. There were also differences in treatment effectiveness by NNT, 5 and 36 for pH7 dependent mesalazine administered.

Conclusion: The results of this meta-analysis, although involving only a small number of studies, suggest that differences in mesalazine delivery may partially account for inconsistencies in the literature. Moreover, pH7 dependent mesalazine may offer an effective treatment for maintaining medically induced remission of Crohn’s disease.

049 TRANSFORMING GROWTH FACTOR-β SIGNALING AND MATRIX METALLOPROTEINASE PATTERN IN INTESTINAL STRICTURES IN CROHN’S DISEASE

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Background and Aims: In addition to its crucial role in dampening tissue damaging immune responses in the gut, TGF-β has a potent profibrogenic action that it exerts by inducing fibroblast proliferation, by downregulating matrix metalloproteinase (MMP) expression, and by enhancing TIMP expression. To elucidate the mechanisms which may underlie intestinal fibrosis and stricture formation in Crohn’s disease (CD), we explored intracellular proteins, whose phosphorylation is involved in activating (pSmad2/3) or inhibiting (Smad7) the TGF-β signal transduction, and MMP pattern in CD.

Methods: Endoscopic biopsy specimens were collected from strictured and non-strictured mucosa of 12 fibrostenosing CD patients. Biopsies from inflamed mucosa of nine non-fibrostenosing CD patients and from 11 controls were also studied. pSmad2/3, Smad7, MMP-3, MMP-12, and TIMP-1 were determined by western blotting. TGF-β transcripts were analysed by RT-PCR.

Results: A lower Smad7 expression was found in strictured than in non-strictured mucosa in CD. As expected, Smad7 was strongly upregulated in CD inflamed mucosa. pSmad2/3 was higher in strictured than in non-strictured mucosa. Strictures expressed greater number of TGF-β transcripts than non-strictures. MMP-3 and MMP-12 were decreased in strictured in comparison to non-strictured mucosa. High expression of MMP-3 and MMP-12 was found at level of CD inflamed lesions. TIMP-1 was higher in strictured than in non-strictured areas.

Conclusion: Our findings of decreased Smad7 and increased pSmad2/3 in strictures support the profibrogenic role of TGF-β in CD. Reduced MMP-3 and MMP-12 together with increased TIMP-1 in strictured mucosa suggest that TGF-β may induce intestinal fibrogenesis by changing the balance between MMP and TIMP expression in CD.

050 ACUTE PSYCHOLOGICAL STRESS INCREASES RECTAL MUCOSAL AND LPS STIMULATED BLOOD RELEASE OF TNF-α IN PATIENTS WITH INACTIVE ULCERATIVE COLITIS

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Introduction: Psychological stress is reported to increase relapse in ulcerative colitis (UC) but the mechanism is unclear. We hypothesised that stress might increase colorectal mucosal and lipopolysaccharide stimulated whole blood (LPS-WB) production of TNF-α.

Aim: To assess the effects of acute stress on the concentration of TNF-α in rectal perimucosal fluid (RPMF), and on the production of TNF-α by LPS-WB in inactive UC.

Methods: For 50 minutes patients with inactive UC (Baron score <2) underwent (1) Stress (n = 25), dichotomous listening test (IQ test during contrasting music in each ear) or (2) Control (n = 10), relaxing music. Autonomic response was assessed by pulse and BP changes. RPFM was collected before and after each protocol from a 7 x 30 mm strip of filter paper placed signiodoscopically against rectal mucosa for 1 min. The filter paper was incubated in 1 ml BSA (0.3%), sodium azide (0.01%), and Tween 20 (0.002%) in PBS for 24 hours; TNF-α in the buffer was measured by ELISA. Before and after each protocol, TNF-α production by 1 ml whole blood incubated with 25 µg/ml LPS at 37°C in 95%O2 /5%CO2 for 24 hours was measured by ELISA (LPS-WB).

Results: The control protocol did not change any variable. Stress increased pulse by 5bpm, systolic BP by 11mmHg, and rectal (RPFM) and LPS-WB TNF-α production by 102% and 54% respectively.

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<table>
<thead>
<tr>
<th>Before</th>
<th>After</th>
</tr>
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<tbody>
<tr>
<td>Pulse rate (bpm)</td>
<td>70 (65–74)</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>118 (113–133)</td>
</tr>
<tr>
<td>RPFM TNF-α (pg/ml)</td>
<td>12.8 (8.6–20.2)</td>
</tr>
<tr>
<td>LPS-WB TNF-α (mg/ml)</td>
<td>28 (17–57)</td>
</tr>
</tbody>
</table>

*p < 0.05 from pre-stress value. Median and IQR shown.

Conclusion: Acute psychological stress increases release of TNF-α by rectal mucosa and by LPS-WB. Both mechanisms could contribute to the pathogenic effects of psychological stress in UC.

051 EXPRESSION OF HUMAN DEFENSIN-5 IN INFLAMMATORY BOWEL DISEASE TISSUE

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Introduction: Human defensin-5 (HD-5) is a major antimicrobial peptide which is present in the lumen in its mature form but stored in normal small intestinal Paneth cells in its precursor form. Alterations in the expression of HD-5 in Paneth cells of Crohn’s small intestine or metaplastic Paneth cells of colon affected by inflammatory bowel disease (IBD) may lead to impaired mucosal innate immunity.

Methods: Surgical resection specimens of terminal ileum (6 normal, 7 Crohn’s disease) and colon (4 normal, 7 IBD) were studied. Tissue sections were used for immunohistochemistry. Paneth cell containing epithelial crypts were stained with HD-5. HD-5 was visualised by immunohistochemistry and western blot analysis. HD-5 expression was measured by ELISA and immunoblotting.

Results: HD-5 was detected by immunohistochemistry and western blot analysis. HD-5 was detected in normal and IBD tissue. HD-5 was detected in normal and IBD tissue. HD-5 expression was measured by ELISA and immunoblotting.

Conclusion: HD-5 expression was measured by ELISA and immunoblotting. HD-5 was detected in normal and IBD tissue.

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from each tissue type had a similar elution profile on the C18 RP-HPLC column (39% acetonitrile). Identical N-terminal sequence (ESLGERADEAT, of precursor form) was found for HD-5 extracted from Crohn’s small intestine (2), IBD colon (2), and normal terminal ileum. Mass of HD-5 purified from normal small intestinal crypts was the same as that predicted for the precursor form (8103.83 Da).

Conclusions: In our studies to date, in Paneth cells of Crohn’s small intestine and in metastatic Paneth cells of IBD colon, HD-5 is stored in the precursor form, identical to HD-5 stored in normal small intestine.

Abstract 53
Remission and clinical response (% of patients)

<table>
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<th>Week</th>
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</tr>
<tr>
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</table>

LOCF, last observation carried forward.

Abstract 54
GNE-WIDE HAPLOTYPIC ANALYSIS DEMONSTRATES NOVEL ASSOCIATION BETWEEN ATP BINDING CASSETTE 3/MULTIDRUG RESISTANCE PROTEIN 3 (ABCC3/MRP3) GENE AND INFLAMMATORY BOWEL DISEASE

Molecular Medicine Centre, University of Edinburgh and Goldstein Laboratories, University College London, UK

Background: Increasing evidence implicates the disruption of xenobiotic defence mechanisms in the pathogenesis of inflammatory bowel disease (IBD). 1, 2 We have recently demonstrated association between variations of the ABCB1/MRP1 gene and UC, microarray data now implicate a series of other genetic determinants involved in the maintenance of intestinal barrier function.

Aim: We have analysed the association of a single of a panel of genes (derived from recent microarray data by Langmann et al) consisting of the Pregnan-X receptor (PXR), ABC2, ABC3, and Mekki genes using a genome wide haplotype tagging approach.

Methods/Results: We have assessed the linkage disequilibrium pattern in these candidate genes by resequencing 24 CEPH white trios leading to the identification of 71 SNPs. A set of 22 haplotype tagging SNPs representing the common variations of these genes, both known and unknown were then selected using the multiple marker criterion of haplotype r2 > 0.8 for all genotyped SNPs. These SNPs were then genotyped in the Scottish cohort consisting of 388 UC, 328 CD, and 338 HC. Within the ABCB3 gene, two haplotype tagging variants demonstrated significant associations with CD (rs739921 C→G, p = 0.005, OR 1.41, 95% CI 1.11 to 1.79) and UC (rs2277624 C/T SNP, p = 0.003, OR 1.52, 95% CI 1.15 to 2.00) respectively. In contrast, no associations were demonstrated at the allelic or haplotypic level (using log-likelihood ratio tests, p = 0.9–0.1) for the other genes studied.

Conclusions: The present data provide the first evidence of the involvement of the ABCB3 gene in determining susceptibility to IBD. ABCB3 gene encodes for multidrug resistance protein 3 (MRP3) which is expressed in the gut and liver. Further fine mapping of associated interval of the implicated SNPs and replication in other datasets are in progress, together with functional and expression data.


ASSOCIATION OF A NONSENSE MUTATION IN THE TUCAN (CARD8) GENE WITH INFLAMMATORY BOWEL DISEASE

M. M. Mirza1, S. A. Fisher1, C. Onnie1, J. Sanderson2, A. Forbes3, J. Mansfield4, C. M. Lewis5, C. G. Mathew1
King’s College London School of Medicine, UK; 2Guy’s and St Thomas’ Hospitals, London, UK; 3St Mark’s Hospital, Harrow, UK; 4University of Newcastle, UK

Background: The TUCAN gene (CARD8, CARDINAL) maps to a region of linkage to inflammatory bowel disease (IBD) on chromosome 19 and is a negative regulator of the transcription factor NF-kB, which has a central role in the inflammatory response. Our aim was to investigate conflicting evidence of a role for TUCAN in IBD susceptibility by sequencing the coding region of the gene in IBD patients and testing single nucleotide polymorphisms for association in a large case control sample.

Methods: The 10 exons, splice sites, promoter, 5’ and 3’ untranslated regions of TUCAN gene were sequenced in 24 IBD (12 CD, 12 UC)
patients. Pairwise linkage disequilibrium coefficients (LD) between SNPs (A and D') were calculated using HAPLOVIEW. Selected SNPs were genotyped in over 1000 IBD cases and 400 controls.

Results: Sequencing detected six SNPs: T29C, T30A, producing a premature stop codon at amino acid 10 (C10X), a frameshift in exon 4 (126insAA–V43fsX67) and synonymous SNPs, G933A in exon 8, G1110A in exon 10 and the rare C1227T in exon 10 (frequency 1%). The five common SNPs fell into four LD groups. The frequency of the C10X SNP was significantly increased, CD in UC and in the combined phenotype of IBD; controls (n = 652) 29.1%, UC (n = 831) 33.2% (p = 0.017, OR 1.21), UC (n = 528) 33.2% (p = 0.033, OR 1.22), IBD (1359) 33.2% (p = 0.009, OR 1.21). However, the frameshift 126insAA was not significantly different in cases of CD (51.5%) and UC (49.1%) compared to controls (58.6%), and no other SNPs were associated with IBD. There was no significant difference in the frequency of C10X in CD cases that did or did not carry one or two mutations in CARD15.

Conclusions: These data suggest that a nonsense mutation, C10X, in the TUCAN/CARD8 gene, which would produce a highly truncated protein, may be associated with a moderately increased risk of IBD. This result requires independent replication in other patient cohorts.

EVIDENCE OF MONOCLINAL ORIGINS IN DYSPLASIA IN ULCERATIVE COLITIS

Aim: Ulcerative colitis (UC) is a chronic inflammatory condition that increases the risk of developing colorectal cancer (CRC). UC associated colorectal cancers (UCACRC) often develop from areas of dysplasia, which can be widespread or multifocal. Loss of heterozygosity (LOH) of important tumour suppressor genes such as denomatous polyposis coli (APC), deleted in colon cancer (DCC) and SMAD4, can occur in UC associated dysplastic tissue. LOH analysis can be used as a simple and reliable marker of clonality. The aim of this study was to use LOH at the above three loci for the assessment of clonality within dysplastic and inflamed tissue in UC to test the hypothesis that dysplastic lesions arise from a single mutated clone.

Methods: Paraffin embedded tissue from coloectomy specimens was obtained from St Marks Hospital pathology library. Tissue was categorised histologically into normal, acute, or chronically inflamed or dysplastic, based on HE & slides. Laser capture microdissection was used to isolate individual crypts. If no normal crypts were available from the tissue, regions of lamina propria or muscularis mucosae were taken to allow LOH analysis comparison. DNA was extracted and amplified for microsatellite markers close to the loci of APC (2q52.11), DCC (18q21), and SMAD4 (18q21.1). PCR product was analysed with ABI 3100 sequencer and genotyper software and abnormal tissue allelic areas were compared with normal tissue allelic areas as a ratio.

Results: LOH for microsatellite markers was found in chronic inflammation in one patient at a low frequency (one marker, 50% of crypts). LOH of the same microsatellite marker was seen in low grade dysplasia at a low frequency (44%) but at a very high frequency across multiple high grade dysplastic patches in different patients (up to 100%). LOH of multiple markers was seen in some patients.

Conclusions: Lower LOH frequency in inflamed and low grade dysplasia compared to high grade dysplasia suggests which marker is lost first, and the earliest lost marker can be used a clonal marker. "Across the patch" loss of the same allele in high grade dysplasia suggests monoclinal derivation. Increased crypt fission is likely to be responsible for mutation spread.

OROFACIAL GRANULOMATOSIS: A TERTIARY REFERRAL CENTRE EXPERIENCE
C. Nunes1, M. Escudier2, P. J. Shirlaw2, S. J. Challacombe3, J. D. Sanderson1. 1Department Gastroenterology, Guy’s & St Thomas’ Hospital; 2Oral Medicine and Pathology, Guy’s, King’s & St Thomas’ Dental Institute, UK.

Background: Orofacial granulomatosis (OGF) is a rare chronic inflammatory disease of unknown aetiology sharing histological features with gut Crohn’s disease (CD). We have been running a combined Oral Medicine/Gastroenterology clinic since 1995 dedicated to patients with OGF. Previous studies addressing the clinical features and natural history of OGF are limited.

Aim: To gain insight into the overall presentation and clinical features in patients with OGF referred to a dedicated OGF tertiary referral centre.

Methods: In a retrospective study, case notes of patients with OGF attending a combined Oral Medicine/Gastroenterology clinic were reviewed. Data were extracted for age of onset, sex, clinical features, blood parameters, concurrent CD, and patch testing. A concurrent diagnosis of CD was established by standard criteria.

Results: Results were available on 73 patients of which 36 (49%) were female. Median age of disease onset was 24 years. Thirty six per cent were referred by maxillo-facial surgeons and only 15% by gastroenterologists. Fifteen (21%) had concurrent CD. Lip swelling (69%) and buccal involvement (72%) were the most common sites involved followed by gingivae and floor of the mouth. Mucosal tags (47% v 28%) and cobblestoning (40% v 19%) were more common in patients with concurrent CD as were haematric deficiencies (53% v 29%) and raised inflammatory (60% v 17%). Those with OGF alone (29% v 9%) were more likely to be patch test positive.

Conclusion: OGF affects predominantly young adults with lip and buccal involvement and is more common in patients with concurrent CD. Mucosal tags and cobblestoning are more likely in those with concurrent CD. Tests for cutaneous sensitivity are more often positive in OGF than CD in keeping with the view that OGF has an allergic component.

Pancreatic symposium

EARLY ADMISSION TO ITU/HDU OF PATIENTS WITH ACUTE PANCREATITIS IN ENGLAND, 2003–04
G. David, A. Al-Sairara, K. Cummins, D. J. Corless, M. Deakin, J. P. Slavin. Department of General Surgery, Leighton Hospital, Crewe CW1 4QJ, UK.

Objectives: British Society of Gastroenterology (BSG) guidelines for management of acute pancreatitis (AP) suggest that severity stratification should be undertaken in all patients within 48 hours of diagnosis and those with predicted severe pancreatitis should be managed on a high dependency or intensive therapy unit with full monitoring and support. We analysed early admissions to ITU/HDU (within three days of presentation) in England for patients admitted with AP during the year April 2003–March 2004.

Methods: Hospital Episode Statistics data for the year 2003–04 were obtained from The Department of Health and imported into a database (Access) for analysis.

Results: There were 16 245 emergency hospital admissions with a diagnosis of AP during the year 2003–04. 1173 (7.22%) were managed on ITU/HDU during their hospital stay. Only 958 (5.90%) patients were admitted to ITU/HDU care within 72 hours of presentation.

Conclusion: Twenty five per cent of patients with AP will be predicted severe if BSG guidelines are being followed, we would have expected to see a much higher proportion of patients admitted to ITU/HDU within the first 72 hours. This clearly has huge implications for ITU/HDU provision.

We would recommend that further work is undertaken to develop the guidelines, looking at levels of monitoring required and where this is best delivered, minimal levels of supportive care, and routine use of scoring systems that would allow the prioritisation of patients with organ dysfunction to a higher level of care.

SOCIOECONOMIC STATUS CORRELATES WITH OUTCOME IN PANCREATIC CANCER
J. J. S. Brown, B. Ashton, R. M. Charnley, D. Forman1, B. C. Jaques. Hepato-Pancreato-Biliary Unit, Freeman Hospital, Newcastle upon Tyne and 1Northern and Yorkshire Cancer Registry, Leeds, UK.

Aim: To investigate the impact of deprivation on outcome in patients with pancreatic cancer, data were collected from the NYCIRS (Northern and Yorkshire Cancer Registry) database for new patients registered from January 1998 to December 2002.

Methods: The IMD2000 score (a validated socioeconomic deprivation tool) was attributed to each patient. Five quintile groups of similar size were generated with graded deprivation profiles, higher scores representing greater deprivation. The difference between the rank of socioeconomic deprivation and average survival in days was also calculated for the cohort of patients who underwent surgery and those who had no surgical intervention.

Results: From a total of 3976 patients the five quintiles had between 739 and 804 patients, the difference of the mean deprivation score between all groups was significant, p<0.0001, using Student’s t test (see table). The mean survival in days, for all treatment modalities between Q1 and Q5, was significantly different, p = 0.0003.
The mean deprivation scores for those undergoing surgery (n = 229) and those not undergoing surgery (n = 3640) were 28.31 and 31.64 respectively, p = 0.002. The mean survival of the surgical cohort in the most deprived quintile (n = 33) was 329 days (95% CI 198 to 460) and the least deprived (n = 53), 424 days (95% CI 320 to 527), p = 0.26. 

Conclusion: Although the cohorts represent a varied casemix, socioeconomic deprivation appears to have a major effect on survival in patients with pancreatic cancer and also correlates with treatment by surgical intervention. Further work is required to determine the underlying cause of this effect.

### IBD/Pathology sections joint symposium

**Abstract 59**

**DETECTION OF MURAMYL DIPEPTIDE SENSING PATHWAY DEFECTS IN PATIENTS WITH CROHN’S DISEASE**

D. A. van Heel1, K. A. Hunt1, S. Ghosh2, K. King2, S. Gaba3, C. G. Mathew2, A. Forbes1, R. J. Ploypail1. 1Imperial College London, 2King’s College London School of Medicine, 3St Mark’s Hospital, UK

**Background and Aims:** Crohn’s disease is strongly associated with double mutations in NOD2/CARD15. Three common mutations (Arg702Trp, Gly908Arg, Leu1007fs) impair innate immune responses to bacterial muramyl dipeptide. Rare NOD2 variants occur, but it is difficult to both identify them and assess their functional effect. We assessed the true frequency of defective muramyl dipeptide sensing in Crohn’s disease and developed a rapid diagnostic assay.

**Methods:** An ex vivo assay was established and validated based on muramyl dipeptide stimulation of peripheral blood mononuclear cell cytokine production. Muramyl dipeptide induced enhancement of IL-8 secretion, and synergistic increase in lipopolysaccharide induced IL-1β secretion were studied. Assay results were compared with NOD2 genotype status (three common mutations and rare variants) in 91 individuals including a prospective cohort of 49 Crohn’s disease patients.

**Results:** The assay was highly sensitive and specific for detection of profound defects in muramyl dipeptide sensing caused by double NOD2 mutations (IL-8 p = 0.0002; IL-1β p = 0.0002). Disease state, active inflammation or concurrent use of immunosuppressive medication did not influence results. Healthy NOD2 heterozygotes had modest impairment of muramyl dipeptide induced IL-8 secretion (p = 0.003). Only one of seven Crohn’s disease patients with both a common mutation and a second amino acid-changing rare variant had a profound muramyl dipeptide sensing defect.

**Conclusions:** Profound defects in muramyl dipeptide sensing were found in 10% of Crohn’s disease patients. Inherited mutations in NOD2 (and not any other genes) accounted for all defects. The ex vivo assay has multiple potential applications as a clinical diagnostic tool to distinguish patients with NOD2 dipeptide sensing defects, and for research investigation.

**Abstract 60**

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**Conclusions:** Profound defects in muramyl dipeptide sensing were found in 10% of Crohn’s disease patients. Inherited mutations in NOD2 (and not any other genes) accounted for all defects. The ex vivo assay has multiple potential applications as a clinical diagnostic tool to distinguish patients with NOD2 dipeptide sensing defects, and for research investigation.

**Abstract 61**

**IGG PLASMA CELLS IN INFLAMMATORY BOWEL DISEASE EXPRESS LARGE QUANTITIES OF STROMELY S IN (MMP-3)**

J. N. Gordon1, K. M. Pickard1, P. M. Goggins2, T. T. MacDonald1. 1Division of Infection, Inflammation and Repair, University of Southampton School of Medicine, UK; 2Department of Gastroenterology, Queen Alexandra Hospital, Portsmouth, UK

**Introduction:** In both ulcerative colitis and Crohn’s disease there is a marked increase in IgG plasma cells in the lamina propria which may be of primary pathogenic significance. In addition, gut plasma cells can secrete functionally active immune mediators capable of driving inflammation in the gut. Using a novel method for isolating gut plasma cells we have previously shown that long lived IgG plasma cells persist in inflammatory bowel disease (IBD) and may contribute to tissue injury. In this study we have investigated the production of MMP-3 by gut plasma cells from normal subjects and patients with IBD.

**Methods:** Biopsy and resection tissue specimens were obtained from patients with active IBD and from normal controls. Lamina propria mononuclear cells were isolated and immunomagnetic selection used to positively select plasma cell populations. MMP-3 expression was investigated using western blotting, and Tanaman PCR. The types of plasma cell making MMP-3 were studied by confocal microscopy.

**Results:** Plasma cells from patients with CD and UC expressed significantly higher levels of MMP-3 protein and transcripts (100 000 fold increase) than controls (p<0.001). Levels of TIEP-1 were not significantly different from controls. In patients with IBD, 92% of IgG+ve plasma cells expressed MMP-3 compared with 20% of IgA+ve cells. In contrast very few plasma cells from controls expressed any MMP-3.

**Conclusion:** We have demonstrated that plasma cells from subjects with IBD express large amounts of MMP-3. Furthermore the primary source of MMP-3 is IgG+ve plasma cells. These results identify a new pathway by which IgG plasma cells can damage the gut.

**Abstract 62**

**POSITION CHANGE IMPROVES LUMINAL DISTENSION DURING COLONOSCOPE WITHDRAWAL: A RANDOMISED, CROSSOVER, BLINDED TRIAL**

J. E. East, N. Suzuki, N. Arebi, D. Swain, N. Palmer, P. Bassett, B. B. Saunders. Wolfson Unit for Endoscopy, St Mark’s Hospital, London, UK

**Background:** Adenoma miss rates may be as high as 27% for lesions <5 mm and 12% if >10 mm. Part of this miss rate may be due to lesions hidden in colon that is inadequately distended to allow complete visualisation of the mucosal surface. Changing the patient’s position during colonoscopy may alter colonic configuration and gas distribution to improve luminal distension, compared to performing the entire withdrawal sequence in the left lateral position.

**Method:** During the withdrawal phase, 14 patients were randomised to one of two sequences first: either examination entirely in the left lateral (LL) position or with position changes (PC). Position change involved examination of caecum (C), ascending colon (AC), and hepatic flexure (HF) in left lateral position; transverse colon (TC) supine; and splenic flexure (SF) and descending colon (DC) in right lateral. At the sigmoid descending junction, the colonoscope was reintroduced to the caecum and the patient was re-examined with the other sequence. Luminal distension was scored on a scale 1–5; 1, total collapse; 5, ideally patent to limit of vision, by the endoscopist (e) and by a blinded video reviewer (v). All patients received lysisine butyramidine 20 mg IV.

**Results:** Scores for each colonic area are expressed as means (table). Scores were significantly different for TC, SF, and DC, paired t test.

<table>
<thead>
<tr>
<th>Segment</th>
<th>C</th>
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<th>HF</th>
<th>TC</th>
<th>SF</th>
<th>DC</th>
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<td>LL (v)</td>
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<td>4.3</td>
<td>2.9</td>
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<td>p Value</td>
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<td>0.63</td>
<td>0.02</td>
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</table>

**Conclusion:** Position change during the withdrawal phase of colonoscopy improves luminal distension in the transverse colon, splenic flexure, and descending colon compared to examination in the left lateral position, and has the potential to reduce adenoma miss rates.
Methods: Neoplastic lesions detected as compared to conventional colonoscopy. We hypothesised that targeted chromoscopy alone with high magnification would improve the detection of intraepithelial neoplastic (IN) lesions in UC compared to controls. A randomised, double blind, placebo controlled trial was undertaken. All seven patients in the steroid group required redilatation and two of these five subsequently required surgery. One of six patients in the placebo group required redilatation, none required surgery. There was a trend to earlier dilatation failure in the steroid group (p = 0.06, log rank test; hazard ratio (steroid to placebo) 6.1 (95% CI 0.7 to 53.0), Cox regression.

Results: Groups were well matched, n=13 (table, median values). Five of seven patients in the steroid group required redilatation and two of these five subsequently required surgery. One of six patients in the placebo group required redilatation, none required surgery. There was a trend to earlier dilatation failure in the steroid group (p = 0.06, log rank test; hazard ratio (steroid to placebo) 6.1 (95% CI 0.7 to 53.0), Cox regression.

Conclusions: Magnification chromoscopy significantly improves the detection of IN in this group. These techniques have important clinical implications and may change current practice guidelines.

064 INTRAEPITHELIAL NEOPLASIA AND COLON CANCER DETECTION IS SIGNIFICANTLY IMPROVED AND CHARACTERISED USING HIGH MAGNIFICATION CHROMOSCOPIC COLONOSCOPY: DO BSG GUIDELINES NOW REQUIRE MODIFICATION?

D. P. Hurlstone 1, D. S. Sanders 1, M. E. McAlindon 1, A. J. Lobo 1, M. Thomson 1, S. Brown 1, S. S. Cross* 1, Gastroenterology, Royal Hallamshire Hospital, Sheffield, *Academic Department of Pathology, Royal Hallamshire Hospital, Sheffield, UK

Background: Data suggest that pan-chromoscopy using methylene blue may improve the detection of intraepithelial neoplastic (IN) lesions in UC surveillance. Infiltrative cancers are known to occur. Steroid injection after stricturodilatation should be reconsidered.

Methods: 39 patients with longstanding UC (n=8 years) underwent surveillance colonoscopy using high magnification imaging. Quadrantic biopsies at 10 cm intervals were taken on extubation in addition to targeted biopsies of abnormal mucosal areas. Defined lesions were further evaluated using modified Kudo crypt pattern analysis and Paris guidelines. Data were compared to disease and extent matched controls who had undergone conventional colonoscopic surveillance between January 2001–April 2005.

Results: Significantly more IN lesions were detected in the magnification chromoscopic group as compared to controls (69/24, p<0.0001). IN was observed in 67 lesions at which 53 (79%) were detected using magnification chromoscopy alone. Chromoscopy increased the number of flat lesions detected with IN as compared to controls (p<0.001).

Conclusion: In this small trial, intrastricture steroid injection post balloon dilatation of Crohn’s disease related ileocolonic anastomotic strictures does not extend time to redilatation and may shorten it. Steroid injection after stricture dilatation should be reconsidered.

065 AUTOFLUORESCENCE IMAGING AND NARROW BAND IMAGING IN COLONOSCOPY: AN EARLY EXPERIENCE

J. E. East, N. Suzuki, N. Palmer, C. Thapar, D. Swain, B. P. Saunders. Wolfson Unit for Endoscopy, St Mark’s Hospital, London, UK

Background: Narrow band imaging (NBI) uses optical filters to improve contrast for superficial mucosal vessels to highlight vascular neoplastic lesions as well as the mucosal (pit) pattern. Autofluorescence imaging (AFI) relies on neoplastic lesions blocking endogenous tissue autofluorescence to provide colour contrast (magenta on green) against the background mucosa.

Method: We report our experience with a third-generation prototype AFI system with high definition and ×100 magnification in colon in the first 92 cases (XCF-H240FLI video colonoscope, XCVL-260HP xenon light source and XCV-260HP video system centre, Olympus Medical System Corp, Tokyo, Japan). We compared the adenoma detection rate in those without a polyposis syndrome or colitis with that of the preceding 92 cases performed with standard colonoscopy (Olympus CF240/260 series).

Results: Mean adenoma detection rate was 0.85 v 0.35/patient, with 47% v 26% having at least one adenoma (range 0–6 v 0–4) for NBI/AFI system vs standard colonoscopy, p<0.005 for patients with at least one adenoma, 2 test. Both NBI and AFI were effective in highlighting adenomas down to 2 mm in size, but image resolution was poorer with AFI which failed to detect some adenomas. NBI and magnification gives a similar appearance to contrast chromoendoscopy but in negative—that is, the pits and grooves look pale and ridges dark; we have been able to detect adenomas <1 mm and determine their Kudo pit pattern. Chromoendoscopy seems to provide a slightly clearer pit pattern and contrast for very small lesions.

Conclusion: The increased adenoma detection rate with this tri-modal system should be interpreted with caution, but is promising. NBI provides many of the advantages of chromoendoscopy without requirements of extra time and equipment, and problems with incomplete mucosal coverage. AFI is not yet consistent enough to replace standard endoscopy but may be a valuable adjunct to NBI in endoscopic assessment of polyps for neoplasia in equivocal cases.

066 COLONIC POLYP TO CANCER: AN ANIMATED STORY

G. J. M. Webster1, R. Doshi2, A. R. Ward3. 1Department of Gastroenterology, University College Hospital, UCLH NHS Foundation Trust; 2AS&K Skylight and 3Remedica, 1 New Oxford Street, London, UK

Background: Embarrassment and ignorance about colonic disease is widespread, yet this needs to be overcome if the national colorectal cancer screening programme is to be a success. Many potential patients do not understand the concept of the ‘polyp-to-cancer sequence’, and this may affect the uptake of screening. Medical textbooks/web information only demonstrate static ‘snapshots’ of the progression from benign polyp to invasive tumour, yet the process is, of course, a dynamic one. Employing state-of-the-art 3D animation and information graphics we have created a dynamic ‘life-like’ visual representation of the process of polyp and tumour development, based on current knowledge about colorectal pathology.

Description of animation: The animation lasts approx 50 seconds and begins in the colon, as if during routine colonoscopy. On advancing proximally, a small sessile polyp is identified. Over several years (spread over 14 seconds of animation), this polyp is seen to grow, become pedunculated and lose blood (this process, and the possibility of faecal occult blood detection, is described in the voice over). Over further years it enlarges and undergoes malignant change (the voice over stresses that only a small proportion of polyps become malignant). Information graphics are used to help convey some of the genetic changes that must occur for the polyp ultimately to become cancerous. The animation then follows the spread of the tumour as it moves through the bowel wall, demonstrating the Duke’s stages of tumour invasion, and including...
haematogenous tumour spread to the liver. We end by showing a snare polypectomy which completely removes the polyp during its premalignant stage.

Conclusion: We hope that this novel way of describing the dynamic nature of disease pathophysiology may be of use to both patients and doctors, and be applicable to other areas of gastroenterology teaching and practice.

Oesophageal free papers

067 SHORTESTING OF THE ABDOMINAL COMPONENT OF THE LOWER OESOPHAGEAL SPHINCTER FOLLOWING A MEAL

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Introduction: There is a high prevalence of intestinal metaplasia and inflammation of the gastric cardia in H pylori negative healthy subjects. This may represent relaxation of the distal (abdominal) portion of the lower oesophageal sphincter (LOS) and consequently, gastric juice damaging the most distal oesophageal squamous mucosa. The LOS is under most strain following a large meal.

Aim: To study the effect of a large meal on the LOS of healthy volunteers.

Method: Fifteen healthy volunteers, all H pylori negative by breath test, fasted on three separate occasions. Baseline slow motorised pull-through (SMPT) manometry was then performed, during quiet respiration, with a standard manometry system. The SMPT was repeated 5 minutes following a battered fish and chip meal. Fasted data were analysed (n=45), each subject acting as their own control. Distances quoted are means and measured from the nares.

Results: Following the meal the total length of the LOS reduced from 4.9 cm to 3.5 cm (p < 0.0001). The upper border position did not change.

- The respiratory inversion point (RIP) elevated from 44.8 cm to 44.2 cm (p < 0.0001).
- The lower border of the LOS elevated from 47.6 cm to 46.0 cm (p < 0.0001).
- The thoracic portion of the LOS reduced from 2.1 cm to 1.7 cm (p < 0.0001).
- The abdominal portion of the LOS reduced from 2.9 cm to 1.8 cm (p < 0.0001).

Conclusion: This study demonstrates shortening of the LOS after a meal due to shortening of the abdominal sphincter. There is also slight shortening of the thoracic sphincter.

Discussion: Shortening of the abdominal segment of the LOS following a large meal is likely to predispose to gastric acid reaching and damaging the squamocolumnar junction. This may explain the high prevalence of carditis and intestinal metaplasia at the squamocolumnar junction.

068 THE CLINICAL IMPACT OF PROLONGED (48 AND 96 HOUR) OESOPHAGEAL pH MONITORING BY THE BRAVO SYSTEM

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Introduction and Aims: The catheter-free Bravo system is designed to record intra-oesophageal pH over 48 hours; however the capsule remains in place for an average of 5-6 days. This provides an opportunity to examine day-to-day variability in pH recordings over an extended period, and the impact of prolonging recorded on the diagnostic yield of gastro-oesophageal reflux disease (GORD).

Method: Fifty six consecutive patients (48 (35–61) years) with reflux symptoms referred for pH monitoring were studied. 43 patients were monitored for two days and 13 patients over four days (returning after 48 hours to download pH data). The day-to-day variability of pH measurements was assessed. Patients were classified with normal or abnormal (≥4.2%/24 hours pH <4) acid exposure during each test period. The potential increase in diagnostic yield of GORD by prolonging pH recording from 24-48 and 96 hours was assessed.

Kappa (κ) values were calculated.

Results: Two-day recordings were available for 47/56 patients (incomplete (n = 8), early detachment (n = 1)). Four-day pH studies were available for 12/13 patients (day 3 detachment (n = 1)). There was no difference between acid exposure day 1-4 (8.2%, 7.8%, 7.9%, 7.3% respectively, p = 0.61); however within patient day-to-day variability was high, ±30% relative to the mean. Pathological acid exposure was present in 29/46 day 1 and 27/46 day 2 (12 patients changed diagnostic classification). Cumulative diagnostic yield increased from 29/46 (48%) day 1 to 34/46 (74%) day 2. Diagnostic reproducibility of 24 hour pH recording was fair (κ = 0.45). Within patient variability between 48 hour test periods was lower than that for 24 hour test periods (±16% v ±30% relative to the mean (p<0.01)). Only 1/12 patients changed diagnostic classification from the first to the second 48 hour test period. Diagnostic reproducibility of 48 hour pH recording was very good (κ = 0.76).

Conclusion: Increasing the duration of pH studies from 24 to 48 hours significantly improved the reliability of clinical measurement and raised the diagnostic yield of GORD by 25%. 96 hour pH studies provided little further improvement. 48 hour pH monitoring provides important advantages in the investigation of reflux symptoms in clinical practice.

069 OESOPHAGITIS IS ASSOCIATED WITH ENLARGED UNBUFFERED POSTPRANDIAL ACID POCKET

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Background: Previous work has demonstrated the presence of an unbuffered pocket of highly acidic juice at the gastric cardia after a meal in healthy volunteers.

Aims: To compare the postprandial acid pocket in healthy volunteers and patients with grade III/IV reflux oesophagitis or Barrett’s oesophagus were studied. At endoscopy radiopaque clips were placed at the proximal gastric folds and at the diaphragmatic pinch and barium meal documented the anatomy. While fasted, a pull-through study was performed using a combined dual pH and solid state manometry catheter, withdrawing at consecutive 1 cm intervals every minute. The position of the pH/manometry apparatus relative to the anatomical landmarks was obtained by identifying the radiopaque clips fluoroscopically. The patients were then fed a standardised fatty meal and 15 minutes after the meal, the pull-through study and x-rays repeated.

Results: A hiatus hernia was identified endoscopically in 13 of the reflux oesophagitis patients and its median length was not significantly altered by the meal (fasting = 1.5 cm, range 0.8 cm to 4.0 cm v postprandial = 2.2 cm, range 0.5 cm to 4.6 cm). There was a significantly longer unbuffered acidic region (pH<2) distal to the proximal margin of the gastric folds in the oesophagitis patients versus healthy volunteers (median length 2 cm, range 0 to 1.5 cm v 0 cm, range 0 cm to 4 cm; p = 0.0004). Its location in the oesophagitis patients corresponded with the hiatus hernia sac, the midpoint of which remained highly acidic (median pH 1.49, range 0.78 to 7.54) after the meal.

Conclusion: Oesophagitis is associated with an enlarged unbuffered postprandial acid pocket. This may be due to the hiatus hernia providing a reservoir of highly acidic gastric juice isolated from food in the main stomach which may reflux into the oesophagus.

070 ARE OESOPHAGEAL PERISTALTIC OR LOWER OESOPHAGEAL SPHINCTER FUNCTIONS GENETICALLY DETERMINED IN GORD? A DISCORDANT CO-TWIN CASE CONTROL STUDY

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Background: Differences in basal lower oesophageal sphincter (LOS) pressure, LOS length and peristaltic function have been described in patients with GORD. However, it is not clear whether these differences contribute to the development of GORD or are caused by GORD. We have examined peristaltic and LOS function in twin pairs who are discordant for GORD symptoms—that is, where one of the pair has GORD symptoms.

Method: Four monozygotic (MZ) and 12 dizygotic (DZ) discordant twin pairs were studied. Manometry assessed basal end-expiratory LOS pressure, total and intra-abdominal LOS length by ten 5 ml water swallows. Ineffective peristaltic function by ten 5 ml water swallows. Ineffective oesophageal motility was defined as at least 30% of contractions less than 30 mmHg or non-transmitted.

Results: MZ twins mean age 63 (range 53–75 years), DZ twins mean age 57 (44-74 years). Univariate analysis revealed no significant differences between twins with GORD symptoms and twins without GORD symptoms for LOS pressure (mean 8.2 mmHg (SD 5.7) v 9.9 mmHg (SD 7.3); p = 0.57). Total LOS length was shorter in GORD twins (median 31 cm (range 22–39 cm) v 39 cm (range 25–54 cm); p = 0.01). Only 1/11 DZ pairs had an ineffective LOS. No differences were found in peristaltic function.
Aims and Method: In this longitudinal, dynamic cohort study (study period 1 October 1984 to 31 December 2004), the aim was to establish the changing trends in the incidence and prevalence of dysplasia in patients with BO attending the General Infirmary at Leeds for endoscopy over the last two decades. Barrett’s oesophagus was defined as specialised intestinal metaplasia (SIM) on histology and dysplasia diagnosis was based on Riddell’s and Vienna criteria. Histology, endoscopy, and case notes were reviewed. Dysplasia on index endoscopy or within six months was defined as prevalent and any subsequent dysplasia as incident. For prevalent dysplasia the denominator was the number of cases of BO and number of OGDs in a year. Prevalent cases were excluded from subsequent incidence measurements and tertiary referrals were excluded.

Results: 5812 episodes of SIM were diagnosed in 2500 patients with BO. 1217 (48%) entered surveillance with a total follow up of 4434 years. 376 episodes of dysplasia were detected in 213 (8.52%) patients, with 4084 OGDs and 1010 biopsies performed. Dysplasia was prevalent in 122 (62%) and incident in 75 (38%). 14 (7%) patients had both prevalent and incident dysplasia. We identified 67 cases of dysplasia in BO (48 male). Median length of follow up was 61 months (range 1–244). After review, 13 patients were downgraded from LGD to no dysplasia (ND) and were subsequently excluded from further analysis. The dysplasia progression data are shown in the table.

**Abstract 72**

<table>
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<tr>
<th>Ddx</th>
<th>Dysplasia progression</th>
<th>Time to dysplasia progression (mean months (range))</th>
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<tr>
<td>BE/ND</td>
<td>(n = 29)</td>
<td>ND→LGD→HGD (n = 3)</td>
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<tr>
<td>BE/LGD</td>
<td>(n = 13)</td>
<td>ND→ID/LGD→AC (n = 5)</td>
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<tr>
<td>BE/HGD</td>
<td>(n = 12)</td>
<td>LGD→ID→AC (n = 3)</td>
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In patients with HGD/AC, 13 had oesophagectomy, three had endoscopic mucosal resection (EMR), and two had radiotherapy. Overall, three out of six patients with persistent HGD had AC on operative histology (50%). All cause mortality was 31.5% (24% BO cancer related deaths).

Conclusion: In our cohort of patients with LGD, 24% progressed to AC over a period of five years, emphasising the fact that this is indeed a high risk group.

**073 CANCER RISK IN BARRETT’S OESOPHAGUS: A META-ANALYSIS**

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Background: The risk of cancer in Barrett’s oesophagus (BO) is uncertain with studies showing variable annual incidence (from 1/52 to 1/450). Recent reports have suggested regional variations in cancer incidence in the west. However no formal meta-analysis has been performed.

Aims and Methods: We aimed to determine by meta-analysis the incidence of oesophageal cancer in patients undergoing surveillance for BO and to examine geographical variation. A MEDLINE, EMBASE, and PubMed search of all English articles from 1966 to 2004, using the key words “Barrett’s oesophagus”, “Oesophageal cancer”, “surveillance”, “short segment Barrett’s” (SSBO) was done. References in retrieved papers and relevant review articles were scrutinised to identify papers missed on the initial search. Studies with patients who had histological confirmation of BO on endoscopy, documented follow up data, and cancer as the outcome measure were included. Heterogeneity statistic (Q value) between studies was significant (p<0.05); hence a random effects model of meta-analysis was used. Conventional BO was defined as length of ≥3 cm.

Results: Forty two articles were included in the analysis for conventional BO and an additional seven articles were included for SSBO. The overall incidence rate for cancer was 8/1000 person-years duration of follow up (ypd) (95% CI 6 to 10). There was some geographical variation, with the incidence rate in UK being 9/1000 ypd (95% CI 4 to 17), USA 10/1000 ypd (95% CI 7 to 15), Europe 10/1000 ypd (95% CI 7 to 15), and others (Canada, Australia, New Zealand) 5/1000 ypd (95% CI 1 to 25).

Conclusion: We found less geographical variation in BO cancer risk than previously suggested between US and UK and a non-significant increase in the risk of cancer in conventional BO compared to SSBO (OR 1.6, 95% CI 0.56 to 4.91, p=0.30).

ARGON PLASMA COAGULATION FOR BARRETT’S OESOPHAGUS: LONG TERM FOLLOW UP

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Background: The long term efficacy of argon plasma coagulation (APC) for treating Barrett’s oesophagus (BO) is uncertain with concern about ‘buried glands’ on histology.

Aims and Methods: To determine the long term efficacy of APC treatment of BO. Follow up data of 50 patients entering an APC trial in 1999 followed up to August 2005 were obtained from endoscopy and pathology; all patients’ GP’s were contacted.

Results: Forty were males, mean age 68 years (range 35–85). The median FU was 38 months (range: 3–75). Median BO length prior to APC was 5 cm (range 3–12) and median length on the last follow up endoscopy was 2 cm (range 1–12). There was a significant reduction in length of Barrett’s mucosa (mean reduction 3.2 cm, 95% CI 1.7 to 3.8, p < 0.001). Although patients were instructed to remain on full dose twice daily PPI, significant reduction in PPI dose (half dose PPI: n = 13, standard dose PPI: n = 37, p < 0.001) was observed. A median of 9.2 biopsies per endoscopy was taken on the last follow up endoscopy. Of the 50 patients, 19 (38%) had a sustained endoscopic response (>90% squamous re-epithelialisation) to APC but only nine (18%) of 50 had complete histological clearance of BO at the end of follow up. The remaining patients (10/19) had either focal or multifocal buried glands on histology. No patient developed dysplasia or cancer. There was a weak but significant negative correlation between initial BO length (r = 0.3, p = 0.02) and eventual histological clearance of BO. Dose of PPI and eventual histological clearance was significantly correlated (r = 0.5, p = 0.006).

Conclusions: Sustained macroscopic clearance of BO following APC occurs in 38%. However 82% patients had histologically proven recurrence including 20% with buried glands. Initial length of Barrett’s mucosa and final dose of maintenance PPI correlate with successful outcome.


PHOTODYNAMIC THERAPY OF EARLY OESOPHAGEAL CARCINOMA

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Background: Surgical resection remains the gold standard treatment of early oesophageal cancer although with an increasingly elderly population many patients are unfit for this radical therapy and less invasive curative options are required.

Aim: To relate our experience of photodynamic therapy (PDT) in treating early oesophageal cancer.

Methods: Thirty oesophageal cancer patients (median age 74 years (range 64–90); 80% adenocarcinoma, 20% squamous) over a six year period were found to have early stage disease based on endoscopic/CT and latterly endoscopic ultrasound(EUS)/CT staging criteria. Patients were deemed medically unfit for major resectional surgery and were selected for PDT. Each patient received iv sodium porphyrin (Photofrin) at a dose of 2 mg/kg as the photosensitising agent 48 hours prior to endoscopy. Red light laser activation of the drug was initiated at endoscopy using a 630 nm fibre delivering a light dose of 300 J/cm. All patients had follow up endoscopy at 6–12 week intervals indefinitely. Routine biopsies of the treated area were obtained. Median follow up was 30 months (range 2–56).

Results: Overall 20/30 patients had an initial complete endoscopic and histological response to therapy at weeks 8 post procedure. Of these 20 patients, 12 developed local recurrence and had further PDT with a median survival of 9/22 days (range: 1–92) and 2/12 cancer related deaths. Eight of 20 patients who had initial complete response remain disease free at follow up of 32.5 months (9–55). Only the latter 14 patients referred for PDT with suspected early cancer had EUS staging. Nine patients had early cancer T1 (n = 8), Tis (n = 1) and all currently disease free at a follow up of 1103 days (249–2039) although 5/9 required one further course of PDT. Five of 14 patients had T2 or 3 disease confirmed by EUS and all these patients have had recurrent disease post PDT. The major complication of PDT in this study was oesophageal strictureting which occurred in 50% of cases. These strictures have required a median of five dilatations (1–31).

Conclusion: PDT is an alternative potentially curative treatment in EUS confirmed early oesophageal carcinoma.

REACTIVE OXYGEN SPECIES INDUCED DNA DAMAGE IN OESOPHAGEAL ADENOCARCINOMA

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Introduction: Oesophageal adenocarcinoma develops in a step-like fashion from Barrett’s oesophagus (BO) through low and high grade dysplasia. Luminal components such as acid and bile salts are thought to contribute to the neoplastic progression. For example, pepsin acid and bile exposure can alter proliferation and differentiation status in ex vivo adenocarcinoma cell lines BIC, SEG, and FLO and Barrett’s (DSBs).

Conclusions: Discriminatory DNA damage in the unaffected hemisphere of stroke patients which is associated with a 30% reduction in short term aspiration.

Aims: To assess the longer term dose response effects of electrical pharyngeal stimulation in dysphagia post stroke.

Methods: Patients admitted with a clinical diagnosis of acute anterior circulation stroke were screened with a standardised videofluoroscopic swallowing assessment. Dysphagic patients were randomised by minimisation to one of four treatment groups or to a control group with age and stroke severity the controlled factors. The four treatment groups received 10 minutes of stimulation daily or three times a day and for three or five days. The control group received no intervention. Change in aspiration severity at the follow up videofluoroscopy at two weeks was then determined.

Results: Of 61 patients who underwent the baseline videofluoroscopy, 22 were found to be dysphagic and completed the study. Fifteen were male with a mean age of 73 (SD 11) years. Six were allocated to the control group with four in each active arm. Group data showed reduced aspiration following daily stimulation (~17% p < 0.02) (fig 1) and three days of stimulation (~12% p < 0.04) (fig 2) compared to controls (~13%).

Conclusion: A dose response treatment of pharyngeal stimulation is effective in dysphagia post stroke.
Other patient groups (inflammatory bowel disease with dyspeptic controls developed week symptoms (mainly pressure, acid regurgitation, etc.).

**Results:** Perception scores and p values are given in the table. Healthy controls were given a scale ranging from 1 to 10, with 1 indicating no symptoms and 10 indicating severe symptoms. The final perception score was calculated as the difference between baseline and post-test perception scores. Data are given as mean (SD), a p value indicating statistical significance.

**Aim:** To determine differences in selective ANS responses for visceral and somatic pain matched for intensity and temporal characteristics. Methods: In 19 healthy adults, SCR, BV, and heart rate (HR) were measured at baseline and in response to oesophageal balloon distension and thermal cutaneous stimuli at pain intensity. Stimuli for each modality were delivered in two runs on balanced order. Phasic SCR latency and rise time (powerlaw), and 1 minute HR and BV blocks (MMedit) were processed offline and aligned with paired student t tests.

**Results:** HR was increased from baseline (mean 69.7±3.2) by 0.05% (p=0.045) and visceral pain (72.7±2.3) by 0.006. There was greater increase in HR by visceral than somatic pain (p=0.017). BV withdrawal from baseline (6.6±0.32) was greater for somatic (6.35±0.29) than visceral pain (6.6±0.27, p=0.007). SCR latency was shorter for visceral (4.5±0.4 seconds) than somatic pain (6.77±0.59, p=0.0002) as was SCR rise time (visceral 8.41±0.67; somatic 11.08±0.77 seconds, p=0.005).

**Conclusion:** In comparison to somatic pain, the larger HR response to visceral pain was mediated by greater sympathetic activation despite lesser central cardiac parasympathetic withdrawal. These differential ANS responses for visceral pain may reflect its greater unpleasantness compared to somatic pain of the same intensity. Selective ANS measures hold promise both for understanding mechanisms and as markers of differences in pain response.

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**079 DIFFERENTIAL SELECTIVE AUTONOMIC RESPONSES IN VISCERAL AND SOMATIC PAIN**

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**Background:** Differences between visceral and somatic pain perception have been explored with brain imaging, however, little attention has been given to differences in autonomic nervous system (ANS) responses such as skin conductance response (SCR) and heart rate variability band variance (BV). These are selective non-invasive central sudomotor sympathetic and cardiac parasympathetic measures respectively.

**Aim:** To determine differences in selective ANS responses for visceral and somatic pain matched for intensity and temporal characteristics. Methods: In 19 healthy adults (eight male) SCR, BV, and heart rate (HR) were measured at baseline and in response to oesophageal balloon distension and thermal cutaneous stimuli at pain intensity. Stimuli for each modality were delivered in two runs on balanced order. Phasic SCR latency and rise time (powerlaw), and 1 minute HR and BV blocks (MMedit) were processed offline and aligned with paired student t tests.

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**Conclusion:** In comparison to somatic pain, the larger HR response to visceral pain was mediated by greater sympathetic activation despite lesser central cardiac parasympathetic withdrawal. These differential ANS responses for visceral pain may reflect its greater unpleasantness compared to somatic pain of the same intensity. Selective ANS measures hold promise both for understanding mechanisms and as markers of differences in pain response.

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**078 HYPERSENSITIVITY AGAINST INTRAgastric CAPSAICIN IN PATIENTS WITH NON-ULCER DYSPESIA**

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**Background:** We have recently demonstrated that chemical stimuli in the small intestine induce sensations comparable to mechanical distension and that chemical hypersensitivity against capsaicin might exist in the pathophysiology of non-ulcer dyspepsia (NUD).

**Aim:** To develop a non-invasive test for the diagnosis of gastric capsaicin sensitivity and to evaluate whether chemical hypersensitivity is involved in the pathophysiology of non-ulcer dyspepsia (NUD).

**Methods:** Twenty healthy controls and 64 outpatients ingested a capsule containing 75 mg capsaicin after an overnight fast. Before and 30 minutes after ingesting the capsule, the severity of nine upper abdominal symptoms, were quantified by a graded questionnaire; an aggregate perception score was calculated by adding all symptom scores. The final perception score was calculated as the difference between pre- and post-test aggregate perception score. Data are given as mean (SD), a p value<0.05 was considered significant.

**Results:** Perception scores and p values are given in the table. Healthy controls developed week symptoms (mainly pressure, acid regurgitation, warmth), scores up to nine comprised 75% of the healthy volunteers and was considered as normal range. N=14 (53.8%) of NUD patients were within the normal range, while n=18 (56.3%) were above that limit. Other patient groups (inflammatory bowel disease with dyspeptic symptoms but no gastric involvement, peptic ulcer, other diseases) had an aggregate perception score comparable to controls, but significantly less than NUD patients.

**Conclusion:** Patients with NUD are hypersensitive against gastric capsaicin. The intragastric capsaicin test is a non-invasive method to detect a subgroup of NUD patients with chemical hypersensitivity. The capsaicin receptor VR-1 is involved in the pathophysiology of more than 55% of NUD patients.

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**080 GUT RESPONSE TO STRESS CAN BE PHARMACOLOGICALLY MODULATED: AMITRIPTYLINE MODIFIES VISCERAL HYPERSENSITIVITY IN IRRITABLE BOWEL SYNDROME**

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**Introduction:** Acute physical stress causes a measurable acute alteration of gut autonomic function and visceral hypersensitivity in patients with irritable bowel syndrome (IBS) (Murray et al. 2004). Low doses of amitriptyline are effective in controlling 50% of IBS patients, through mechanisms that are unclear. We present the first report of the effects of amitriptyline on the gut neural response to acute stress.

**Methods:** Nineteen patients with constipation-predominant IBS (16 female, mean age 32, range 19–58) were given amitriptyline 25–50 mg at night. Patients underwent stress assessment at baseline and after three months of treatment. Stress assessment comprised a physical (cold pressor) and psychological (dichotomous listening) stress given in random order at least one day (median 1, range 1–4 days) apart. Physiological parameters measured included: perception of stress (visual analogue scale); systemic autonomic tone (heart rate and blood pressure); gut specific autonomic innervation (laser Doppler flowmetry of rectal mucosal blood flow (RMBF)); and visceral sensitivity (rectal pressure). 13 patients underwent barostat assessment of rectal sensitivity.

**Results:** Fourteen of 19 (74%) patients were symptomatically improved after three months of amitriptyline (median dose 25 mg). Acute stress resulted in increased perception of stress and systemic autonomic tone, and reduced RMBF, which was similar in responders and non-responders (p=0.05 for all). In contrast, all non-responders and only three out of 14 of responders, continued to exhibit stress-induced reduced pain threshold at three months (change from baseline −31% v
Pregabalin, a Second Generation α2,δ Ligand Reduces Hypersensitivity to Rectal Distension in Patients with Irritable Bowel Syndrome

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Background: Visceral hypersensitivity is an important pathophysiologic factor in irritable bowel syndrome (IBS). Preclinical data indicate that pregabalin reduces trinitrobenzene sulfonic acid (TNBS)-induced hypersensitivity but not basal sensitivity to colonic distension.

Aim: To assess the effect of pregabalin on the perception of rectal distension in hypersensitive IBS patients.

Methods: Twenty-six rectally hypersensitive Rome II IBS patients (aged 18–46 years, 7 male) were included in a randomised, double-blind, placebo controlled, parallel group study in which they received either three weeks oral pregabalin (titrated: 50 mg tid days 1–3, 100 mg tid days 4–7, 150 mg tid days 8–11; fixed: 200 mg tid days 12–21) or placebo control. Rectal sensitivity was assessed using a barostat technique, in which sensory thresholds were determined using the ascending methods of limits followed by tracking, both prior to treatment (baseline) and on day 21 ± 4 of treatment. Rectal hypersensitivity at baseline was defined as a pain threshold of <28 mmHg.

Results: Pregabalin significantly increased the sensory thresholds from baseline for first sensation (median difference from placebo: 95% CI): 2.0 mmHg (0 to 4.0 mmHg; p = 0.045), stool (6.0 mmHg (2.0 to 10.0 mmHg; p = 0.008), and pain (5.4 mmHg (0.12 to 11.25 mmHg; p = 0.048) compared with placebo. Baseline sensory thresholds were comparable between treatment groups. An emx model provided the best fit to the compliance data. Pregabalin significantly increased rectal compliance (slope of the volume pressure curve was 1.96 steeper than placebo (95% CI: 1.50 to 2.41; p < 0.0001).

Conclusions: Pregabalin increases the pain threshold to distension in IBS patients with rectal hypersensitivity. This may result from an increase in rectal compliance. These data suggest that α2,δ ligands might prove useful in the treatment of the visceral pain disorders, such as IBS.

Conclusion: COX-2 expression was demonstrated in the majority of colonic adenomas. Localisation of this was mainly in stromal cells. The stromal microenvironment of colonic adenomas and its interface with neoplastic epithelium may be important in cellular transformation towards malignancy, and warrants further investigation.

**085** MITOCHONDRIAL DNA (MTDNA) MUTATIONS IN HUMAN COLONIC CRYPTS: A NOVEL BIOMARKER OF COLORECTAL CANCER

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Background: There is considerable interest in the quest for a reliable “biomarker” of colorectal cancer (CRC). Mitochondrial DNA (mtDNA) mutations have been suggested to play a role in ageing and given that CRC occurs more commonly as we age there may be an association. Furthermore, mtDNA mutations have been shown to accumulate within colonic crypt stem cells to levels that result in respiratory chain deficiency. The presence of mtDNA mutations within colonic crypt stem cells suggests that these mutations are present before the development of colorectal cancer, thus it is not unreasonable to suggest that mtDNA mutations may prove to be a putative biomarker of risk of CRC.

Aim: To characterise mtDNA mutational load in colonic crypts of patients with macroscopically normal colorectal mucosa.

Methods: Fresh frozen colonic tissue from 21 patients (8 males) with macroscopically normal colorectal mucosa were analysed histologically and histochemically. Standard H&E histology was performed as well as COX histochemistry to determine respiratory deficiency within crypts. 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.

<table>
<thead>
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<th>Table 1: % of COX deficient crypts</th>
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<tr>
<td>Mean age = 54 years (range 29-71)</td>
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<td>Total (n = 21)</td>
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<td>Mean (SD) % of COX deficient crypts</td>
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Results: See table. These are results from the initial pilot study. COX deficiency was identified in colonic crypts of patients with macroscopically normal colorectal mucosa. The mitochondrial mutational load was significantly higher in those over 50 years of age (Wilcoxon signed ranks; p = 0.016), compared to those under 50 years. These findings lend further support to the hypothesis that mtDNA mutational rate increases with age. Given that CRC occurs more commonly as we age there could be an association.

Conclusions: We have shown that COX deficient colonic crypts have been identified in the macroscopically normal colon. Hence, mtDNA mutations may prove to be a useful putative biomarker of CRC risk especially in those over 50 years. Further studies on the influence of dietary intake on mtDNA mutational load are ongoing.

**086** EVALUATION OF AUTOFLUORESCENCE COLONOSCOPY FOR THE DETECTION AND DIAGNOSIS OF COLONIC POLyps

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Background: Autofluorescence (AF) has been developed to enhance conventional white light (WL) endoscopy in the diagnosis of neoplastic lesions of the GI tract. It is based on the stimulation of endogenous fluorophores and produces a pseudo-colour image of tissue. Metaplastic polyps are common and do not need to be treated, whereas adenomatous polyps carry a neoplastic potential. It would therefore be helpful to be able to distinguish between adenomatous polyps and metaplastic polyps when performing colonoscopy.

Aim: To evaluate AF for the endoscopic detection and differentiation of colorectal polyps.

Methods: Patients were invited to attend for colonic assessment with both AF and WL colonoscopy. The intensity of autofluorescence (AI) is quantified automatically and readings, pictures, and biopsies were recorded of any visible pathology or areas of high AF. The biopsy results were analysed and an AI reading for each biopsy site obtained by subtracting the actual AI reading from the background reading for the rectum of each patient.

Results: A total of 47 patients were assessed with AF and WL colonoscopy. A total of 33 polyps were detected (19 adenomatous and 14 metaplastic polyps). We found that adenomatous polyps had higher AI readings (median 0.53, IQR 0.15–1.05), than metaplastic polyps (median 0.09, IQR 0.06–0.10) (Mann-Whitney U test: p = 0.00003).

Conclusion: These early data suggest that autofluorescence colonoscopy has the potential to differentiate between metaplastic and adenomatous polyps and may have a role as a new diagnostic technique for the improved detection of colonic dysplasia and early malignancy.

**Plenary session**

**087** ALPHA-FETO PROTEIN SPECIFIC CD4+ T CELL RESPONSES ARE UNMASKED DURING TRANSARTERIAL EMBOLISATION IN HEPATOCELLULAR CARCINOMA

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Background: Tumours regulate immune responses and may mask anti-tumour immunity. We hypothesised that necrosis produced by transarterial embolisation (TAE) of HCC may induce and/or expand pre-existing T cell responses to tumour rejection antigens such as AFP. We have recently reported the presence of AFP14, 34, 373 reactive CD4+ T cells in HCC patients (Clin Can Res 2005). Here we aimed to identify population of CD4+ T cells unmasked by TAE and characterise further epitopes which could be targeted in an AFP based vaccine against HCC.

Methods: In the peripheral blood of 31 untreated HCC patients and 24 controls (chronic liver disease, liver metastases, normal), AFP specific CD4+ T cell responses to a panel of 59 AFP derived peptides were analysed using intracellular cytokine assays for IFN-γ, IL-2, and IL-5. Blocking HLA antibodies were used to determine the presenting MHC class II molecules. Six patients were recruited from a randomised trial of TAE versus chemoembolisation (TACE) and the presence of AFP reactive CD4+ T cell responses analysed longitudinally for six months.

Results: Two novel AFP derived CD4+ T cell epitopes, AFP29 and AFP14, were identified that were recognised by circulating lymphocytes in association with HLA-DR. Of the 31 untreated HCC patients had CD4+ T responses to AFP14, 34, 373, one to AFP 32, and none to AFP 94. There were no detectable responses in the controls. In all treated patients, AFP-reactive CD4+ T cells were expanded in vivo during therapy and then declined in frequency. Preliminary data point to an association between clinical responses (as assessed by CT criteria) and high frequencies of AFP specific CD4+ T cells.

Conclusion: Necrosis produced by TACE/TAE unmask AFP specific CD4+ T cell responses and provides a potential window for successful immunotherapy. We have identified novel AFP derived CD4+ T cell epitopes which could be targeted in an AFP based vaccine against HCC.

**088** REAL-TIME IMAGING AND FUNCTIONAL ANALYSIS OF HUMAN COLONIC CRYPT RENEWAL EX VIVO

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Background: Following on from classical animal studies and work on adenocarcinoma cell lines, recent gene targeted and transgenic mice studies have provided profound insights into the molecular determinants of epithelial renewal in the intestine. Despite, and because of, this progress, there is an increasing call for a complementary in vitro model of the intact human colonic epithelium.

Aims: To apply bio-imaging and functional genomic approaches to the study of intestinal tissue renewal in cultured human colonic crypts.

Methods: Colonic crypts were isolated from tissue biopsies obtained at sigmoidoscopy from healthy subjects (ethical approval). Isolated crypts
were attached to collagen coated coverslips and cultured for 24 hours–7 days in serum-free DMEM (5%CO2/37°C). Expression constructs and siRNA oligonucleotide duplexes were introduced to cells by low voltage electroporation. Gross morphology was monitored in real-time by digital video time lapse microscopy (24–48 hours). For immunofluorescence studies cultured crypts were fixed in 4% paraformaldehyde and specific protein expression probed for by a primary antibody and visualised using a FITC conjugated secondary antibody in conjunction with confocal microscopy. A range of markers for cell proliferation (for example, BrDU incorporation for example, BrDU incorporation and Ki67), and viability (for example, propidium iodide) were employed. Cell migration was assessed by monitoring Hoechst 33342 or α-tubulin-GFP labelled cells. Intracellular calcium signalling was monitored in FITC loaded crypts.

**Results:** Colonic crypts maintained their gross morphological flask-like appearance bounded by a distinctive lumen for at least seven days in culture. Expression of basolateral membrane transporters (for example, NKCC1) and membrane receptors (for example, M3ACHR) continued throughout the culture period as did the topological gradient of expression along the crypt axis. Accordingly, the colonic crypt calcium wave signature induced by acetylcholine maintained its site of initiation at the base and unidirectional propagation along the crypt axis. The proliferative zone was maintained at the crypt base (Ki67 positive). Actinomycin Dogenetic signals were confirmed by the presence of nuclear β-catenin in cells located at the crypt base; all other cells exhibited membranous β-catenin labelling. BrDU labelled cells migrated to the upper crypt (Ki67 negative) over the course of 48 hours. Tracking of Hoechst 33342 and GFP labelled cells revealed a migration rate of approximately 10–15 μm/hour. Cells were shed at crypt mouth and were positive for propidium iodide, whereas cells located elsewhere in the crypt excluded propidium iodide. Cell viability was compromised in lower crypt compartments by siRNA knockdown of β-catenin.

**Conclusions:** Isolated human colonic crypts are amenable to real-time imaging and can be used as a model for studies of colonic epithelial function. We have demonstrated that many of the cellular processes associated with rapid renewal of the colonic epithelium are recapitulated ex vivo.

### **Gastrointestinal physiology associates group**

#### **089 IMPROVING THE EXPERIENCE OF PATIENTS HAVING AN ENDOSCOPY WITH THE ENDOSCOPY GLOBAL RATING SCALE**

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The endoscopy Global Rating Scale (GRS) is a web based instrument designed to help endoscopy units deliver a patient focused service and assess how well they are doing. The GRS includes 12 items that reflect the experience of a patient having an endoscopy. The items are ranked into four levels: D to A. Level D is very basic and A is excellent. All endoscopy units in England were invited to complete the GRS on two census dates: April and October 2005. Of registered units 80% completed scores in April and 66% in October (to date). The results are presented as the percentage of A and B scores for each of the items. The very high completion rates of the GRS indicate that the service finds the GRS acceptable and useful. All items showed an increase in the percentage of A and B scores between the two census dates. These changes reflect real improvements in the processes that underpin the experience of a patient having an endoscopy and/or the ability of the service to demonstrate that it provides high quality care. These data show that the GRS is an effective service improvement tool.

#### **090 ASPIRIN FOR THE PREVENTION OF RECURRENT COLORECTAL ADENOMAS: RESULTS OF THE UKCAP TRIAL**

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**Background:** Many observational studies have found regular aspirin use is associated with a reduced risk of colorectal (CR) cancer and two randomised trials have shown that aspirin reduces risk of recurrent CR adenomas, although results were not wholly consistent. We report the preliminary aspirin results of a large factorial trial of aspirin (enteric 300 mg/day) and folate supplements in patients under surveillance for recurrent CR adenomas.

**Methods:** A double blind, placebo controlled randomised trial was carried out in 10 centres (nine in the UK and one in Denmark). Patients who had one or more adenomas (>0.5 cm) removed in the six months before enrolment were randomised to receive either aspirin (enteric 300 mg/day) or placebo. All participants were followed up at intervals of four months to assess compliance, with a second colonoscopy arranged for three years after the date of trial entry. The primary outcome measure was a histologically confirmed CR adenoma or cancer either at the end examination or during the course of the trial.

**Results:** 945 patients were recruited into the study, of which 853 (434 receiving aspirin and 419 placebo) underwent a second colonoscopy and were included in an intention to treat analysis. Full compliance with trial medication was reported by 700 patients. In total, 101 (23.3%) patients receiving aspirin had a recurrent adenoma compared with 120 (28.6%) patients who received placebo (relative risk = 0.81; 95% CI 0.65 to 1.02). 103 advanced CR adenomas were observed (on the basis of villous/tubulovillous features, size >1 cm or evidence of severe dysplasia or cancer); 39 (9.0%) of these were in the aspirin group and 64 (15.3%) in the placebo group (RR = 0.59; 95% CI 0.40 to 0.86), 11 CR cancers were included among these (3 aspirin and 8 placebo).

**Conclusion:** Aspirin use (300 mg/day) resulted in a 19% reduction in risk of any colorectal adenoma recurrence and a marked, statistically significant, 41% reduction in risk of advanced adenoma development.
ACETYLCOLINE STIMULATION OF THE NKCC1 TRANSPORTER IS CALCIUM DEPENDENT AND IS RAPIDLY DESENSITISED BY ENDOCYTOSIS: IMPLICATIONS FOR INTESTINAL FLUID SECRETION

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Background: Intestinal fluid secretion is driven by transcellular active transport of chloride. NKCC1 mediates basolateral uptake of chloride and is emerging as a master controller of intestinal fluid secretion. Although it has long been established that acetylcholine (ACh) stimulates transient intestinal fluid secretion, the regulation of NKCC1 activation and its role in governing the nature of this response has not been investigated in the intact human colonic epithelium.

Aim: To characterise NKCC1 expression along the human colonic crypt axis and study its activation by propagating cholinergic calcium signals. Methods: Colonic crypts were isolated from tissue biopsies obtained at sigmoidoscopy from healthy subjects (ethical approval). Isolated crypts were attached to collagen-coated coverslips and cultured for 24 hours–7 days in serum-free DMEM (5%CO₂/37°C). Total NKCC1 expression was assessed in 48 h by probing for a panel of polyclonal antibodies. Labelling was visualised using a FITC conjugated secondary antibody in conjunction with confocal microscopy and semi-quantitative image analysis. Results: Phospho-NKCC1 was detected using a specific polyclonal antibody raised against a diphosphopeptide containing Thr171 and Thr172. For calcium imaging experiments colonic crypts were loaded with the calcium sensitive dye Fluo-3 AM. Results: NKCC1 exhibited an expression gradient along the crypt axis; labelling was basolateral and predominated at the crypt base. The secretagogue acetylcholine (ACh) initiated calcium signals at the human colonic crypt base, which propagated in a unidirectional fashion along the entire crypt axis. Calcium responses were greater at the crypt base and progressively diminished towards the crypt mouth (n=30, p<0.01). Calcium signal intensity and degree of propagation along the crypt axis was concentration dependent (EC₅₀ = 1-10 μM; n=20, p<0.01). ACh stimulated phospho-NKCC1 labelling exhibited a similar concentration dependency to the calcium response. TMB-8 (100 μM), an inhibitor of intracellular calcium mobilisation, abolished ACh stimulated calcium signals and NKCC1 phosphorylation. Phospho-NKCC1 levels peaked at 3 minutes post-stimulation and diminished in the continued presence of ACh (10 μM). After prolonged exposure (15 minutes) NKCC1 membrane labelling diminished and NKCC1 levels accumulated in cytosolic vesicles juxtaposed to the luminal apical pole. Conclusions: A striking spatial correlation exists between ACh induced colonic crypt calcium signals, and calcium dependent NKCC1 activation. These observations suggest that propagating cholinergic calcium signals coordinate fluid secretion along the human colonic crypt axis and that NKCC1 endocytosis may be an important mechanism in downregulating the secretory response. This work was supported by the BBSRC.

GASTRODUODENAL FREE PAPERS

PREDICTING CLINICAL OUTCOME IN UPPER GASTROINTESTINAL BLEEDING COMPLICATING LOW DOSE ASPIRIN AND ANTI-TROMBOTHRYTIC THERAPY

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Background and Aims: Current risk stratification systems have not specifically corrected for the intake of low dose aspirin and other anti-thrombotic drugs. As the incidence of upper gastrointestinal bleeding (UGIB) related to these agents has been increasing, we aimed at testing the Blatchford scoring system in predicting the clinical outcome in bleeders using these drugs.

Methods: The Blatchford scores cover risk factors and associated components measured on admission (Lancer 2000;356:1318–21). These include blood urea, haemoglobin, systolic blood pressure, pulse, melena, syncope, hepatic disease, and cardiac failure. We assessed the validity of this system to predict the clinical outcome of UGIB in 529 patients attending a single centre, including 129 on low dose aspirin, 46 on other anti-thrombotic drugs, and 68 on NSAIDs.

Results: The median scores were as follows: no risk factors, 5; NSAIDs, 8; aspirin, 7; other anti-thrombotics, 6; excess alcohol, 4; multiple risk factors, 7; (p=0.003, Kruskal-Wallis). Scores in all groups except excess alcohol users were elevated relative to those with no risk factors (p<0.05). Scores correlated positively with the duration of admission in the entire study group (r²=0.267, p<0.001) and in those taking aspirin and other anti-thrombotics (r²=0.189, p=0.017). The median scores in patients requiring blood transfusion were 10 in the entire study group and 10 in users of aspirin or anti-thrombotic drugs, compared with 3 and 4 respectively in those not transfused (p<0.001).

Conclusions: The Blatchford scores, derived from admission data, are significantly elevated in users of NSAIDs, low dose aspirin, and other anti-thrombotic drugs. They also correlate positively with the duration of admission, and can predict the need for transfusion in such patients.

HELICOBACTER PYLORI INFECTION CONFRNS AN INCREASE IN 10 YEAR MORTALITY FROM ALL CAUSES: DATA FROM A COMMUNITY SCREENING PROGRAMME

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Introduction: Population screening and treatment of Helicobacter pylori has been advocated to reduce mortality from gastric cancer. Screening programmes have been conducted in the West, but follow up was at two years. We therefore long term mortality data are not available. Methods: This was a 10 year follow up study of individuals currently aged 50–59 years, previously recruited into a screening and treatment programme for H pylori. Those testing positive were randomised to receive either eradication therapy, or placebo. All those involved were traced with a list cleaning service provided by the Office for National Statistics, and death certificates were obtained for deceased individuals.

Results: Of 8407 original participants, 140 (1.7%) were dead at 10 years. 92 (66%) were male. 64 (46%) deaths were due to cancer, and 31 (22%) to ischaemic heart disease (IHD). Mortality from all causes of IHD were significantly increased in H pylori positives compared to negatives (add odds ratios (OR) 1.65, 95% CI 1.15 to 2.36 and 2.46, 95% CI 1.13 to 5.32 respectively) but there was no difference in cancer mortality (OR 1.37, 95% CI 0.78 to 2.36) following logistic regression controlling for age at study entry, gender, tobacco and alcohol consumption, and social class, all-cause mortality remained significantly higher in H pylori positives (OR 1.46, 95% CI 1.02 to 2.09). There was a trend towards higher all-cause mortality and mortality from IHD in those receiving eradication therapy at 10 years compared to placebo (relative risks 1.46, 95% CI 0.85 to 2.49 and 2.0, 95% CI 0.69 to 5.84 respectively), though neither were statistically significant.

Conclusions: Infection with H pylori is associated with an increased mortality from all causes, even when possible confounding factors are controlled for. However, screening and treatment of positive individuals may confer an increased risk of death from IHD, which should be borne in mind when recommending the adoption of such a strategy.

INNATE IMMUNE RESPONSE GENRE POLYMORPHISMS AND THEIR ROLE IN H PYLORI INDUCED PRECANCEROSO CHANGES

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Background: The innate immune system plays a crucial role in the initial handling of H pylori infection. Toll-like receptors (TLRs) are important members of this system and at least five TLRs (TLR2, 4, 5, 9, and 11) are involved in recognising bacterially derived pathogen associated molecular patterns. Most of these genes have functionally relevant polymorphisms but apart from TLR5 these polymorphisms have not been associated with gastric cancer. Toll-like receptor 4 (TLR4) is involved in recognising bacterial lipopolysaccharide and LPS. TLR5 polymorphism (TLR5 Stop) affects the activity of TLR5 which is involved in recognising flagellin. TLR9 polymorphism (TLR9 1237 C/T) is involved in recognising DNA molecules. Polymorphisms in the TLR4, TLR5, TLR9 and TLR9 polymorphisms are associated with gastric cancer risk.

Aim: We examined whether SNPs in TLR2 (TLR2 Arg753Gln), TLR5 (TLR5 Stop), TLR9 (TLR9 1237 C/T), and CD14 (CD14 159 C/T) influenced the risk of developing gastric atrophy and hypochlorhydria (ATR/HC), the most important precursors of gastric cancer.

Subjects and Methods: We used PCR-RFLP and 5' nuclease assays to genotype the four SNPs in 170 healthy gastric cancer relatives (GCR) and 100 population controls.
**Results:** There was a significant association between carriage of TLR9-1237G/A and CD14-159C/T SNPs and presence of hypochlorhydria and gastric atrophy. Compared to infected subjects who did not develop H. pylori, the odds ratio for H. pylori induced H. pylori and H. pylori in subjects with the TLR9-1237G/A was 3.9 (95% CI 1.7 to 8.6) and CD14-159 C/T was 3.8 (95% CI 1.4 to 9.8). Although the functional consequences of the TLR9 promoter polymorphism are unknown, in silico analysis indicates disruption of an NF-kB binding site. In contrast, the functional CD14 polymorphism affects binding of the GC box and also S5 proteins.

**Conclusions:** Our results indicate that carriage of the TLR9-1237G/A and CD14-159 C/T polymorphisms predispose H. pylori infected subjects to a severe phenotype characterised by hypochlorhydria and gastric atrophy. These findings call for further evaluation of innate immune gene polymorphisms in the context of H. pylori induced gastric cancer.

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**GASTRIN INCREASES MCL-1 EXPRESSION IN AGS, GASTRIC EPITHELIAL CELLS TO CAUSE SUPPRESSION OF APOPTOSIS**

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**Introduction:** The gastric antral hormone gastrin acts as a cofactor during gastric carcinogenesis and has been shown to regulate important cellular processes in the stomach including proliferation, migration, and differentiation. In addition, several previous studies have shown that gastrin inhibits apoptosis. The mechanisms responsible for the anti-apoptotic action of gastrin are currently not fully understood.

**Methods:** AGS cells, a human gastric carcinoma cell line stably transfected with the CCK-2 receptor were used. The expression of genes involved in the regulation of apoptosis was investigated by pathway specific cDNA microarray following treatment with 10 mM gastrin for six hours. Abundance and subcellular location of mcl-1 protein was subsequently assessed by Western blotting and immunofluorescence. Various inhibitors were used to investigate relevant downstream signalling pathways. The functional consequences of mcl-1 upon apoptosis were investigated using mcl-1 siRNA.

**Results:** Treatment of AGS cells with 10 nM gastrin for six hours resulted in increased expression of mcl-1 transcripts by cDNA microarray and increased protein abundance was confirmed by western blot analysis. Immunofluorescence showed increased cytoplasmic accumulation of mcl-1 following gastrin treatment. Increased mcl-1 abundance was inhibited by a transcription inhibitor actinomycin D and by a protein synthesis inhibitor cycloheximide. Downstream signalling occurred via the CCK-2 receptor, protein kinase C, and MAP kinase pathways, but not via PI3 kinase. Transfection with mcl-1 siRNA for 90% suppression of mcl-1 protein abundance and accumulation of mcl-1 following gastrin treatment. Increased mcl-1 abundance was confirmed by western blotting and immunofluorescence. Various inhibitors were used to investigate relevant downstream signalling pathways. The functional consequences of mcl-1 upon apoptosis were investigated using mcl-1 siRNA.

**Conclusions:** Gastrin signals via the CCK-2 receptor, PKC, and MAP kinase to induce expression of the anti-apoptotic protein mcl-1. Mcl-1 prevents induction of apoptosis following addition of gastrin. This demonstrates a novel pathway by which gastrin suppresses gastric epithelial apoptosis.

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**THE MAGNITUDE OF VISCERO-VERBAL AND VISCEROSENSOMATIC SENSITISATION INDUCED BY INTRADUODENAL CAPSAICIN INFUSION IS DOSE DEPENDENT**

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**Background:** Capsaicin activates TRPV-1 receptors on spiral and vagal afferents and its infusion into the jejunum evokes burning and cramping sensations, the intensity of which is dose dependent. In this study we wished to determine if capsaicin infusion into the proximal duodenum would result in increased excitability of spiral dorsal horn neurones and the development of sensitisation of convergent visceral and somatic structures.

**Methods:** We recruited 16 subjects (12 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 (ADR) on the abdominal wall and control region (Foot). Capsaicin was then infused into the duodenum (2 ml/min for 30 minutes). The concentrations of capsaicin used were 100 and 200 µg/ml with a saline control. Subjects were studied on four occasions (1×100 µg/ml, 2×200 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 five minute intervals during the infusion and a short McGill pain questionnaire was used.

**Results:** Significant and reproducible reductions in oesophageal PT were seen on both occasions at 200 µg/ml (9.2 mA and -11 mA, p=0.04) but this was not significant at 100 µg/ml (-6.3 mA, p=0.06) or with saline (-0.7 mA, p=0.77). Significant reductions in AOR PT were seen on both occasions at 200 µg/ml (-4.9 mA and -4 mA, p=0.004) and 100 µg/ml (-2.7 mA, p=0.001) but not with saline (0.7 mA ± 12, p=0.77). No differences were seen in foot PT. VAS scores for pain were higher that for the other psychophysical measures and highest at the 200 µg/ml concentration. The most common verbal descriptors used to describe the capsaicin infusion were cramping, hot burning, and aching.

**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. The magnitude of sensitisation increases with increasing concentrations of capsaicin as does the subjective awareness of the infusion. These data provide further evidence that central sensitisation plays an important role in the development of visceral hypersensitivity.

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**Inflammatory bowel disease section symposium**

**FULLY HUMAN ANTI-TNF ADALIMUMAB MAINTAINS REMISSION FOR ONE YEAR IN PATIENTS WITH ACTIVE CROHN’S DISEASE: A RANDOMISED, CONTROLLED COHORT**


**Aim:** To assess the efficacy and safety of adalimumab (ADA) in maintaining remission in patients with CD.

**Methods:** All patients completing CLASSIC I, a four week, randomised controlled trial of ADA in patients with moderately to severely active CD, were eligible to receive ADA 40 mg sc at weeks 0 and 2 of CLASSIC II. Patients in remission (CDAI < 150) at weeks 0 and 4 of CLASSIC II were randomised to receive ADA 40 mg every other week (eow) or 40 mg/week, or placebo (PBO) for up to one year. Patients with CDAI > 150 entered an open label adalimumab cohort (results reported separately). CDAI and adverse events (AE) were assessed at each visit. Results: Of 55 eligible patients randomised, 44 completed one year (33 randomised and 11 OL). ADA treated patients stayed in remission over time (table). Overall, AEs were mild to moderate in severity. Serious AEs occurred in two patients with PBO and one patient with ADA 40 mg eow therapy. Conclusions: In this exploratory cohort, remission was maintained in patients treated for up to one year with adalimumab. Adalimumab was well tolerated. A definitive study powered to assess long term adalimumab efficacy is ongoing.
Mesorolamine (5-ASA), but not hydrocortisone, inhibits E. coli induced IL-8 release from colonic epithelial cells at therapeutic concentrations

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Background and Aims: Inflammatory bowel disease colonic mucosal E. coli isolates release interleukin-8 (IL-8) from colonic epithelial cells (Gastroenterology 2004;127:80–93). We have now investigated the effect of 5-ASA and hydrocortisone on this IL-8 response.

Materials and Methods: Preliminary experiments showed that 0.2 μm filtered supernatant, pooled from six E. coli mucosal isolates from 3 UC patients, induced a substantial IL-8 response from HT29 colon epithelial cells (pooled supernatant, 1262 (SD 110) pg/ml; pooled whole bacteria, IL-8 1901 (SD 67) pg/ml). HT29 colon cell monolayers were therefore pre-treated for one hour with 2.5–20 mM 5-ASA or 10–100 μM hydrocortisone followed by addition of the pooled supernatant. After four hour treatment, IL-8 release was measured by EUSA. In parallel experiments, IL-8 release was assessed in the presence and absence of BAY11-7082, an NFκB inhibitor.

Results: 5-ASA dose dependently inhibited the IL-8 response to a pooled E. coli supernatant, with reductions of 22 (SD 15)% at 2.5 mM, 45 (SD 5)% (5 mM), 51 (SD 11)% (10 mM), and 97 (SD 1)% at 20 mM (all p < 0.01; ANOVA). Hydrocortisone only caused significant inhibition of the IL-8 response (13% (p > 0.05)) at a supra-therapeutic concentration (100 μM). This is in keeping with the fact that inhibition of NFκB only had a modest effect on IL-8 release (mean reduction 39 (SD 35)%), n = 21). In a separate experiment, 5-ASA (5 mM) and hydrocortisone (100 μM) in combination inhibited IL-8 release by 82 (SD 7)% compared with 38 (SD 8)% for 5-ASA alone and 51 (SD 6)% for hydrocortisone alone (p < 0.001).

Conclusions: 5-ASA, at therapeutic concentrations, markedly inhibits the release of IL-8 by colon epithelial cells in response to mucosal E. coli whereas hydrocortisone only has a significant inhibitory effect at concentrations almost 20-fold greater than are likely to be seen therapeutically. This confirms the epithelial cell as the target for mesorolamine (JEM 2005;201:1205–15) but implies that other cell types probably represent therapeutic targets for corticosteroids in IBD.

Cell/molecular biology free papers

Deoxycholic acid damages DNA through its production of reactive oxygen species: antioxidants prevent this damage

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DNA damage induction is a key initiating mechanism in cancer development in most tissue types. Recent reports have shown that Barrett’s tissues carry higher levels of DNA damage than squamous tissue, suggesting that Barrett’s tissues are exposed to DNA damaging agents. Bile acids are implicated in oesophageal adenocarcinoma induction, although there is some contention as to whether they can cause DNA damage and it not known how they do so. Hence, we assessed whether a range of bile acids were capable of inducing DNA damage in cultured oesophageal cells. Using the cytokinesis blocked micronucleus assay, we showed that DCA was the only bile acid tested that caused DNA damage in these oesophageal carcinomas. We further showed that this damage was induced at both neutral and acidic pH (pH6). DCA was also shown to induce point mutations in the human p53 gene, using the restriction site mutation assay. Hence DCA is a genotoxin, but how does it damage DNA?

As bile acids do not bind to DNA directly, we suspected that DCA’s ability to induce DNA damage involved the generation of reactive oxygen species. Indeed, using an ROS sensitive fluorescent dye (H2DCFDA), we were able to show the induction of reactive oxygen species (ROS) by DCA in oesophageal cells (OE33 and KYSE). In order to demonstrate that these ROS were responsible for DCA’s genotoxicity, we co-exposed cells to DCA and two antioxidants (vitamin C and curcumin). Both antioxidants prevented DCA from damaging DNA. These data correlate well with previous data from our lab, showing that DCA’s activation of NFκB is ROS dependent and can be blocked by the same antioxidants on this mechanism. Therefore, we can conclude that bile acids can damage DNA (and activate NFκB) by inducing ROS. Hence antioxidant supplementation may be an effective chemopreventative strategy in Barrett’s patients. These observations are supported by epidemiological data showing that there is an inverse correlation between fruit and vegetable intake and cancer progression in Barrett’s patients.

Monoclonal conversion of human gastric glands provides insights into stem cell and clonal architecture


Studies on the intestine of animals and man have confirmed, beyond reasonable doubt, that the structural units, the crypts, are clonally derived. The unit found in the stomach, the gastric gland, especially in the human, remains an enigma. Some animal reports show clonal derivation, whereas others show that a minority of glands remain polyclonal, suggesting the possibility of multiple, possibly independent stem cells. In the human, results are also mixed.

We have used mutations in the mitochondrial cytochrome c oxidase subunit 1 gene (COXsu1), as a clonal marker (J Clin Invest 2003;112), detecting COXsu1 in conjunction with a nuclear encoded oxidative enzyme, succinate dehydrogenase (SDH), by double enzyme histochemistry. We have observed both body-type gastric glands which are partially filled with mutated cells, and others glands where all the cells in the gland are mutated (COXsu1−, SDH+). These suggest that a stem cell bearing this mutation expands to fill the entire gastric gland. Early observations suggest that all cell lineages in these mutated body-type glands are involved in this process. Moreover, the mutated gland then appears to spread in the mucosa by gland fission.

Several conclusions are made possible by these observations:

1. Gastric glands undergo a process of monoclonal conversion, where the gland becomes gradually replaced by mutated cells.

2. Human gastric glands are maintained by a number of stem cells.

3. Each body-type gland is derived ultimately from a single stem cell which gives rise to all the contained lineages, and are therefore multi-potential.

4. These mutated glands then appear to expand by gland fission, even in the adult stomach.

Use of growth hormone releasing peptide-6 for the prevention of hepatic and multi-organ failure

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Background/Aims: Novel therapies for the treatment of multiple organ failure are required.

Methods: We examined the effect of synthetic growth hormone releasing hormone peptide-6 (GHRP-6) on cell migration and proliferation using rat intestinal epithelial (IEC-6) and human colonic cancer (HT29) cells in vitro models of injury. In addition, we examined its efficacy when given alone and in combination with the potent protective factor epidermal growth factor (EGF) in an in vivo model of multi-organ failure (using two hepatic vessel ischemia-reperfusion protocols; 45 min ischemia-45 min reperfusion and 90 min ischemia-120 min reperfusion).

Results: In vitro studies showed GHRP-6 directly influenced gut epithelial function as its addition caused a threefold increase in the rate of cell migration of IEC-6 and HT29 cells (p < 0.01) but did not increase proliferation ([3H]-thymidine incorporation). In vivo studies showed that, compared to baseline values, ischemia/reperfusion caused marked hepatic and intestinal damage (histological scoring), neutrophil infiltration (MPD assay, fivefold increase) and lipid peroxidation (MDA assay, fourfold increase). Pretreatment with GHRP-6 (120 μg/kg sc) alone truncated these effects by 50–85% (all p < 0.05) and additional benefit was seen when GHRP-6 was used in combination with EGF (1 mg/kg sc). Lung and renal injuries were also reduced by these pretreatments.

Conclusion: Administration of GHRP-6, given alone or in combination with EGF to enhance effects, may provide a novel, simple approach for the prevention and treatment of multi-organ failure and other injuries of the gastrointestinal tract. Further studies appear justified.
103 HYPERAMMONEMIA ALTERS THE LPS INDUCED ACTIVATION OF TNF-α IN PERIPHERAL BLOOD MONONUCLEAR CELLS

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Background: Patients with liver dysfunction are prone to infection which is frequently a precipitant of decomposition associated with hepatic encephalopathy, renal failure, and shock. Bacterial infections in patients with cirrhosis are poorly tolerated and responsible for 30–50% of deaths. We have shown that hyperammonemia impairs neutrophil phagocytosis and induces spontaneous oxidative burst but the effect on peripheral blood mononuclear cells (PBMCs) has not been studied. TNF-α, sTNFR1, and sTNFR2 were measured from cell supernatants at 48 hours with ELISA. Live cell counts were obtained using the trypan blue exclusion assay.

Methods: PBMCs were isolated from healthy volunteers on a Ficoll-Paque gradient. Cells were incubated with 0–125 μM ammonium chloride (NH₄Cl) immediately, or after 24 hours, when a 1 ng/ml lipopolysaccharide (LPS) challenge was administered. TNF-α, sTNFR1, and sTNFR2 were measured from cell supernatants at 48 hours with ELISA. Live cell counts were obtained using the trypan blue exclusion assay.

Results: Significant TNF-α release occurred only in the presence of LPS stimulation, and NH₄Cl caused a concentration related decrease in TNF-α (20–48%) reduction with 125 μM NH₄Cl (p<0.05). sTNFR was produced in the absence of LPS stimulation, however 125 μM NH₄Cl potentiated the LPS induced rise of sTNFR by 21.4% (p<0.0005). sTNFR1 was measured in the absence of LPS stimulation, however 125 μM NH₄Cl potentiated the LPS induced rise of sTNFR by 21.4% (p<0.00005) and of sTNFR1 by 9.9% (p<0.005). A linear relationship was demonstrated between sTNFRI and sTNFR1 in their regulation by LPS and NH₄Cl.

Conclusion: Hyperammonaemia influences endotoxin induced release of TNF-α and soluble receptors. This may have implications for resisting infections in liver disease.

104 COLONIC STEM CELLS ARE UNABLE TO SELECTIVELY SEGREGATE GENOME AT THE TIME OF MITOSIS: REPLICATION ERRORS SURVIVE


Background: There is evidence that one way in which small intestinal stem cells are able to protect themselves from errors of DNA replication is by segregating their genome at the time of cell division; always retaining the old (or “template”) strand and passing on only the newly synthesised DNA strand to their progeny (Potten et al. J Cell Sci 2002). Here, we try to establish whether or not the same process takes place in the colon at a time when new stem cells and new “template” strands are being produce following a single dose of ionising radiation.

Methods: Thirty Min and 20 C57Bl/6J mice underwent whole body irradiation at a dose of 8 Gy, followed by six hourly i.p. injections of tritiated thymidine (H³ThdR) over 48 hours. The mice were then left for eight days and a cohort sacrificed. The remaining mice were injected with bromodeoxyuridine (BrdUrd) i.p. every six hours for 48 hours and sacrificed at time points from 40 minutes to 25 days following the final injection. The colons of all mice were removed post mortem and stained with the anti-BrdUrd antibody, before autoradiography was performed. Crypts were counted and labelled cells mapped on a positional basis.

Results: After eight days 1.9% of cells were labelled with H³ThdR, with none seen after 20 days. Labelled cells were distributed equally throughout the length of the crypt and there fewer labelled cells in the Min mice. BrdUrd labelling was almost complete throughout the crypt at one day, but declined sharply 3–5 days after the last injection, with no labelled cells seen after 25 days. Cells containing both proliferative markers were very rare indeed and occurred only in the first 24 hours.

Conclusion: Since the stem cell cycle time is reduced by irradiation, the presence of H³ThdR at eight days is indicative of retention of part of the genome. The disappearance of the label over the following 12 days and the dilution of BrdUrd at the same rate, suggests that this process is stochastic and there is no mechanism in the colon selectively retaining the “template” strand at the time of mitosis. This may contribute to the higher incidence of tumours found in the colon compared to the small intestine.

105 TARGETED KILLING OF COLORECTAL CELL LINES AND MURINE ADENOMAS USING A MONOCLONAL ANTIBODY AGAINST MEMBRANE BOUND CARCINOEMBRYONIC ANTIGEN

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Introduction: The anti-CEA antibody PR1A3 binds only membrane-bound CEA. The distribution of carcinoembryonic antigen (CEA) in colorectal cancer (CRC) differs from that in normal colorectal tissue, being found throughout the cell membrane of the cells, thus enabling access to intravenous antibody. Our aim is to assess whether PR1A3 is suitable to be considered as a therapeutic agent in the treatment of CRC.

Methods: Humanised PR1A3 was assessed in vitro cytotoxic assays with CEA positive and negative colorectal cell lines using peripheral blood mononuclear cells as a source of natural killer (NK) cells. In addition PR1A3 was injected intraperitoneally twice weekly for six weeks into a transgenic murine model of CRC which expresses human CEA on adenomatous polyposis predominantly in the small bowel (MIN CEA mice).

Results: PR1A3 demonstrated antibody dependent and CEA dependent killing of tumour cell lines by human effector cells. The effect increased with increasing concentration of antibody and was lost by antibody to block the Fc-γ receptor which is found predominantly on NK cells. Tumour cell lysis increased by a mean of 25% (range 15–38%) compared to spontaneous killing in the absence of antibody. 46 transgenic MIN CEA mice treated with PR1A3 had a 24% reduction in average adenoma size (p=0.0014) compared to 33 untreated controls.

Discussion: PR1A3 mediates NK killing of CEA-positive tumour cells in vitro and in vivo. This killing is dependent on effector cells binding the Fc portion of the antibody and so is likely to act via antibody dependent cellular cytotoxicity and not by blocking cellular function. These findings suggest promising therapeutic potential in CRC.

Pathology free papers

106 EVOLUTION OF HELICOBACTER PYLORI VIRULENCE FACTORS IN INDIVIDUALS AND FAMILIES FROM AN ISOLATED AFRICAN POPULATION

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Background: Helicobacter pylori are constantly evolving and are passed between individuals. We have previously studied virulence factor evolution in strains from Scottish families and more recently Nottingham individuals. We have now studied H pylori evolution in a rural Black, South African community (Ogies Tribe from Mpumulanga).

Methods: The study collection consists of 90 individuals. Initially 10 single colony isolates were taken from a single gastric biopsy specimen from each of nine individuals. Evolution in the H pylori virulence genes vacA, cagA, and iceA was determined by PCR typing and nucleotide sequencing and OipA protein status was determined by western blot analysis. Similarties between strains were determined by RAPD-PCR.

Results: RAPD-PCR revealed that each stomach had a single unique strain. However, their strains had evolved to change vacA (4/9) and oipA. We found multiple vacA alleles within the same stomach at a higher frequency then in a UK population (4/9 African strains compared to 2/49 Nottingham strains showed deviation within vacA, p=0.001 Fisher’s exact test). Variation in oipA functionality was investigated following a six hour co-culture with gastric epithelial (AGS) cells. OipA is believed to cause IL-8 secretion. However, in this case no difference was found between the levels of IL-8 secretion induced by oipA “on” and “off” strains.

Conclusion: We have shown evolution of H pylori by recombination. Evolution occurs commonly within individual stomachs, particularly in Africa where infection is very common. This may be due to increased contact between strains. We speculate that this may allow H pylori to adapt and rapidly to its environment. This result in H pylori evolving to become more or less virulent and, if the latter, it may help explain the low incidence of H pylori associated disease in Africa (the African enigma).


**Introduction:** Helicobacter pylori (Hp), the major cause of peptic ulcer disease, provokes a vigorous immune response. Despite this, however, most infections are persistent. We hypothesise that Hp subverts regulatory T cells (Tregs) to suppress protective immunity and gastric inflammation and promote co-existence. The aim of this study was to characterise the human Treg response to Hp.

**Methods:** Gastric antral biopsies were collected from 63 consenting patients attending the Queen’s Medical Centre, Nottingham for an upper GI tract endoscopy. Flow cytometry was used to quantify Tregs by staining for the markers CD4 and CD25 and also interleukin-10 (IL-10). Expression of the natural Treg-specific gene FOXP3 was quantified by real-time PCR.

**Results:** Elevated frequencies of CD4\(^+\)CD25\(^+\) regulatory T cells were detected in the gastric mucosa of Hp infected compared with uninfected donors (p = 0.04). A 12-fold higher frequency of CD4\(^+\)CD25\(^+\)IL-10\(^+\) cells was found amongst gastric cells from infected compared to uninfected donors (p = 0.002). Up to 95% of the gastric CD4\(^+\)CD25\(^+\) cells from infected donors were IL-10\(^+\) (median 61.3%; IQR 32.2–83.3%), and the proportion of IL10\(^+\) Tregs was 18-fold greater than that obtained with cells from uninfected donors (median 3.5%; IQR 0.0–24.3%; p = 0.002), suggesting that suppression of the normal T-cell response may be IL-10-mediated.

Real-time PCR revealed a sevenfold increase in FOXP3 expression in gastric tissues from infected compared to uninfected donors (p = 0.003), indicating the presence of natural Tregs during infection. To address the hypothesis that Tregs responses influence the inflammatory response to infection, the frequency of CD4\(^+\)CD25\(^+\)IL-10\(^+\) cells in the gastric mucosa of Hp positive patients diagnosed with or without peptic ulcer disease was compared. Significantly elevated frequencies of Tregs were found in the tissues of patients without peptic ulcer disease (median 2263; IQR 1766–3636) compared to 12 patients with disease (median 946; IQR 593–1538; p = 0.04). A 12-fold higher frequency of CD4\(^+\) cells in the gastric mucosa from infected compared to uninfected donors (p = 0.002). Up to 95% of the gastric CD4\(^+\) cells from infected donors were IL-10\(^+\) (median 3.5%; IQR 0.0–24.3%; p = 0.002), suggesting that suppression of the normal T-cell response may be IL-10-mediated.

**Background:** The stomach periglandular fibroblast sheath forms a protective fenestrated sheath around the stem cell niche at the isthmus/neck of the gastric gland and is important coordinating cells that possess significant influence on their environment by virtue of their antibody type 1 was negative. In the light of ultrasound and CT findings cancer if the patient had a history of carcinoma, short duration of symptoms, difficulty/inability in passing the endoscope through the OG neck, and difficulty in the patient's nutrition. Learning points: (1) Both achalasia and pseudoachalasia can produce identical manometric appearances. (2) In dysphagia patients with manometric features of achalasia consider pseudoachalasia if the patient had a history of carcinoma, short duration of symptoms, difficulty/inability in passing the endoscope through the OG junction.

**Conclusion:** Elastic stains are useful and practical in evaluation of VI status in CRC, and we recommend implementing these stains in routine pathological practice.

**Trainee/Trainers computer workshop**

**BEWARE OF THE DIAGNOSTIC IMITATION IN DYSPHAGIA!**

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**Case report:** A 39 year old school teacher was referred by her GP for open access gastroscopy with six weeks’ history of mid-retrosternal dysphagia to solids. There was no history of chest pain, vomiting or weight loss, arthralgia, or Raynaud’s phenomenon. Gastroscopy showed a benign looking 3 cm stricture near OG junction through which only a paediatric scope could be passed. Biopsies showed chronic active carditis. Patient was commenced on empirical PPI therapy and at repeat gastroscopy the stricture was dilated up to 20 mm with Microvasive balloon with no improvement in symptom. Repeat biopsies showed no dysplasia/malignancy. Barium swallow study and oesophageal manometry were carried out. Oesophageal manometry showed changes consistent with diagnosis of achalasia. Further history revealed lupemoptomy and axillary node clearance for ductal carcinoma in 1996 for which she received chemotherapy and was commenced on Tamoxifen. In 1997 she developed contralateral carcinoma which led to left mastectomy. She was regularly followed up in the breast clinic with no evidence of recurrent disease and remained in good health until she developed dysphagia which led to her referral for gastroscopy. Routine blood tests revealed abnormal liver function test. Ultrasound scan of the liver showed multiple hypoechoic lesions consistent with metastases. A CT scan showed circumferential thickening of the lower oesophagus, metastases in the liver, lungs, vertebral body. Antineuronal nuclear antibody type 1 was negative. In the light of ultrasound and CT findings and the previous history of breast carcinoma a diagnosis of pseudoachalasia was made and she was referred to the oesophagologist for chemotherapy. A percutaneous gastrostomy tube was placed to provide her nutrition. Learning points: (1) Both achalasia and pseudoachalasia can produce identical manometric appearances. (2) In dysphagic patients with manometric features of achalasia consider pseudoachalasia if the patient had a history of carcinoma, short duration of symptoms, difficulty/inability in passing the endoscope through the OG junction.
AN UNUSUAL ENDOSCOPIC DUODENAL APPEARANCE

R. P. Willer1, S. M. Weerasinghe2, D. A. F. Lynch1, 1Gastroenterology and 2Histopathology Departments Blackburn Royal Infirmary, Blackburn, Blackburn BB2 3JR, UK

Case report: A 59 year old female non-smoker initially presented in 2000 with progressive weight loss of 8 kg (BMI 22) and painless, watery diarrhoea. There was no history of foreign travel. Stool cultures were negative for cysts, ova, and parasites. Her full blood count, U&Es, LFTs, glucose, inflammatory markers, haematocrits, and thyroid function were all normal and her anti-endomysial antibodies were negative. A CXR suggested evidence of basal bronchiectasis. She underwent a gastroscopy with duodenal biopsies, received a specific therapy, and was lost to follow up.

Five years later she represented with further progressive weight loss of 1.5 kg (BMI 17) but with no change in bowel habit, pain, or systemic symptoms. Examination was unremarkable apart from vitiligo and coarse nasal crinkles in keeping with her bronchiectasis.

Repeat bloods and stool cultures were again all normal and her anti-endomysial antibodies remained negative. An ultrasound scan demonstrated mild splenomegaly but her pancreas, biliary tree, and liver were normal. A repeat gastroscopy was performed which demonstrated an unusual appearance in the duodenum and further duodenal biopsies were taken.

This case discusses the differential cause for the abnormal duodenal findings and the appropriate investigations and treatment required in this uncommon condition.

AN UNUSUAL CAUSE OF FACIAL SWELLING IN A JAUNDICED PATIENT

J. Gasem, S. Khalid, M. Babores. Macclesfield General District Hospital, Macclesfield, UK

Case report: A 63 year old gentleman was admitted to hospital complaining of feeling unwell for six months, with jaundice, weight loss of 1½ stones in two years, poor appetite, leg ulcers for one month, and loose stools. He had no significant medical history prior to admission and had no risk factors for liver disease. On examination he had jaundice, finger clubbing, and an ulcerating skin rash on his legs. Abdominal examination was unremarkable. His blood results confirmed microcytic anaemia with cholestasis and a bilirubin of 139 mol/l (2–20). His CRP was raised at CRP 93 mg/l (0–8), and his albumin was reduced at Albumin of 16 g/l (30–50). His chest x-ray was normal. CT scan of the liver failed to reveal biliary obstruction. Colonoscopy and biopsy confirmed ulcerative colitis with a moderately well differentiated rectal adenocarcinoma. He was treated with high dose steroids and supportive therapy, the patient died a few days later.

This case discusses the differential cause for the abnormal duodenal findings and the appropriate investigations and treatment required in this uncommon condition.

A RASH CAN CAUSE GI BLEEDING?

J. Parr, D. A. Burke, C. E. Macdonald. Cumberland Infirmary, Carlisle CA2 7HY, UK

Case report: A 19 year old man presented after two days of dyspepsia and witnessed haematemesis. He had a history of ulcerative colitis (UC), well controlled on oral Asacol. He had been taking a tetracycline for acne. He was otherwise well. O/E he had tachycardia, postural drop in BP, and mild epigastric tenderness. No rash, fever, or other significant findings noted. Admission biochemistry showed AST was normal but the WCC = 21.4 x 109/l and CRP = 143 mg/l. Urinalysis was negative. An OGD was carried out. Thickened cobblestone like mucosa, superficial ulceration, and oozing of blood was noted to extend from the OG junction along the lesser curve. Biopsies (Bx) were taken and he was started on IV PPI. CLO test was negative. Oxytetracycline was stopped. The Bx showed haemorrhagic acute gastritis with ulceration. Also present was vasculitis with fibrinoid change and leukocytoclasis at the small vessels. No granulomata were seen. Special stains for bacteria and fungi were negative. Autoantibodies and viral hepatitis screen was requested. This showed normal complement levels, ANA, immunoglobulins, and hepatitis serology, there was cANCA 1/160 present, with a positive precipitin with which cANCA 1/400. Rpt OGD at day 10 showed dramatic change with only minor generalised patchy erythema noted. Chronic active inflammation was noted in the gastric Bx mainly around the vessels and was still suspicious for vasculitis. H pylori not seen. Given the persistently raised cANCA, tetracycline use, and vasculitis on Bx, he was diagnosed with microscopic polyangiitis (MPA) of the stomach.

Discussion: MPA is identical to polyarteritis nodosa (PAN) except for the presence of vasculitis in vessels smaller than arteries. Presentation is similar in both, though GI tract involvement is more common in PAN. The lesions in MPA are thought to represent a hypersensitivity reaction and can involve skin, GI tract, and other organs. Autoimmune phenomena (incl MPA) are well recognised with tetracycline use. MPA affecting the skin has been associated with ulcerative colitis. Most cases of MPA require no treatment. UC patients have PANCA positivity in 60–80%. cANCA is uncommon in UC but positive in 25% of MPA.

Conclusion: Vasculitis can affect any organ of the body, and although rare, GI involvement should be considered.

A FATAL PULMONARY EMBOLISM SECONDARY TO A RARE SMALL BOWEL INFECTION

A. H. Shenoy, N. A. Shepherd, J. L Brown. Gloucestershire Royal Hospital, Gloucester GL1 3NN, UK

Case report: A 76 year old man presented with diarrhoea, barbor-hygri, and weight loss of a month’s duration. There was no rectal bleeding or abdominal pain. His symptoms started on return from a holiday in Portugal. His stool culture and microscopy were negative and he did not respond to oral tinidazole for suspected giardiasis. He had been on long term low dose prednisolone and methotrexate orally for rheumatoid arthritis, which had been quiescent for a long time. He had suffered a single episode of deep vein thrombosis many years ago. There was no other comorbidity or any symptoms of gastrointestinal disease in the past.

At presentation he was anaemic with haemoglobin of 9.1 g/dl due to iron and folate deficiency. C reactive protein (CRP) was 38 mg/l (normal <10 mg/l) and albumin was 26 g/dl (35–44). A repeat stool test and other blood tests including vitamin B12 levels, thyroid function tests, glucose, anti-endomysial antibody were normal. Flexible sigmoidoscopy and colonoscopy were normal. Gastric biopsy showed a granular and finely nodular appearance of duodenum. Duodenal histology showed subtotal villous atrophy, dilated lymphatics, and abundant PAS positive inclusion filled macrophages infiltrating the submucosa, which are diagnostic of the chronic small bowel infectious disease this patient was suffering from.

Soon after the diagnosis, before any treatment could be initiated, the patient suddenly took ill with pleuritic chest pain and severe shortness of breath. The electrocardiogram and echocardiogram showed severe right heart strain suggesting massive pulmonary embolism (PE) from which he died. The risk factors for the PE were likely to be related to the DVT and possibly the underlying small bowel disease.

A BLEEDING CATCH-22

G. Pritchard1, E. Roche2, P. Foster2, 1Royal Liverpool University Hospital, UK; 2Macclesfield District General Hospital, UK

Case report: We report a 56 year old patient who sustained recurrent bleeding from oesophagogastric varices over a four year period while on lifelong warfarin for a previous mesenteric vein thrombosis and femoral deep vein thrombosis. CT scanning demonstrated extensive thrombosis involving the portal, splenic, and superior mesenteric veins. Work up to determine the cause of his underlying condition, need for oral anticoagulation, and the therapeutic procedures used to treat varices resulted in significant and challenging complications.

Discussion: We discuss the management of extra-hepatic portal vein thrombosis in light of the current literature, with a particular focus on aetiology, anticoagulation in the setting of varices, techniques to prevent rebleeding, and the implications of the presented complications.
A 33 year old man was admitted with a four week history of pain in the right iliac fossa. His haemoglobin was 10.6 g/dl (13–18), and on admission his amylase was 341 U/l with an albumin of 28 g/l and normal U&E and LFTs. His haemoglobin dropped from 11.9 g/dl to 7.3 g/dl during admission. A repeat OGD showed mild duodenitis, and colonoscopy showed diverticular disease. Ultrasound examination of his abdomen showed a dilated common bile duct at 8 mm and an echo poor mass in the pancreatic head. The gall bladder was normal. His CA 19-9 was 80. A contrast enhanced CT scan of the abdomen was performed which showed a bulky pancreatic head and a well circumscribed intensely enhancing lesion in it. This was suggestive of a splenic artery pseudoaneurysm secondary to chronic pancreatitis.

He underwent mesenteric angiogram a few days later which failed to show the aneurysm. A repeat CT scan confirmed that the aneurysm is thrombosed. To date he did not have a further episode of GI bleed. In this case the aneurysm thrombosed spontaneously and this may have had a therapeutic effect preventing further admissions with haemorrhage.

Haemobilia is an uncommon cause of GI bleeding which is often overlooked. Pseudoaneurysms of branches of coeliac axis are rare causes of haemobilia. Aneurysms arising from hepatic artery, gastro duodenal artery, splenic artery, cysic artery, and left gastric artery have been reported.

RAISED SERUM HCG: AN ACUTE SURGICAL PROBLEM


Case report: A 47 year old lady was admitted as an emergency with abdominal pain and vomiting. Investigations revealed a raised serum hCG and evidence of renal failure. Pregnancy was excluded by ultrasound scanning. Subsequently a mass lesion in the apex of left lung was demonstrated on the chest x-ray, and a contrast follow through revealed a jejunal intussusception, both of which were confirmed by CT scanning. The patient underwent a laparotomy, where a polypoidal mass was resected. Histology revealed an angiosarcomatoid carcinoma with positive cytokeratin, EMA, and TTF-1 staining, which was suggestive of metastasis from carcinoma of the lung. A PET scan failed to show any additional site of activity other than the lung lesion. A left upper lobectomy was performed, showing concordant histology with the previously excised jejunal mass. The patient is currently under follow up and is clinically asymptomatic at six months. The serum hCG level has now returned to normal.

A FLUKE DIAGNOSIS?

A. J. Lawson1, A. Zaitoun2, G. P. Aithal1. 1Wolfson Digestive Disease Centre, University Hospital, Nottingham, UK; 2Department of Histopathology, University Hospital, Nottingham, UK

Case report: A 33 year old man was admitted with a four week history of diarrhoea and abdominal pain. He described 3-4 loose motions per 24 hours, associated with occasional blood per rectum. He was originally from Zimbabwe but had been living in the UK for 18 months. On examination he had a temperature of 38.1°C and he was mildly tender in the right iliac fossa. His haemoglobin was 10.6 g/dl (13–18), platelets 442 x 10^9 (140–400), and ESR 133 mm/hr. There had been no positive culture from two stool samples sent by his general practitioner. Flexible sigmoidoscopy was performed to the transverse colon with the finding of several small ulcers in both the sigmoid and distal transverse colon with normal intervening mucosa. The histological appearances of specimens from the colon threw up a surprising finding.
bowell. Histological examination of these lesions confirmed the presence of ectopic endometrial tissue.

Endometriosis is a rare cause of haemorrhagic ascites, with only 41 cases having been described in the world literature since 1951.

122 SKIN BLISTERS AND LIVER

Y. Reddy, D. Das. Stepping Hill Hospital, Stockport, UK

Case report: A 63 year old female was referred to a dermatologist with blistering, non-pruritic lesions on the dorsum of both hands, and excoriations on her face which did not improve with one week of oral corticosteroids. Apart from lansoprazole she was not on any medications. She was a non-smoker but drank 20 units of alcohol a week on average. Her body mass index was 33 and there were no signs of chronic liver disease.

Liver function tests showed bilirubin 15 μmol/l, AST 155 IU/l, ALT 199 IU/l, GGT 599 IU/l, Alk Phos 114 IU/l. She tested negative to presence of viral B&C markers and auto-antibodies. Ultrasound scan revealed a heterogeneous architecture of the liver. Her fasting serum ferritin was 12320 μg/l and transferrin saturation was 50%. Genetic screening for haemochromatosis showed a heterozygous status for H63D mutation. Liver biopsy appearances were in keeping with steato-hepatitis and grade 1 siderosis. No porphyrin crystals were identified in the unstained section of liver.

High levels of porphyrins were detected both in plasma and urine. A diagnosis of porphyria cutanea tarda (PCT) was made on the basis of a positive fluorescence emission at 620 nm, fluorescence excitation and chromatographic retention characteristics of uroporphyrin/creatinine at a level of 626.9 (4.4 μmol/mol) in the urine. Red blood cell protoporphyrin was not elevated.

She was commenced on regular venesection. After nine sessions of venesection the skin lesions began to disappear, her LFTs returned to normal, serum ferritin came down to 7, and the uroporphyrin/creatinine levels fell to 53.4 μmol/mol.

PCT should always be considered in any patient with blistering skin lesions in the background of high alcohol intake and abnormal LFTs and venesection is effective in preventing relapses and reducing tissue damage.

123 CAPSULE ENDOCOSPY: FRIEND OR FOE?

E. Wood, S. McCartney, S. Bloom. Department of Gastroenterology, Middlesex Hospital, UCLH NHS Trust, Mortimer Street, London W1T 3AA, UK

Introduction: We describe the case of an 81 year old man with known ischaemic and valvular heart disease (aortic stenosis (AS) with a gradient of 52 mmHg) and non-insulin dependent diabetes mellitus who had been previously investigated for an episodic transfusion requiring anaemia. He was also known to have a chronically infected prosthetic. OGD and colonoscopy at that time were unremarkable and subsequent bone marrow sampling to exclude myelodysplasia revealed normal, serum ferritin came down to 7, and the uroporphyrin/creatinine of the extent of the underlying pathology. The patient has since had two further admissions for transfusion in the last two months.

Case report: A 76 year old lady underwent surgery for intraductal breast carcinoma which was followed by three courses of radiotherapy. Two months after starting her radiotherapy she developed severe watery diarrhoea opening her bowels 8-10 times per day. There was no family history of bowel disease and she had not been abroad recently. After two weeks of persistent diarrhoea she was admitted to hospital. On examination she was noted to have perianal aphthous ulceration, a temperature of 38.5˚C, and bilateral leg oedema. Her CRP was raised. Blood and urine cultures were negative. Stool samples were sent for Clostridium difficile toxin, ova, cysts and parasites, and electron microscopy and were all negative. Early morning urine for TB was negative. CT abdomen showed some thickening of ascending colon. A limited unprepared colonoscopy was performed and the scope was passed to the distal ascending colon. Colon biopsy histology revealed non-specific chronic inflammation. Her pyrexia and diarrhoea continued which necessitated further investigation to exclude an unusual infective cause.

In this case we discuss how we investigated this patient and how appropriate treatment controlled her colitis.

124 AN UNUSUAL PRESENTATION OF CHRONIC DIARRHOEA

A. Dias, G. Eryian, I. Crapley, O. Epstein. Royal Free Hospital, Pond Street, London NW3 2QG, UK

Case report: A 76 year old lady underwent surgery for intraductal breast carcinoma which was followed by three courses of radiotherapy. Two months after starting her radiotherapy she developed severe watery diarrhoea opening her bowels 8-10 times per day. There was no family history of bowel disease and she had not been abroad recently. After two weeks of persistent diarrhoea she was admitted to hospital. On examination she was noted to have perianal aphthous ulceration, a temperature of 38.5˚C, and bilateral leg oedema. Her CRP was raised. Blood and urine cultures were negative. Stool samples were sent for Clostridium difficile toxin, ova, cysts and parasites, and electron microscopy and were all negative. Early morning urine for TB was negative. CT abdomen showed some thickening of ascending colon. A limited unprepared colonoscopy was performed and the scope was passed to the distal ascending colon. Colon biopsy histology revealed non-specific chronic inflammation. Her pyrexia and diarrhoea continued which necessitated further investigation to exclude an unusual infective cause.

In this case we discuss how we investigated this patient and how appropriate treatment controlled her colitis.

Plenary posters

125 ROLE OF PROTEIN KINASE C IN ALDOSTERONE INDUCED NON-GENOMIC INHIBITION OF BASOLATERAL POTASSIUM CHANNELS IN HUMAN COLONIC CRYPTS

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Background: Aldosterone has a rapid, non-genomic, inhibitory effect on Ca2+-sensitive basolateral intermediate conductance K+ (IKCa) channels in human colonic crypt cells, which reduces the colon’s Cl− secretory capacity. However, the intracellular second messenger pathways involved in this effect are unclear.

Aim: To evaluate the role of protein kinase C (PKC) in aldosterone’s non-genomic inhibitory effect on basolateral IKCa channels in human colonic crypt cells, using the patch-clamp technique.

Methods: With informed consent, biopsies were obtained from healthy sigmoid colon during colonoscopy, and intact colonic crypts isolated by enzymatic digestion. With informed consent, biopsies were obtained from healthy sigmoid colon during colonoscopy, and intact colonic crypts isolated by enzymatic digestion.

EGFR INHIBITION IMPROVES HELICOBACTER PYLORI INDUCED PATHOLOGY AND EPITHELIAL CELLULAR KINETICS IN VIVO

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Introduction: H pylori has been shown to transactivate the EGFR receptor (EGFR) in gastric epithelial cells. H pylori activation of the EGFR signalling pathway may be relevant to the epithelial hyperproliferation and increased risk of gastric carcinogenesis associated with infection.
The aim of this study was to examine whether inhibition of the EGFR with the specific inhibitor EKB-569 would alter H pylori induced pathology in the Mongolian gerbil model.

**Methods:** Male Mongolian gerbils were infected with H. pylori (SS1 strain). Six weeks post-infection, infected and uninfected controls were fed on either, control, or EKB-569 (10 mg/g gerbil/day) supplemented diet. Gerbils were killed at 38 weeks post-infection. Gastric pathology was assessed and epithelial proliferation and apoptosis quantified respectively by anti-BrDU and activated caspase-3 histochromistry.

**Results:** No difference in antral pathology was observed in treated and untreated infected gerbils. EKB-569 treatment in infected gerbils resulted in a significant reduction in corpus atrophy (p < 0.03) and mucus metaplasia (p < 0.05), but chronic corpus inflammation was similar to untreated gerbils. There was significant (p < 0.05) reduction in submucosal herniations in EKB-569 treated gerbils. Increased epithelial proliferation (p < 0.001) was observed in the antrum and corpus of both infected groups. Apoptosis was only significantly increased (p < 0.001) in the EKB treated group compared to uninfected control groups. There was a marked increase in apoptotic subepithelial mononuclear cells in the EKB-569 treated infected gerbils. In infected gerbils, the proliferation/apoptosis ratio in the untreated group was significantly greater (p < 0.05) in both the antrum and corpus than in the EKB-569 treated group, where the ratio was comparable to uninfected controls.

**Conclusion:** EGFR inhibition reduces H pylori induced corpus pathology in vivo and promotes apoptosis in both epithelial and subepithelial mononuclear cells.

**THE COLORECTAL NURSE PRACTITIONER TRAINING IN COLONOSCOPY AND POLYPECTOMY**

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**Background and Aim:** An audit of the colorectal nurse practitioner’s (CNP), MTC, performance in lower GI endoscopy, between January 2003 and January 2004, revealed that CNP had performed 374 lower GI procedures and 104 polyps were found. The CNP with the assistance of the supervising consultant excised 52 (50%) of the polyps that were <2 cm. Polyps >2 cm was dealt by the consultant. It was proposed that given a specific programme of training there was a significant opportunity for the CNP to excise successfully and safely polyps <2 cm.

**Method:** Review of practice before and after one to one focussed training in colonic polypectomy.

**Results:** After a six month period of intensive supervised learning, 240 lower gastrointestinalal procedures were performed independently by the CNP from July 2004-May 2005, (101 colonoscopy and 139 flexible sigmoidoscopy). One hundred and fifty six (65%) patients were female and the median age was 55. Eighty nine (88%) of colonoscopies were carried out to the caecum. Cancers were detected in 13 (5%) of patients. In addition 65 polyps were found in 54 (23%) patients. Out of the 65 polyps, seven (11%) measured >2 cm and were referred to the consultant, as were two other patients with polyps each on warfarin. Fifty six (86%) polyps measured <2 cm and were safely snared or hot biopsied by the CNP. There were no immediate or late (30 days) complications.

**Conclusion:** After a period of one-to-one learning and supervisory practice it is safe for the CNP to perform polypectomy on polyps measuring up to 2 cm. With limited NHS resources and the introduction of bowel cancer screening, the role of CNP may be extended to colonoscopy and polypectomy.

**THE THREAT TO SPECIALIST TRAINING FROM THE EUROPEAN WORKING TIME DIRECTIVE: RESULTS FROM THE BSG TRAINING COMMITTEE SURVEY OF SPRS**

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**Introduction:** The implementation of the European Working Time Directive (EWTD) on 1 August 2004 has created major changes in the specificities of regional training and must be fulfilled within the constraints of the EWTD, the BSG Training Committee sent a questionnaire to SPRS in Gastroenterology.

**Methods:** Each SPR in a training programme in Gastroenterology was asked to complete a questionnaire in April 2005 (chosen as the month when training was least likely to be affected by major meetings, public holidays or annual leave). Sprs stated the number of total number training opportunities in their timetable and the number their working patterns allowed them to attend.

**Results:** 110 responses (~40%) were received. Seventy (67%) were in the first three years of training. Less than 10% took any leave during the study month. As a result of the EWTD (excluding leave), SPRs were unable to attend 26% of scheduled clinics, 25% of supervised endoscopy lists, 34% of consultant-led ward rounds, 40% of cancer MDT meetings, 18% of histopathology meetings, and 45% of journal clubs. In addition, 24% of regional training days were not attended. A maximum of 48 supervised endoscopy lists, 66 clinics and 60 consultant-led rounds could be attended over the course of a year.

**Conclusions:** Implementing the EWTD has reduced training for SPRs by 25% to 40%. As a result, the number of specialist training in Gastroenterology are not being met. The service commitment for acute medicine is highly damaging to specialty training.

**THE EFFECT OF FOOD COMPOSITION AND PREPARATION ON REFLUX SEVERITY IN PATIENTS WITH REFLUX DISEASE**


**Introduction:** Patients with gastro-oesophageal reflux disease (GORD) are often told to avoid fatty food in the hope that this will decrease acid reflux; however evidence from healthy volunteers suggests that reflux severity may not be associated with fat content per se but calorie density. Moreover effects of meal preparation on reflux have never been studied.

**Method:** Twenty one patients referred for investigation of reflux symptoms were studied. Bravo was placed under sedation at endoscopy. All meals were supplied, providing 24 hours in each “dietary condition”. Patients returned after 48 hours and 96 hours to download data. Friedman test was used to identify associations of food composition and preparation with acid reflux.

**Results:** Data were available from 15 patients (9 female, median age 48 (26–70) years, BMI 26 (21–35) kg/m²). Demographic variables and meal sequence had no effect on reflux parameters. Acid reflux was reduced 18% in low compared to high calorie meals (fat constant) 5.5 v. 8.4% time pH<4 (p < 0.01). No difference was observed between low and high fat meals (calories constant); 8.6 v. 8.2% time pH<4 (p = NS). Food preparation did not affect reflux parameters (p = NS).

**Conclusion:** Prolonged pH recordings by BRAVO allowed the first detailed comparison of dietary conditions on reflux severity in GORD. A clinically relevant (~40%) decrease in reflux severity was found on a low calorie, low fat diet compared with an isovolumetric high calorie, low fat diet. In contrast, no difference in reflux parameters was seen after a high fat meal compared with an isocaloric and isovolumetric low fat meal. GORD patients should be advised that lowering the calorie density (richness) of meals can significantly reduce acid reflux.

**THE MALLORY WEISS TEAR**


**Introduction:** Bleeding from Mallory Weiss Tear (MWT) is generally considered to be trivial, self-limiting, and rarely requiring acute intervention. There are, however, only limited community based published data to support this benign perception. The 10 year prospectively collected data from the Aberdeen Gastrointestinal Bleeding Unit (AGIBU) have given us the opportunity to evaluate this further.

**Aim:** To evaluate the natural history of Mallory Weiss Tears in the stable at risk population (458 536) of Grampian over a 10 year period.
Method: Prospectively collected data on all admissions with gastrointestinal bleeding to the AGIBU were stored on a Microsoft Access database. Analyses were then performed on the data collected from all admissions with bleeding from Mallory Weiss Tears.

Results: From October 1991 to October 2001, 9.3% (n=668) of admissions to the AGIBU, with suspected upper GI bleeding, bled from a MWT. A positive correlation (r=0.0001) was seen with young male patients, acute and chronic alcohol intake, smoking, and a history of retching or vomiting, and a history of vomiting when compared to the other AGIBU admissions. Of those with haematemesis, 36% did not have a prior history of retching or vomiting. The bleeding episode was defined as significant (haemodynamic compromise, Hb<10 g/dl) in 36.7%. The proportion with significant bleeding increased with age (p<0.01) and was more common in females (p=0.0001) than males. The majority had a short hospital admission with no complications. However 5% (n=28) rebleed within 30 days and 1.71% (n=9) died within 30 days. All of the deaths were associated with significant comorbid disease.

Conclusions: Contrary to popular belief bleeding from MWT is not only common but is often significant. It often occurs without retching or prior vomiting and can be associated with rebleeding. There is a small but significant mortality.

131 ATTENTIONAL MODULATION OF VISCERAL AND SOMATIC PAIN

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Background: Hypervigilance, an increased state of guardedness, watchfulness, or attention, has been proposed as a possible underlying aetiology in irritable bowel syndrome. As hypervigilance must be a centrally mediated process, functional magnetic resonance imaging of the brain can be used to test this hypothesis. However, a better understanding of the normal attentional mechanisms during visceral pain in health is initially required. The aim of this experiment was to identify the neural correlates underlying the attentional modulation of visceral and matched somatic pain.

Methods: Twelve healthy, pain-free, right handed subjects were recruited for the study. Simultaneous electrical pulses and auditory tones lasting 6 seconds were delivered to the subjects during a whole-brain functional scan acquisition. The electrical catheter was placed into the rectum for the visceral scan and onto the lower abdomen for the somatic scan. Subjects were instructed to attend to and count either the auditory tones or electrical pulses. Electrical pulses and auditory tones were delivered at either 2, 3.5, or 4.3 Hz thereby varying the cognitive demand of the tasks. Pain intensity, unpleasantness, and tone/pulse count were recorded after each stimulus.

Results: During the 3.5 Hz and 4.3 Hz conditions alone, distraction by the auditory tones resulted in a significant reduction in pain report (p<0.05) in both sensory modalities. There was a marked spatial overlap in group statistical activation maps during somatic and visceral pain. The typical ‘pain matrix’ was used. Using pain intensity values as regressors in a group level regression analysis, the primary somatosensory cortex (SI) increased in activity with increasing pain report, independent of attentional direction. Likewise the primary auditory cortex (AI) increased in activation with decreased pain report. Right dorsolateral prefrontal cortex (DLPFC) activity correlated positively with pain intensity during somatic pain.

Conclusions: Pain perception during attentional modulation is reflected in the primary sensory cortex activity and may be influenced in a top-down manner by the right DLPFC during somatic pain.

132 DEVELOPING A NOVEL STIMULATION PARADIGM FOR ENHANCING HUMAN BRAIN-SWALLOWING PATHWAYS

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Background: Neuronal excitability can be amplified by the synchronous activity of two afferent stimuli. This process, known as paired associative stimulation (PAS), has been successfully applied in enhancing hand motor cortex excitability. The effect of PAS on the swallowing motor cortex, which is bilaterally represented, remains unknown.

Aims: We investigated the optimal timing for the two stimuli of PAS for altering bi-hemispheric swallowing motor cortex excitability.

Methods: Healthy volunteers underwent transcranial magnetic stimulation with resultant pharyngeal electromyography (EMG) traces recorded through an intraluminal catheter. Mean EMG amplitude representing cortical excitability was assessed before and after PAS (paired pharyngeal electrical and transcranial magnetic stimuli every 20 s for 30 minutes). Twelve subjects attended on four occasions to test the effect of various interstimulus intervals (ISI) between the two PAS pulses (50, 75, 100, and 125 ms). In six further subjects, the effect on the contralateral hemisphere was assessed.

Results: PAS with a 100 ms ISI produced an immediate increase in cortical excitability that reached 130% compared to baseline and was sustained at 2 hours (fig 1). All other ISIs produced less than 40% change in cortical excitability (p<0.02). The contralateral hemisphere showed a smaller but non-significant increase in cortical excitability (fig 2, p=0.2).

Conclusion: PAS applied to swallowing motor cortex can induce sustained increases in cortical excitability of the stimulated hemisphere. These changes may have implications for the rehabilitation of dysphagic stroke patients.
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135 A STUDY TO ASSESS EXPERTISE AND TRAINING IN TRANSCUTANEOUS LIVER BIOPSY AMONG TRAINEE GASTROENTEROLOGISTS

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Background: The JCHMT Gastroenterology Curriculum Feb 2005 states trainees should be skilled in liver biopsy. Increasingly transcutaneous liver biopsy is conducted under ultrasound guidance by radiologists suggesting trainee gastroenterologists are no longer routinely experienced in the procedure despite the stated curriculum aims.

Aim: This study aims to determine the level of training and competence in transcutaneous liver biopsies amongst SpRs in gastroenterology in a training region (Wessex deanery).

Methods: All gastroenterology SpRs in the Wessex deanery received a questionnaire aimed at assessing their training in liver biopsy and knowledge of the current British Society of Gastroenterology guidelines on the use of liver biopsy in clinical practice.

Results: Thirty one SpRs were eligible for the study and 77% responded. None currently worked in a trust where transcutaneous liver biopsy was routinely conducted by a gastroenterologist. Only 54% had practical experience of liver biopsy under supervision and 29% without supervision. Just 25% had a written record of this training. None had conducted a liver biopsy in the last twelve months. Only 4% knew the pre-procedure platelet count quoted as safe in the BSG guidelines, although 94% knew the safe level of INR. With regards to pain post procedure and significant haemorrhage only 4% and 16% respectively knew guidelines figures. Only 25% could quote accurate mortality figures post liver biopsy. No respondent had received training in transabdominal ultrasound although 45% felt gastroenterologists should be trained in conducting liver biopsies.

Conclusion: This study shows trainees in gastroenterology have a low level of practical and theoretical knowledge with regards to transcutaneous liver biopsy. Only a more comprehensive survey can determine if this is a national phenomenon. If stated JCHMT curriculum aims are to be addressed training in transabdominal ultrasound scanning may need to be compulsory for trainees.

134 DECOMPENSAED ALCOHOLIC LIVER DISEASE: DETERMINANTS OF SUBSEQUENT DRINKING BEHAVIOUR

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Background: In patients with decompensated alcoholic liver disease (ALD), continued heavy drinking is associated with mortality. Its determinants are not well understood.

Aim: Evaluation of drinking behaviour after diagnosis of decompensated ALD.

Methods: Review of records of 190 consecutive patients discharged from hospital following admission with first episode of decompensated ALD; phone calls as required to patient, family, and GP. Drinking behaviour since discharge up to 1/4/05 or to death evaluated in all patients and classified as grade 1–4 (see below). Time to first drinking relapse was also recorded. In the 130 Sheffield residents, Townsend and Jarman indices of social deprivation were derived from postcodes.

Results: The proportion of patients remaining abstinent after 3, 12, and 24 months was 42%, 31%, and 24% respectively. Predictors of relapse by Cox regression analysis were younger age and living alone. 49 patients were fully abstinent (drinking grade 1), 54 drank (18 occasionally, 36 regularly) below the safety limits (grade 2), 44 patients reduced their previous intake to a level above the safety limits (15 binge drinkers, 29 regular drinkers) (grade 3), and 49 patients failed to reduce previously heavy intake (grade 4). Patients with drinking grade 4 (a) had higher alcohol intake prior to admission (median 1.42 v 105 U/wk) and higher Townsend (4.1 v 0.9) and Jarman (21 v 5) scores (all p<0.01 by Mann-Whitney) and (b) were more likely to live alone and to have failed to stop drinking prior to admission (p<0.01 by χ²), compared to patients with grades 1–3, between which these parameters did not differ. Patients treated with corticosteroids and 3–4 were younger than those with grades 1–2 (median age 45 v 50 years). Gender and MELD score on admission were not associated with drinking behaviour.

Conclusions: After hospital discharge, continued heavy drinking in patients with decompensated ALD is associated with young age, previous heavy drinking, failure to stop drinking, social deprivation, and living alone. These associations may help target interventions to modify drinking behaviour.

133 WHO CONSULTS WITH DYSPEPSIA? A 10 YEAR CROSS SECTIONAL SURVEY

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Introduction: Dyspepsia is a chronic relapsing, remitting disorder, the natural history of which has been studied extensively. However, there are few studies examining factors that influence likelihood of consulting a general practitioner (GP) with symptoms in those who are symptomatic, particularly over a long time period.

Methods: The authors performed a 10 year follow up cross sectional survey of individuals recruited into a community screening and treatment programme for Helicobacter pylori. All surviving, traceable participants were contacted, by validated postal dyspepsia questionnaire. Baseline demographic data, quality of life at study entry, and dyspepsia and irritable bowel syndrome (IBS) symptom data were already on file. Written informed consent was sought to examine primary care records, and data on NSAID and aspirin use, and number of dyspepsia related consultations over the 10 year period were extracted from these.

Results: Of 8407 individuals originally involved, 3266 (39%) gave consent to examination of primary care records. The mean age of included individuals was 55 years, and 1799 (55%) were female. 1738 (33%) had dyspepsia at any point during 10 year follow up, when dichotomised according to questionnaire data. Of these, 729 (42%) consulted their GP. The mean number of consultations in these individuals was 3.5 (range 1 to 23). Univariate analysis revealed that H pylori infection, female gender, tobacco use, Asian ethnicity, lower social class, lower quality of life at study entry, IBS, and NSAID or aspirin use significantly increased likelihood of consultation, while the opposite applied to regular alcohol use. Following logistic regression H pylori infection, lower social class, lower quality of life at study entry, and aspirin use remained independent risk factors for consultation.

Conclusions: The reasons for consulting a GP with dyspepsia are multifactorial, but H pylori infection, aspirin use, low social class, and poor quality of life are independent predictors of consultation.

136 PREVALENCE AND CHARACTERISTICS OF OVERLAP SYNDROMES IN AUTOIMMUNE LIVER DISEASE, A 20 YEAR COHORT FROM A DEFINED COMMUNITY IN SOUTH WALES

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Background: The characteristics and relative frequency of overlap syndromes between autoimmune hepatitis (AIH) and both primary biliary cirrhosis (PBC) primary sclerosing cholangitis (PSC) are well described. Published data come from tertiary centres rather than a community setting and so may be affected by referral bias.

Aim: To describe the characteristics of 252 consecutive cases of autoimmune liver disease have been followed prospectively from 1984–2005 in a community hospital serving a stable population of 250 000 (98.6% white) in South Wales, UK. 27 overlap syndromes have been seen among the 121 cases of PBC, 78 of AIH, and 53 of PSC. Overlap syndromes were defined by clinical, biochemical, histological, serological, and cholangiographic features. Antimitochondrial antibody (AMA) negative PBC cases were excluded. 27 cases (22 female) aged 11–74 years (median 58) at presentation, have been followed for 1–29 years (median 11), 314 patient-years.

Results: There were 21 PBC/AIH, 4 AIH/PSC, 1 PBC/PSC, and 1 sequential overlap between PSC, PBC, and AIH. The dominant clinical picture was PBC in 7, PBC with bouts of AIH in 4, PBC evolving to AIH in 1; AIH in 6, AIH evolving to PBC in 2; PSC in 2, PSC with bouts of AIH in 3 and asymptomatic cirrhosis in 2. The biochemical pattern was cholestasis in 16, hepatitis in 12, both in 6 and mild mixed enzyme elevations in 5. Anti nuclear ± – anti-smooth muscle antibodies (mean titre 1:640) were seen in 21, AMA (mean titre 1:640) in 14, both in 10. Histologically 6 had PBC, 5 AIH, while 10 showed features of both; 11 were cirrhotic at initial biopsy. There have been 6 liver related and 2 unrelated deaths and one liver transplant while 18 are in remission. 16 patients were treated with corticosteroids and 10 with Ursodiol. Steroid induced osteoporosis was particularly common in PBC/AIH overlaps. Outcome reflected the dominant clinical picture and did not differ from the whole cohort with autoimmune liver disease.

Conclusion: In this community setting over a 21 year period, overlaps were seen in 22 of 199 patients with AIH or PBC (11%), five of 131 patients with AIH or PSC (4%), and two of 174 patients with PBC or PSC (1%). The PBC/PSC overlap is a newly recognised syndrome.
REMITFENTANIL VERSUS MIDAZOLAM AND PETHIDINE SEDATION DURING COLONOSCOPY: A PROSPECTIVE, RANDOMISED STUDY

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Background and Aims: Our study sought to compare the safety and efficacy of remifentanil (group A) versus the standard regimen of midazolam and pethidine (group B) for sedation during colonoscopy. To the best of our knowledge, this is the only prospective, randomised comparative study for the two regimens.

Methods: 116 consecutive patients undergoing colonoscopy were randomly assigned to groups A or B. In group A, patients were started with a loading dose of 1 μg/kg/min remifentanil followed by a continuous infusion at an initial rate of 0.05 μg/kg/min, adjusted accordingly. Patients in group B (n=56) received intravenously 4.3 (SD 1) mg midazolam and 81.7 (SD 21) mg pethidine. The quality of the anaesthesia was assessed with a four point scale; recovery level was evaluated with the Aldrete score, while patients’ suitability to home readiness was evaluated by a Modified Post Anesthesia Discharge Scoring system (MPADS). Patients’ comfort level was assessed 24 hours after the procedure.

Results: Recovery time and time to home readiness was significantly shorter for the group A than for group B (Aldrete: 10: 0 v 70.7 (SD 13.6) minutes and MPADS of 10: 28.7 (SD 4.3) v 157.8 (SD 34.2) minutes) (p<0.01). Multivariate stepwise logistic regression analysis revealed that among sex, age, duration of the test, ASA grade, and the type of sedation, the latter was the only factor associated with a quicker patient recovery time (χ²=160.6, p<0.01). Patient satisfaction was significantly higher in group B patients than group A (p<0.05).

Conclusions: Our data suggest that remifentanil sedation during colonoscopy provides sufficient pain relief, better hemodynamic stability, less respiratory depression, and significantly faster recovery comparing to midazolam/pethidine. However, the use of midazolam/pethidine was associated with a higher patient satisfaction.

IS A PHOTOGRAPH OF THE CAECUM OR TERMINAL ILEUM RELIABLE ENOUGH FOR DOCUMENTING COMPLETION OF COLONOSCOPY? A PROSPECTIVE STUDY

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Introduction and Aim: Documenting colonoscopy completion may become an important aspect of quality assurance if a suitable tool becomes available. The aim of this study was to independently assess the reliability of caecal or terminal ileal photographs as a proof of colonoscopy completion.

Materials and Methods: Colonoscopists were requested to take a convincing photograph of the caecum or terminal ileum to document completion of their examination during a prospective colonoscopy audit. Caecal photographs captured the following landmarks in various combinations (appendical opening, ileocaecal valve and tri-radiate fold). Terminal ileal photographs were either taken after water flush (to enhance the villi) or without. 177 photographs were collected over eight months and a further 23 bluffed photographs were added randomly. Eight clinicians (surgeons and gastroenterologists) were requested to categorise the photos as “caecum, terminal ileum or not sure”. Those identified as caecum and terminal ileum were further graded as 1, 2, or 3 depending on the level of certainty.

Results: A total of 200 photographs were used. The true locations were caecal in 91 (45.5%) cases, terminal ileal in 86 (43%) cases, and 23 (11.5%) were bluffed photographs. Thirty eight per cent of the caecal photographs, 71% of the terminal ileal photographs (combined), and 85.8% of the terminal ileal photographs with water flush technique were identified with a certainty of grade 2 or 3. When all the grades were considered, 70.9% of the terminal ileal photographs with water flush technique were identified. Interestingly 15% of the bluffed photographs were interpreted as caecum and a further 15% as terminal ileum.

Conclusion: A photograph of the terminal ileum after flushing with water appears to be a reliable and safe technique for documenting colonoscopy completion. This is less invasive when compared to terminal ileal biopsy. Caecal photographs do not appear to be a reliable way to document completion due to high interobserver variability.
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using the Q homogeneity statistic and if significant (p<0.05) a random effects model of meta-analysis was used.

Results: Twenty one surveillance studies met the inclusion criteria. This included 2808 patients with chronic ulcerative colitis on surveillance of which 534 had either flat LGD or LGD with dysplasia associated lesion or mass. An average of four colonoscopies were done/patient (range: 1.5–8.4) over an average duration of 12 years (range: 4–22). An average of 19 biopsies taken per colonoscopy (range: 8–56) detected 69 advanced lesions (cancer or high grade dysplasia) preoperatively. The average duration of colitis before LGD was diagnosed was 17 years (range: 11.5–33.8). The cancer incidence was 13/1000 pyd and the average of 19 biopsies taken per colonoscopy (range: 8–56) detected 20 hours and IL-8 assayed by ELISA. 

E coli strains and specific TLR agonists and antagonists were then added one to

Background and Aims: There is increasing interest in the use of probiotics as modulators of intestinal inflammation and gut flora homeostasis. Although the mechanism involved is unknown, it is likely to involve an interaction with gastrointestinal epithelial cells. The aim of this study was to study probiotic suppression of E coli induced IL-8 production in epithelial cell lines and investigate the potential role of toll-like receptors (TLR) in this interaction.

Methods: HT29 and Caco-2 cells were grown until confluent. Probiotic strains and specific TLR agonists and antagonists were then added one hour before stimulation with E coli. Supernatants were collected at 20 hours and IL-8 assayed by ELISA. E coli adherence was assessed by culture of washed lysed cells on MacConkey’s agar.

Results: The addition of E coli induced significant IL-8 production in both cell lines. Pretreatment with B longum or lactis and L casei, acidophilus, pentosus, or plantarum probiotics completely blocked E coli induced IL-8 production. Culture of recoverable E coli was in keeping with loss of adherence. The TLR-2 agonist lipoteichoic acid (LTA) reduced IL-8 production in HT29 and Caco-2 cells by 60%. Although LPS on its own only produced a low response, the TLR-4 antagonist Polymixin B was 20% less in HT29 and Caco-2 cells respectively compared to E coli K12 supporting a role for TLR-4.

Conclusions: Probiotics demonstrate potent inhibition of E coli induced IL-8 production and loss of adherence in vitro highlighting their therapeutic potential in gut inflammation. These findings suggest a role for TLR-2 and TLR-4 receptors in these suppressive probiotic effects.

Results: No significant differences in the mean or median values were found for transcripts of the apical membrane sodium-linked bile acid transporter ASBT, the cytoplasmic ileal bile acid binding protein IBABP, or the putative basolateral organic solute transporters alpha and beta. However there was no significant correlation between ASBT and IBABP in controls although they were related in those with diarrhoea. Expression of transcription factors previously shown to affect ASBT or IBABP expression was then measured. Mean or median values for FXR, LXR-1, SHP, and CDX2 were not significant different between groups. However the relationships of expression of these factors with ASBT and IBABP differed. Multiple stepwise regression showed that ASBT was significantly associated with LXR-1 and SHP in controls, and with SHP and CDX2, but not LXR-1, in diarrhoea. IBABP was associated with LXR-1, SHP, and CDX2 in controls, but only with CDX2 in diarrhoea.

Conclusion: Bile acid transporters were expressed at similar levels in patients with chronic diarrhoea and controls, but ASBT and IBABP may be regulated differently in patients with chronic diarrhoea.

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[142] PROBIOTIC BACTERIA INHIBIT EPITHELIAL CELL IL-8 PRODUCTION: ROLE OF TOLL-LIKE RECEPTOR ENGAGEMENT


Background and Aims: There is increasing interest in the use of probiotics as modulators of intestinal inflammation and gut flora homeostasis. Although the mechanism involved is unknown, it is likely to involve an interaction with gastrointestinal epithelial cells. The aim of this study was to study probiotic suppression of E coli induced IL-8 production in epithelial cell lines and investigate the potential role of toll-like receptors (TLR) in this interaction.

Methods: HT29 and Caco-2 cells were grown until confluent. Probiotic strains and specific TLR agonists and antagonists were then added one hour before stimulation with E coli. Supernatants were collected at 20 hours and IL-8 assayed by ELISA. E coli adherence was assessed by culture of washed lysed cells on MacConkey’s agar.

Results: The addition of E coli induced significant IL-8 production in both cell lines. Pretreatment with B longum or lactis and L casei, acidophilus, pentosus, or plantarum probiotics completely blocked E coli induced IL-8 production. Culture of recoverable E coli was in keeping with loss of adherence. The TLR-2 agonist lipoteichoic acid (LTA) reduced IL-8 production in HT29 and Caco-2 cells by 60%. Although LPS on its own only produced a low response, the TLR-4 antagonist Polymixin B was 20% less in HT29 and Caco-2 cells respectively compared to E coli K12 supporting a role for TLR-4.

Conclusions: Probiotics demonstrate potent inhibition of E coli induced IL-8 production and loss of adherence in vitro highlighting their therapeutic potential in gut inflammation. These findings suggest a role for TLR-2 and TLR-4 receptors in these suppressive probiotic effects.

[144] H63D MUTATION AND LIVER DISEASE

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Background: Haemochromatosis was first described by Von Recklinghausen in 1889 but the phenotypic heterogeneity became apparent only since the discovery of candidate genes in the early 90s. 90% of patients with haemochromatosis have C282Y mutation and its clinical effects are well known. The effects of H63D mutation remain unclear despite its world wide prevalence. Data available from the available studies show that H63D disease remains clinically silent in the majority and is not associated with significant hepatic iron overload or scarring.

Methods and Results: We looked at our database of 57 cases of haemochromatosis diagnosed between 1998 and 2005. Six homozygous H63D patients (1 female, 5 males) presenting with serum ferritin of 16, 350, 200, 801, 263 respectively. Four patients underwent liver biopsy for clinical indications not related to iron overload. The severity of iron overload in none of these biopsies was greater than grade 1. Three cases displayed a minor degree of portal fibrosis. One case progressed from mild fatty change to micro nodular cirrhosis in three years time and developed severe portal hypertension. His alcohol consumption was moderate (<=20 g/day) and viral markers were negative. His ferritin remained normal throughout and no other cause for the progression of his liver disease was found.

Conclusion: We suspect that in the background of his genetic predisposition this risk of moderate alcohol consumption could have triggered the onset of cirrhosis. The safety of moderate alcohol drinking should be reviewed in H63D homozygous individuals.

[145] REGENERATION IS INCREASED IN JNK2 KNOCKOUT LIVER

C. M. Bates, N. C. Henderson, K. J. Simpson (introduced by P. C. Hayes), Centre for Liver and Digestive Disorders, Royal Infirmary of Edinburgh, UK

Background: The ability for liver to regenerate following toxic injury or resection is almost unique and involves the complex interaction of multiple factors to produce a rapid regenerative response. C-Jun N terminal kinase (JNK) is a mitogen activated protein kinase (MAPK), involved in intracellular signalling. Upon activation by stress signals, proinflammatory stimuli, and mitogens, its main action is the phosphorylation of the transcription factor c-jun. JNK intracellular signalling pathway has a crucial role in liver regeneration. Three isoforms JNK1, JNK2, and JNK3 exist, JNK3 being mainly confined to brain, heart and testis. JNK1 is the main isoform involved in phosphorylation of c-jun and is a positive regulator of cellular proliferation. JNK2 in contrast is the main isoform that facilitates ubiquitination of c-jun and subsequent proteasome degradation, therefore is possibly a negative regulator of proliferation.

Methods and Results: Using genetically modified JNK2 knockout mice we investigated if JNK2 knockout liver has increased hepatocyte proliferation compared to wild-type littermate controls following toxic liver injury. Three isoforms JNK1, JNK2, and JNK3 exist, JNK3 being mainly confined to brain, heart and testis. JNK1 is the main isoform involved in phosphorylation of c-jun and is a positive regulator of cellular proliferation. JNK2 in contrast is the main isoform that facilitates ubiquitination of c-jun and subsequent proteasome degradation, therefore is possibly a negative regulator of proliferation.

Conclusion: Bile acid transporters were expressed at similar levels in patients with chronic diarrhoea and controls, but ASBT and IBABP may be regulated differently in patients with chronic diarrhoea.
into nuclei synthesising DNA, BrdU positive nuclei per 1000 nuclei were counted and calculated for each time point, and also western blot for cell cycle related cyclin-cyclin D1.

Results: At 30 hours post CCl4 injection hepatocyte proliferation was significantly increased in the JNK2 KO mice as determined by BrdU incorporation (JNK2 KO 2.47 (SD 0.86) nuclei per high power field control 0.4 (SD 0.17); n=4). Expression of cyclin D1 was significantly elevated at 30 hours in JNK2 KO mice compared with littermate controls. This research has demonstrated earlier and increased hepatocyte proliferation in a murine model of toxic injury in JNK2 knockout liver.

146 PRACTICAL MODIFICATIONS OF THE 13C-METHACETIN BREATH TEST STILL FULFIL CLINICAL DEMANDS FOR THE QUANTITATIVE ASSESSMENT OF LIVER FUNCTION

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Background and Aims: The 13C-methacetin breath test measures the activity of the cytochrome P450 dependent enzyme system and has been developed to assess the functional hepatic mass. We evaluated simple modifications of the 13C-methacetin breath test in order to further increase its practicability and therewith clinical acceptance.

Methods: 104 patients with different chronic liver diseases (including 35 patients with histologically proven cirrhosis) and 65 healthy controls underwent the 13C-methacetin breath test. Breath test results of two-point measurements at baseline and 5, 10, 20, 25, and 30 minutes after ingestion of the test solution, respectively, were compared to conventional breath test results (cumulative recovery after 30 minutes) and liver histology.

Results: The receiver operator curve analysis revealed the two-point measurement at 15 minutes (Delta over baseline value at 15 minutes DOB) best compared to the cumulative recovery at 30 minutes and the presence of cirrhosis in histology. Using a cut-off <14.6% the DOB 15 minutes reached 92.6% sensitivity and 94.1% specificity with respect to the presence of cirrhosis in liver histology. However, even the two-point measurement at 5 and 10 minutes provided good discrimination between cirrhotic and non-cirrhotic subjects.

Conclusion: The 13C-methacetin breath test reliably indicates decreased liver function in liver cirrhosis, even in its modification as two-point measurement using breath samples at baseline and after 15 minutes. This simplification of the 13C-methacetin increases practicability and cost efficiency and therewith will facilitate its clinical acceptance and distribution.

147 COVERED STENT GRAFTS FOR TIPS INSERTION PROVIDE IMPROVED CLINICAL OUTCOME: A DECADE OF EXPERIENCE

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Introduction: The principal disadvantages of TIPS are the development of shunt dysfunction and hepatic encephalopathy. The introduction of covered stent-grafts is thought to improve shunt patency with a theoretical consequent increase in hepatic encephalopathy. We report on 10 years’ experience in a single centre.

Methods: Data was collected prospectively at the time of TIPS insertion and surveillance portography were correlated with retrospective case note analysis. Complete data were available for 192 patients.

Results: Most patients were male (62.4%) with alcoholic liver disease (66.7%) and bleeding varices (86.6%). The procedure was unsuccessful in eight. There were 35 deaths within one month and a further five patients underwent liver transplantation during the same admission. A further seven were lost to follow up. No further analysis was undertaken on these 55. TIPS was created using a covered stent-graft in 58 patients and a bare stent in the remainder. Successful portal pressure reduction was achieved in all patients. In patients who had surveillance portography, primary patency at 1 year was 86.7% v 53.4% for the covered and bare stents respectively. Shunt insufficiency requiring intervention occurred in 5 v 35 patients requiring a total of 8 v 60 interventions during mean follow up of 19.8 (SD 1.7) v 43.2 (SD 4.1) years respectively. Hepatic encephalopathy developed in 52 (38.8%) patients. HE was present within three months of TIPS insertion in 26 patients but completely resolved thereafter in 10. HE may have contributed to the death of 10 patients. In three of these the TIPS was radiologically occluded but none of these improved prior to death. HE occurred with equal frequency after both covered (37.9%) and bare stents (39.4%).

Conclusion: Newer covered stents appear to improve patency compared to bare stents with implications for surveillance and intervention. Clinically important hepatic encephalopathy develops in a minority of patients and there is no increase in frequency with covered stents.

148 ACUTE LIVER FAILURE IN SCOTLAND: 13 YEAR OBSERVATIONAL STUDY

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Acute or fulminant hepatic failure (FHF) is a rare, life threatening condition with no specific treatment except liver transplant. Paracetamol is the commonest cause of FHF in the UK. Legislative changes to paracetamol packaging were introduced 1998 in order to reduce the number of overdoses and the prevalence of FHF. The incidence, causes or outcomes of FHF in Scotland are unknown. A prospectively collected database was analysed to obtain information on patients admitted to the Scottish Liver Transplant Unit (SLTU) with FHF.

Between November 1992 and 1 November 2005 there have been 783 admissions to SLTU with FHF, 351 males (45%) and 432 (55%) females. 948 patients had taken a paracetamol overdose (POD). Other causes included non A–E hepatitis, 59 (7.5%); idiosyncratic drug reactions, 36 (4.6%); Budd Chiari syndrome,15 (2.0%); and ischaemic hepatitis,14 (1.8%). 157 PODS (27.9%) met poor prognostic criteria, 84 (53.3%) were considered transplant candidates and 41, (49%) died prior to transplant. In patients with non-POD FHF more patients met poor prognostic criteria (85 patients, 38.6%), more were candidates (76 patients, 89%) and 57 patients (75%) survived to transplant. Paracetamol was taken as a staggered overdose in 140 (24.9%) cases—associated with increased morbidity and greater percent of patients being too sick for transplant (22 patients (56%) were candidates, 64% became too sick). Mortality was increased with staggered mortality, 34.3% v non-staggered mortality, 21.8%.

The legislative changes have not significantly decreased admissions to SLTU (275 admissions Nov 92–Sept 98 compared with 285 admissions Oct 98–Nov 05). Increased numbers of patients met KCH criteria for transplant. Paracetamol overdose remains the commonest reason for admission to SLTU. Legislative changes have not significantly reduced the number of admissions or deaths. Staggered overdoses have increased since the legislative change and are associated with poorer prognosis.

149 WHAT IS THE DELAY TO DIAGNOSIS IN PATIENTS REFERRED WITH ABNORMAL LIVER BIOCHEMISTRY?

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Introduction: Clear guidelines exist for the management of many of the patients seen in the primary care setting. Many of the tests to screen patients for the various causes of abnormalities in liver biochemistry are available to primary care practitioners and if employed as part of a suitable guideline may reduce only time to diagnosis.

Aims and Methods: The aim of this study was to determine the extent to which patients who were referred because of abnormalities in liver biochemistry were investigated prior to referral to hospital, and the time to final diagnosis after referral. Patients with abnormalities in liver biochemistry who were referred over a one year period between October 2002 and October 2003 were identified. Their presenting complaint, investigations requested by their general practitioner, eventual diagnosis and time to diagnosis and management were analysed from the medical records.

Results: The notes of 38 patients were reviewed; 25 were new referrals during the study period. Abnormalities in liver biochemistry were an incidental finding in 16. Four patients had associated abdominal pain, three had jaundice, three had pruritis, three had weight loss, one with fatigue and one with an abdominal mass. 11 patients had an ultrasound scan prior to referral; viral serology had been checked in five, with three patients having had a ferritin estimation, and three had autoimmunity antibodies. None of the patients had had the full complement of tests at the time of referral. The time to diagnosis was non-alcoholic fatty liver disease (NAFLD) in seven patients and alcohol related liver disease in five patients; four patients had autoimmune liver disease.
NON-INVASIVE MARKERS OF FIBROSIS IN NAFLD: A SYSTEMATIC REVIEW

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Background: Long term studies suggest that the presence of fibrosis within non-alcoholic fatty liver disease (NAFLD) has the most significant prognostic implication. Currently liver biopsy is the gold standard diagnostic test for liver fibrosis but due to its limitations there is a need to develop effective non-invasive tests.

Methods: We conducted a systematic review of the performance of non-invasive tests in NAFLD. Data were extracted from electronic databases 1996–September 2005: Cochrane Library 2004, MEDLINE, and EMBASE. Key measures of diagnostic accuracy and variables statistically associated with fibrosis were extracted. Inclusion criteria: NAFLD proven on biopsy, n>30 and analysis of fibrosis stages.

Results: Electronic search yielded 1781 abstracts; 27 primary studies in separate populations were included in the final analysis. Only four studies produced a true diagnostic score with details of an AUC and sensitivities and specificities at critical cut-off points. The majority of studies presented associations of variables with fibrosis found by univariate (UVA) or multivariate analysis (MVA). 17 studies compared severe to mild fibrosis, four studies compared mild fibrosis to moderate fibrosis, and six studies compared no fibrosis to any fibrosis. The most frequent variables associated with severe fibrosis were: increased age, presence of diabetes, raised AST/ALT ratio, raised homeostatic model assessment (HOMA-IR), increased BMI, raised serum hyaluronic acid, raised serum ferritin, and elevated platelet count. The data are extremely heterogeneous and presentation of odds ratios, by UVA or MVA, was variable and did not allow meta-analysis for strength of association.

Conclusion: Simple clinical and biochemical parameters appear to be associated with fibrosis in NAFLD. Studies incorporating these variables into non-invasive tests have started to emerge. It is likely that accuracy will continue to improve with refinement of these diagnostic algorithms by the addition of novel biomarkers.

SERUM UNDERCARBOXYLATED PROTHROMBIN (PIVKA II) HAS AN INVERSE RELATIONSHIP WITH HEPATIC STEATOSIS


Background and Aims: Hepatic steatosis is a condition with an increasing prevalence and can progress to hepatic inflammation and fibrosis. The functional activity of vitamin K dependent clotting factors synthesised in the liver is dependent on the integrity of the microsomal γ-glutamyl carboxylation system. This converts the inactive protein precursors to their active forms. In the absence of adequate hepatic function, the precursors may be secreted into the systemic circulation and can be detected (Proteins Induced by Vitamin K Absence or Antagonism, PIVKA II). Previous studies have shown that PIVKA II estimation to predict subclinical coagulopathy in liver failure, and may predict prognosis on treatment in hepatocellular carcinoma. The aim of the present study is to determine the relationship between PIVKA II levels and hepatic steatosis.

Methods: We studied PIVKA II levels in 85 patients investigated for abnormal liver function tests who have had liver biopsies. The biopsies were assessed and reported by a pathologist blinded to the PIVKA II measurements, and steatosis was graded as absent, mild, moderate or severe graded 0–4. PIVKA II levels were measured by enzyme linked immunosorbent assay (ELISA). Patients with bilirical stasis or obstructive jaundice were excluded.

Results: Of the 85 patients, 25 had chronic hepatitis C, seven chronic hepatitis B, one STE, two auto immune hepatitis, 12 alcoholic liver disease, five methotrexate induced liver fibrosis, and one sarcoidosis. Patients with no steatosis on liver biopsy had a significantly higher PIVKA II level when compared with patients with severe steatosis (1.27 ± 0.43, p = 0.01). PIVKA II levels did not correlate with hepatic fibrosis.

Conclusion: These preliminary results may indicate an augmented mechanism of vitamin K metabolism in the presence of hepatic steatosis. Whilst PIVKA II did not correlate with fibrosis it may be a useful non-invasive marker of hepatic steatosis and warrants further investigation.

NON-INVASIVE MARKERS OF FIBROSIS IN NAFLD: A SYSTEMATIC REVIEW

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Introduction: Type 2 diabetes is recognised as a risk factor for non-alcoholic fatty liver disease (NAFLD). We examined the incidence of elevated (>35 U/l) alanine transaminase (ALT), as a surrogate marker for NAFLD, in patients with newly diagnosed type 2 diabetes.

Results: Retrospective analysis of ALT levels and various routine metabolic parameters from 668 consecutive patients presenting to our district wide education sessions for newly diagnosed type 2 diabetes.

Conclusions: There is a high incidence of elevated ALT levels in our well defined population of newly diagnosed type 2 diabetics, but no significant correlation between ALT and glycaemic control. Rather, an elevated ALT is associated with increasing age, obesity, elevated triglycerides and lower HDL cholesterol levels. These observations are in keeping with the currently understood pathogenesis of NAFLD as a hepatic manifestation of the metabolic syndrome and may help identify individuals at increased risk of developing chronic liver disease who should be investigated further.

IS THE METABOLIC SYNDROME A USEFUL CRITERION IN THE DECISION TO BIOPSY IN NON-ALCOHOLIC FATTY LIVER DISEASE?

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Introduction: NAFLD represents a spectrum of disorders with NASH only representing a stage within it. Liver biopsy at present is the only way of distinguishing those with NASH from fatty liver alone. It cannot be predicted reliably on clinical or laboratory grounds. Patients with NASH are at risk of progression of their disease and therefore need to be identified. A recent study showed that those with three or more criteria for the metabolic syndrome were at significantly increased risk of NASH rather than fatty liver alone.

Aim: To measure the prevalence of the metabolic syndrome in patients with NAFLD and to verify that these patients are more likely to have NASH, with or without fibrosis. There is a need for criteria to distinguish those at greater risk of NASH and therefore at risk of more advanced disease. With this goal in mind, we reviewed a group of patients with biopsy proven NAFLD and identified the most culturally relevant criteria for the syndrome that are associated with the diagnosis of NASH.
risk of progression of their liver disease. The metabolic syndrome may be a useful criterion and larger studies are needed to verify this.


154 LAMIVUDINE IN ACUTE HEPATITIS B INFEC TION: A CASE SERIES

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Background: Lamivudine is a nucleoside analogue that improves outcomes in chronic hepatitis B infection. It is not licensed for other indications but may have a role in acute hepatitis B infection. We present here our experience of this treatment.

Methods: Case note review of patients treated between 2001 and 2004. We recorded clinical and serological findings at presentation and after treatment. Treatment protocol for patients with clinically severe hepatitis was lamivudine 100 mg daily for six months.

Results: Six patients were treated (median age 35 years, range 16–75; 5M: 1F; five white, one south Asian). No patient had a prior history of liver disease. At presentation median ALT level was 1150 iu/l (range 468–5847) and median bilirubin level was 225 µmol/l (range 12–85). All patients were HBsAg and anti-HBc IgM positive; one was HBsAg positive. Hepatitis B DNA levels in four patients were < 400, 2700, 72,000, and 80,000 iu/ml. Liver biopsy was done in two older patients and revealed active hepatitis without cirrhosis. After four weeks of lamivudine, ALT fell to a median of 116 iu/l (range 34–506) and median bilirubin was 25 µmol/l (range 12–85). At 12 weeks liver function had normalised in all patients; median ALT was 25 iu/l (range 16–37) and median bilirubin was 11 µmol/l (range 7–17). One patient was then lost to follow up; all remaining patients were HBsAg negative by completion of therapy at six months. No adverse effects of the treatment were reported and no patient had recurrent disease thereafter (median follow up 10 months, range 3–22).

Conclusions: This uncontrolled series suggests a favourable role for lamivudine in acute hepatitis B infection; further case series or controlled studies may help to confirm this.

155 RESISTANCE AND SENSITIVITY TO INSULIN AFFECT THE RESPONSE TO INTERFERON IN PATIENTS WITH CHRONIC HEPATITIS C

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Aims: Insulin resistance (IR) is related to hepatic inflammation in patients with CHC infection. The possible association with fibrosis development and the response to treatment is under intense research; we therefore studied IR in patients with chronic hepatitis C (CHC) in relation to these parameters.

Patients and Methods: Seventy patients with biopsy proven CHC were included: 23 before any treatment, 18 with sustained virological response (SVR) after interferon and ribavirin, 19 non-responders, and 10 relapsers. We evaluated IR (HOMA-IR), sensitivity to insulin (Quicki) and CD8+ cell function (HOMA-B) of the patients and related to BMI, steatosis and Ishak’s stage; we also measured serum factors linked to fibrosis: laminin, leptin, hyaluronic acid, CD8+ and collagen IV and TGF-β.

Results: HOMA-IR was significantly lower (p<0.05) and Quicki higher (p<0.05) in those who responded to treatment compared to non-responders or relapsers. HOMA-B was found significantly lower in relation to steatosis and advanced fibrosis (p<0.05). Hyaluronic acid (395 µg/µl; 63.5–182.1; SD 24.3; p=0.0003) and collagen IV (65.8 SD 11.4) and 38.5 SD 2.2; p=0.0006) were statistically higher in advanced compared to early fibrosis, while laminin, leptin, and TGF-β did not have statistical correlation with fibrosis nor with response to treatment.

Conclusions: Resistance and sensitivity to insulin was related to the response to interferon treatment in patients with CHC, while CD8+ cell function correlated with steatosis and advanced fibrosis. Serum hyaluronic acid and collagen IV were the best discriminators between early and advanced fibrosis.

156 ACTIVATION OF EFFECTOR CD8+ T CELLS FROM THE LIVER TISSUE MICROENVIRONMENT IN PATIENTS WITH CHRONIC VIRAL HEPATITIS


Background: CD8+ T cells mediate liver damage and protection in hepatitis B and C virus infection. Activation of CD8+ T cells requires a number of signals that include recognition of MHC class I and costimulatory molecules such as CD28 and NKG2D. CD8+ T cells capable of activating and *killing* infected hepatocytes in patients with viral hepatitis are usually CD28- and NKG2D-. CD8+ T cell function is determined by the microenvironment surrounding them.

Aims: To determine the activation status of CD8+ T cells from patients with chronic viral hepatitis.

Methods: Peripheral blood lymphocytes and intrahepatic lymphocytes from 30 patients with viral hepatitis were studied. Five patients undergoing resection of liver metastases were included as controls. Phenotypic NKG2D/CD28 expression on CD8+ T cells was investigated. Functional study of CD28/NKG2D co-stimulatory ability was analysed in lymphocytes (intrahepatic and circulating) and in HBV-specific CD8+ NKG2D+ CD28low T cell clones.

Results: Intrahepatic CD8+ T cells phenotypically display increased NKG2D and low CD28 in patients with viral hepatitis. In contrast, circulating CD8+ T cells show a high level of CD28 positivity with low NKG2D expression. Consistent with this, CD28 has a profound co-stimulatory effect in the activation of circulating CD8+ cells, while the co-stimulatory effect of CD28/NKG2D is minimal on intrahepatic T cells. IL-15 however could induce NKG2D co-stimulation on purified intrahepatic CD8+ T cell clones. Furthermore, NKG2D had the ability to modulate antigen specific recognition of HBV specific CD8+ NKG2D+CD28low T cell clones.

Conclusions: Both phenotypic and co-stimulatory requirements of intrahepatic and circulating CD8+ T cells differ. The NKG2D co-stimulatory function of intrahepatic CD8+ T cell activation is IL-15 dependent. Cytokine profile of the liver microenvironment in chronic viral hepatitis can influence CD8+ T cell activation and disease profile.
Conclusion: Majority of our patients were compliant to treatment (97%). All patients were satisfied with the information and care provided by the nurse consultant during treatment. This study emphasizes the importance of specialist nurses in the management of chronic hepatitis C infection.


[158] SERIAL MEASUREMENTS OF HYALURONIC ACID: A USEFUL MARKER OF CIRRHOSIS IN HEPATITIS C

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Background and Aim: Hyaluronic acid (HA) is a linear polysaccharide that has been shown to correlate with fibrosis in patients with chronic hepatitis C. The use of serial measurements in monitoring fibrosis over time has not been established. The aim of this study was to evaluate the usefulness of serial HA measurements in predicting cirrhosis in hepatitis C haemophilia patients.

Method: Single centre retrospective observational study. We identified 97 haemophilia (A or B) or von Willebrand patients with active or past hepatitis C infection. From this group we selected 19 patients with at least three serial HA measurements of which at least one value was >100 (group 1) and 10 patients who had serial HA levels persistently <100 (group 2). Only HA levels measured after 1998 were included as the assay was changed at that time. Patients were classified as cirrhotic based on a combination of clinicopathological parameters including ALT/platelet ratio index (APRI) >2.0, AST/ALT ratio >1.0, U/S evidence of portal hypertension or histology. Hepatitis C PCR status was also recorded.

Results: In group 1 (18 males; 1 female), mean age was 50 (range 28–77 years) and Hep C PCR was positive in 11. 13 patients had previously undergone treatment for hep C. The mean HA over a median four year follow up period was 112. In those in whom HA values were persistently >100 (at least two consecutive values) (n=10; group 1a), eight (80%) were classified as cirrhotic. In those in whom HA was >100 once or intermittently (not consecutive values) (n=9; group 1b) none were classified as cirrhotic. Of the two patients in group 1a classified as non-cirrhotic one had severe arthropathy and the other was one of two with cirrhosis classified as cirrhotic one had severe arthropathy and the other was one of two with cirrhosis.

Conclusion: In haemophilia patients with serum HA levels persistently >100, cirrhosis is generally present. In those in whom HA <100 or intermittently >100, cirrhosis is generally absent. Serial measurements of HA are more value than single HA estimations.


Aims: To report the clinical and treatment outcomes of hepatitis C patient care in a single centre hepatitis C service.

Methods: We prospectively recorded demographic information, hepatitis status, liver biopsy results, and treatment outcomes on a viral hepatitis database.

Results: 1235 patients with viral hepatitis were referred; hepatitis C, n=1185 (96%); hepatitis B, n=50 (4%). HCV genotypes were known in 453 cases; 209 (46%) genotype 1; 244 (54%) genotype 2 and 3. Liver biopsies were performed in 228 patients, 25 (11%) cirrhotic. Of patients attending, nine (1.03%) developed hepatocellular carcinoma and 44 (5.04%) died of which 14 (32%) were related to liver disease. 691 patients (56%) have been discharged from the service due to non-attendance. The table shows sustained response (SR) rate to three treatment regimens.

Conclusions: (1) Treatment response rates in clinical practice were lower than published data. In particularly only 16% of HCV genotype 1 patients achieved sustained response. (2) An overall 5.04% mortality rate, with 1.6% liver related deaths was observed in those attending. (3) The high non-attendance rate indicates the need to establish alternative methods of delivery of care.

Table 1

<table>
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<tr>
<th>Treatment</th>
<th>Peg interferon + ribavirin monotherapy</th>
<th>Peg interferon + ribavirin monotherapy</th>
<th>Peg interferon + ribavirin monotherapy</th>
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<td>0.55</td>
<td>94%</td>
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<tr>
<td>F0–3</td>
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<td>&lt;0.001</td>
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<td>92%</td>
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<td>90%</td>
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Conclusion: The ELF markers can be used in the assessment of liver fibrosis in CHC either as an adjunct to, or in place of liver biopsy where appropriate.

[160] EUROPEAN LIVER FIBROSIS MARKERS ACCURATELY DISTINGUISH FIBROSIS SEVERITY IN CHRONIC HEPATITIS C

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Introduction: Liver biopsy is the reference method for assessing liver fibrosis. However this is painful, hazardous, costly, and inaccurate as it is subject to significant sampling error and problems with processing and interpretation. The quest for accurate non-invasive markers of liver fibrosis has led to the development of a panel of highly sensitive serum assays that measure matrix components and enzymes involved in their turnover. We have previously shown that these European liver fibrosis (ELF) markers are accurate in assessing liver fibrosis in a range of chronic liver disorders. Here we present the validation of the performance of the ELF markers in an independent cohort of patients with chronic hepatitis C (CHC).

Methods: Subjects were 173 patients with CHC in the Trent Cohort, naïve to antiviral treatment, for whom serum samples were available and linked to a liver biopsy obtained within six months. All biopsies were scored by a single pathologist using the Ishak staging system. TIMP-1, PIINP, and HA were measured in the samples, all of which were anonymous to the investigators. Discriminant scores (DS) were derived using the published ELF algorithm. The area under the curve (AUC) for receiver operator characteristic curves was measured along with sensitivity (Sens) and specificity (Spec) for distinguishing between different degrees of severity of fibrosis.

Results: See table.

Table 1

<table>
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<tr>
<th>Stage</th>
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<th>p Value</th>
<th>DS</th>
<th>Sens</th>
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<tr>
<td>F0,1</td>
<td>0.79</td>
<td>0.72–0.86</td>
<td>&lt;0.001</td>
<td>1.03</td>
<td>90%</td>
</tr>
</tbody>
</table>

Conclusion: The ELF markers can be used in the assessment of liver fibrosis in CHC either as an adjunct to, or in place of liver biopsy where appropriate.

[161] AN EPIDEMIOLOGICAL STUDY OF HEPATITIS C GENOTYPE RELATED TO URBAN/RURAL LIVING

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Background: Little is known about the geographic breakdown of hepatitis C genotypes between urban and rural areas. We analysed the genotype of all hepatitis C positive patients attending the liver clinic at Lancaster Royal Infirmary and Furness General Hospital between 1997 and 2004. Results of the genotyping were then geographically mapped according to postcode.

Methods/Results: 105 patients were studied. There was a noticeable increase in the numbers of patients diagnosed during 2000 and 2001 (24 and 18 patients respectively). 44.8% of patients (n = 47) were genotype 3a, 43.8% (n = 46) were genotype 1 with the reminder being genotype 2 or other subtypes. Only a small number of patients (n = 10) lived in rural postcodes. The majority of patients (n = 95) were clustered around urban areas.

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There was no noticeable difference between the distribution of genotypes between urban and rural areas. The increase in numbers of patients diagnosed with hepatitis C during 2000 and 2001 may have been related to a co-existing research trial during that period and may indicate an underlying undiagnosed larger population with hepatitis C within Morecambe bay. The relatively higher incidence of genotype 3a in our patients has implications for local funding for Hepatitis C treatment. NICE guidelines currently recommend 48 weeks treatment with Ribavirin and Peg-interferon for genotype 1 disease but only 24 weeks treatment for genotype 2 and 3. According to the NNF the cost difference is £6199 (for a 70 kg man). Urban clustering may follow the fact that hepatitis C infection is largely contracted through IV drug use. Cheaper accommodation costs in the Northwest particularly in Lancaster, Morecambe, and Barrow may attract current or reformed drug users who are hepatitis C positive. Rural lifestyle is associated with a much lower prevalence.

**Conclusion:** Larger regional studies into the geographic breakdown of hepatitis C genotypes are needed to elucidate small trends within urban and rural areas.

### RESULTS OF COMBINATION TREATMENT WITH PEGYLATED INTERFERON AND RIBAVIRIN IN CIRROTIC PATIENTS WITH HEPATITIS C INFECTION

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**Background:** The treatment of hepatitis C patients with advanced cirrhotic liver disease remains challenging. These patients were excluded from the registration trials of pegylated interferon and ribavirin, so data on the outcome of treatment for this patient group are limited.

**Patients and Methods:** Between September 2000 and August 2004, 61 (42 male, age range: 29–69 years, 26 Asian) patients with either biopsy proven cirrhosis, or blood tests suggestive of cirrhosis, started treatment with pegylated interferon and ribavirin. None had evidence of significant hepatic decompensation at start of treatment.

**Results:** Forty three of 61 (70%) patients were serum HCV RNA negative at the end of treatment and 24 (39%) achieved a SVR. SVR was achieved for 35 (6 of 17) of patients with genotype 1, and for 39% (16 of 41) with genotype 3. Comparison of SVR rates for Asian versus white patients infected by genotype 3 demonstrated a higher cure rate for white patients (SVR observed for 10/18 = 56%) than for Asians (10/24 = 25%). No female Asian patient achieved a SVR (9 treated). Failure to achieve SVR was associated with baseline features including a lower platelet count, neutrophil count, and albumin compared to those who achieved SVR. 22 patients (39%) did not finish the treatment course 10 patients decompensated during therapy. Two patients died. Patients who experienced hepatic decompensation tended to be older at baseline (>45 years) and to have baseline characteristics associated with more advanced liver disease.

**Conclusion:** The treatment of patients with advanced liver disease from hepatitis C is challenging, though a significant number can achieve a sustained virological response. Significant toxicity is experienced and there is treatment-related mortality. This balance of efficacy and toxicity needs to be considered before commencement of treatment. Older patients and those with more advanced cirrhosis should be told about the significant risk of hepatic decompensation.

### WHY IS GAMMAGLOUTAMYLTRANSPERIDASE ACTIVITY INCREASED IN PATIENTS WITH CHRONIC HEPATITIS C?

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**Background:** Serum gammaglutamyltranspeptidase activity (GGT) is often increased in chronic hepatitis C. The factor predicting poor response to antiviral treatment is the mechanism involved in this effect is unclear, although hepatic steatosis has been identified as a possible cause in unselected patients. The aim of our study was to assess factors affecting GGT activity in patient with chronic hepatitis C by carefully selecting patients with no present or past history of alcohol intake.

**Methods:** We selected 63 consecutive patients with biopsy proven chronic hepatitis C and no history of alcohol consumption. We measured anthropometric parameters, insulin resistance (HOMA IR) and the conventional virological and serological liver tests. Liver histology was classified according to Knodell and hepatic steatosis according to Brunt. All patients were treated with Peg-IFNα-2a 1.5 μg/kg/weekly plus ribavirin (800–1200 mg/day according to body weight).

**Results:** Thirty eight patients had pretreatment GGT > 1 the upper limit of normal, and 25 had values within the normal range. There was no difference in pretreatment viral load and genotype distribution among the two groups. Peptide-C (mean (SD): 2.98 (SD 1.66) ng/ml vs. 2.04 ± 0.90 ng/ml, p = 0.0175), insulin resistance (2.83 (SD 1.9) vs. 1.79 (SD 1.12), p = 0.023), and hepatic steatosis score (0.78 (SD 0.5) vs. 0.22 (SD 0.43), p = 0.001) were significantly higher in patients with high than in those with normal GGT. Insulin resistance (r=0.467, p<0.001), hepatic staging (r=0.313, p<0.05) and steatosis (r=0.399, p<0.007) were significantly correlated (Pearson correlation) with serum GGT. Hepatic steatosis was the only parameter independently correlated with serum GGT (r=0.510, p<0.007) at multiple regression.

**Conclusion:** This study confirms that serum GGT is increased in a substantial proportion of patients with chronic hepatitis C that are not alcohol consumers. This effect is independent of virological characteristics and is attributable and is surrogate marker of hepatic non-alcoholic steatosis.

### MANAGEMENT OF VARICEAL BLEEDING: A SINGLE CENTRE EXPERIENCE

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**Background/Aims:** Variceal bleeding is an important. We aim to audit our current practice and assess the efficacy of our management strategies.

**Methods:** A retrospective study on the management of variceal hemorrhage in a single tertiary referral centre from April 2002–July 2004. 92 patients were identified using clinical coding. Data were collected and analysed in a dedicated database.

**Results:** The mean follow up was 11.4 (SD 12.2) months. The mean age was 52.8 (SD 14.9) years. The male to female ratio was 3:1. Alcoholic
A significant number of patients required a TIPSS. Adherence to pre-endoscopic therapy, particularly antibiotics, needs to be optimised.

The use of Conclusions:

variceal re-bleeding.

84% of patients had an endoscopy within 24 hours. 18% of patients were ventilated. Average time spent in intensive care was 1.6 (0–18) days, and total hospital stay was 13 (1–70) days. 38% of patients received vasconstrictor therapy, while 86% of patients received antibiotics. The most used initial endoscopic therapy for acute bleeding was variceal band ligation (79%) followed by sclerotherapy (62%) and others (13%). 59% of patients went on to have TIPSS (70% in Child’s grade C), where there was failure of acute hemostasis or variceal rebleeding. The average volume of transfusion (blood) received by each patient was 4.5 (SD 4.9) units. Cumulative survival rates at 6 weeks, 1 year, and 2 years were 71%, 57%, and 53% respectively. Six week, 1 year, and 2 year rates of variceal rebleeding were 53%, 57%, and 61% respectively. Independent variables predicting poor survival were a Child’s score of >10 (p<0.001) and a creatinine >110 (p<0.001). Failure to administer antibiotics (p=0.02) and a Child’s score >10 (p<0.05) were independent variables predicting variceal re-bleeding.

Conclusions: Our experience highlights the poor outcome of patients with variceal bleeding, especially within the first six weeks, which reflects the fact that most had significantly impaired liver function. The use of pre-endoscopic therapy, particularly antibiotics, needs to be optimised. A significant number of patients required a TIPSS. Adherence to recommended guidelines is essential and needs to be improved.

166 SPORADIC HEPATITIS E IS MORE COMMON THAN PREVIOUSLY THOUGHT: A SINGLE CENTRE EXPERIENCE

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Background: Hepatitis E (HEV) is an oro-faecal borne viral infection which is endemic in parts of Asia. The incidence of autochthonous hepatitis E is poorly documented in the United Kingdom but one study estimated the sero-prevalence of anti-HEV IgG in London between 3.9% to 8.8%. A possible source of autochthonous infections is believed to be the UK pig herd in which there is an estimated sero-prevalence of 85%. We present nine cases of non travel associated HEV which occurred over the last 18 months. The incidence of HEV in our mixed urban and rural population is far higher than expected.

Results: Nine cases of unexplained hepatocellular jaundice tested positive for HEV IgM/IgG antibodies over an 18 month period, six of whom were PCR +ve. Three cases were PCR –ve but IgM and IgG titres were consistent with acute HEV. There were six males and the mean age was 66 (range 35–83) years. All cases exhibited symptoms of an acute hepatitis. In all cases liver function recovered completely and no patient lived within a 10 mile radius from the shore but none lived in proximity to or worked on a farm. None had travelled to an endemic area. Four had regular contact with domesticated animals. All PCR positive cases were genotype 3 and phylogenetic analysis revealed high homology to HEV genomes infecting both humans and pigs in the UK and those seen in the UK pig herd.

Conclusion: The incidence of acute HEV amongst our catchment population is far higher than expected. The high sequence homology between these cases and those seen in the pig herd raise the possibility of zoonotic transmission. Hepatitis E virus is a public health issue in the United Kingdom.

167 A SYSTEMATIC REVIEW OF ACUTE HEPATITIS E VIRUS INFECTION IN A SEMI-RURAL POPULATION IN THE UK

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Background: Hepatitis E virus (HEV) infection in the UK has previously been considered an infection predominantly associated with travel to the HEV endemic and epidemic countries of Asia, Africa, and Mexico. Method/Results: HEV serology at County Hospital, Hereford (a semi-rural population of 220 000) was reviewed over a 12 month period (2004–05). Seven patients had evidence of HEV infection with four patients demonstrating acute HEV on serological testing and three showing evidence of past infection. Two acute HEV cases were elderly patients (85): one developed acute hepatitis with jaundice lasting 3–4 weeks and died from hepatoencephalopathy, the other developed fulminant liver failure complicated by a fatal myocardial infarction. The two other cases of acute HEV (ages 49, 61) presented with acute, severe viral hepatitis requiring admission to hospital with jaundice lasting 3–4 weeks and both patients subsequently made a full recovery. Only one of the four cases of acute HEV gave a history of recent foreign travel (Spain and Australia). In our review none of the cases of HEV were found to be associated with travel to recognised HEV endemic countries.

A previous report of 186 cases of acute HEV diagnosed in England and Wales between 1996 and 2003 revealed 17 cases with no history of recent foreign travel but identified risk factors of coastal and estuary settings and increased age.

Conclusion: HEV now appears to be endemic across the UK and acute HEV infection should be considered in all patients with acute viral hepatitis of uncertain aetiology in a UK setting. The infection is particularly notable in children, pregnant women, and immunosuppressed individuals.

168 HEPATOTOXICITY ASSOCIATED WITH ATORVASTATIN USE

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Background: Atorvastatin, an HMG-CoA reductase inhibitor, is widely used in the treatment of dyslipidaemia. A transient rise in serum transaminases occurs in up to 3% of patients but this is usually self-limiting and inconsequential. Recent literature has indicated some potential for serious but rare idiosyncratic reactions related to this drug. Method/Results: We report seven cases of significant liver dysfunction related to atorvastatin use from one centre during the period 2002–05, with one death. No cases of hepatotoxicity with other statins were noted at this centre. A total of seven other patients are reported in the literature. The 14 patients were usually over 60 years, had a female: male ratio of 2:1 and showed a mixed cholestatic/hepatic cellular reaction. Six patients had marked hyperbilirubinaemia (>100 µmol/L). The daily dose of atorvastatin varied with five patients taking 10 mg, four 20 mg, one 30 mg, two 80 mg, and two unrecorded. Seven patients had liver biopsies with four demonstrating a cholestatic pattern and three a hepatic pattern. The mean interval to onset of reaction was nine weeks and the liver often took several months to recover. Three deaths occurred.

In Scotland there were 0.91M prescriptions for atorvastatin and 1.62M for simvastatin in the year ending March 2005. Adverse drug reaction reports from the UK Committee on Safety of Medicines reveal four deaths due to hepatobiological disease with atorvastatin treatment over eight years. Simvastatin had no fatalities reported over 15 years and pravastatin one death in 14 years. It is possible that atorvastatin is more likely than other statins to occasionally cause serious idiosyncratic hepato-cellular reaction. Mechanisms might include longer duration of action, drug interactions with CYP 3A4 or more pronounced lowering of LDL influencing membrane integrity.

Conclusion: While significant hepatotoxicity with atorvastatin remains uncommon, any persistent abnormality in liver function should be treated with caution.

169 HIGH PREVALENCE OF HISTOLOGICAL ABNORMALITIES IS COMMON IN INCIDENTALLY REMOVED GALLBLADERS


Introduction: Gallbladder disease accounts for a significant proportion of acute and elective surgery. Previous prevalence studies of gallbladder disease have been autopsy or radiological based and little detailed histological research has been reported. Cholecystectomy is carried out during liver resection as necessitated by the surgical technique. Our aim was to define the prevalence of abnormalities detected in these incidentally removed gallbladders.

Methods: 228 liver resections were carried out between January 2000 and December 2003. We excluded gallbladders removed in cirrhosis for hepatocellular carcinoma, cholangiocarcinomas or those with colorectal metastasis within 5 cm of the gallbladder bed. Statistical comparisons were made between prevalence of abnormalities between men and women, and sex, and preoperative chemotherapy.

Results: 155 gallbladders (96 males/59 females; mean age 60.9, SE 5.9 to 69) were included. 66/155 (43%) had abnormal histology including...
chronic cholecystitis and cholesterolosis and 13% of the total had incidental gallstones. No statistically significant differences were seen between age groups, sex, or with preoperative chemotherapy.

**Conclusions:** High prevalence of abnormalities exists in gallbladders removed incidentally at time of liver resections. Whilst the prevalence of gallstones is comparable to published autopsy series, the degree of histological abnormalities is unexplained and may represent changes in the natural history. Chemotherapy does not seem to alter the prevalence of chronic inflammation. Prevalence of abnormal histological features seems to be significantly higher than previously appreciated and may reflect the existence of undiagnosed abnormalities in the general population.

170 ASSOCIATION BETWEEN COELIAC DISEASE AND PRIMARY BILIARY CIRRHOSIS

K. Baird, D. Dos, Y. Reddy. Department of Gastroenterology, Stepping Hill Hospital, Stockport, UK

**Introduction:** Coeliac disease and primary biliary cirrhosis are thought to be associated with each other, since they share similar autoimmune features. Many studies have sought to prove a definite link between these two diseases, but the results are often conflicting. This small systematic review seeks to summarise the findings of several studies to aid in the investigation of a link between coeliac disease and primary biliary cirrhosis.

**Methods:** A comprehensive search was undertaken in MEDLINE (1966 to June week 1 2005), EMBASE (1980 to 2005 week 24), CINAHL (1985 to June week 1 2005), and SIGLE databases. Studies meeting inclusion criteria were critically appraised using a self-designed appraisal form based on several epidemiological and prognostic checklists. The results of these studies were collated allowing for an overall estimated prevalence to be calculated, which was analysed using the χ² test.

**Results:** Eight articles reported the prevalence of coeliac disease among patients with primary biliary cirrhosis, which revealed that coeliac disease was more common in the primary biliary cirrhosis group when compared to controls (0.28% vs 0%, p = 0.01). Two articles reported the prevalence of primary biliary cirrhosis amongst patients diagnosed with coeliac disease, both of which revealed that primary biliary cirrhosis was more common in the coeliac group compared to controls (0.24% vs 0.05%, p < 0.0001).

**Conclusions:** There is a statistically significant association between coeliac disease and primary biliary cirrhosis according to this systematic review.

171 WITHDRAWN

172 DID CELTS REACH ROME ON THE EAST SIDE OF APPENNINI MOUNTAINS? AN OPEN POPULATION SCREENING STUDY FOR HFE GENE MAJOR MUTATIONS IN CENTRAL ITALY

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**Background:** Two HFE genotypes are strongly associated with hereditary haemochromatosis (HH): homozygosis or the C282Y mutation and compound heterozygosis C282Y and H63D mutation seem to have a Celtic origin. It is still debated whether Celt migrations reached Italy on the east or on the west side of Appennini Mountains. According to the literature, the allele frequency of C282Y mutation decreases from North to Southern Italy, however in Central Italy there are no studies on HFE mutations.

**Aims:** To investigate the allele frequency of HFE mutations and the association between mutations and cases of HH or other liver diseases in an open population of Central Italy.

**Patients and Methods:** This study is part of a survey for liver and methabolic diseases in an open population of East Appennini. Arsita is a mountain village with a high rate of inbreeding and scarce exchanges with neighbouring areas. Its population likely derives from old Latin groups. Five hundred and two subjects (299 F and 203 M), aged >18 years (1004 chromosomes), were tested for C282Y, H63D, and S65C mutations of the HFE gene by Taqman probes. All subjects had transferrin, ferritinemia, serum iron, liver function tests, HCV and HBV assay, Homa test. Information on alcohol intake and diet were collected with a questionnaire. Liver ultrasound was performed in 334 (66.5%) subjects. Data were analysed by logistic regression analysis.

**Results:** Allele frequencies for C282Y, H63D and S65C were 1.9%, 14.8%, and 0.01% respectively. Genotype distribution was within Hardy-Weinberg equilibrium for all three mutations. C282Y -/- was found in 19 subjects (3.8%), H63D +/ - in 127 (25.3%), H63D +/- in 11 (2.2%), S65C +/ - in 1 (0.2%). No homozygosity for C282Y or compound mutation (C282Y/H63D) was found in the study population, however 227 subjects (5.4%) had TSTOP >45 (including 10 subjects with high SF). Overall, 49 subjects (9.8%) were found HCV-RNA positive. Univariate analysis showed a significant correlation between SF and the following parameters: steatosis at ultrasound (any grade), alcohol intake (>40 g/day), insulin sensitivity (HOMA), age >54 years, BMI >30, liver enzymes, and male gender. Logistic regression analysis indicated that male gender (p = 0.000) and hepatic steatosis (p = 0.017) were independent variables related to high SF.

**Conclusions:** This study confirms that C282Y HFE mutation is less frequent in Central Italy than in Northern Italy. This results are in favour of the hypothesis that Celtic groups never reached these mountain areas of East Appennini. HH in this area might be associated with other mutations on genes involved in iron metabolism.

173 DOES VENESECTION AND SUBSEQUENT IRON DEPLETION REVERSE ARTERIAL STIFFENING SEEN IN HEREDITARY HAEOMOCROMATOSIS?

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**Introduction:** Increased cardiovascular risk has been associated with heterozygosity for the HFE gene and with states of iron overload, including hereditary haemochromatosis (HH). The mechanism could be either genetic or a direct effect of excess iron causing vascular dysfunction and increased arterial stiffening.

**Aims:** To assess the effect of venesection on arterial stiffness in HH.

**Methods:** We have used the non-invasive technique of pulse wave analysis (PWA) to study arterial stiffness in patients with HH. PWA uses application technology to record the radial artery pressure waveform non-invasively. Each waveform is composed of a forward and reflected wave. The compliance of the vascular tree can be expressed quantitatively as the augmentation index (Aix), following application of a validated transfer function, which is expressed as a percentage change in height of the pulse waveform as a result of the reflected wave.

**Patients:** The Aix of 10 patients (nine male) with haemochromatosis (diagnosed by homozygosity for the cy282tyr mutation or appropriate hepatic histology) was recorded following a 10 hour fast. Each patient then entered a standard venesestion protocol and had subsequent Aix recordings taken at 6 weeks, 3 months, and 6 months under the same conditions.

**Results:** The mean Aix of the 10 patients dropped from 20.30% (SD 11.8) at initial attendance to 13.04% (SD 9.26) at six months representing a reduction in arterial stiffness over this time. There was a strong correlation between iron reduction and Aix, r² = 0.85. There was no significant difference in other variables including blood pressure, body mass index, or smoking status during the study period.

**Conclusions:** These results confirm, using a non-invasive, in vivo technique that arterial stiffness diminishes during venesection for haemochromatosis. This suggests that it is the excess iron rather than other genetic factors which produces the vascular damage in haemochromatosis.

174 A PROSPECTIVE AUDIT INTO THE INCIDENCE, DIAGNOSIS, AND TREATMENT OF SPONTANEOUS BACTERIAL PERITONITIS IN CIRRHOTIC INPATIENTS WITH ASCITES IN A UK HOSPITAL

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**Background:** Spontaneous bacterial peritonitis (SBP) in cirrhotic patients with low protein ascites is often fatal. Early diagnosis, treatment, and secondary prophylaxis are indicated. Prophylaxis may cause microbial resistance. We prospectively audited local guidelines on diagnosis, treatment, and prophylaxis of SBP, monitoring local incidence, microbiology, and antibiotic resistance.
Methods: Clinical Audit Department registration was obtained. Admissions of cirrhotic patients with ascites were included and data including patient demographics and indications for and results of diagnostic paracentesis were collected. An ascitic FNM count of >250 mm⁻³ was considered diagnostic of SBP, and "on admission" if performed within 24 hours of admission.

Results: Fifty admissions (42 patients, M = 28, F = 14, mean age 50.86 years) were included. SBP was diagnosed during nine admissions (18%) with 55.5% (n = 5) of cases diagnosed on admission. In 44.4% (n = 4) the causative organism was not identified. 100% (n = 5) of cases of culture positive SBP were isolated by injecting ascites into blood culture bottles. 44.4% (n = 4) were due to Gram negative infection. 11.1% (n = 1) were due to Gram positive infection. Two cases of quinolone resistance were identified.

Conclusion: There are no data on frequency and microbiology of SBP in the UK. SBP frequency in this unit is consistent with published rates from Europe and the USA. Of culture positive cases gram negative bacteria were most commonly identified. Inoculating ascites into blood culture bottles improves the yield and this guideline will be emphasised in our unit as a result of this audit.

175 MORBIDITY AND MORTALITY ASSOCIATED WITH ALCOHOLIC LIVER DISEASE FOLLOWING ADMISSION TO ST GEORGE’S HOSPITAL HDU/ICU

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Introduction: Alcoholic liver disease (ALD) is associated with significant mortality in the ICU setting. Decompensated liver disease with three organ dysfunction (OD) has a reported mortality of >85%. Much of these data are from transplant centres based on patients referred from other hospitals. It is likely they have had organ(s) failure/disfunction for sometime before referral.

Aims: We hypothesise that early admission to HDU/ICU and introduction of aggressive therapy would improve expected mortality.

Methods: We prospectively monitored patients with ALD admitted to the HDU/ICU for 11 months; clinical, biochemical, and physiological parameters were recorded, including Child-Pugh (CP), APACHE, and SOFA scores.

Results: See table.

Abstract 175

<table>
<thead>
<tr>
<th>OD</th>
<th>Patients</th>
<th>SOFA</th>
<th>CP</th>
<th>Lactate (mmol/l)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23/120</td>
<td>12 ± 3</td>
<td>5 ± 1</td>
<td>2.8 ± 1.0</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>45/120</td>
<td>18 ± 4</td>
<td>5 ± 1</td>
<td>3.2 ± 2.7</td>
<td>19</td>
</tr>
<tr>
<td>3</td>
<td>36/120</td>
<td>23 ± 3</td>
<td>9 ± 2</td>
<td>4.9 ± 3.3</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>54/120</td>
<td>24</td>
<td>13 ± 2</td>
<td>8.2 ± 2.3</td>
<td>50</td>
</tr>
</tbody>
</table>

1 = liver only; 2 = liver+inotropes; 3 = liver+inotropes+renal support; 4 = liver+inotropes+renal support+ventilation.

Conclusion: Increasing organ dysfunction associated with ALD leads to increasing morbidity and mortality. Mortality for the severe group is maximally 50%. This is markedly better survival than data from similar studies. We postulate that this difference is due early referral, admission, and aggressive treatment usually within 24 hours of organ dysfunction.

176 DECOMPENSATED ALCOHOLIC LIVER DISEASE: FACTORS ASSOCIATED WITH MEDIUM TERM MORTALITY FOLLOWING HOSPITAL DISCHARGE

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Background: In patients with decompensated alcoholic liver disease (ALD), continued heavy drinking is associated with mortality. Whether continued drinking at a lower level affects mortality is unclear. Other determinants of medium term outcome are not well characterised.

Aim: Evaluation of factors associated with mortality over 1–4 years after diagnosis of decompensated ALD.

Methods: Review of records of 198 consecutive patients discharged from hospital following admission with first episode of decompensated ALD; phone calls as needed to patient, family, and GP. Drinking behaviour from discharge to 1/4/05 or to death was classified as: fully abstinent (grade 1), drinking below the safety limits (grade 2), reduced drinking but above the safety limits (grade 3), and failure to reduce previously heavy intake (grade 4).

Results: By Cox regression analysis, higher drinking grade, higher Townsend and Jarman social deprivation scores (available in 130 Sheffield residents), and female sex were independently associated with mortality. With analysis confined to patients with grades 1–3 and grades 1–2, the association of mortality with drinking grade disappeared but that with social deprivation remained. Age and admission MELD score were not independently associated with mortality.

Conclusions: Following discharge from hospital, mortality in decompensated ALD is associated with failure to reduce alcohol intake, female sex, and social deprivation. Continued drinking below safety limits may not prejudice survival.

177 DECOMPENSATED ALCOHOLIC LIVER DISEASE: ACCURACY OF GLASGOW, MELD, MADDREY, AND CHILD PROGNOSTIC SCORES

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Background: The Glasgow prognostic score (Forrest. Gut 2003;54:1174) may be more accurate that the MELD, Child, and Maddrey scores in predicting early mortality in patients with presumed alcoholic hepatitis (defined as ALD with serum bilirubin >80 µmol/l).

Aim: Evaluation of these scores in prediction of early mortality in a broader range of patients with first presentation of decompensated ALD (defined as Child grade B or C).

Methods: Review of 199 patients presenting consecutively between 01/04/98 and 31/03/05, who did not receive corticosteroids. Predictive value of prognostic scores (calculated on admission (day 1) and on day 7) with respect to 28 and 84 day mortality was assessed by comparing areas under ROC curves (AUROC) and accuracy (ACC, % of cases correctly assigned using published cut-off values).

Results: 28 and 84 day mortality was 12.2% and 21.3% respectively. The table shows results for prediction of 28 day mortality.

Abstract 177

<table>
<thead>
<tr>
<th>Drinking grade</th>
<th>n</th>
<th>1 year</th>
<th>2 year</th>
<th>3 year</th>
<th>4 year</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>84 (5)</td>
<td>81 (3)</td>
<td>76 (7)</td>
<td>76 (7)</td>
</tr>
<tr>
<td>2</td>
<td>54</td>
<td>88 (4)</td>
<td>79 (6)</td>
<td>68 (7)</td>
<td>68 (7)</td>
</tr>
<tr>
<td>3</td>
<td>44</td>
<td>91 (4)</td>
<td>78 (6)</td>
<td>62 (8)</td>
<td>53 (9)</td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>65 (8)</td>
<td>62 (8)</td>
<td>34 (9)</td>
<td>28 (9)</td>
</tr>
</tbody>
</table>

Table shows % survival (mean (SEM)) with time. Patients with drinking grade 4 had reduced survival (p < 0.05), compared to grades 1–3, which were not significantly different from one another.

For prediction of 84 day mortality, accuracies of the Glasgow, MELD, and Maddrey scores (82, 81, and 76% for day 1 values; 85, 84 and 80% for day 7 values) were similar to one another but were greater (p < 0.01) than that of the Child scores (57% for day 1 and 61% for day 7). Accuracy of the Glasgow score was not diminished by including patients with bilirubin <80 µmol/l.

Conclusions: Accuracy of the Glasgow and MELD scores is similar and is greater than accuracy of Maddrey and Child scores for prediction of
early mortality in decompensated ALD. Accuracy of the Glasgow score is preserved in patients with serum bilirubin <80 μmol/l.

178 MORTALITY AND MORBIDITY TRENDS DUE TO ALCOHOLIC LIVER DISEASE IN A DISTRICT GENERAL HOSPITAL POPULATION IN NORTH EASTERN UK

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Introduction: With the advent of International Classification of Disease tenth revision (ICD-10) ONS (Office of National Statistics) data until 2003 show that alcohol related death (ARD) is still on the rise and is second highest in northeastern part of the UK. Moreover alcoholic liver disease (ALD) and its related complications constitute a significant proportion of hospital admissions and prolonged hospital stay.

Aims and Methods: We aimed to ascertain the current mortality and morbidity trends from ALD in University Hospital Harlaxton (UHH), a small town in northeast UK with a population of approximately 90 000. ALD patients admitted during the period of January 2002 to December 2004 were identified using ICD-10 code K70.

Results: Out of 99 patients (68 male; 31 female) majority, both sex inclusive, belonged to age group 40–60 years peaking at 50–60 years. There were 29 deaths (male 19; female 10) in the two year study period, as estimated in 2003 by ONS, which confirms that ALD is the major cause of all ARDs. Also mortality rate from ALD in UHH is almost equal to total ARD rate in the area, as estimated in 2003 by ONS, which confirms that ALD is the major cause of all ARDs. Also mortality rate from ALD in UHH is twice in males than in females and younger age groups show a much higher mortality and morbidity trends as would be expected from current national trends.

Conclusion: Mortality rate due to ALD in UHH is almost equal to total ARD rate in the area, as estimated in 2003 by ONS, which confirms that ALD is the major cause of all ARDs. Also mortality rate from ALD in UHH is twice in males than in females and younger age groups show a much higher mortality and morbidity trends as would be expected from current national trends.


179 DOES THE GLASGOW ALCOHOLIC HEPATITIS SCORE (GAHS) ACCURATELY PREDICT SURVIVAL IN SEVERE ALCOHOLIC HEPATITIS?

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Introduction: Approximately 30%–40% of patients with a discriminant function >32 die within six months but many physicians are reluctant to use corticosteroids because of the potential risk of steroid side effects in this patient population. GAHS has been developed to more accurately predict poor outcome.

Method: We identified 38 patients with a DF >32 who underwent transjugular liver biopsy. The GAHS was calculated from five parameters at admission (age, leucocyte count, bilirubin, prothrombin ratio, urea. Forrest, Gut 2003) and compared to survival at 28 and 84 days and to accepted histological features of alcoholic hepatitis scored semiquantitatively from 0 to 4.

Results: Only six patients received corticosteroids, 1/6 died within 84 days. Of six histological variables (steatosis, portal inflammation, lobular infiltration with neutrophils and monocytes, ballooning and Mallory's hyaline), only higher scores for Mallory's hyaline were correlated with the GAHS. A GAHS <7 accurately predicts 28 day survival without treatment in alcoholic hepatitis (DF >32). The extent of Mallory's hyaline deposition is the only histological feature that correlates with clinical predictors of survival.

180 HETEROGENEITY OF LIVER HISTOLOGY IN SEVERE ALCOHOLIC HEPATITIS DIAGNOSED ON CLINICAL CRITERIA

A. S. Austin, P. Kaye, G. P. Aithal, S. D. Ryder. Liver Units, Derby City General Hospital, Uttoxeter Road, Derby, DE22 3NE and Queens Medical Centre, Nottingham NG7 2UH, UK

Introduction: Recent studies suggest up to 20% of patients thought to have severe alcoholic hepatitis (AH) on clinical grounds will not have histological criteria for this diagnosis. Forrest et al. (Gut 2002 #51). Furthermore, it is possible that patients with a discriminant function greater than 32 may have a severe histological lesion yet do not manifest the clinical criteria and might be denied treatment if a biopsy is not undertaken. We sought to compare the histological findings in jaundiced patients with a discriminant function greater than 32 with and without clinical stigmata.

Method: Transjugular liver biopsies from jaundiced patients with alcoholic liver disease (ALD [DF >32, n = 36, group 1] and 21 controls with stable ALD [bilirubin <100, group 2]) were scored semiquantitatively from 0 to 4 for four histological features of AH: a single experienced liver pathologist. Clinical features suggestive of AH were tender hepatomegaly, leucocytosis >12 000/mm³, fever, hepatic bruit, and encephalopathy.

Results: Biopsies had median length 12–14 mm (3–28) and width 0.6–0.7 (0.4–0.9) and were similar between groups. All biopsies were cirrhotic (Ishak 6), had pericellular fibrosis consistent with an alcoholic aetiology and scored similarly for steatosis and cholestasis. The alcoholic hepatitis activity index (lobular neutrophils and monocytes, ballooning and Mallory's) (AHAI–maximum score 16) was greater in the absence of clinical features (median 10 (2–13)) compared to the presence (8 (4–13)) (p = 0.483) and compared to controls (4 (1–9) (both p<0.001).

Conclusion: In jaundiced patients with severe alcoholic hepatitis the histological picture varies widely but there is no difference in liver injury/inflammation observed in groups with and without accepted clinical criteria. Clinical criteria should not be used to determine those suitable for therapeutic intervention.

181 ‘ALCOHOLIC HEPATITIS’ AFTER GASTROINTESTINAL BLEEDING HAS A GOOD PROGNOSIS


Introduction and Aims: The management of alcoholic hepatitis (AH) remains controversial. Trials of treatment have variably included or excluded those patients who present with gastrointestinal (GI) bleeding. We aimed to look at patients with AH who presented with GI bleeding to determine whether the natural history of such patients differs from those without GI bleeding.

Method: We retrospectively examined the records of patients presenting with GI bleeding who developed a clinical picture in keeping with AH: a history of excess alcohol in last four weeks, serum bilirubin >80 μmol/l, AST <500 iu. The modified Discriminant Function (mDF) and Glasgow Alcoholic Hepatitis Score (GAHS) were calculated on admission and two days after stabilisation from the GI bleed. Outcome at 28 days was determined and a comparison was made with a historical control group with a clinical diagnosis of AH but without GI bleeding (n = 163). Neither group received corticosteroids or pentoxifylline.

Results: Forty patients were identified of whom 28 (70%) were male and three of whom had coexistent chronic hepatitis C. Variceal haemorrhage occurred in 32 (80%) patients and three patients required a TIPSS. Two days after stabilisation 35 (87.5%) patients had a mDF >32 and 15 (37.5%) had GAHS >9. Overall survival at 28 days was 90%. Kaplan-Meier analysis demonstrated a significant 28 day survival advantage for patients presenting with GI bleeding compared with non-bleeding historical controls for patients with a mDF >32 (87% v 65%, p = 0.0077) and a GAHS >9 (80% v 41%; p = 0.0143).

Conclusions: The 28 day outcome of patients with apparent AH 48 hours after stabilisation from a GI bleed appears to be significantly better compared with those who do not present with GI bleeding. Standard clinical criteria for the diagnosis of AH may not be applicable to this group of patients and such patients might be best excluded from clinical trials of AH treatments.

Abstract 179

<table>
<thead>
<tr>
<th>GAHS</th>
<th>Survival — survived/total (%)</th>
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<tbody>
<tr>
<td>&lt;7</td>
<td>8/8</td>
</tr>
<tr>
<td>8</td>
<td>28/24</td>
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<tr>
<td>9</td>
<td>2/6</td>
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<tr>
<td>10</td>
<td>0/5</td>
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Day 28: 0/14 (100) 12/18 (67) 24/26 (92) 2/6 (33)
Day 84: 8/11 (73) 4/14 (29) 12/20 (60) 0/5 (0)
**A82 CONTRAST ENHANCED ULTRASOUND SCAN IN THE MANAGEMENT OF FOCAL LIVER LESIONS**

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**Background:** Focal liver lesions (FLL) present a diagnostic and management dilemma for almost all specialties of medicine including surgery, general medicine, general practice, and gynaecology. This study evaluates the sensitivity, specificity, positive and negative predictive values, and accuracy of contrast enhanced ultrasound (CEUS) in the assessment of focal liver lesions (FLL).

**Methods:** 109 patients attending the Cardiff Liver unit at the University Hospital of Wales, Cardiff, between 01/10/03 and 01/05/05, who were found to have focal liver lesions underwent Contrast enhanced ultrasound with Sonavue as the contrast. The results of the scan were analysed retrospectively in comparison with the gold standard investigation like CT scan, MRI, or PET scans and histopathology if the patients were operated on.

**Results:** The accuracy of CEUS in diagnosing FLL as hepatocellular carcinoma is 100%, metastases is 97%, cholangiocarcinoma is 99%, haemangioma is 100%, focal nodular hyperplasia is 99%, and as benign condition is 97%.

**Conclusions:** Our results suggest that CEUS should be considered as a standard investigation in every patient with incidental FLL.

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**A83 IS INSERTION OF UNCOVERED TRANSJUGULAR INTRAHEPATIC PORTO SYSTEMIC STEM SHUNTS REALLY A RISK FACTOR FOR DEVELOPMENT OF HEPATOCELLULAR CARCINOMA?**

N. Kochar1, D. Tripathi1, T. E. Delahooke1, D. N. Redhead2, H. Ireland2, P. C. Hayes1. 1Departments of Hepatology; 2Radiology, Royal Infirmary of Edinburgh, UK

**Introduction:** Hepatocellular carcinoma (HCC) is a major complication of cirrhosis which necessitates surveillance by regular ultrasound examinations and alfabetoprotein measurements. A recent retrospective study reported an increased incidence of HCC in cirrhotic patients with unrevealed transjugular intrahepatic porto systemic stem shunts (TIPSS). 1

**Aim:** To determine whether the patients treated with non-covered TIPSS for complications of cirrhosis have higher incidence of HCC.

**Methods:** Retrospective study; patients identified from a dedicated database. Inclusion criteria: Patients with uncovered TIPSS with >6 months of follow up. Exclusion criteria: HCC diagnosis within 6 months of TIPSS, <6 months follow up, deaths/transplants with in 6 months of TIPSS.

**Results:** Of 732 TIPSS insertions over a 14 year period, 518 were uncovered stents, of which 203 were excluded due to various exclusion criteria. Of the remaining 315, HCC was diagnosed in eight patients (median age 64 years). Aetiology of cirrhosis: alcoholic, 7 and hepatitis C, 1; Child's A/B/C –1/2/5. Indication for TIPSS: variceal bleed, 6 and ascites, 2. Median time from TIPSS to HCC diagnosis was 36.5 (18–89) months. Five patients have died and one has had a transplant at a median time of 8 (1–32) months.

**Conclusions:** We could not find an increased incidence of HCC in patients with uncovered TIPSS, when we compared it with the HCC incidence in patients with cirrhosis of any aetiology (1–3% per year). Higher frequency of HCC surveillance is probably not indicated.

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**A85 PREVALENCE AND MANAGEMENT OF ANAEMIA AFTER LIVER TRANSPLANTATION**

C. Preston, V. Mills, M. Arundel, A. McVerry, C. Millson. Department of Hepatology, St James’s University Hospital, Leeds, UK

**Background:** Anaemia is well recognised after solid organ transplantation. Specific data on its prevalence in adults after liver transplantation are not available and little is known about how to manage anaemia during long term follow up post-liver transplant.

**Aims:** To investigate the prevalence of anaemia in our post-transplant population during long term follow up. To establish a pragmatic algorithm for the management of this anaemia and to assess whether our current practice approaches to this algorithm.

**Methods:** We identified all post-transplant patients under follow up in this institution who were more than 6 months post-transplant. We included them in our analysis if they were found to be anaemic. We defined anaemia as Hb<12 in males, Hb<11 in females, persisting for six months or more. Patients’ notes were examined to determine the following: (1) Has the anaemia been noted? (2) Have relevant aspects of the history been sought? (3) Have basic blood tests been performed? (4) If iron deficient, have endoscopic investigations been considered? (5) Has a referral to a haematologist been made?

**Results:** Sixty five patients fulfilled criteria. This represents 14% of the total post transplant population of 456. The average age was 52 years (range 27–78 years). Mean Hb=9.8. The anaemia was noted in 36/65 (55%). All 65 patients were on potentially myelosuppressive medications. Haematocrits were measured in 22/36. 24/36 underwent endoscopic investigations. 7/36 patients were referred for a haematological opinion. The aetiology of the anaemia was multifactorial and included; myelosuppressive medications, iron deficiency, and hypersplenism.

**Conclusion:** Anaemia after liver transplant represents a significant problem in our in our institution with a prevalence of 1.4%. Our review identifies shortfalls in our current approach to these, patients probably due to the lack of existing information about how this problem should be managed. We intend to implement the management algorithm used in our study in the outpatient setting.

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**A86 POSTOPERATIVE COURSE AFTER LIVER RESECTION IS NOT INFLUENCED BY THE USE OF PORTAL INFLOW COMPRESSION (PRINGLE’S MANOEUVRE)**


**Introduction:** Portal inflow compression (PIC) is used to reduce blood loss at the time of parenchymal transection though hepatic ischaemia with reperfusion injury has been a theoretical possibility. Emerging evidence seems to indicate intermittent PIC may precondition the liver to tolerate ischaemia with some hepatoprotection. Our aim was to compare the post operative recovery and outcome of patients who had PIC at the time of major liver resection (>2 segments) with those who did not.

**Methods:** The biochemical and haematological data of patients were recovered from our prospectively maintained database for the period from January 2004 to June 2005. All patients who had undergone a neoadjuvant chemotherapy for downstaging of colorectal liver metastasis with concerns about impairment of liver regeneration. We compared the viability of hepatocytes (and cells/gram of digested liver) in patients who had received oxaliplatin and those who were chemotherapy naive.

**Methods:** All patients with colorectal liver metastasis who underwent liver resection between January 2003 and June 2005 had a specimen of normal liver analysed and cultured by UKHTB were included in the study. Two sample t test was used to compare the mean percentage of viable cells (and cells per gram of digested liver tissue) between the group that received oxaliplatin based neo adjuvant chemotherapy and the group that was chemotherapy naive.

**Results:** Eighty seven liver samples (11 oxaliplatin group/76 chemotheraphy naive group) were included in our study. The groups were similar in age and sex distribution. The mean percentage of viable cells in the chemotherapy naive group and the oxaliplatin group was 78.28 and 82.28 respectively though this was not statistically significant with a p value of 0.275 (95% confidence interval: –1.12 to 3.2). No difference was noticed in the postoperative biochemical profile between the two groups or length of stay in hospital.

**Conclusions:** Oxaliplatin based neoadjuvant therapy does not reduce the viability of hepatocytes or alter the post operative course of liver resection.
major liver resection were included in our study. The change in haemoglobin concentration, the perioperative blood transfusion, liver function test, and coagulation profile were all compared between the two groups along with the length of hospital stay.

Results: A total of 102 (81 with no PIC v 21 with PIC) were included in the study. The two groups were similar in age and sex distribution and type of liver resection. The postoperative course did not show any statistically significant difference in peak elevation of liver function tests, change in haemoglobin concentration, postoperative morbidity, and length of hospital stay. The blood product transfusion rates were similar in both groups with no statistically significant difference.

Conclusions: PIC does not seem to influence the postoperative recovery of patients undergoing liver resection and can be safely used without fear of postoperative hepatic dysfunction. However, there seems to be no difference in the perioperative blood usage in both groups. PIC is a safe technique to be used in liver resection.

ANTHROPOMETRIC MARKERS AND OUTCOME FROM LIVER TRANSPLANT

D. G. Oliver, J. Barbour, B. Davidson, D. Mans, N. P. Thompson. Freeman Hospital, Newcastle-upon-Tyne, UK

Introduction: Malnutrition is common among patients undergoing liver transplantation and is often difficult to quantity because of confounding factors such as diabetes and oedema. Anthropometric tests such as hand grip strength (GS), mid-arm circumference (MAC), triceps skin fold thickness (TSF) and mid-arm muscle circumference (MAMC) provide additional information. It is unclear whether poor nutrition is simply a marker for severity of liver disease or an independent and treatable risk factor for poor outcome.

Aims: To assess whether preoperative anthropometry in patients undergoing elective liver transplantation is associated with duration of time ventilated, stay on the intensive therapy unit (ITU) and hospital stay overall.

Methods: Retrospective study of patients transplanted for end-stage chronic liver disease.

Results: Nutritional records were obtained for 173 (72%) of 241 consecutive transplants between 1997 and 2005. Anthropometry had been performed during pre-transplant assessment in 72 (42%) patients. Indicators of liver transplant were as follows: autoimmune liver disease 25 (35%), alcoholic liver disease 24 (33%), cryptogenic cirrhosis 6 (8%), viral hepatitis 2 (3%), other 15 (21%). Seven patients had co-existent hepatocellular carcinoma. 90 day and 12 month mortality were both 6%. Significant inverse relationships were found for MAC, TSF and MAMC with days spent on ITU (r² = -0.26, p = 0.048; r² = -0.28, p = 0.036; r² = -0.26, p = 0.048 respectively) and for TSF with total days in hospital (r² = -0.36, p = 0.007). The effect of nutritional status was more pronounced for those transplanted for alcoholic or cryptogenic aetiologies than for others. Patients who died within 90 days had higher initial MAC and MAMC with days spent on ITU (0.05=10/05) were studied. Demographic features, severity of CLD and presence of key OF were reviewed in TP (n %) or median (interquartile range). Dataset validation is ongoing.

Results: Analysis of ICU patients revealed that cumulative cardiovascular, renal and neurological failure resulted in 100% mortality (p<0.0001). Other determinants: Age>50, Child Pugh (CP) class C and 1 key OF >70% mortality (p>0.0001). In 101 TP, 23% CP A, 44% CP B, and 31% CP C, MELD median 9 (6–33). 21% had no OF, 34% 1, 30% 2, and 16% 3 OF. The CP (p<0.01), MELD (p<0.001) and key OF (CNS p<0.008, CVS p<0.006, renal p<0.05) predicted outcome. Of TP 63% had renal dysfunction CCl76 ml/min (0–194). 45% had CVS dysfunction, 35% structural LV/cardiac pathology and 9% conduction abnormalities. 32% TP had CNS dysfunction. During the study period 9% died (70% all key OF) and 9% underwent liver transplantation.

Conclusions: Patients with CLD requiring admission to ICU with all key OF have 100% mortality. Those not requiring ICU admission have a high prevalence of organ dysfunction. Of the patients who died, 70% had three key OF. With ongoing data collection, these prognostic scores will to highlight the clinical importance of extrathoracic OF in the assessment of patients with CLD both on the ward and in intensive care.

Pancreas posters

EVALUATION ON A MEXICAN COHORT OF A COMPUTER MODEL DEVELOPED TO PREDICT SEVERITY OF ACUTE PANCREATITIS

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Background: It has been reported (BSG March 2004) that a computer model using eight admission variables (age, C-reactive protein (CRP), respiratory rate, pO2 on air, creatinine, pH, serum creatinine, white cell count, and GCIs) created using UK data can provide accurate severity prediction in acute pancreatitis (AP). An evaluation of this model on a dataset from a different geographical and social setting (Monterrey, Mexico) is presented. Severity and organ failure were defined by Atlanta criteria.

Method: Admission data were collected from 202 Monterrey patients with a diagnosis of AP between October 2002 and November 2004. The data were retrospectively evaluated using the UK computer model, and the area under the receiver operating characteristic curve (AUC) was used to evaluate its accuracy in predicting severity in AP.

Results: Forty two patients (20.8%) developed severe AP, and three died (1.5%). 11 patients (5.4%) developed renal failure, and 23 respiratory failure (11.4%). 146 patients had a biliary aetiology (73.2%), 25 alcohol (12.4%), 17 other aetiology (5.4%), and 14 idiopathic (6.9%). The UK model predicted severity in the Monterrey patients with an AUC of 0.81 (identical to the figure obtained previously in UK patients). This gives an optimum sensitivity and specificity of 0.80 and 0.77 and compares favourably with the CREED system developed in Mexico (AUC 0.70) and admission CRP (AUC 0.76; p=0.001) in the same patients.

Conclusions: This study can provide a predictor within a few hours of admission, and is more accurate than admission CRP or APACHE-II. The validation of the model on a separate cohort of patients confirms the merit of the computer assisted approach. A prospective multicentre study using the Southampton computer system is required.

MANAGEMENT AND OUTCOME OF ACUTE PANCREATITIS VARIATES BETWEEN CENTRES

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Introduction: National guidelines suggest pancreatectomy should be managed as an acute emergency with severity scoring and stratification of patients with a high score to either HDU/ITU. In this study we compared the management and outcome of acute pancreatitis in two DGHs (RLI at Lancaster and FGH at Barrow in Furness). This retrospective study was undertaken between January 2003 and December 2004 and a total of 60 patients at RLI and 44 at FGH were reviewed.

Results: The groups were similar for age and sex. The aetiology of pancreatitis at RLI was gallstones 47% v 53% at FGH, alcohol 18% v 3%, idiopathic 22% v 18%, others including trauma and viral were 1.4% v 6%. Only 7% of patients at FGH v 55% at RLI had severity scoring done at 48 hours. A retrospective calculation revealed 36% at FGH had severe scores at any given time of which only 37% were admitted to HDU/ITU v 8% with severe scores at RLI of which 60% were admitted to HDU/ITU. Of the 28 patients with gall stone pancreatitis at RLI, three had scores consistent with severe pancreatitis. A total of 12 patients underwent ERCP of which two were from the severe pancreatitis group.
At FGH 8/24 patients had severe gall stone pancreatitis. A total of two patients underwent ERCP, but none from the severe pancreatitis group. In the severe pancreatitis group 67% underwent ERCP at RLI v 0% at FGH. The overall mortality at FGH was 18% and in the severe pancreatitis group was 37% which was higher than the nationally accepted levels of 10% and 30% respectively. In contrast, the overall mortality at RLI was 2% and 20% in the severe group.

Conclusion: We conclude that severity scores are useful in stratifying patients for HDU/ITU treatment where appropriate. Patients who underwent ERCP for gall stone pancreatitis had a better outcome as reflected by the low mortality and higher number of ERCPs performed at RLI.

191 AUTOIMMUNE PANCREATITIS: RESPONSE TO THERAPY IN A UK SERIES

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Background: Autoimmune pancreatitis (AIP) is a rare condition which usually presents with a pancreatic mass, biliary and pancreatic duct strictureing, jaundice, and a raised serum IgG4. A response to steroids is a diagnostic criterion, although historical data from our unit suggest that spontaneous improvement may occur. This is the first UK series of AIP patients in which objective responses to active treatment are reported.

Methods: All nine patients treated for AIP at our centre in 2004–05 were included. Intravenous/hilar strictureing was present in eight at diagnosis, and, for treatment and dominant CBD/hilar strictures were sited at ERCP in five (although four patients remained jaundiced despite apparently optimal stenting). Oral prednisolone 30 mg OD was commenced in all patients, with gradual dose reduction over 4 weeks.

In cases of disease relapse following steroid reduction, azathioprine was commenced. Response was assessed in terms of pre- and post-steroid symptoms, liver biochemistry and radiological appearances.

Results: Within 4 weeks of starting steroids, all patients reported significant symptomatic improvement. After 8 weeks, median bilirubin levels had fallen from 38 μmol/l (range 8–232) to 9 μmol/l (5–27), (p = 0.004 by Wilcoxon matched pairs test); median ALT from 88 IU/l (22–276) to 57 IU/l (26–76), (p = 0.008), and ALP from 496 IU/l (149–1928) to 193 IU/l (64–424), (p = 0.004 by Wilcoxon matched pairs test); median ALT from 88 IU/l (22–276) to 57 IU/l (26–76), (p = 0.008), and ALP from 496 IU/l (149–1928) to 193 IU/l (64–424), (p = 0.004). Repeat ERCP (seven patients) and MRCP (two patients) after 3–6 months showed improvement in pancreatic and extrapancreatic/intrapancreatic biliary strictureing in all cases, with almost complete resolution in four. Biliary stents were removed in all cases, with no recurrence of jaundice (median follow up 4, range 3–12 months). CT/MRI showed resolution of mass lesions in three, and spontaneous improvement may occur. This is the first UK series of AIP patients in which objective responses to active treatment are reported.

Conclusion: These data suggest palliative bypass surgery improves long term survival with an acceptable procedure related mortality and support surgical exploration of patients with pancreatic cancer in the absence of metastatic disease.

192 BILIARY STENTING VERSUS PALLIATIVE BYPASS SURGERY IN LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA


Background: The role of palliative bypass surgery versus biliary stenting in patients with locally advanced pancreatic cancer is controversial with no randomised study to date.

Methods: After exclusion of patients with resectable disease, 56 consecutive patients with proven pancreatic adenocarcinoma presenting to two units were studied. One unit advocated stent insertion for all patients unless there was evidence of gastric outlet obstruction. The other unit favoured palliative bypass surgery if there was no laparoscopic evidence of metastatic disease.

Results: Twenty three patients underwent palliative surgery and 33 patients underwent stent insertion. CA19.9 was the only significant demographic difference between the two groups (mean 5537.55 μU/l in stent group versus 2282.56 μU/l, p = 0.04). There was no difference in total admission duration. There was a lower emergency readmission rate for the surgical group (17% v 30%) and more surgical patients underwent chemotherapy (61% v 18%, p = 0.004). 30 day mortality for the surgical group was 4% v 18% in the stent group. There was a significant improvement in long term survival for the surgical patients with median survival of 382 days v 135 days in the stent group (log rank test p = 0.03).

Conclusion: These data suggest palliative bypass surgery improves long term survival with an acceptable procedure related mortality and support surgical exploration of patients with pancreatic cancer in the absence of metastatic disease.

193 CT AND ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS AND STAGING OF PANCREATIC AND PERIAMPULLARY MALIGNANCY

S. D. Mansfield, J. Scott1, K. Oppong, D. L. Richardson1, G. Sen, B. C. Jaques, C. B. O’Sullivanobhain, D. M. Manas, R. M. Charnley. Departments of Hepato-Pancreato-Biliary Surgery and 1Radiology, Freeman Hospital, Newcastle-upon-Tyne, UK

Introduction: Multislice CT, which offers improved scanning speed and resolution compared to conventional CT, was compared with endoscopic ultrasound (EUS) in patients with pancreatic and periampullary malignancy.

Methods: Prospective data collection on all suspected pancreatic and periampullary cancers between June 2002 and June 2004. Dynamic triple phase multislice CT and EUS were performed where clinically indicated. For quality reasons only in-house CTs were accepted for the analysis. Presence of malignancy, portal vein invasion and resectability were compared using McNemar’s test of paired proportions (table).

Results: Of 345 patients, 134 underwent in-house multislice CT, 188 EUS and 84 both. Of these, 35 underwent laparotomy. The use of EUS guided fine needle aspiration was not assessed.

No significant difference was demonstrated between the modalities either in the whole cohort or when small tumours (<20 mm) were analysed separately. When the clinical impact was assessed EUS had most impact in the following groups of patients: benign on CT – 5/21, 23.8%; portal vein invasion and resectability were compared using McNemar’s test of paired proportions (table).

Conclusion: Multislice CT is the primary imaging modality in assessing these tumours. EUS is not indicated in those patients in whom CT confidently demonstrates a resectable tumour. In those patients in whom CT suggests benign disease or borderline vascular invasion, however, EUS has an important role in determining resectability.

Abstract 193

<table>
<thead>
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<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>CT</td>
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<td>57%</td>
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Endoscopy posters

194 DOES A TWO DAY ON-SITE REGIONAL TRAINING PROGRAMME IMPROVE COLONOSCOPY SERVICE IN A DISTRICT GENERAL HOSPITAL: A PROSPECTIVE STUDY

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Background and Aims: Three national and seven regional training centres have been funded to support endoscopy training in England in view of the low national completion rate and the imminent Bowel Cancer Screening Programme. The aim of this study was to assess the effect of this training programme on our endoscopy unit.

Materials and Methods: A prospective audit of our colonoscopy service was undertaken between August 2003 and March 2005. After an initial data collection period of nine months, a two day on-site training course facilitated by the regional training centre was offered to all our colonoscopists using Magnetic Endoscopy Imager (MEI) in April 2004. The MEI was available for a further three weeks and the colonoscopists completed a questionnaire at the end. A grace period of three months then elapsed. Follow-up for this further audit data collection was continued for eight months until March 2005. Independent endoscopists who contributed to both study periods were included. Variables such as completion rate, sedation doses, and complications were compared between the periods.

Result: 93% of the colonoscopists felt that this would help improve their technique while 95% felt that the course had a significant impact on their sedation usage practise. Seven colonoscopists contributed to the study undertaking 408 and 569 procedures before and after the training. The mean adjusted completion rates were 82.3% (73.5–94.2%) before and 82.4% (62–95%) after the training. The mean pethidine doses fell from 43.3 mg to 34.38 mg and the mean sedative doses fell from 4.31 mg to 3.2 mg. Complication rates did not change (rectal bleeding in three patients and abdominal pain in four). There were no perforations or deaths.

Conclusion: Colonoscopists rated the course very high. There was a significant reduction in the doses of analgesics and sedatives used while maintaining the same caecal intubation rate. The sample size may be too small to detect changes in complication rates. Further training is required for some to improve our unit’s intubation rates.

195 PERCEIVED VALUE OF TEACHING COMPONENTS USED ON COLONOSCOPY TRAINING COURSES

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Background: Endoscopy training courses are a recommended component of learning endoscopy. Trainees often have their training recorded on video/ DVD. It is unclear how trainees rate the different components of the training courses and in particular whether they value watching recordings of their own performance.

Methods: A questionnaire was sent to 62 trainees who had attended a colonoscopy course at least three months earlier. All trainees were from centres that gave trainees video recordings of their own performance. Trainees were asked to rate 11 possible course components on a 6 point Likert scale and comment on the use of video recording of their training.

Results: There was a 63% response rate and the course components were ranked as shown in the table. Less than half of trainees video of their own training while on the course. Although most trainees felt video recordings should be kept, 29% never watched their videos and of those who did the mean number of times recordings were watched was only twice.

Discussion: There are potential benefits to using video feedback for endoscopy training but at present videos appear under utilised. Its long term usefulness is also limited by data protection and patient confidentiality issues. The course components currently most valued by trainees are hands-on experience and the magnetic endoscopic imager.

196 ONE-TO-ONE HANDS-ON COLONOSCOPY TRAINING COURSE IMPROVES COLONOSCOPY PERFORMANCE

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Background: Poor performance and inadequate training in colonoscopy in the UK has been reported. Ten centres across the UK run intensive hands-on training courses but their efficacy has not been established.

Aim: To assess whether a four day course delivering one-to-one training can improve colonoscopy performance.

Methods: Forty one specialist registrars (24 physicians, 14 surgeons) and three nurses have individually attended the course since the unit became a national training centre (15 months). The course objectives were to increase core knowledge and improve the basic hand skills required for colonoscopy. Trainees attended three microteaching, two computer simulator, and four hands-on training sessions. They performed two multiple choice question (MCQ) papers (previously validated and shown to be of equal difficulty). Performance parameters measured at the beginning and the end of the course included the MCQ time taken to complete the simulator test cases and Direct Observation of Procedural Skills (DOPS) using 100 point visual analogue scales for all aspects of colonoscopy technique. Trainees completed an anonymous feedback form to evaluate the course content.

Results: The MCQ score significantly increased: mean score 56.6% v 65.7% (p = 0.001). Mean total time taken to complete simulator test case improved significantly from 700 seconds v 500 seconds (p = 0.02). Trainees performed a median number of 16 cases during the course. DOPS demonstrated an improvement in clinical skills. Pre and post course mean scores were generally improved (7.5 v 8.1 (p = 0.007), basic handling technique 5.9 v 6.7 (p = 0.002), understanding and control of looping 5.4 v 6.7 (p = 0.001), caecal/ileal intubation 6.1 v 7.6 (p = 0.001) and exurement technique 6.5 v 7.7 (p = 0.001) respectively. All trainees had a high level of satisfaction and found the hands-on training most beneficial.

Conclusion: This intensive course improves core knowledge and clinical skills in colonoscopy. One-to-one tuition maximises hands-on training which may accelerate the learning curve.


197 ENDOSCOPE TRAINING AND ADVERSE OUTCOMES (30 DAY POST PROCEDURE MORTALITY): AN AUDIT OF 5715 PROCEDURES IN A LARGE TEACHING HOSPITAL

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Introduction: Although it is widely believed that endoscopy outcome is operator dependent, only recently have endoscopy training, quality, and adverse outcomes been pushed to the forefront of the debate. The two main reasons are; firstly, the NCEPOD report “scoping our practice”, and secondly, the imminent national bowel cancer screening programme. JAG and the Endoscopy Modernisation Agency have the task to improve endoscopy standards and training.

Aim: To determine whether training and in training in endoscopy has adverse patient outcomes as measured by the 30 day post procedure mortality (PPM).

Methods: 5715 consecutive endoscopic procedures were audited from 01/03/05 to 31/07/05 after being identified by endoscribe database. The hospital IT middleware system and coding was used to identify patients that died (PPM).

Results: Forty seven different users (endoscopists) performed 5715 procedures; including 22 trainees (TR) (performed 18% (22% if included supervised), 12 Consultants (CON) (perform 20% (26% if supervised included)), seven Non-Training Grade (NTG) (perform 27%), and six Nurse Specialists (perform 35%). PPM was 1.2% (n = 69; mean age 74.2 and ASA Score 3 (mode 4); all inpatients). This included 32 patients who

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A REGIONAL OUT OF HOURS ENDOSCOPY SERVICE IS AN EFFECTIVE WAY OF PROVIDING COVER FOR GI BLEEDING ACROSS A NUMBER OF DIFFERENT HOSPITALS

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Background and Aim: In 2004, a region-wide out of hours endoscopy service for gastrointestinal bleeding was introduced to cover five hospitals in South London (St George’s Tooting, the Royal Marsden Sutton, Epsom General Hospital, Epsom, Surrey, UK)

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Background and Aim: In 2004, a region-wide out of hours endoscopy service for gastrointestinal bleeding was introduced to cover five hospitals in South London (St George’s Tooting, the Royal Marsden Sutton, Epsom General Hospital, Epsom, Surrey, UK)

METHODS: Over a two month period, the SpRs were asked to complete two forms each time they were on call, one detailing the calls received, the other clinical details of endoscopies performed.

Results: Data for 32 days (24 weekdays and 6 weekend days) were available. Forty-four calls were received during this period, 26 during the week, 18 at weekends. 66% of calls were from St George’s Hospital. Seventeen calls resulted in out of hours endoscopy, 19 led to telephone advice being given about GI bleed patients, and eight calls were about non-GI bleed matters (for example, PEG fallen out, general gastroenterology advice). Of the 17 endoscopies (all upper GI performed), three occurred after midnight. The mean age of the patients was 68, and the mean Rockall score prior to endoscopy was 4.4. All patients had iv access on arrival for endoscopy, but 47% were haemodynamically compromised on arrival. Five cases revealed oesophageal varices, five peptic ulcer disease. Only one endoscopy was entirely normal. Endoscopic therapy was undertaken in 71%. One patient died from the GI bleed, eight went to ITU and subsequently recovered.

Conclusions: The regional GI bleed service in South London is a new initiative which has been successful and has enabled a number of hospitals to provide an effective and safe out of hours endoscopy service.

ENDOSCOPISTS’ ATTITUDES ON THE PUBLICATION OF “QUALITY” DATA FOR ENDOSCOPIC PROCEDURES

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Background: The public now have access to experience, mortality & morbidity data for certain surgical procedures (BMJ 2005; 330:506–10). Such “quality” data for endoscopy are not generally available, although Cotton has suggested this (Am J Gastro 2002;97:922). We studied endoscopists’ attitudes to and the practicality of these data being published.

Methods: We sent a questionnaire to all consultant GI surgeons, physicians, and gastroenterology registrars in the Northern region who currently endoscope (n = 132). We recorded doctor demographics, current bowel preparation, and the acceptability and utility (5 point Likert scale; higher = less useful/acceptable) of nine items describing endoscopic “quality” (for example, mortality, complication, and completion rates).

Results: 103 (78%) doctors responded of whom 79 were consultants (77%), 61 physicians (59%), and 90 male (87%). 77 (75%) collect any “quality” data. The most frequently collected item was colonoscopy completion rate (57, 74%). Data were collected for audit by 26 (34%), clinical governance by 30 (39%), and appraisal by 62 (81%). For 42 (54%) these data were only available to themselves, 34 (44%) to other doctors, and just one (1%) to the public. Respondents consistently considered data publication as more acceptable than useful (p < 0.01). The most acceptable/useful data item was annual number of endoscopies performed (mean acceptability = 1.9, utility 2.3), and the least was crude upper GI bleeding mortality (2.9, 3.2). Surgeons rated information less acceptable (2.9 v 1.9, p < 0.01) and less useful (3.0 v 2.4, p < 0.01) than physicians. Acceptability and utility scores were not related to gender, length of experience or current intensity levels. Registrars rated utility better than consultants (2.0 v 2.7, p < 0.01). Only two respondents thought all items totally unacceptable and useless.

Conclusions: The majority of endoscopists currently collect “quality” data for their practice although this is not widely available. If these data were to be made available, consideration must be given to the value of such data and their acceptability. The majority of endoscopists do not find this completely unacceptable.

IMPACT OF ENDOSCOPIST PERFORMED TRANSABDOMINAL ULTRASOUND ON INVESTIGATION OF DYSPEPSIA IN DIRECT ACCESS ENDOSCOPY LISTS

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Introduction: Endoscopy (OGD) and transabdominal ultrasound (TAUS) are complementary investigations in the investigation of upper GI bleeding. In the UK, OGD and TAUS are traditionally undertaken by different personnel in different departments thus fragmenting the investigation of dyspepsia, increasing the workloads in the departments, resulting in multiple hospital visits and delaying the diagnosis and management.

Methods: Our consultant gastroenterologist (SL) undertook formal training in TAUS in line with Royal College of Radiology guidelines for medical non-radiologists. A scanner was purchased for the endoscopy unit from charitable funds. Patients attending for direct access OGD underwent concurrent TAUS on this endoscopist’s lists. Outcomes were compared with the pattern for six intensity levels.

Results: 1204 sequential patients attended for investigation of dyspepsia during the study period. Undertaking concurrent TAUS had no impact on the throughput of the endoscopy lists (mean time in procedure room for OGD alone was 10.4 minutes, TAUS + OGD 10.6 minutes). With concurrent TAUS + OGD, investigations for dyspepsia were completed in 100% of cases during a single hospital visit. On the OGD alone lists, investigations were concluded in only 87% during the initial visit. Concurrent TAUS thus substantially reduced follow up visits, outpatient clinic workload, and waiting times. Several patients who had diagnoses made on TAUS that precluded the need for OGD.

Conclusion: Abdominal ultrasound scanning by endoscopists is feasible and leads to major efficiency gains in the investigation of dyspepsia, accelerating diagnosis, minimising hospital visits, and improving waiting times, all without detriment to the throughput of endoscopy lists. We recommend that all UK endoscopists consider training in ultrasound, in view of the efficiency gains and earlier diagnosis that this would bring. Two other endoscopists are now training in ultrasound in our unit, and the rest may follow suit.

COMPARISON OF THE EFFICACY, ACCEPTABILITY, AND SAFETY OF A NEW TWO LITRE PEG-E GUT CLEANSING SOLUTION VERSUS TWO ESTABLISHED COLON CLEANSING REGIMENS

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Aim: To compare the efficacy, safety and acceptability of a new 2 L PEG-E oral gut cleansing solution (MOVIPREP) to a standard 4 L PEG-E or sodium phosphate solution (NaP) as bowel preparation prior to colonoscopy.

Methods: Two similar randomised, single blinded, active controlled, multicentre studies were performed and datasets combined. Gut lavage solutions were taken either as single dose the day before the colonoscopy or as split dose with half dose the evening before followed by the other half on the morning of the colonoscopy. Primary efficacy criterion was the gut cleansing quality, as judged by a blinded expert panel on the basis of videotapes. Secondary endpoints were the degree of gut cleansing in predefined gut segments, overall quality of gut
cleansing, evaluation of taste, patient’s satisfaction and acceptability, and a full safety assessment. Results: A total of 699 patients (349 with Moviprep, 179 with 4 l PEG-E and 171 with NaP) in 27 centres received study medication. 580 patients (290 with Moviprep, 155 with 4 l PEG-E and 143 with NaP) were analysed for the primary efficacy endpoint using the available video tapes. The overall success rate was 81.4% in the MOVIPREP group versus 94.8% in the 4 l PEG-E group and 64.3% in the NaP group. Similarly, the scores of gut cleansing per colon segment were: 0 (SD 0.8) to 2.8 (SD 0.8) in the MOVIPREP group versus 2.3 (SD 0.5) to 2.5 (SD 0.6) in the 4 l PEG-E group and 1.9 (SD 0.9) (colon ascending) to 2.8 (SD 0.8) in the NaP group. Patients consistently preferred MOVIPREP over 4 l PEG-E (patient satisfaction, overall acceptability and taste, satisfaction with bowel cleanliness and professional/social impact). Both PEG-E containing solutions were well tolerated and had similar mild adverse event profiles. No relevant shifts in the laboratory tests were observed. In contrast, NaP was more frequently associated with the occurrence of adverse events and clinical significant laboratory shifts. Two cases of serious hypopotassemia were observed after the intake of NaP.

Conclusions: MOVIPREP is at least as effective as established gut cleansing regimens. Patients consistently preferred MOVIPREP as gut lavage solution to the established comparators. In summary, this new 2 l PEG-E bowel cleansing solution provides a better patient acceptability without any loss of efficacy or enhanced safety concerns for colon cleansing prior to colonoscopies.

202 WHAT HAPPENS TO PATIENTS WITH IRON DEFICIENCY ANAEMIA IN WHOM NO CAUSE IS FOUND?

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Background: All adults with iron deficiency anaemia (IDA) need upper and lower GI tract investigation to exclude malignancy (BSG guidelines). In our series 15% of patients had cancer and 11% benign pathology to explain their IDA.

Aim: To follow up patients with unexplained IDA to see if they were re-investigated for persistent IDA and if our approach had missed malignancy or other causes of IDA.

Methods: We investigate all adults with IDA by endoscopy with duodenal biopsy and colonoscopy. All patients investigated by this means from 01/05/1999 to 01/05/2002 were identified. In those where no cause was identified the hospital records system (PAS) was used to identify their GP. GPs were sent a questionnaire about these patients.

If there was no reply a further questionnaire was sent and if not returned this was followed by a telephone call. PAS was used to identify patients who died and patients who had been diagnosed with GI malignancy since investigation.

Results: Forty five patients had unexplained IDA. 33 replies were received from GPs. PAS showed 0 of 12 about whom we got no replies had died. Three of 33 patients had died; 1 hypothyroidism, 1 MI, and 1 stroke. No patient was diagnosed with GI malignancy since investigation. Seventeen of 33 patients had recurrent IDA with four diagnoses; 1 thalassemia trait, 1 prosthetic valve haemolysis, 1 GORD, and 1 GI angiodysplasia. The other 24 of 33 patients did not have recurrent IDA but one developed a colorectal fistula due to diverticular disease and one an acute GI bleed and endoscopy revealed oesophageal varices.

Conclusion: Investigation of patients with IDA by endoscopy with duodenal biopsy and colonoscopy is adequate. This approach does not seem to miss malignancies though one angiodysplasia and was probably “missed” and one patient later was found to have varices though in the absence of IDA.

203 ANTIBIOTIC PROPHYLAXIS FOR INFECTIVE ENDOCARDITIS: IMPACT OF NEW BRITISH CARDIAC SOCIETY GUIDELINES

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Background: The British Cardiac Society (BCS) recently updated their guidelines for antibiotic prophylaxis of infective endocarditis, proposing a more aggressive approach. These contrast with those of the British Society of Gastroenterology (BSG), American Gastroenterological Association (AGA), American Heart Association (AHA), and European Society of Cardiology (ESC). Although there remains consensus regarding prophylaxis for patients at high risk of endocarditis undergoing diagnostic endoscopy, the BCS also propose prophylaxis for patients at moderate risk with acquired valvar lesions.

Methods: Prospective study to assess the prevalence of patients with moderate or high risk cardiac lesions attending for diagnostic endoscopy. Patients underwent cardiovascular examination before the procedure. Clinical records and endoscopy referral forms were reviewed to confirm the presence or absence of known structural cardiac lesions.

Results: Sixty two patients (mean age 67 years) were examined. Of these, 40 (64.5%) underwent gastroscopy and 22 (35.5%) underwent colonoscopy. Eleven patients (17.7%) were found to have haemodynamically significant valvar lesions on clinical examination. Of these 11, the lesion had been previously documented in four patients (36.4%). No patient would have received antibiotics under BSG guidelines. If BCS guidelines were implemented in our Trust (7000 procedures/year), it would result in 1239 extra doses of antibiotics/year.

Conclusions: More than one in six patients attending for diagnostic endoscopy has a clinically detectable valvar lesion. These patients would receive broad spectrum antibiotics under BCS guidelines, without clear evidence of benefit. Latorgenic complications from anaphylaxis, C difficile diarrhoea, previously unknown penicillin allergy, and antibiotic resistance may be incurred. Implications extend to cost, workload and training of nurse endoscopists for cardiac examination. Clearly, the BCS guidelines need to be reassessed urgently, possibly in collaboration with the AHA, ECS, AGA, and BSG.

204 PREDICTORS OF RE-INTERVENTION IN ENDOSCOPIC PALLIATION OF MALIGNANT GASTRODUODENAL OR COLORECTAL OBSTRUCTION WITH SELF-EXPANDABLE METAL STENTS

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Aims: Enteral stenting is a minimally invasive option for the palliation of malignant obstruction. We sought to evaluate potential factors that may predispose to re-intervention in enteric and colonic stent failures in long term survivors.

Methods: Patients undergoing palliation of malignant gastroduodenal or colonic obstruction with self-expandable metallic stents (SEMS) were identified from our endoscopic database over a six year period. In patients surviving 30 days or more an analysis was made of potential factors which may predispose to re-intervention including stent angulation and post-stenting survival. Stent angulation was graded: 1 (no angulation), 2 (1–15˚), 3 (16–45˚), 4 (46–90˚), 5 (<90˚).

Results: Eighty eight patients (49 male, mean age 71 years) were identified (47 gastroduodenal and 41 colocolonic obstruction). Immediate technical success was achieved in 79/84 (94%) cases (four lost to follow up). With stenting symptoms resolved and oral intake resumed in 74/79 (94%) patients. Overall median survival following stenting was 71 days (range 2–785) and 101 days for the 52 patients surviving 30 days or longer. 16 of these patients required re-intervention due to stent obstruction (n=13) or migration (n=3) at a median time of 85 days (range 34–481). The mean stent angulation score for these patients was 3.94; the mean score in the group not requiring re-intervention was 2.89 (p = 0.004). Patients with post-stenting survival > 60 days were likely to need reintervention (p = 0.01). The site of obstruction, type of primary malignancy, concurrent chemoradiotherapy did not influence stent functional longevity.

Conclusion: SEMS provide excellent palliation of malignant gastrointestinal or colonic obstruction. Re-intervention is necessary in almost 1/3 of long term survivors. Initial stent angulation and duration of survival post-stenting may be predictive of the need for re-intervention in patients surviving 30 days or longer. In strictures that are severely angulated, primary intervention with longer or more flexible SEMS may avoid the need for re-intervention.

205 DOES SENDING A VIDEO TO PATIENTS LEAD TO BETTER INFORMED CONSENT?

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Introduction: Informed consent is the cornerstone of good medical practice. We have previously assessed the level of understanding of consent in patients undergoing endoscopy and found it to be deficient in around one third. This study investigates whether understanding can be improved by sending a video of the procedure to patients prior to an upper GI endoscopy.
Method: Eighty-five patients were sent a video prepared in-house, with professional support, detailing the procedure, showing images of the endoscope and detailing risks and alternative procedures as recommended in DOH guide to informed consent. Patients were then consented in the unit on the day of the procedure. Following obtaining consent and prior to the procedure their level of understanding was assessed using previously audited criteria to decide if consent was good, fair, poor, or displayed no understanding.

Results: Of the 85 patients sent videos only 74 had watched it. The 11 who did not watch cited reasons of “too frightened” (no), “couldn’t be bothered” (no), no video at home (no). Of the 74 who watched the video, 95% had good overall understanding, 90% understood the benefits, but only 70% understood the risks compared to 63%, 65%, and 68%, respectively in the previous study. Whereas in the patients who watched the video these results are impressive, if those who did not watch it are included, there is no significant overall difference. Some patients (64, 86%) commented the video was helpful, others found it frightening (9, 12%), 1 felt the same.

Conclusions: The use of videos can help the understanding of some patients undergoing an endoscopic procedure but given that 13% do not watch such material the overall group level of understanding is not improved. We suggest for those patients who express an interest, such material should be available in the endoscopy unit, but routine sending is not warranted.

The British Society of Gastroenterology (BSG) guidelines recommend all patients referred to our unit for endoscopy who have a macrocytic/normocytic anaemia in the context of elevated, normal, or undetermined serum ferritin concentrations. For comparison we studied patients without evidence of IDA (p < 0.05) with microcytic/hypochromic red cell indices or reduced serum ferritin concentrations. Unfortunately, endoscopy units receive many referrals for invasive investigation of patients with anaemia in the absence of supporting evidence of iron deficiency.

Aim: To discover potential aetiological factors in patients referred for endoscopic investigation of anaemia. Endoscopic findings were then categorised according to biochemical classification of anaemia. Blood samples from within three months of endoscopy were analysed for serum ferritin, serum iron, and iron binding capacity (TIBC). The classifications were: (1) IDA defined as either low ferritin, or low iron and high TIBC; (2) ACD defined as low iron and low TIBC in the absence of low ferritin; and (3) mixed anaemia (MA). Endoscopically diagnosed bleeding lesions were cancer, ulceration, angiodysplasia, telangiectasia, and collitis.

Results: Ninety three patients over the age of 75 years (mean age 82 years) underwent endoscopic investigation for anaemia between July 2004 and October 2005. All underwent colonoscopy, and 75 underwent gastroscopy.

Table: Endoscopic Investigation Must Be Considered in Patients with Severe Unexplained Anaemia Irrespective of MCV

<table>
<thead>
<tr>
<th>Measure</th>
<th>BSG Targets</th>
<th>UHND Audit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low haemoglobin</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Reduced MCV</td>
<td>100%</td>
<td>91%</td>
</tr>
<tr>
<td>Reduced ferritin</td>
<td>100%</td>
<td>91%</td>
</tr>
<tr>
<td>UGIF ± colon/barium enema</td>
<td>90%</td>
<td>71%</td>
</tr>
<tr>
<td>Screening for coeliac disease</td>
<td>90%</td>
<td>81%</td>
</tr>
<tr>
<td>Iron replacement</td>
<td>90%</td>
<td>57%</td>
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Conclusions: Biochemical IDA was present in a small minority (7.5%) of elderly patients referred for investigation of anaemia. Many patients (39.8%) were found to have ACD, and these were least likely to have endoscopic pathology. The majority had MA, surprisingly the best predictor of endoscopic pathology. Therefore, the absence of classical iron deficiency in the elderly must not preclude endoscopic investigation. However, the paucity of endoscopic pathology in patients with ACD suggests that in frail patients investigation may be deferred, at least until more convincing indications for endoscopy emerge.

209 THE CHANGING FACE OF OGD AND COLONOSCOPY IN A TERTIARY REFERRAL CENTRE: 11 YEAR AUDIT OF ENDOSCOPIC PRACTICE
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Background: Colonoscopy is performed poorly in the UK, with caecal intubation rates (CIR) <60% in a recent national audit. Upper GI endoscopy (OGD) can have significant cardiorespiratory morbidity in part attributed to poor sedation practise. We were interested to examine whether changes in awareness of problems, sedation guidelines, and endoscopy training during the last 10 years had altered our practice.

Aim: To examine OGD and colonoscopy practise in a large University Hospital over 11 years and compare with current advisory guidelines.

Methods: A database of 75 956 procedures was used 1994–2005 (OGD: 65 728; colonoscopy: 10228). Recorded parameters for both were analysed: sedation/opiate use, therapeutic trends, caecal intubation rates (CIRs), reporting practise and use of LA spray for OGD. Statistical analyses included log rank analysis (LRA) and MWT using MINITAB 13 software.

Results: 90% OGD (59017) and 73% c/scopy (7506) reports had complete data for analysis. OGD analysis—a significant decrease (p<0.001) in midazolam dose (1994 mean 5.9 mg, range 1–20 mg; 2005 mean 3.1 mg, range 1–8 mg) LA spray use has not changed (mean 60%, range 45–56%) but use of pethidine has increased (p<0.001) in parallel with therapeutic OGD (r²=0.69 p<0.001). Colonoscopy had a similar reduction in midazolam use (1994 mean 7.4 mg, range 2–20 mg; 2005 mean 3.6 mg, range 1–8 mg) and pethidine use has risen from 17% in 1994 to 87% in 2005 (p<0.0001). This parallels improvement in CIR: 70% 1994 to 85% 2005 (r²=0.8 p<0.0001). Therapeutic colonoscopy has also risen from 9% 1994 to 26% in 2005 (r²=0.9 p<0.0001) in part representing better patient selection. Reporting practise for both OGD and c/scopy has improved significantly from 1994–2005: 30% of 1994 reports did not accurately state drug doses of with only 3% in 2005 (r²=0.8 p<0.0001).

Conclusion: Sedation dose has reduced in line with current guidelines and parallels improved training of SpRs. CIRs have risen over the last 11 years and reporting practise has improved. Further improvements in audited outcomes require more accurate recording of details of selection and clinical outcomes.

210 CHANGING PRACTICES IN BENZODIAZEPINE SEDATION FOR ENDOSCOPY
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Background: Most endoscopic procedures are performed under conscious sedation with a short acting benzodiazepine such as midazolam. The 2004 NCEPPOD report “Scoping our Practice” found that in 14% of peri-endoscopy deaths the cause of death was inadequately explained. Awareness of safe practice in sedation is increasing in part due to guidelines from the BSG and other authorities. The 2003 BSG Safety and Sedation During Endoscopic Procedures Guidelines recommend that the “dosage of benzodiazepines … should be kept to a minimum to achieve sedation.’’ The aim of this study was to determine whether our use of midazolam sedation for endoscopy has changed over the last six years.

Methods: A snapshot retrospective review of sedation records for all gastroscopies (OGDs), colonoscopies and ERCPs performed in one of the Trust’s endoscopy units during the year 2000 and 2005.

Results: A total of 11 359 OGDs, 989 colonoscopies, and 82 ERCPs were performed with iv sedation in 2000; 840 OGDs, 987 colonoscopies, and 120 ERCPs were performed with iv sedation (to date) in 2005. Benzodiazepine doses used for all endoscopies and the use of sedation for upper GI endoscopy have reduced significantly between 2000 and 2005. This encouraging trend highlights the increasing awareness of safe sedation practices among endoscopists.

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Background: A national audit into colonoscopy practice revealed high average doses of midazolam (5 mg) and pethidine (50 mg) being used resulting in oversedation in 3.4% of cases (CJA Bowles, R Leicester et al. Gut 2004). When previously audited in 2000 we found high doses of sedatives were often administered and following this earlier audit in-house re-education and training took place. In 2002 skills courses were regularly carried out in the unit. We re-audited our practice to assess the impact of these on our sedation practice.

Method: We analysed 14 521 colonoscopies in our department from 1992 and 2004 to determine changes in sedation practice and sedation related complication rates in particular comparing practice before and after our previous audit. Oversedation was defined as the need to administer naloxone or flumazenil or being noted as a specific complication on the endoscopy report.

Results: 6849 colonoscopy results were available in the 1992–99 period and 7672 between 2000–04. Fortral was used at a mean dose of 29.5 mg (SD 3.2), between 1992–2002 and diazemuls at a mean dose of 6.1 mg (SD 2.4). Between 1992–2004 midazolam was used at a mean dose of 3.9 mg (SD 1.4). Between 1993-2004 pethidine was used at a mean dose of 40.9 (SD 13.5). Between the 1990s and 2000s there has been a significant reduction in the dosages of midazolam (4.6 mg v 3.1 mg p<0.001) and pethidine (47.3 mg v 31.6 mg p<0.0001), no changes were seen with fortal or diazemuls. 61 cases of oversedation were recorded (0.4%) with 46 cases in the 90s (0.7%) and 15 cases in the 2000s (0.2%) (p<0.003).

Conclusion: Regular auditing and re-education can help to improve endoscopic standards and reduce the dosages of sedatives administered and subsequent oversedation.

212 DOES BODY MASS INDEX INFLUENCE PAIN FOLLOWING COLONOSCOPY?
P. S. A. de Silva, J. M. Sayer. Department of Gastroenterology, Doncaster Royal Infirmary, Thorne Road, Doncaster DN2 5LT, UK

Introduction: The incidence of obesity is growing in the United Kingdom. This has resulted in more overweight and obese subjects undergoing colonoscopy. There is an increasing interest in assessing complication outcomes and suitable remedial action in this category.

Aims: To assess the incidence of pain in obese patients who underwent colonoscopy in a district general hospital over a four month period.

Methods: Data were collected from HCNScribe database and a questionnaire from all patients who consented to participate. Patients were asked to complete and return a questionnaire stating any symptoms that they experienced up to two weeks after their procedure. Case notes were also reviewed. Inaccurately/incompletely filled questionnaires were excluded from data analysis. BMI values were calculated from weight and height measurements on the day of the procedure and classified according to British Heart Foundation criteria. Corresponding details of sedation type, dosage, and procedures undertaken during colonoscopy were obtained from HCNScribe.

Results: During the study 508 patients underwent colonoscopy. 462 had a valid BMI recording. A total of 162 with valid BMIs had accurately completed questionnaires: 38 obese, 60 overweight, 41 normal, 3 underweight.

121 had complications (abdominal pain, bleeding, vomiting, faint, respiratory or urinary tract infections, non-specific) Pain was noted in 97
(78.2%) — 34 obese, 35 overweight, 27 normal, and 1 underweight. There was no significance in the incidence of pain among the different groups. 124 patients had sedation. There was no significant difference amongst BMI groups, occurrence of pain, administration of sedation (type, dosage, single or combined administration) and incidence of procedures undertaken during colonoscopy. Sedatives used were pethidine, midazolam, buscopan, and nubain.

**Conclusion:** This study reveals that BMI does not affect the incidence of pain after colonoscopy irrespective of sedation administered and procedures undertaken.

### 213 Unsedated Colonoscopy: For the Many or For the Few?

A. Sarkar, K. S. Smith, S. S. Johal, M. T. Donnelly. Department of Gastroenterology, Northern General Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Herries Road, Sheffield S5 7AU, UK

**Introduction:** A colorectal screening programme, with colonoscopy at its centre, is imminent in the United Kingdom. Perhaps the most dangerous aspect of colonoscopy is intravenous (iv) sedation related complication.

**Aim:** The aim of this study was to discover whether unsedated colonoscopy could be well tolerated by a large group of UK patients.

**Methods:** We retrospectively analysed sedated and unsedated colonoscopies carried out on our unit over a period of January 2002 to September 2005. All patients had their tolerance of the procedure independently assessed by an experienced endoscopy nurse on a four point scale ("good", "acceptable", poorly tolerated", "not tolerated"). We correlated these assessments with demographic and other data.

**Results:** Between January 2002 and September 2005 we performed 1442 unsedated colonoscopies, 1901 with Entonox only, and 4617 with intravenous midazolam. The age range of the patients was 16-95 years. As can be seen from the table, patients who were unsedated or received nitrous oxide alone tolerated colonoscopy significantly better than those who received intravenous sedation.

**Abstract 213**

<table>
<thead>
<tr>
<th>Total</th>
<th>&quot;Good&quot; or &quot;acceptable&quot;</th>
<th>&quot;Poor&quot; or &quot;Not tolerated&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrous oxide alone</td>
<td>1442</td>
<td>1417</td>
</tr>
<tr>
<td>No sedation</td>
<td>3283</td>
<td>3168</td>
</tr>
<tr>
<td>Intravenous sedation</td>
<td>4617</td>
<td>4115</td>
</tr>
</tbody>
</table>

The nitrous oxide or no sedation group and the no sedation group both tolerated colonoscopy better than the iv sedation group (p < 0.001, z test).

**Conclusion:** Significant numbers of patients can tolerate colonoscopy without sedation or by using nitrous oxide alone. Patients who choose to have colonoscopy without sedation or with nitrous oxide tolerate colonoscopy better than those who choose to have iv sedation. These data encourage the practice of unsedated colonoscopy.

### 214 Endoscopy in High Risk Cardiovascular Patients

G. Parkes, P. Fairclough, J. O. Lindsay. Department of Gastroenterology, Royal London Hospital, London, UK

**Background:** Early percutaneous transarterial coronary angioplasty (PTCA) improves outcomes in patients with acute coronary syndromes (ACS). Many cardiologists require endoscopic investigation of patients with angina or evidence of a GI bleed prior to PTCA, resulting in an increase in the number of procedures in patients with a recent history of ACS. The diagnostic yield in this patient group has not been reported; furthermore, performing endoscopy within three months of ACS may be associated with increased morbidity and mortality.

**Objectives:** To review the incidence of complications and diagnostic yield in patients undergoing endoscopy with recent ACS compared to matched controls, over one year period in a London teaching hospital with a large interventional cardiology department.

**Methods:** A retrospective review was performed using the Adam endoscopic reporting system. Patients referred for endoscopic procedures with a history of ACS within the previous 60 days were identified. The control group consisted of inpatients referred for endoscopic procedures, matched for age, sex, and indication.

**Results:** Over a one year period 57 patients with ACS within the previous 60 days underwent a combination of gastroscopy (40) and colonoscopy (17). The median (range) time between ACS and endoscopy was 4.16 (1–58) days. Three cardiovascular complications were reported in the ACS group—one acute MI (5.7%), two episodes of profound hypotension (5.2%); compared to none in the control group. There were no fatalities in either group. The yield of important diagnoses in the ACS group was 37% of cases compared to 51% in the control group. The diagnostic yield in ACS patients referred for angina as opposed to GI bleed was 24% v 38% in control.

**Conclusion:** This small study suggests that endoscopic procedures in patients with a recent history of ACS are associated with increased morbidity compared to non-cardiac inpatient endoscopy. The diagnostic yield in ACS patients is low, suggesting the need for more specific referral criteria.

### 215 Cardiovascular Assessment in Patients Following Bowel Preparation Without Intravenous Fluid Replacement: Increased Age Does Not Mean Decreased Function

S. E. Noblett, A. F. Horgan. Department of Colorectal Surgery, Freeman Hospital, Newcastle Upon Tyne, UK

**Introduction:** It is recognised that bowel preparation prior to colonoscopy-colorectal surgical procedures has a dehydrating effect such that many advocate intravenous fluid replacement, particularly in elderly patients. We compared the cardiovascular effects of bowel preparation in patients under 65 and over 65 years of age.

**Method:** Thirty nine patients having bowel preparation prior to elective colorectal surgery were prospectively assessed. All received bowel preparation using sodium picosulphate without intravenous fluid replacement. Data collected included age, POSSUM physiology score, and preoperative cardiovascular parameters which were measured in all patients using an oesophageal doppler; these included stroke volume (SV), cardiac index (CI), declining aortic flow time (FTc), heart rate (HR), and mean arterial pressure (MAP). The patients under 65 years of age were compared with those over 65 years. Data were compared using Student’s t test or Mann-Whitney U test as appropriate.

**Results:** Patients less than 65 years (group 1) had a median age of 55 years (range 24–63), the over 65 group (group 2) had a median age of 77 years (66–93). As could be expected the medical comorbidity assessed by the POSSUM physiology dataset was increased in group 2 (16.8 v 13.7, p < 0.001). No differences were found in routinely measured indices, HR (73 bpm v 65 bpm, p = 0.079) or MAP (74 mmHg v 79 mmHg, p = 0.122) between the two groups. Similarly, no significant differences were found in the cardiac function parameters SV (77.2 ml v 79.9 ml, p = 0.908), CI (2.92 l/min/m² v 2.86 l/min/m², p = 0.915), or FTc (6.1 v 6.2, p = 0.547).

**Conclusion:** The use of bowel preparation without supplementary intravenous fluid replacement did not significantly reduce cardiac function in our elderly patient group compared with younger patients. With an increasingly elderly patient population combined with pressures on resources and a drive towards day-case procedures, our finding that despite being a susceptible group for bowel purgative induced dehydration, no significant difference in cardiac function is reassuring.

### 216 Conscious Sedation and Colonoscopy. Are We Neglecting Patient’s Comfort for Safety?

J. M. Hancock1, D. Nylander2, K. Tiru1, S. Zubais1, R. Kasturi1, M. Connolly1, B. Gilbain1, J. Painter1, G. D. Bell1, S. E. Noblett, A. F. Horgan. Department of Colorectal Surgery, Freeman Hospital, Newcastle Upon Tyne, UK

**Introduction:** Several of us who either regularly teach colonoscopy on courses held at different Regional and National Centres (IH, DM, JP, GDB) or alternatively supervised trainees who had attended such courses (MC) wondered if the admirable trend to using much smaller doses of sedation and analgesia might, at times, have gone too far and thus patient comfort might be suffering. MC, a largely self-taught colonoscopist, had a sedation practice which was known to be markedly different to that of the other trainees. MC, a largely self-taught colonoscopist, had a sedation practice which was known to be markedly different from that of the other trainees and he agreed to take part in a comparative prospective audit to monitor patients’ experience and overall satisfaction with their colonoscopy.

**Method:** 132 patients undergoing a colonoscopic examination (at which trainees were present) agreed to complete a patient satisfaction questionnaire. The form included an assessment of pre-procedure worries, estimated degree of discomfort, severity of pain experienced...
Objective: The aim of this study is to derive and evaluate diagnostic determinants of gastro-oesophageal cancer based on patients’ symptomatic profile derived from an upper GI PCQ.

Method: A detailed upper GI PCQ was sent to all patients coming for first time endoscopy. All symptoms and diagnostic outcomes were collected and stored in the EPR to create a databank.

Results: 402 patients were included. 4% of these had cancer, 31.3% of which had curative surgery. Univariate and multivariate analysis resulted in four factors being positive predictors for cancer. These were age, retrosternal dysphagia, duration of abdominal pain less than six months, and worsening abdominal pain. On the other hand there were two negative predictors, those being female sex and abdominal pain, which is more than six months and not progressive. When the generated scoring system was tested on the other cohorts it excluded 40% of the workload and detected cancer in 10% with AUC (area under curve) of 0.87 in the ROC (receiver-operating characteristic) analysis.

Conclusion: Scoring system for upper GI symptoms as predictor of cancer is possible and it will result in reducing the workload in endoscopy by prioritisation of referrals.

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**IS SEDATION PRACTICE LINKED WITH ADVERSE ENDOSCOPIC OUTCOME? AN AUDIT IN RESPONSE TO THE NCEPOD REPORT**


Introduction: The NCEPOD report “Scoping our practice” (2004) emphasised sedation practice as a possible contributor to endoscopy related mortality (ERM). Recommendations included regular audit and national guidelines for sedation. Current BSG and Academy of Medical Royal Colleges guidelines recommend the use of no more than 5 mg midazolam (MD) and for reduced doses in the elderly or in combination with opioids (COM).

Aim: To audit endoscopy sedation practice to establish rates of procedure-related complications (PRC) (including ERM and immediate complication rate) for all diagnostic and therapeutic upper and lower endoscopy (excludes ERCP).

Methods: 7234 consecutive procedures performed in 5999 patients were audited. Patients were identified from Endoscopy database and deaths correlated using the hospital Medway IT system. Death certificates were reviewed in all fatalities.

Results: Sedation was used in 53% of procedures. Mean MD dose (SD) was 4.87 mg (2.5). 18.75% (6/32) endoscopists used doses >5 mg. Overall 30 day mortality was 0.73% (n=53) but true ERM was 0.25%. The lower ERM was seen in non-sedated versus sedated patients (0.09% v 0.4%; p=0.02) perhaps reflected a younger age group (p=0.001) underlying many non-therapeutic procedures (97% v 65%). PRC was again lower in the non-sedated group (0.18% v 1.1%; p<0.001). Mean doses of MD were lower in ERM patients than survivors (2.6 mg v 4.9 mg p=0.001) with none receiving >5 mg or COM. Also, MD doses were comparable for those with or without any complication (p=0.2). There were no differences in PRC when comparing patients receiving <5 mg versus >5 mg MD (1 v 1.4%; p=0.4) or MD only versus COM (1.1 v 0.95; p=0.7). Endoscopists consistently using >5 mg MD did not have greater ERM or PRC compared to other operators (p=0.7 and 0.2).

Conclusions: We found no strong evidence to link higher sedation doses or the use of combined sedation with endoscopic related mortality (ERM) or procedural related complications (PRC). Endoscopists who exceeded recommended doses had comparable outcomes. This suggests that the heavy emphasis placed on sedation practice by NCEPOD on mortality was unfounded and highlights the need to audit both favourable and adverse outcomes.

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**AN AUDIT OF MORTALITY FOLLOWING PEG INSERTION AND THE IMPACT OF A NURSE LED PRE-ASSESSMENT SERVICE**

R. Riley, M. M. Ahmed. Department of Gastroenterology, Good Hope Hospital, Birmingham B75 7NB, UK

Introduction: Percutaneous endoscopic gastrostomy (PEG) is a common procedure that provides enteral access for the administration of tube feeding in patients who are unable to obtain adequate nutrition by mouth. The recent NCEPOD report (Oct 2004) has raised concerns over improper PEG usage and recommends in-depth assessment of the patient to determine potential benefit prior to PEG insertion.

Aim: We performed a two year audit (01/01/03–31/12/04) to examine mortality after PEG insertion and determine the impact of a nurse led pre-assessment service which was set up one year into the audit (01/01/04).

Method/Patients: Over the two years, 102 patients (51 female, 41 male) were fitted with a Fresenius Freka (9 or 15 French) pull through gastrostomy tube. A prospective database of all patients was kept.

Results: See table.

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**UPPER GASTROINTESTINAL POLyps: WHY BIOPSY?**

S. Cherian, M. M. Ahmed. Good Hope Hospital NHS Trust, Sutton Coldfield B75 7NB, UK

Aim: Polyps are a common finding at oesophage-gastro-duodenoscopy (OGD). Up to 90% of gastric polyps are reported to be hyperplastic. We conducted a retrospective audit on all patients in whom a polyp was detected at OGD to establish the yield from biopsies of these polyps.
mimicking phantom, we have previously estimated the max error of the T1 cancer of the oesophagus. As part of their staging a CT of thorax/patients (5 F/9 M, mean age 72/65 years respectively), diagnosed with methods:

Between 2002 and 2005, we retrospectively studied, 14 methods:

Aims:

To investigate the use of 3D EUS as a means to provide detailed and accurate information in the staging and localisation of T1 cancers of the oesophagus.

Methods:

Between 2002 and 2005, we retrospectively studied, 14 patients (5 F/9 M, mean age 72/65 years respectively), diagnosed with T1 cancer of the oesophagus. As part of their staging a CT of thorax/abdomen and EUS with subsequent 3D reconstruction (3D-EUS) were performed. A reconstruction of the oesophagus was generated from images acquired during a free pullback of the echo-endoscope at a constant speed and at a rate of 12.5 fps. Using an oesophagus mimicking phantom, we have previously estimated the max error of the 3D EUS technique in estimating length and depth of tumour as <2.5%.

Results:

In all cases there was agreement between standard EUS and 3D EUS in the staging of the disease (T1). The tumour was not visible by CT scan in any of the cases. Seven patients had upper/mid oesophageal Ca, six patients at lower third, and one junctional tumour. No definite lymphadenopathy seen by EUS or CT. In addition to standard EUS, 3D EUS provided more information and accurately determined tumour dimensions, layer involvement and in particular length relative to reference anatomical structures such as the aortic arch, subcarinal area, or the OGI. Four of seven patients with upper/mid tumour received radiotherapy. Conclusion: 3D EUS provided additional detailed information regarding tumour dimensions and layer involvement in early (T1) disease. Such information can be of use in treatment planning, in particular in cases treated by radiotherapy in order to accurately localise tumour in the absence of tumour imaging by CT and focus the administration of radiotherapy.

Abstract 220

<table>
<thead>
<tr>
<th>Histology</th>
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<th>Duodenal</th>
</tr>
</thead>
<tbody>
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<td></td>
</tr>
<tr>
<td>High grade dysplasia</td>
<td>01</td>
<td></td>
</tr>
<tr>
<td>TVA with high grade dysplasia</td>
<td>03</td>
<td>01</td>
</tr>
<tr>
<td>Intraduodenal adenocarcinoma</td>
<td>03</td>
<td></td>
</tr>
<tr>
<td>Poorly differentiated adenocarcinoma</td>
<td>03</td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td>09</td>
<td></td>
</tr>
<tr>
<td>GIST</td>
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</tr>
<tr>
<td>MALT</td>
<td>01</td>
<td></td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>02</td>
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</tbody>
</table>

Methods: All OGDs performed over a nine year period (1996 to 2005) were reviewed and cases where a polyp was detected were identified and analysed further.

Results: 367 patients (225 male) underwent 425 OGDs. The median age was 69 years. Polyp location was: gastric (412), duodenal (1) and both (12). In 254 of 425 cases, polyps were multiple. Polyps were >10 mm in size in 38 procedures, 6–10 mm in 63 and 0–5 mm in 184. Polypectomy was performed in 11 procedures (2 endoscopic mucosal resections). Argon plasma coagulation was used to ablate polyps in two cases. Adrenaline injections were used to control post-polypectomy bleeding in two patients. Biopsies were performed in 225 procedures: 89 were fundic gland polyps/cystic glandular polyps, 10 were Corpus glandular and 57 were either inflammatory, hyperplastic or regenerative. Normal mucosa was detected in 42. Significant histology was detected in 29 procedures. These are listed in the table. Conclusion: Significant diagnostic yield from upper gastrointestinal polyp sampling is not as low as sometimes assumed. In addition when polyps are found, the biopsy result can alter patient management. Hence we recommend that histological confirmation be obtained in all new polyps.

Abstract 221

VALUE OF 3D EUS IN STAGING AND DETAILED ACCURATE LOCALISATION OF EARLY OESOPHAGEAL CANCER PRIOR TO TREATMENT

S. Inglis, S. Patterson-Brown1, D. Patel2, J. N. Plevris3. Departments of Medical Physics, 1Surgery, 2Radiology, and 3Centre for Liver & Digestive Disorders, The Royal Infirmary of Edinburgh, UK

Background: Endoscopic ultrasound (EUS) is routinely used in the staging of oesophageal cancer. The majority of these tumours at diagnosis are advanced, but when the disease is diagnosed early there are several treatment options available depending on patient fitness, age and their preference of treatment.

Aims: To investigate the use of 3D EUS as a means to provide detailed and accurate information in the staging and localisation of T1 cancers of the oesophagus.

Methods: Between 2002 and 2005, we retrospectively studied, 14 patients (5 F/9 M, mean age 72/65 years respectively), diagnosed with T1 cancer of the oesophagus. As part of their staging a CT of thorax/abdomen and EUS with subsequent 3D reconstruction (3D-EUS) were performed. A reconstruction of the oesophagus was generated from images acquired during a free pullback of the echo-endoscope at a constant speed and at a rate of 12.5 fps. Using an oesophagus mimicking phantom, we have previously estimated the max error of the 3D EUS technique in estimating length and depth of tumour as <2.5%.

Results: In all cases there was agreement between standard EUS and 3D EUS in the staging of the disease (T1). The tumour was not visible by CT scan in any of the cases. Seven patients had upper/mid oesophageal Ca, six patients at lower third, and one junctional tumour. No definite lymphadenopathy seen by EUS or CT. In addition to standard EUS, 3D EUS provided more information and accurately determined tumour dimensions, layer involvement and in particular length relative to reference anatomical structures such as the aortic arch, subcarinal area, or the OGI. Four of seven patients with upper/mid tumour received radiotherapy. Conclusion: 3D EUS provided additional detailed information regarding tumour dimensions and layer involvement in early (T1) disease. Such information can be of use in treatment planning, in particular in cases treated by radiotherapy in order to accurately localise tumour in the absence of tumour imaging by CT and focus the administration of radiotherapy.

Abstract 222

THE VALUE OF REPEATING UPPER GI ENDOSCOPY AFTER NORMAL INITIAL FINDINGS

C. P. C. Boger, S. Bridger. Dorset County Hospital, Dorchester, Dorset, UK

Introduction: Repeat endoscopy on patients who have already had a normal upper gastrointestinal investigation often seems unrewarding. Despite this observation no study has investigated whether repeating endoscopy in these patients yields any additional pathology in particular new cancers.

Method: We conducted a review of our endoscopy database over a seven year period between July 1997 and July 2004. We included all patients who had undergone two or more upper GI endoscopies with a normal first endoscopy. We then looked at all subsequent endoscopies for that patient to ascertain the number of new cancers discovered.

Results: 15 758 patients underwent an endoscopy during this time period with 2991 patients (19%) having two or more procedures. 1379 patients (8.8%) underwent repeat endoscopy despite a normal initial procedure. In this group only 20 new cancers (1.5%) were found; seven within one year at the first endoscopy, two between 1–2 years, five between 2–3 years, and five over three years. Of those found in the first year, all seven (35%) were probable missed cancers that had undergone repeat procedures prompted by continuing or new worrying symptoms, or other additional investigation. Of those cancers picked up after one year, only one was a probable miss with the rest again prompted by worrying symptoms.

Discussion: A large number of endoscopies are performed on patients who have already had a normal initial endoscopy using up valuable resources. With such a low yield of cancer the necessity of repeating the procedure should be strongly considered, and only undertaken on those with continuing worrying symptoms.

Abstract 223

WIRELESS CAPSULE OESOPHAGOSCOPY (PILLCAM ESO) COMPARED TO UPPER GI ENDOSCOPY IN THE DETECTION OF OESOPHAGEAL VARI...
224  CLINICOPATHOLOGICAL VARIABLES PREDICT MORBIDITY AND EARLY MORTALITY FOLLOWING COMBINED BILIARY STENTING: A MULTIVARIATE RISK FACTOR ANALYSIS


Introduction: Combined percutaneous and endoscopic biliary stenting permits drainage of biliary obstruction not treatable by ERCP alone, but is associated with significant morbidity and mortality. We present the largest reported series of combined procedures and examine factors that may predict procedure associated morbidity and mortality.

Methods: A retrospective study of patients undergoing a combined procedure for biliary decompensation between January 2001 and December 2004. Sixteen pre-procedure clinicopathological and laboratory variables were correlated with outcome and significance determined using the chi-squared test for morbidity and the log rank test and Cox regression analysis for mortality.

Results: Combined biliary stenting was attempted in 80 patients over the study period and was technically successful in 72 cases. Underlying pathology in those stented included carcinoma of the pancreas (n = 31), cholangiocarcinoma (n = 19), metastatic disease (n = 13), benign pathology (n = 7), and ampullary carcinoma (n = 2). Inpatient morbidity was 30% and 30 day mortality 21%. Low serum albumin, low haemoglobin, elevated white cell count, and clinical evidence of sepsis were significantly associated with morbidity (p < 0.05). High ASA grade (p = 0.011), elevated serum creatinine (p = 0.01), low serum albumin (p = 0.01), elevated white cell count (p = 0.003), and clinical evidence of sepsis (p = 0.0002) were associated with increased 30 day mortality on univariate analysis. Of these factors, high ASA grade (p = 0.009) and elevated white cell count (p = 0.04) were independently associated with increased 30 day mortality.

Conclusion: Combined biliary stenting is associated with a high technical success rate and acceptable morbidity and mortality in our centre. Clinicopathological and laboratory variables predict poor outcome following combined biliary drainage and optimisation of patient status may reduce procedure associated risk.

225  SERIAL INCREMENTAL STENTING OF SYMPTOMATIC COMMON BILE DUCT STRICTURES SECONDARY TO PANCREATITIS

P. M. Lynch, A. A. Bailey, E. Y. T. Lee, T. L. C. Lee, S. J. Williams, M. J. Bourke. Endoscopy Unit, Westmead Hospital, Sydney, Australia

Aims: Common bile duct (CBD) strictures occur in 1/3 of patients with chronic pancreatitis. Operative management carries significant morbidity and potential mortality. Single placed CBD stents are associated with early symptomatic stricture recurrence. Our aim was to determine the clinical and biochemical benefit of multiple simultaneous stents for symptomatic distal CBD strictures due to pancreatic fibrosis.

Methods: Patients with symptomatic distal CBD strictures secondary to pancreatitis were managed by a standardised protocol of serial incremental stenting at ERCP; the therapeutic goal being placement of two 10F biliary stents. Three monthly stent exchanges were performed over one year. Stents were then removed and the patients followed with three monthly LFTs. Three 10F stents were placed for refractory strictures.

Results: From July 2000 to May 2005 ten patients with symptomatic CBD stricture related pancreatic fibrosis were included (chronic pancreatitis: n = 8; acute pancreatitis: n = 2). All patients were male (mean age 57 years; range 39–77 years). Clinical features at presentation were indicative of biliary obstruction. Eight patients had two (10F) stents placed simultaneously, while two patients with refractory strictures required three (10F) stents. At mean follow up (15 months; range 2–46) after initial stent placement there was a significant reduction in mean ALP level from 282 to 106 U/l (p = 0.012). Of eight patients presenting with abdominal pain, pain persisted in only one patient post treatment. Mean initial distal CBD stricture diameter was 2.0 mm. In all cases a 15 mm balloon could be drawn through the stricture at stent removal. Six patients have completed the treatment protocol with a mean stent free follow up of 12 months; of which one had recurrent CBD stenting at one year after stent removal, requiring reintervention with triple stenting.

Conclusions: Our results suggest that serial incremental stenting for symptomatic biliary stricture related to pancreatic fibrosis results in symptom resolution, biochemical improvement and radiographic improvement in CBD diameter with minimal complications.

226  ERCP BRUSH CYTOLOGY OR EUS-FNA FOR TISSUE DIAGNOSIS OF OBSTRUCTIVE JAUNDICE SECONDARY TO BILIARY STRICTURES

D. Raine, S. Ramakrishnan, V. Wadehra1, M. Egash1, R. M. Charnley, K. Oppong. HPB Unit Freeman Hospital and 1Department of Cellular Pathology (Cytopathology) Royal Victoria Infirmary Newcastle upon Tyne, UK

Background: ERCP guided biliary brushings (ERCP-BB) has a reported sensitivity for malignancy between 64–96%. However there have been few direct comparisons of the two sampling techniques.

Methods: Retrospective study of patients with obstructive jaundice secondary to a mass or stricture (on CT) who required biliary drainage, EUS staging, and a tissue diagnosis prior to surgery or palliative chemotherapy. 17 consecutive patients (9F, 8M) were identified in whom EUS-FNA and ERCP-BB were performed during the same session (6 patients) or within a few days (11). The results of the first sampling technique were not known at the time of the second procedure. EUS-FNA and biliary brushings were performed using standard techniques. Malignant cytology by either technique, surgical histology, or one year follow up were used to determine final diagnosis.

Results: Fifteen individuals had tissue diagnosis (14 malignant) or follow up (1 benign). Five of these had surgery. 10 of the biliary brushings were indicative of malignancy (5 definite, 5 suggestive). There were four false negatives (atypia) and one benign. Sensitivity 71%, specificity 100%, NPV 20%. For EUS-FNA there were also 10 indicative of malignancy (7 definite, 3 suggestive) There were four false negatives (2 benign, 2 low cellularity/unsatisfactory aspirates) and one benign. Sensitivity 71%, Specificity 100%, NPV 20%. Excluding the unsatisfactory aspirates sensitivity was 83%. Combining the two tests sensitivity 93% specificity 100%, NPV 50%.

Conclusion: In this series the sensitivity of EUS-FNA and ERCP-BB are the same, whilst the combination is associated with an improved sensitivity and NPV. Therefore individuals undergoing ERCP and EUS-FNA either simultaneously or in quick succession should have both BB and FNA performed.

227  ENDOSCOPIC CYSTGASTROSTOMY FOR Pancreatic pseudocysts: AN OUTCOME ASSESSMENT

S. Nair, S. Ramakrishnan, R. M. Charnley, K. Oppong. Hepatobiliary Unit, Freeman Hospital, Newcastle Upon Tyne, UK

Background: Endoscopic cystgastrostomy is increasingly used as therapy for pancreatic pseudocysts (PP). Endoscopic ultrasound (EUS) guidance has been advocated to facilitate the procedure and reduce complications.

Aim: To evaluate the efficacy and safety of Endoscopic drainage of pancreatic pseudocysts and evaluation of EUS use.

Methods: A retrospective study of all patients considered for Endoscopic cystgastrostomy in a 3 year period of pancreaticobiliary referral centre between 1 June 2002 and 30 July 2005.

Results: Thirty two patients underwent an endoscopic procedure with intent to drain a pancreatic pseudocyst during the study period. Data were available for 26 of the 32 patients (15 men, 11 female; median age 54 years). Three patients did not undergo pseudocyst drainage following a EUS examination. These three patients subsequently showed complete resolution on repeat imaging without any further intervention. 23 patients underwent cystgastrostomy; four patients with a duodeno-scope without EUS assessment, seven with a radial EUS assessment using a duodenoscope and 12 with EUS assessment and subsequent drainage using a therapeutic linear echoendoscope. During a median follow up period of 14.5 months, Endoscopic drainage was successful in 20 of the 23 patients (87%). Of these 20 patients, eight had complete resolution after the first procedure (40%) while 12 required multiple Endoscopic procedures (60%). Of the remaining three, one required additional percutaneous radiological pseudocyst drainage and two required surgical cystgastrostomy for complete resolution. The site of drainage was gastric body in 16, antrum in two, cardia in one, and duodenum in one. Following the initial endoscopic procedure complications occurred in seven of these patients (35%) within 30 days. Puncture site bleeding in three (requiring transfusion in two), pancreatitis in one, secondary cyst infection in two, and pneumonia necessitating HDU care in one. All complications were managed conservatively and there were no deaths.

Conclusion: Endoscopic cystogastrostomy is an effective treatment for PP in carefully selected individuals. However this is associated with a 35% complication rate. Prior EUS examination altered management in 11%.

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**ENDOSCOPIC PALLIATION OF CONCOMITANT MALIGNANT BILIARY STRICTURE AND GASTRODUODENAL OUTFLOW OBSTRUCTION**

A. Anderloni, F. Montino, M. Del Piano. Azienda Ospedaliera “Maggiore della Carità”, Novara, Italy.

Background: Malignant biliary stricture (MBS) is a well known condition often complicating duodenal, bilipancreatic or hepatic malignancies. Nowadays endoscopic stenting is the treatment of choice of MBS palliation. More than 15% of the cases are complicated by gastro-duodenal outflow obstruction (GOO). Recently Yim et al., Wang et al., and Del Piano et al. proposed self expanding metallic stents (SEMS) as the best palliation in GOO if compared with surgical treatment. In the majority of the cases MBS precedes GOO but sometimes the two complications occur concomitantly. In such situation a surgical bypass could be a good option but due to the short life expectancy of these patients an endoscopic approach can be proposed.

Aim: To evaluate the efficacy and the feasibility of endoscopic palliation of concomitant MBS and GOO.

Materials and Methods: Between January 1997 and February 2005, 10 consecutive patients (4 male, aged 66–82) presenting concomitant MBS and GOO were enrolled. All these patients underwent CT scan, MRCP, and perendoscopic duodenal and jejunal x ray during stenting procedure. The patients were sedated with diazepam and meperidine. The following two steps procedure was performed: (1) Enteral Wallstent 9 × 2 cm was positionned without dilation; (2) 24 hours later, the enteral stent was fully dilated with a 2 cm diameter balloon. Then, using the balloon lightly deflated as guide, the duodenoscope was introduced and, if feasible, a biliary stent was positioned. The 24 hour waiting time between step 1 and step 2 would be necessary to permit a sufficient stent expansion and anchorage to duodenal wall.

Results: The duodenal stent was successfully positioned in all patients. Three anatomic conformation types were found: (A) biliary outlet proximal to the stricture (1 pt), (B) at the stricture (4 patients), or (C) distal to the stricture (5 patients). Biliary endoscopic stenting was successful in all patients with conformation type A and C and only one out of four patients with conformation type B. The remaining type B patients were managed by PTC. No procedure related mortality or morbidity were observed.

Conclusions: This procedure is a feasible and safe treatment for concomitant MBS and GOO. 70% success rate was achieved and these patients were discharged after 48–72 hours.

**COMPARISON OF DIAGNOSTIC YIELD BETWEEN BILIARY BRUSHINGS AND BILIARY BIOPSY: RESULTS OF A PILOT STUDY**

F. Ali 1, D. Richards 1, G. Anagnostopoulos 2, A. Zaitoun 3, P. Griffiths 1, N. Tolazzi 2, K. Ragunath 2, G. Ashraf 1. Morriston Hospital, Swansea; 2Queen’s Medical Centre, Nottingham, UK

Purpose: To evaluate the diagnostic accuracy of Mighty Bite biliary forcep biopsy compared with biliary brush cytology in the analysis of suspected malignant biliary strictures at ERCP.

Methods: A two centre collaborative prospective study was carried out involving 47 patients (21 male, 28 female; mean age 70 years) undergoing ERCP for suspected malignant strictures. Both forceps biopsies and brush cytology taken in each patient. First tissue sampling technique randomised. Sample size and difficulty with sampling recorded. The histology and cytology samples were analysed separately. The final diagnosis was confirmed at surgery, further pathology, or subsequent clinical course.

Results: Available in 44 cases (23 Swansea, 21 QMC). Five excluded (1 no results, 4 sampling not possible). There were 42 malignant strictures incl. 17 pancreatic and 23 cholangiocarcinomas. Overall sensitivity of Mighty Bite was 44% (57% Swansea, 30% QMC) 95% CI 28 to 66% v 55% (45% Swansea, 65% QMC) 95% CI 39 to 70% for brush cytology. Specificity and positive predictive value was 100% in both groups. Diagnostic accuracy was 46.5% v 56.8%. Overall sensitivity improved to 69% (95% CI 53 to 82%) for combined sampling. Sensitivities were greater for cholangiocarcinoma compared to pancreatic cancer (brushings 61% v 47%, Mighty Bite 44% v 37%). Sensitivity of mighty bite improved from 35% to 53% if Mighty Bite preceded cytology. There were no immediate or late complications in either technique.

Conclusion: Mighty Bite cannot be recommended as a single sampling modality. However, it is generally safe and can improve diagnostic yield if combined with brush cytology in the investigation of suspected malignant biliary strictures.

**LONG TERM OUTCOME OF PATIENTS WITH SPHINCTER OF ODDI DYSFUNCTION AFTER ENDOSCOPIC SPHINCTEROTOMY: A PROSPECTIVE STUDY**

S. P. Pereira 1, A. Gillam 2, N. S. Sgouros 3, G. J. M. Webster 1, A. R. W. Haffield 3. Departments of Gastroenterology and Radiology, University College Hospital, UCL Hospitals NHS Foundation Trust, London, UK.

Background and Aims: Sphincter of Oddi manometry (SOM) is the gold standard for the diagnosis of sphincter of Oddi dysfunction (SOD) and predicts response to sphincterotomy. However, most studies have had relatively short follow up and there are few data from the UK. We aimed to assess the long term outcome of consecutive patients with suspected SOD II (pancreaticobiliary-type pain + duct dilatation or abnormal liver biochemistry/recurrent pancreatitis) or III (pain alone) who were referred for SOM ± sphincterotomy.

Methods: SOM was performed using a standard water perfused manometry catheter, and SOD diagnosed when the mean basal sphincter pressure was >40 mm Hg (sustained for >30 seconds and observed in both leads). Where indicated, an endoscopic sphincterotomy of the affected segment (biliary, pancreatic, or both) was performed. Patients were assessed clinically before SOM and at outpatient review or by telephone after discharge. Patients were asked to rate their symptoms on an 11-point Likert scale (0=no pain at all, 10=worst pain imaginable).

Results: Of 47 patients (M/F 9/38; mean age 46 years, range 27–69 years) referred for SOM, 27 (57%) had manometrically proven SOD: 16 type II and 11 type III. During a mean follow up of 31.6 months (range 17–44 months), patients with SOD type II experienced a significant reduction in symptoms (mean Likert score 9.0 v 1.6, p=0.0002), as did those with normal SOM who did not undergo sphincterotomy (8.0 v 4.0; p=0.03). However, in patients with SOD type III there was no improvement in mean pain scores after sphincterotomy (8.0 v 6.1; p=0.24). Patients with SOD II were more likely to benefit from endotherapy than those with SOD III (p=0.0009).

Conclusions: Patients with manometrically proven SOD type II derive a sustained benefit from endoscopic sphincterotomy of the affected segment, in contrast to those with SOD type III.

Gastroenterological posters

**IMPLEMENTATION OF CONVENTIONAL AND REAL-TIME PCR FOR ROUTINE DIAGNOSIS OF HELICOBACTER PYLORI INFECTION AND ANTIBIOTIC RESISTANCE**

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Background: Culture from gastric biopsy is the standard approach to determine H pylori antibiotic susceptibility. However test sensitivity may be compromised by the fastidiousness of H pylori, by effects of therapy, and by loss of viability and/or overgrowth of contaminating microorganisms. We demonstrated previously the excellent sensitivity and specificity of a multiplex PCR assay when applied to gastric biopsies for detection of H pylori and/or “"H heilmannii”-like organisms (HHLOs), and of two real-time probe hybridisation assays for clarithromycin and tetracycline susceptibility testing.

Methods: To evaluate the implementation of a specialist molecular service for detection and susceptibility testing of helicobacters from gastric biopsies.

Results: From 2003 to date, gastric biopsies from 154 patients, of whom at least 50% were known treatment failures, were tested. None was HHLOs PCR positive. Of the 63 H pylori culture positive biopsies (41%), 62 were PCR positive (98% sensitive). Interestingly for the culture negative biopsies, PCR identified a further 25 H pylori positive patients (16% of all patients). Of these, overgrowth of microbial contamination was recorded for 10 samples, while three samples underwent severe transport delays. In spite of the failure to obtain culture from these 25 samples, susceptibilities to clarithromycin (17 resistant, seven sensitive) and tetracycline (23 sensitive, one resistant) could be determined in 24 biopsies by real-time PCR.

Conclusions: PCR assays are an invaluable adjunct to culture methods for the diagnosis and drug resistance determination of H pylori infection.

Discussion: Routine PCR based testing was particularly useful in instances where the specimen was contaminated or underwent severe transport delays. Of the 88 H pylori positive results, 25 (28%) were
**GASTRIC HISTOLOGY, SEROLOGICAL MARKERS AND AGE AS PREDICTORS OF GASTRIC ACID SECRETION IN H PYLORI INFECTED SUBJECTS**

M. H. Derakhshan, E. El-Omar, K. Oien, D. Gillen, V. Fyfe, J. E. Crabtree, K. E. L. McCall. Department of Medicine and Therapeutics, University of Glasgow, UK

**Background and Aim:** Acid secretion is intimately associated with most upper gastrointestinal diseases. H pylori infection is a major environmental factor modifying acid secretion. We have studied the association between the pattern of H pylori gastritis and gastric secretory function in a large number of subjects without specific upper GI disease.

**Method and Materials:** Maximal acid output was measured in a total of 255 dyspeptic patients with normal endoscopy. Activity and severity of gastritis, atrophy, and H pylori infection were assessed in body and antral biopsies. The correlations of histologic parameters as well as age, gender, height, weight, smoking, serum gastrin, pepsinogen I, II, and their ratio with acid output were determined. We used multiple linear regression to show possible best predictors of acid output.

**Results:** Negative relationships: Body atrophy and body combined (active and chronic) inflammatory scores showed potent inverse correlation with acid output (correlation coefficients (CC): 0.59, p < 0.01 and CC: 0.50, p < 0.01 respectively). Body/antral chronic inflammation ratio and combined inflammatory scores (CC: 0.49, p < 0.01) were also inversely correlated with acid output. Positive relationships: Serum pepsinogen I, body H pylori density/combined inflammatory ratio and pepsinogen I/II ratio with CC: 0.38 (p < 0.01), 0.38 (p < 0.01), and 0.30 (p < 0.01) respectively, correlated with acid output. The H pylori density/combined inflammation of both antrum and body positively correlated with acid output (CC: 0.29 and CC: 0.38 respectively). Male gender and patient height also positively correlated with acid output. Modelling showed that body combined inflammatory score, body atrophy, age, and serum pepsinogen I are independent predictors of acid output (p < 0.02)

**Conclusion:** Combination of body inflammation, body atrophy, age, and serum PGI can be used for prediction of acid secretory state in H pylori infected population.

**GASTRIC EPITHELIAL APOTOPSIS IN VIVO**

M. H. Derakhshan, E. El-Omar, K. Oien, D. Gillen, V. Fyfe, J. E. Crabtree, K. E. L. McCall. Department of Medicine and Therapeutics, University of Glasgow, UK

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**Conclusion:** Combination of body inflammation, body atrophy, age, and serum PGI can be used for prediction of acid secretory state in H pylori infected population.
236 HOW SIGNIFICANT IS A HISTORY OF COFFEE-GROUND VOMITING?
D. Gavin, O. Saraj, D. Ng. General Hospital, St Helier, Jersey, UK

Objectives: Many clinicians believe that a history of vomiting coffee-grounds is a poor predictor for the presence of a significant haemorrhagic lesion in the upper gastrointestinal tract. We aimed to test this hypothesis.

Methods: This was a retrospective study of patients presenting to an island district general hospital with upper gastrointestinal bleeding over a three year period. The case notes for each patient were reviewed and the history of presenting complaint scrutinised for a history of "coffee-ground vomiting", "fresh haematemesis", or "melaena". The endoscopic findings for these patients were then reviewed.

Results: A total of 100 patients were identified. Of these, 33 had a history of "coffee-ground vomiting", 38 "haematemesis", and 29 "melaena".

Conclusion: We can conclude from this series that a history of coffee-ground vomiting alone is a poor predictor for the presence of a significant haemorrhagic lesion at endoscopy. It would be reasonable to manage these patients without inpatient endoscopy. A history of fresh haematemesis and particularly of melaena is a strong predictor and these patients should undergo endoscopy as part of their acute management.

Abstract 236
Endoscopic findings (%)

<table>
<thead>
<tr>
<th>Coffee grounds</th>
<th>Haematemesis</th>
<th>Melaena</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>38</td>
<td>24</td>
</tr>
<tr>
<td>Maller-Weyss</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Oesophagogastric duodenitis</td>
<td>53</td>
<td>33</td>
</tr>
<tr>
<td>Osophagued ulcer</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Varices</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Gastric/duodenal ulcer</td>
<td>0</td>
<td>29</td>
</tr>
</tbody>
</table>

237 GASTROINTESTINAL SYMPTOMS IN PATIENTS UNDERGOING HAEMODIALYSIS TREATMENT

Background: Gastrointestinal (GI) symptoms are said to be common in patients with end-stage renal disease undergoing maintenance haemodialysis treatment (HD), but few data are available.

Aims: To assess the prevalence of GI symptoms in patients with end-stage renal failure undergoing HD, and to compare them to sex and age matched (±10 years) general medical outpatients without renal failure, as well as community subjects.

Methods: Patients and hospital controls completed a locally validated Rome II questionnaire. Community controls received and returned questionnaires by post.

Results: Of 104 patients on HD treatment 100 (96%) completed the study. The prevalence of various gastrointestinal symptoms was compared with that of 100 general medical outpatients and 100 community controls. Some of the comparisons are shown in the table.

Abstract 237

<table>
<thead>
<tr>
<th></th>
<th>HD Outpatients</th>
<th>Community controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>F:M</td>
<td>48:52</td>
<td>48:52</td>
</tr>
<tr>
<td>Heartburn</td>
<td>20 (20%)</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>6 (6%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>IBS</td>
<td>21 (21%)</td>
<td>4 (4%)*</td>
</tr>
<tr>
<td>Constipation</td>
<td>23 (23%)</td>
<td>7 (7%)*</td>
</tr>
<tr>
<td>Laxative use</td>
<td>43 (43%)</td>
<td>8 (8%)*</td>
</tr>
</tbody>
</table>

IBS, irritable bowel syndrome. *p<0.05. **p<0.01. ***p<0.001, CAPP compared with either outpatients or community controls using χ² test

238 COMPARISON OF ZINC VERSUS TWO BISMUTH BASED THERAPIES AFTER FAILURE TO ERADICATE HELICOBACTER PYLORI WITH STANDARD TRIPLE TREATMENT
B. Baburajan, S. Bridge, D. Ling, R. P. H. Thompson. Guy’s and St Thomas’s Hospitals NHS Trust; Worcestershire Acute Hospitals NHS Trust; The Rayne Institute, King’s College, London, UK

Background: Treatment failure of Helicobacter pylori remains a problem. There are limited data on the efficacy of second line regimens. Increasing antibiotic resistance is probably a factor in primary and secondary treatment failure. Metal based approaches may reduce antibiotic resistance and have a synergistic antibiotic effect.

Aim: To compare bismuth and zinc based quadruple regimens in peptic ulcer patients with H pylori refractory to triple treatment.

Methods: Eighty consecutive patients with peptic ulcer disease with positive 13-C urea breath tests at least four weeks after standard triple treatment, received one of three regimes: (1) ranitidine bismuth citrate 400 mg bd (B), omeprazole 200 mg bd (O), amoxicillin 1 g bd (A) and clarithromycin 500 mg bd (C) (BOAC); (2) BOA and metronidazole 400 mg bd (M) (BOAM) or (3) Salazinc 125 mg tds (Z) and OAM (ZOAM). Eradication was defined as a negative breath test at least one month after completing therapy.

Results: Per protocol eradication was achieved in 20/22 (90.9%) with BOAC, 29/34 (85.3%) BOAM, and 10/18 (55.6%) with ZOAM. Intention-to-treat eradication was 20/25 (80%), 29/36 (80.6%), and 10/19 (52.6%), respectively. The bismuth based regimes were both significantly better than the zinc regimen, with a combined odds ratio of 5.5 (95% confidence limits 1.6–19, p=0.0034). Metronidazole was not significantly different from Clarithromycin.

Conclusion: Ranitidine bismuth citrate, omeprazole, amoxicillin, and either clarithromycin or metronidazole is an effective quadruple combination for salvage treatment of H pylori without knowledge of antibiotic resistances. Zinc was not as effective as bismuth.

239 EVALUATION OF THE EFFICACY OF HELICOBACTER PYLORI ERADICATION IN A DISTRICT GENERAL HOSPITAL

Introduction: Helicobacter pylori is a very important pathogenic factor in peptic ulcer disease and its eradication can lead to cure. Thus the National Institute of Health recommended in 1994 giving H pylori eradication treatment to all patients with active peptic ulcer disease or a history of the same and proven infection. Likewise, the European Helicobacter Study Group in 1996 made similar recommendations while adding bleeding peptic ulcers and low grade MALT lymphoma to the list of those requiring eradication therapy. The combination of proton pump inhibitor and two antibiotics (triple therapy) is widely used for eradication but most GI endoscopy units do not routinely check the efficacy of this treatment.

Aim: To evaluate the efficacy of H pylori eradication in a British district general hospital, using the C13-urea breath test (UBT).

Methods: Retrospective analysis was performed of 399 UBT results from patients treated for H pylori infection identified at gastroscopy during the period February 2001 to December 2004 in a district general hospital in provincial UK, serving both rural and urban populations. There were 235 (59%) males and 164 (41%) females with a male:female ratio of 1.4:1. Indications for the diagnostic gastroscopy included dyspepsia 119 patients (29.7%), epigastric pain 41 patients (10.2%), gastro-oesophageal reflux symptoms in 37 patients (9.2%), and nausea 25 patients (6.2%).

Results: 374 (93.7%) of the 399 patients who received eradication therapy were UBT negative 8–12 weeks post treatment. The 25 patients (6.3%) with positive UBT results received a further course of triple therapy and of these 15 patients produced a negative UBT when this was repeated at 12 weeks post treatment. The remaining 10 patients received a further course of eradication and six remained UBT positive. Four of these patients had a third course of treatment, comprising quadruple therapy and of these two patients became breath test negative.
negative. The two patients who remained positive did not attend for further testing.

**Conclusions:** This high eradication rate (93.7%) after one course of triple therapy is reassuring and concurs with published results (BHJ 1998;156:649–54). This was achieved with the combination of Lansoprazole, Amoxycillin, and Clarithromycin, except when sensitivities or adverse drug reactions suggested that alternative agents should be used, usually Metronidazole or Ciprofloxacin. Patients who were HIV positive post eradication (6.3%) were assumed to be either poorly compliant with treatment or their organism was resistant to one or more of the antibiotics.

**Methods:** In this small group of patients H pylori eradication continued to be difficult with >24% remaining positive after a second course of eradication treatment and 50% after a third. This raises two questions: (1) are those patients with persistent H pylori infection more liable to complication and (2) should they be the subject of further testing to determine whether their particular organism is either cagA or cagB positive—analysis that might help to decide whether successful eradication must continue to be pursued?

**240 PREVALENCE OF DYSPEPSIA SYMPTOMS IN THE ELDERLY: HOW THEY VARY WITH SEX AND INCREASING AGE, AND THE EFFECT ON RESOURCE USE**

S. J. Philpott1, K. Sundaram3, M. Mendall1. 1Mayday Hospital, Croydon, CR7 7YE; 2St Georges Hospital, London SW17 1UK

**Background:** The burden of dyspepsia and reflux disease has not been studied in extreme old age in a community sample. It is likely that at extreme old age, with autonomic failure, symptoms may become less severe due to the fact that pathology is likely to become more severe. We therefore aimed to determine the prevalence of reflux and dyspepsia symptoms in an elderly community sample and sought to determine whether symptoms do indeed become less prevalent as age progresses or whether they differ for men and women. We also examined dyspepsia-related resource use and how it varied with extreme age.

**Method:** Cross-sectional, retrospective study. Patients aged 60+ were randomly selected from local GP lists in Croydon and sent a questionnaire containing Leeds Dyspepsia questions. GP list were scrutinised for baseline demographic information on both total number of siblings, and their order of birth. Data concerning other social conditions in childhood were stored on file from the original study.

**Results:** 3928 (47%) of the 8407 original participants provided data. Prevalence of H pylori infection increased steadily according to total number of siblings, from 20% in those with no siblings, to 63% with eight or more. Odds of infection were significantly increased with three or more siblings (OR = 1.59; 95% CI 1.34 to 1.89), and a clear gradient of effect continued up to eight or more siblings (OR = 6.66; 95% CI 3.94 to 11.44). Odds of infection became significantly higher with two older siblings (OR = 1.32; 95% CI 1.04 to 1.68), and again increased steadily up to six (OR = 3.78; 95% CI 1.51 to 9.74). Even among firstborn individuals, prevalence of infection significantly increased with three or more siblings (OR = 1.59; 95% CI 1.02 to 2.44). When number of siblings, and other social conditions in childhood were controlled for in a logistic regression model, the association between birth order and odds of H pylori infection was no longer statistically significant.

**Conclusions:** Number of siblings and birth order appear to influence prevalence of H pylori infection, though the observed effect of birth order may be due to confounding by other factors in childhood.

**241 H PYLORI, SEX, AND THE RELATION OF EXTREME OLD AGE TO DYSPEPSIA**

S. J. Philpott1, K. Sundaram2, M. Mendall1. 1Mayday Hospital, Croydon, CR7 7YE; 2St Georges Hospital, London SW17 1RE, UK

**Background:** H pylori (HP) is a risk factor for dyspepsia (non-ulcer and ulcer associated). However this association has only been studied in extreme old age in a community sample. There is also controversy as to whether HP through destroying the acid making capability of the stomach may actually protect against reflux disease. The best population to observe this effect on would be the elderly in whom HP infection would have run the longest course. We aimed to investigate the association of HP with reflux and dyspeptic symptoms in an elderly population.

**Methods:** Cross-sectional, retrospective study. Patients aged 60+ were randomly selected from local GP lists in Croydon and sent a questionnaire containing the Leeds Dyspepsia questionnaire, and a kit for saliva collection to determine HP status. Medical records were examined for all events over a five year period. HP status was determined using ELISA and Western blotting methods as previously described. Participants: 2100 patients were randomly selected from 28 GP lists, of which 1116 patients responded (60%). Patients were divided into three age groups: (1) 60–69 years (n = 564), (2) 70–79 years (n = 390), and (3) 80+ years (n = 162).

**Results:** 137/499 men and 167/617 women were HP positive. Dyspepsia was prevalent in 23% men and 35% women and did not change with age, and reflux in 31% men and 34% women. Reflux symptoms decreased with age for men only. HP infection increased with age for men (21% in group 1 v 34% in groups 2 & 3) but not for women (27%, 28%, and 25%). In men, 31% with HP had dyspepsia v 20% without (p = 0.01). This risk was not seen in the 80+ group (21% with HP v 17% without). There was no association with reflux. In women those with HP were less likely to have any reflux symptoms than those without (29% v 37%), although this was not significant (p = 0.06), and did not differ by age group.

**Conclusion:** In men, HP was associated with having dyspepsia, but this effect was not seen in extreme old age suggesting the effect of HP reduces with age. We found that HP may be protective against reflux but this was more marked in women.

**242 EFFECT OF SIBLING NUMBER AND BIRTH ORDER ON HELICOBACTER PYLORI PREVALENCE: A CROSS SECTIONAL SURVEY**

A. C. Ford1, A. G. Bailey1, D. Forman2, A. T. R. Axon1, P. Moayyedi3,1Centre for Digestive Diseases, Leeds General Infirmary, Leeds; 2Centre for Epidemiology and Biostatistics, Leeds University Medical School; 3Gastroenterology Division, Health Sciences Centre, Hamilton, Canada

**Introduction:** Social conditions influencing the acquisition of Helicobacter pylori in childhood are well recognised, but the effect of number of siblings, and birth order on prevalence of H pylori has not been extensively reported.

**Methods:** The authors performed a 10 year follow up cross sectional survey of individuals previously enrolled in a community screening and treatment programme for H pylori. Prevalence of H pylori was assessed with 13C urea breath testing. All individuals who were alive, and could be traced were contacted by postal questionnaire, to obtain information on both total number of siblings, and their order of birth.

**Results:** 3928 (47%) of the 8407 original participants provided data. Prevalence of H pylori infection increased steadily according to total number of siblings, from 20% in those with no siblings, to 63% with eight or more. Odds of infection were significantly increased with three or more siblings (OR = 1.59; 95% CI 1.34 to 2.38), and a clear gradient of effect continued up to eight or more siblings (OR = 6.66; 95% CI 3.94 to 11.44). Odds of infection became significantly higher with two older siblings (OR = 1.32; 95% CI 1.04 to 1.68), and again increased steadily up to six (OR = 3.78; 95% CI 1.51 to 9.74). Even among firstborn individuals, prevalence of infection significantly increased with three or more siblings (OR = 1.59; 95% CI 1.02 to 2.44). When number of siblings, and other social conditions in childhood were controlled for in a logistic regression model, the association between birth order and odds of H pylori infection was no longer statistically significant.

**Conclusions:** Number of siblings and birth order appear to influence prevalence of H pylori infection, though the observed effect of birth order may be due to confounding by other factors in childhood.

**243 A 10 YEAR NATURAL HISTORY OF GASTROESOPHAGEAL REFLUX DISEASE**

A. C. Ford1, A. G. Bailey1, D. Forman2, A. T. R. Axon1, P. Moayyedi3,1Centre for Digestive Diseases, Leeds General Infirmary, Leeds; 2Centre for Epidemiology and Biostatistics, Leeds University Medical School; 3Gastroenterology Division, Health Sciences Centre, Hamilton, Canada

**Introduction:** Gastroesophageal reflux disease (GORD) is common in the general population, with a reported incidence as high as 20%. However, there is little information regarding the long term natural history of the disorder.

**Methods:** The authors performed a 10 year follow up cross sectional survey of individuals recruited into a community screening and treatment programme for Helicobacter pylori. All surviving, traceable participants were contacted, by validated postal dyspepsia questionnaire, which contained items relating to GORD symptoms. Baseline demographic data and GORD symptom data were stored on file from the original study.

**Results:** Of 8407 individuals, 4003 (48%) responded to the questionnaire. The mean age of responders was 55 years, and 2247 (56%) were female. Males, those with dyspepsia at baseline, smokers, and

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individuals with GORD remained symptomatic, while in those without symptoms at baseline over five percent had developed new onset GORD symptoms at a frequency of once a week or more.

Conclusions: During 10 years of follow up approximately a third of individuals with GORD remained symptomatic, while in those without symptoms at baseline over five percent had developed new onset symptoms.

**Endoscopy posters**

### 244 A CROSS SECTIONAL SURVEY OF THE RELATIONSHIP BETWEEN GASTROESOPHAGEAL REFUX DISEASE AND CHRONIC COUGH

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**Introduction:** Gastroesophageal reflux disease (GORD) has been recognised as an important cause of chronic cough, but the frequency with which this is reported to be related varies widely.

**Methods:** The authors performed a cross sectional survey to establish prevalence of self-reported chronic cough and its relationship to GORD. The study was performed as part of a 10-year follow up of individuals recruited into a population Helicobacter pylori screening programme. All surviving, traceable participants were contacted, by validated postal dyspepsia questionnaire, and were also asked how often in the last two months they had experienced bouts of coughing, rated on a five-point Likert scale. Baseline demographic data were already on file.

**Results:** Of 8407 individuals originally involved, 3880 (46%) responded. 425 (11%) of whom had GORD at 10 years. The odds ratio (OR) for GORD increased with frequency of cough (cough less than once a month OR 1.79; 95% CI 1.66 to 3.30, once a week OR 2.35; 95% CI 1.66 to 3.30, once a week or more, and heartburn remained the predominant symptom in 167 (30%) of these, while 301 (55%) had symptoms less than once a week or were entirely asymptomatic. Of the 3421 individuals who were asymptomatic at baseline, 629 (18%) had heartburn at a frequency of once a month or more, 196 (5.7%) once a week or more, and 29 (1.1%) once a day or more. Heartburn was the predominant dyspeptic symptom in 540 (16%) of these individuals at 10 years.

**Conclusions:** During 10 years of follow up approximately a third of individuals with GORD remained symptomatic, while in those without symptoms at baseline over five percent had developed new onset GORD symptoms at a frequency of once a week or more.

### 245 PROSPECTIVE 19 MONTH AUDIT OF THE CLINICAL USE OF CAPSULE ENDOSCOPY: THE ROYAL LONDON HOSPITAL EXPERIENCE

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**Background:** Capsule Endoscopy (CE) was co-developed by Professor Paul Swain at Royal London Hospital in 2001. Despite widespread use in N America and Europe, CE uptake and service provision has been slower in the UK.

**Methods:** Prospective data on demographics, indications, findings, and complications were collected in a database since February 2004. The database was examined from February 2004 until September 2005. Summary statistics were calculated.

**Results:** 101 patients (49M), mean age was 49 (range 13–86). Indications included suspected Crohn’s disease (CD) (30/101), iron deficiency anaemia (IDA) (28/101), overt GI bleed (21/101), obscure GI bleed (4/101), anaemia of unknown aetiology (10/101), suspected Peutz Jeghers (PJ) (2/101), chronic abdominal pain (3/101), and 1/101 each of refractory coeliac disease, suspected small intestinal lymphoma, and suspected Behcets disease. Mean gastric and small bowel emptying time were 36.4 and 240 minutes respectively. CE explained the cause of IDA in 14/28 patients, the cause of suspected CD in 11/30, the cause of GI bleed in 15/21 (all 15 angiodysplasias). Each of 4/101 with obscure GI bleed had findings to explain their symptoms. One of the 2/101 with suspected PJ syndrome had a positive result. A single complication of capsule retention occurred in a single patient but resolved with conservative management. Image quality was good in 93/101 cases performed.

**Conclusion:** CE was diagnostic in 45% of patients, having a higher yield in patients with overt/obscure GI bleed than in suspected CD and IDA. CE is an extremely valuable tool for further evaluation of a difficult diagnostic group of patients.

### 246 CLINICAL IMPACT OF NORMAL AND ABNORMAL CAPSULE ENDOSCOPY FINDINGS IN 150 CONSECUTIVE PATIENTS

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**Background:** Capsule endoscopy (CE) is useful for investigating small bowel disease. Its value in altering the clinical management of patients with a normal result has not been studied.

**Methods:** We conducted a prospective analysis of all the cases of CE undertaken in St Mark’s Hospital over 20 months. Diagnostic yield and the impact of the findings on further clinical management were determined from the CE database and patient interviews.

**Results:** During the period under study 150 consecutive cases were performed. The indications were obscure gastrointestinal bleed (OIB) (100), Peutz-Jeghers Polyposis (PJ) (30), abdominal pain (10), Crohn’s disease (CD) (6), and others (4). CE was reported as normal in 52 (35%), abnormal in 73 (49%), equivocal in 16 (10%), and incomplete in nine (6%) cases. The overall diagnostic yield was 48.7%. The yield according to the indication was 39% for overt OIB, 46% for occult OIB, 83% for PJ, 11% for pain, 50% for CD, 25% for suspected CD, and 50% for other indications. In group with normal results 31/52 cases were contacted; 5/31 (16%) had a cause for symptoms identified while 26/31 (84%) had no cause identified by further investigations. A normal result changed clinical management in 15 of these 26 patients (58%). From the abnormal group 47/73 cases were contacted: 25 had PJ and 22 had other abnormalities. In the PJ group, the CE result led to a change in management in seven patients (28%) but had no influence on clinical management in 18 (72%). In the non-polyp group, the abnormality was treated with symptom resolution in 19 patients (86%) but had no effect on outcome in three (14%) cases where further intervention did not detect the lesion noted on CE. Although PJ had the highest diagnostic yield, it had the lowest impact on clinical management.

**Conclusion:** This study suggests that the value of CE should be assessed by the clinical outcome of patients with both normal and abnormal results in addition to the diagnostic yield. Future studies on the benefit of CE in clinical management should include the impact of a normal result on future management decisions.

### 247 THE ROLE OF CAPSULE ENDOSCOPY IN SMALL BOWEL SURVEILLANCE OF ADULTS WITH PEUTZ-JEGHERS SYNDROME

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**Introduction:** Capsule Endoscopy (CE) is a novel radiation-free tool for imaging the entire small bowel (SB), and has enormous potential in Peutz-Jeghers syndrome (PJS). We compared the performance of CE with barium follow through (BFT), the current standard, for the detection of significant SB polyps (SSBPs) in PJS patients.

**Methods:** Adults with PJS undergoing routine surveillance underwent both CE and BFT, which were reported blindly. SB polyps 1 cm or more were considered significant. The total number of SSBPs detected by each test was compared. Participants stated their preference for future surveillance.

**Results:** There were 19 participants (10 women; mean age 37); 10 had the BFT first. All capsules were excreted naturally. The caecum was visualised in 12 patients and the ileocaecal valve in a further two. The median total number of SSBPs detected in each participant by CE was four (range 0–18) and by BFT was one (range 0–5; p = 0.008). 12 participants had SSBPs by both CE and BFT; a further five had SSBPs by
Wireless oesophageal video capsule endoscopy (WOVCE) is a non-invasive, disposable imaging methodology for visualisation of the upper GI tract. These attributes make WOVCE a desirable investigative tool in select patients, notably those who may constitute a public health risk through transmissible infections and those who cannot tolerate conventional endoscopy.

Methods: In Edinburgh we have investigated an initial seven patients who fall into these categories. WOVCE was performed after a standard six hour fast, correct placement of the recording electrodes, electrolyte replacement, and administration of metoclopramide (5 mg) 20 minutes prior to capsule ingestion. These protocol modifications resulted in improved gastric images showing no significant pathology and visualisation of a normal proximal duodenum.

Results: From this early experience we consider that WOVCE is a valuable oesophageal imaging modality, for use in those patients where conventional endoscopic techniques are not possible, or as a non-invasive screening method. Modifications to protocols can enhance images recorded and result in a more detailed investigation of the upper GI tract, particularly the duodenum.

DOUBLE BALLOON ENTEROSCOPY UNDER CONSCIOUS SEDATION: PATIENT SAFETY, COMFORT, AND TOLERABILITY COMPARED TO OTHER ENDOSCOPIC PROCEDURES


Introduction: Double balloon enteroscopy (DBE) allows examination of the whole small bowel with therapeutic capability. It may be prolonged procedure associated with discomfort, raising the question as to whether it should be performed under conscious sedation or general anaesthetic.

Aim: To assess patient safety, comfort and tolerability of DBE under conscious sedation and compare it to other endoscopic tests.

Method: Nineteen patients with suspected small bowel disease were examined (17 oral and two anal). Data were recorded on sedation and reversal agents used and conscious level during procedure, depth of insertion and intubation distance of 118 cm. The mean duration of DBE was 248 minutes. Indications included: 6/19 recurrent anaemia/obscure GI bleeding (32%), 9/19 overt GI bleeding (47%), 3/19 diagnosis of inflammatory bowel disease (16%), and 1/19 "other"). Of those 15 patients who previously had capsule endoscopy (CE) performed, DBE confirmed CE findings in 8/15 (53%), while in 6/15 (40%) patients, DBE was normal where CE had suggested pathology, and in one a small bowel neoplasm was misdiagnosed as a Dieulafoy lesion on CE. Directed biopsies were performed in 6/19 (32%) and therapy in 8/19 (42%), 7 APC, 1 ileal stricture dilatation. Of the seven patients who underwent APC, 3/7 (43%) had had ongoing bleeding. In 4/7 (57%) they had had either no or reduced blood transfusion requirements. No complications were observed either during or in the short term post-procedure period.

Conclusion: DBE is an exciting advance within GI endoscopy. It appears to be well tolerated and safe. For the first time, it provides the means to endoscopically investigate and treat disorders of the SI that have previously been inaccessible to conventional endoscopy. It has demonstrable attributes to CE. Indications for its use continue to be defined.

CHROMOENDOSCOPY IN THE DIAGNOSIS OF EARLY OESOPHAEGAL NEOPLASIA


Introduction: Chromoendoscopy has shown great potential in diagnosis of early cancers. The procedure is more time consuming compared to conventional endoscopy reducing the number of endoscopies per session with obvious cost implications. This study aims to clarify the role of chromoendoscopy in improving the diagnosis and management of early oesophageal neoplasia.

Methods: A mixture of N-acetyl cystine and simethicone was administered per os prior to the endoscopy. Indigo carmine (0.4%) dye spray was used to detect subtle mucosal abnormalities. Acetic acid (3%) and Lugol's Iodine (2.0%) and/or methylene blue (0.5%) was used to characterise lesions in suspected Barrett's oesophagus and Lugol's iodine (2.0%) in suspected squamous dysplasia. Pre- and post-chromoendoscopy histology data was collected and its influence on clinical management decisions noted.

McNemar's test was applied (SPSS) to the paired categorical data with respect to the change in histological staging.

Results: Seventy three consecutive patients undergoing oesophageal chromoendoscopy were analysed and divided into two groups. Group A consisted of 47 patients undergoing routine Barrett's surveillance and group B of 26 patients who presented as a diagnostic challenge based on previous endoscopy and histology. Thirty two of the 47 patients in group A were found to have indeterminate dysplasia. In group B, chromoendoscopy led to an alteration in histological grading in 14 of 26 patients,
resulting in a p value of <0.001. Of the 16 patients with either high grade dysplasia or cancer, chromoendoscopy delineated focal lesions in seven patients so well that potentially curative endoscopic mucosal resection (EMR) could be performed. In the nine remaining patients the lesion was either multifocal or not well delineated so either PDT or surgery was required. Chromoendoscopy assisted in rationalising future surveillance intervals in the 10 patients with lower grades of dysplasia.

Conclusion: This series shows the potential of chromoendoscopy as a staging tool in the management of patients with suspected oesophageal dysplasia or early cancer. Its role in routine Barrett’s surveillance remains uncertain and calls for larger studies.

252 OPTICAL MICROANGIOGRAPHY: HIGH DEFINITION ZOOM COLONOSCOPY WITH NARROW BAND IMAGING TECHNIQUE FOR VISUALISING MUCOSAL CAPILLARIES AND RED BLOOD CELLS IN THE LARGE INTESTINE

K. Yao1, G. K. Anagnostopoulos1, A. U. Jawhari1, P. Kaye2, C. J. Hawkey1, K. Ragunath1. Wolfson Digestive Disease Centre and 1Department of Pathology, University Hospital Nottingham, UK

Introduction: The recent advances in zoom endoscopy techniques had enabled endoscopists to observe the organ specific subepithelial capillary network (SECN) pattern in gastrointestinal mucosa. However, we had not been able to visualise a honeycomb-like SECN pattern which has been proved to be the normal microvasculature in the large intestine by anatomical study. Recently, a new optical method called NBI technique, designed to help specifically the visualisation of superficial microvasculature, has been developed. The aim of this study was to investigate whether High definition zoom colonoscopy with NBI is useful for visualising capillaries and RBC in the large intestine.

Methods: Total colonoscopies were performed in six patients with abdominal symptoms using a high definition zoom colonoscope (CF-H260Z, Olympus) and a prototype high definition electronic endoscopy system that incorporates NBI function (Hyperpro, Olympus). Each part of the large intestine (caecum, ascending, transverse, descending, sigmoid colon and rectum) was observed at maximal magnification (X150), with NBI and without NBI, alternatively. The SECN pattern and RBC movement in the capillaries were recorded for each part of the large intestine. The colonoscopies and biopsies were normal.

Results: In all patients, high definition zoom colonoscopy with NBI could constantly visualise a honeycomb-like SECN pattern together with RBC movement in each part of the large intestine except for the rectum. In contrast, without NBI, neither such SECN pattern nor RBC movement could be detected.

Conclusion: This method could be a new optical method that facilitates non-invasive investigation for both microvascular architecture and microcirculation without any contrast materials.

253 OLYMPUS LUCERA HIB VASCULAR ECTASIA MAPPING IN COMBINATION WITH THE NAGATA TYPE V(C) CRYPT PATTERN FOR INVASIVE DEPTH ESTIMATION IN PARIS TYPE II COLORECTAL CANCERS: A COMPARATIVE PROSPECTIVE ANALYSIS TO 20 MHZ MINI PROBE ULTRASOUND

D. P. Hurlstone1, D. S. Sanders1, S. Brown1, M. Thomson1, S. S. Cross2. 1Gastroenterology, Royal Hallamshire Hospital, Sheffield; 2Academic Department of Pathology, Royal Hallamshire Hospital, Sheffield, UK

Introduction: We have previously shown that 20 MHz high frequency EUS is superior to the modified type V Nagata crypt criteria when differentiating T1/2 disease in Paris type II neoplastic lesions. 20 MHz EUS has a high PPV for sm3 differentiation. Hib differential vascular mapping permits visualisation of superficial neoplastic vascular structure in combination with magnification endoscopy where neoplastic superficial “vascular ectasia” (VE) may be an additional marker for sm3 disease.

Aims: To assess the efficacy of the Nagata type (c) crypt pattern in combination with Hib vascular mapping for the invasive depth of Paris type II neoplasia as compared to 20 MHz EUS.

Methods: Paris type II neoplastic lesions were imaged using HMCC followed by 20/12.5 MHz EUS. Crystal violet staining permitted Nagata crypt criteria to be defined. Sm3+ invasion was defined at ultrasound by the presence or absence of a disrupted third sonographic layer. Neoplastic superficial VE using Hib was defined as vascular disruption/tortuosity. Predicted T0/1/NO lesions were resected using EMR with the remaining referred for surgery. The EUS and HMCC staging was then compared to the resected histopathological specimens.

Results: n=68 (12 sm1/13 sm2/27 sm3+). EUS was significantly more accurate for invasive depth staging as compared to Nagata stage alone (p<0.0001). Combining Nagata (c) with VE positive criteria although not superior to EUS (p=0.05) significantly improved T2 staging accuracy (p=0.02). The sensitivity for lymph node metastasis detection using ultrasound and combined VE/Nagata (c) was 80% and 68% respectively (p<0.001).

Conclusions: Combination Nagata (c) and + VE criteria permit an acceptable in vivo staging modality without the requirement for repeat 20 MHz imaging. Sm3+ invasion was associated with nodal metastasis.

254 DETECTION OF HELICOBACTER PYLORI GASTRITIS AND GASTRIC ATROPHY BY REAL TIME HIGH RESOLUTION MAGNIFICATION ENDOSCOPY

G. K. Anagnostopoulos, K. Yao, C. J. Hawkey, K. Ragunath. Wolfson Digestive Diseases Centre, University Hospital, Nottingham, UK

Background: High resolution magnification endoscopy (HRME) offers the ability to examine the gastric mucosa in detail that is not visible by conventional endoscopy. The aim of our study was to correlate the magnified endoscopy findings with histopathology of normal stomach, Helicobacter pylori (HP) associated gastritis, and gastric atrophy.

Methods: One hundred consecutive patients (57 male, mean age 59 years) scheduled to undergo gastrointestinal endoscopy were enrolled. Conventional and magnifying endoscopies were performed with the Olympus GIF Q240Z endoscope (x115). Biopsies were taken from the sites observed, and according to Sydney protocol.

Results: The magnified findings in gastric body were classified into five types: (A) honeycomb-type subepithelial capillary network (SECN)/normal collecting venules (CVs), (B) loss of normal SECN/irregular CVs, (C) normal SECN/loss of CVs, (D) loss of normal SECN-CVs/enlarged white pits/erythema, and (E) atypical type SECN in gastric body. Normal mucosa corresponded to type A, gastric atrophy to type B, and HP gastritis to types C–E. 33 patients had magnified endoscopic evidence of HP infection (18C, 11D, 4E) and 22 had histology positive for HP. 23 patients had findings suggestive of gastric atrophy and 22 had histologically proven gastric atrophy. The sensitivity/specificity/predictive values of: type A for the prediction of normal gastric mucosa, type B for the prediction of gastric atrophy, and types C, D for the prediction of HP gastritis are shown in the table. All four cases with type E mucosa corresponded to HP gastritis.

Conclusion: HRME has the potential for real time diagnosis of H pylori associated gastritis and gastric atrophy during endoscopy.

255 NOVEL ZOOM ENDOSCOPY TECHNIQUE BASED ON GASTRIC MICROVASCULAR ARCHITECTURE IS USEFUL TO DIFFERENTIATE BETWEEN FLAT EARLY GASTRIC CANCERS AND GASTRITIS

K. Yao1, A. Ivashita2, S. Sou1, T. Nagahama1, H. Tanabe1, T. Yao1, T. Matsui1 (introduced by K Ragunath)1. 1Department of Gastroenterology and 2Pathology, Fukuoka University Chikushi Hospital, Fukuoka, Japan

Introduction: During gastroscopy we frequently encounter flat reddened lesions in the stomach. In order to diagnose a flat, small, early gastric cancer, it is common practice to obtain multiple biopsies from such...
lesions. We investigated the diagnostic accuracy of magnified endoscopic findings for differentiating between redened mucosa due to gastritis and flat redened gastric cancer, prospectively and blindly. Methods: Six hundred and three consecutive patients were examined by zoom endoscopy (GIF-Q240Z, Olympus, ∓80) and the prevalence of each of the following magnified endoscopic findings, which had been already reported as characteristic for differentiated carcinoma, was recorded. (1) Presence of a demarcation line between the redened lesion and the surrounding mucosa, (2) disappearance of the regular subepithelial capillary network (SECN) pattern, and (3) presence of an irregular microvascular pattern (IMVP) within the flat redened lesion. Results: One hundred and fifty seven flat redened lesions from 157 patients were detected. Pathologically, 144 flat redened lesions showed only gastritis, while 13 lesions were newly diagnosed as differentiated carcinoma. The prevalence of the findings is shown in table. Conclusion: The novel zoom endoscopic findings based on microvascular architecture are useful for making a differential diagnosis between flat early gastric carcinoma and gastritis.

**Table 1**

<table>
<thead>
<tr>
<th>Incident types</th>
<th>Gastritis (95% CI)</th>
<th>Gastric cancer (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demarcation line</td>
<td>25.3% (18.6–32.8%)</td>
<td>100%</td>
</tr>
<tr>
<td>Disappearance of SECN</td>
<td>22.9% (16.2–29.8%)</td>
<td>100%</td>
</tr>
<tr>
<td>IMVP</td>
<td>7% (0–2.1%)</td>
<td>92.3% (77.8–100%)</td>
</tr>
</tbody>
</table>

The diagnostic accuracy of IMVP was 98.7%.

**Abstract 256**

**Kudo classification**

<table>
<thead>
<tr>
<th>Polype type</th>
<th>I</th>
<th>II</th>
<th>III/IV</th>
<th>Neoplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ad (n = 13)</td>
<td>0/2</td>
<td>4/4</td>
<td>8/5</td>
<td>0/2</td>
</tr>
<tr>
<td>Hp (n = 4)</td>
<td>0/1</td>
<td>2/3</td>
<td>1/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Inf (n = 4)</td>
<td>0/0</td>
<td>0/0</td>
<td>3/2</td>
<td>0/0</td>
</tr>
</tbody>
</table>

**Ad, adenomatous; Hp, hyperplastic; Inf, inflammatory.**

**Abstract 255**

**Demarcation line**

<table>
<thead>
<tr>
<th>Presence of SECN</th>
<th>IMVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence</td>
<td>25.3% (18.6–32.8%)</td>
</tr>
<tr>
<td>Absence</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Abstract 257**

**IMMEDIATE COLONOSCOPY COMPLICATIONS 1992–2004: AN AUDIT OF 14 521 CASES**

T. Sivayakan, R. Leicester, A. Poullis. St George’s Hospital, London, UK

**Background:** A national audit into colonoscopy complications revealed a perforation rate of one in 769, a post procedure minor bleed rate of one in 263, and major haemorrhage rate of one in 1537 (Bowles, Leicester, et al. Gut 2004). We audited our units results to compare them to the national results.

**Method:** We analysed 14 521 colonoscopies in our department from 1992 and 2004 to determine immediate colonoscopy complication rates. Hospital records were reviewed to obtain more details of the complications and determine their severity.

**Results:** There were five perforations (one in 2904); two cases occurred post polypectomy, two cases occurred in patients with diverticular disease, and one occurred in a patient with radiation colitis. All five required surgery. 26 cases of post procedural bleeding occurred. 14 were immediately controlled without the need for hospital admission. In 12 cases bleeding was immediately controlled but the patient was admitted for observation. One patient required a blood transfusion but contraindicated for neoplastic or non-neoplastic. Pattern intensity alone gives a sensitivity of 77% and specificity 75%, PPV 83%, NPV 75%. Pattern intensity alone gives a sensitivity of 77% and specificity 75%, PPV 83%, NPV 75%. Pattern intensity alone gives a sensitivity of 77% and specificity 75%, PPV 83%, NPV 75%.

**Conclusion:** The perforation rate in this series is one in 2904. The risk of a moderate post polypectomy bleed is one in 1210, that of a significant haemorrhage is one in 14,521. The risk of a complication is increased for therapeutic procedures and in those with an underlying abnormality. Regular reviews of complication rates after endoscopy are an important part of clinical governance.

**Flexigastroscopy: is time running out?**

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**Introduction:** Population based screening for colorectal cancer, validation of colonoscopists and virtual colonoscopy are all going to impact on UK endoscopy services. Flexible sigmoidoscopy (flexisig) is seen as a valid investigation for cancer screening and is stated to take one unit of endoscopy time. Full colonoscopy is allocated two units of endoscopy time. A full list should comprise five or six colonoscopies or 10 flexisigs.

**Aims:** To see if the units of endoscopy time allocated to the two procedures reflect time actually taken.

**Methods:** Six colonoscopists in our unit were timed during colonoscopy by endoscopy nurses. Three time-points were recorded: (1) time to the point the endoscopist felt he would have achieved satisfactory flexisig, (2) time to caecal/terminal ileal intubation, and (3) time to exuation. Times for procedures where the caecum was not reached were discarded. Data for 121 completed colonoscopies over a two month period were obtained.

**Results:** The overall mean colonoscopy time was 17.7 minutes. Flexisig was achieved a mean of 6.0 minutes after intubation and the caecum reached after a mean of 13.5 minutes. The terminal ileum was accessed in 22 cases. The fastest colonoscopist averaged 12 minutes for total colonoscopy. 17 of the 22 terminal ileal intubations were achieved by the two fastest colonoscopists (out of 48 colonoscopies).

**Discussion:** Allocating two units of endoscopy time to colonoscopy and one unit to flexible sigmoidoscopy appears justified in terms of the relative times taken. One unit of endoscopy time does not equate to 20 minutes. A list of six colonoscopies would take 1 hour 46.2 minutes of endoscopy time. The extra time needed to convert a flexible sigmoidoscopy to a full colonoscopy is only 7.5 minutes and this small difference does not support intentionally limiting the scope of a large bowel investigation to trade-off for increased patient throughput.
TERMINAL ILEAL BIOPSY IS UNNECESSARY TO CONFIRM COMPLETE COLONOSCOPY

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Background: Objective proof of completion at colonoscopy is best obtained by terminal ileal (TI) intubation and biopsy. However, with increasing demands on histopathologists and the predicted increase in the number of colonoscopies in 2007 as a result of a national bowel cancer screening programme in Scotland, we wished to assess whether this manoeuvre was of value in confirming completion when performed by an experienced colonoscopist.

Methods: TI biopsies collected prospectively to confirm completion at colonoscopy in patients with intact colons were audited. All colonoscopies were performed either by or under the direct supervision of one colonoscopist. Cases referred for TI intubation in light of imaging studies suggesting ileal pathology were excluded. Data were retrieved to establish if TI biopsy correlated with histology and to assess the incidence of histologically confirmed ileal pathology.

Results: 642 TI biopsies were audited. In two cases submitted specimens were too small for processing. Three cases were reported as biopsies of colonic mucosa with no evidence of ileal tissue. Four patients had coincidental abnormal histology (0.06%), comprising one carcinoid tumour, one adenocarcinoma, and two Crohn’s disease. Three of these four cases were clinically diagnosed at the time of ileal intubation. Normal terminal ileal mucosa was confirmed in 633 cases (98.6%).

Conclusion: TI biopsy is unnecessary for colonoscopists who can regularly intubate the ileocaecal valve and should therefore be reserved for those cases where ileal pathology is encountered or clinically suspected, avoiding both considerable expense (£245 per biopsy) and histopathology time. Simple alternatives such as photography after dye spraying should be used to record ileal intubation.

ARE PARIS TYPE I AND II HYPERPLASTIC POLYPS ASSOCIATED WITH SYNCHRONOUS COLORECTAL CARCINOMA? A PROSPECTIVE 1000 PATIENT CHARACTERISATION USING HIGH MAGNIFICATION CHROMOSCOPIC COLONOSCOPY

D. P. Hurlstone1, D. S. Sanders1, S. Brown1, M. Thomson1, S. S. Cross2. 1Gastroenterology, Royal Hallamshire Hospital, Sheffield, 2Academic department of Pathology, Royal Hallamshire Hospital, Sheffield, UK

Background: We have previously reported an increased prevalence of right hemicolonic Paris type II hyperplastic (HP) polyps in HNPCC using high magnification chromoscopy (HMCC). Recent data now suggest that patients with right hemicolonic Paris type II lesions in addition to high density diminutive left hemicolonic lesions may be at increased risk of colorectal neoplasia.

Aims: To establish the prevalence, morphology, anatomical location, and relationship of HP to synchronous colorectal cancer.

Methods: 1000 patients underwent HMCC using the Olympus CF240Z and 0.5% indigo carmine pan-chromoscopy. Lesion morphology was classified according to Paris guidelines and crypt analysis as per modified Kudo criteria. Biopsy and resection practice was performed as per recommended practice (Hurlstone DP et al. Gut 2004;53:284–90).

Results: n=1000; median age 66 (range 24–92 years).

Conclusions: Intermediate/large Paris type II HPs cluster within the right hemicolon and represent valid biomarkers of synchronous neoplasia. HMCC screening colonoscopy protocols may require revision.

FACTORS PREDICTING A SUCCESSFUL COLONOSCOPY

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Objective: UK colorectal screening is around the corner but a recent national colonoscopy audit suggest most endoscopy centres do not achieve the unadjusted completion rate of 85% or more to qualify as a screening centre. We have recently completed a five year colonoscopy audit in a district hospital setting and our unadjusted completion rate was 74.6% which was similar to the recent national colonoscopy audit.1 We looked at factors that may predict the colonoscopy completion rate.

Methods: Retrospective audit from June 1999 to May 2004. We performed multiple logistic regression analysis to calculate the odds ratio and to determine the predictive factors for successful colonoscopy. We excluded colonoscopist performing less than 100 procedures for the multiple logistic regression analysis.

Results: 3873 colonoscopic examinations were done but 674 were excluded, hence 3199 procedures were available for analysis. The unadjusted completion rate remained at 74%. The gender ratio was one to one. The mean age was 61.2 years old (2SD= 31.4 to 90.9 years old).

Abstract 261

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of procedure (v 1999)</td>
<td>1.15</td>
<td>1.08 to 1.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1</td>
<td>0.99 to 1</td>
<td>0.29</td>
</tr>
<tr>
<td>Colonoscopy number (v 101–200)</td>
<td>201–300</td>
<td>1.61</td>
<td>1 to 2.6</td>
</tr>
<tr>
<td>301–400</td>
<td>1.57</td>
<td>1 to 2.44</td>
<td>0.45</td>
</tr>
<tr>
<td>&gt;401</td>
<td>1.93</td>
<td>1.38 to 2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (male to female ratio)</td>
<td>1.49</td>
<td>1.26 to 1.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Speciality (GI surgeon to GI physician ratio) (1700:1392)</td>
<td>0.40</td>
<td>0.29 to 0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Use of Midazolam (n=3019)</td>
<td>1.96</td>
<td>1.25 to 3.08</td>
<td>0.003</td>
</tr>
<tr>
<td>Use of Fentanyl (n=530)</td>
<td>0.7</td>
<td>0.38 to 1.35</td>
<td>0.3</td>
</tr>
<tr>
<td>Use of Pethidine (n=420)</td>
<td>0.43</td>
<td>0.17 to 0.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Use of Foral (n=1216)</td>
<td>0.98</td>
<td>0.94 to 1.01</td>
<td>0.13</td>
</tr>
<tr>
<td>Quality of bowel prep</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: There is a significant improvement trend for successful colonoscopy over the five year audit period. We would recommend performing at least 200 colonoscopy examinations per year to maintain your skill. The use of midazolam, male patient and trained GI physician are independent predictors for successful colonoscopy.


RETROFLEXION IN FLEXIBLE POUCHOSCOPY CAN INCREASE ADENOMA DETECTION IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS AFTER RESTORATIVE PROCTOCOLECTOMY

R. F. S. Man1, C. Fraser1, B. P. Saunders1. 1.Wolfson Unit for Endoscopy, St Mark’s Hospital, Harrow, UK

Introduction: Restorative proctocolectomy eliminates the risk of colorectal cancer in patients with familial adenomatous polyposis. However, approximately 35% (Parc2001) of these patients have reported to

<table>
<thead>
<tr>
<th>Lesion size (mm)</th>
<th>n</th>
<th>Prevalence</th>
<th>Synchronous HP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6</td>
<td>9146</td>
<td>599</td>
<td>61%</td>
</tr>
<tr>
<td>6–10</td>
<td>451</td>
<td>121</td>
<td>16/120</td>
</tr>
<tr>
<td>&gt;10</td>
<td>196</td>
<td>26</td>
<td>1/26</td>
</tr>
</tbody>
</table>

Association between synchronous CRC (21% (212/1000)): <6 mm HP OR 1.0 (p=NS); 6–10 mm HP OR 3.1 (p<0.05); >10 mm HP OR 6.2 (p<0.001).
develop adenomas after the formation of ileal pouch anal anastomosis (pouch). The most common areas of developing adenomas are in the ileo-anal vault especially at the anal-pouch anastomotic site and the columnar cuff. This is possibly due to the presence of some residue rectal tissue despite mucosectomy. In fact, cancers in these areas have been reported in patients who had regular endoscopic surveillance suggested the possibility of missed adenomas during their examination (Ooi et al 2003, Vrouwenraets et al 2004). Studies have demonstrated retroflexion can increase adenomas detection in the rectal vault (Hanson et al 2001) when performing colonoscopy (Heitmiller et al 2001). Therefore, retroflexion in pouch is often not performed despite the risk of causing perforation is unknown.

**Aims:** This study is aimed to demonstrate retroflexion can increase adenoma detection in the ileo-anal vault in FAP patients with ileal pouch-anal anastomosis.

**Methods:** A prospective study of 105 FAP patients with ileal pouch endo-anal anastomosis (IPAA) whom had undergoing surveillance unsedated flexible pouchoscopy (Olympus CF200) by a single nurse endoscopist (RM) between March 2003 to July 2005.

**Results:** One hundred and twenty two patients were seen during this period. Seven patients were excluded due to tight/strictureing anal anastomosis. Forty eight patients (about 42.5%) were found to have polyps seen on retroflexion (mean interval of IPAA formation was 8.8 years). All polyps were removed either by endoscopic resection or transanal excision surgically. Only one patient required a permanent ileostomy for extensive polyposis in the whole pouch. With the adenomas found, 12 (28/%) of these were ileal pouch mucosa type. The remaining 27 adenomas (72%) where found to be arising from the residual rectal tissue. No endoscopic complications such as pain or perforation were reported. More importantly, no adverse reactions were reported during a follow up period of two and half years in this patient group.

**Conclusion:** This study has demonstrated an increased in adenoma detection when retroflexion is performed in flexible pouchoscopy than the previous literatures. This technique is simple and safe to perform in surveillance endoscopy. Early detection of these adenomas in these patients can lead to early removal of these premalignant lesions; hence can prevent cancer and avoid the need for permanent ileostomy.

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**264 ASSESSING PAIN DURING COLONOSCOPY: WHO GUIDES SEDATION?**

B. H. Hayee, M. Wong, D. S. Rowbotham, V. Saxena, A. McNair. Queen Elizabeth Hospital, Woolwich, London SE18 4QH, UK

**Introduction:** Accurate assessment of pain during colonoscopy allows the dose of intravenous sedation and analgesia to be titrated to minimise patient discomfort. Patients who remember a painful colonoscopy may decline repeat examinations and this may be a significant issue for the institution of a national screening programme for colorectal cancer.

**Aims and Methods:** We sought to determine whether the assessments of pain by endoscopists and nurses during colonoscopy correlated with patients’ reports and whether this influenced sedation or procedure time. Information was collected using visual analogue scales (VASs) and patient questionnaires.

**Results:** The mean patient post-endoscopy VAS score for 167 patients (93 female) was 21.4 (SE 23.8). Mean VAS scores from endoscopists and nurses from patients pre-endoscopy (patients anticipation of pain) tended to be higher than the patient’s post-endoscopy score. Correlation coefficients between patients’ post-endoscopy VAS scores and pre-endoscopy scores, endoscopist VAS and nurse VAS were 0.15, 0.39 and 0.41 respectively. 28 patients received a “step up” sedative dose. Mean endoscopist and nurse VAS scores for these patients were higher than patients not requiring additional sedation/analgesia (54.03 ± 27.58, p ≤ 0.0005 and 50.74 ± 17.58, p ≤ 0.0005), as were pre- and post-endoscopy scores (37.42 ± 31, p = 0.07 and 38.48 ± 17.42, p = 0.025 respectively) and trended to be higher than patients undergoing routine TI biopsy is very low. All patients with microscopic disease alone had an abnormal colonoscopy.

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**265 TERMINAL ILEUM VILLI PHOTOGRAPHY TO DOCUMENT EXTENT OF COLONOSCOPY**

N. Powell, B. Hayee, D. Yeoh, D. Rowbotham, V. Saxena, A. McNair. Gastroenterology Dept, Queen Elizabeth Hospital, Woolwich, London, UK

**Background:** Colonoscopy can be demanding and may be accompanied by significant patient discomfort. This study aims to use virtual colonoscopy (VC) measurements to predict difficulty in advance of optical colonoscopy.

**Methods:** Eighty two out of 87 endoscopic procedures were completed. All patients subsequently underwent same day optical colonoscopy. The images were processed using V3D software which allowed accurate measurements of colon segments and angulation of landmark flexures. These images were independently evaluated by three gastroenterologists and categorised as “definitely”, “probably”, and “definitely not” depicting villi.

**Results:** Histological assessment of TI biopsies confirmed small bowel mucosa in 202 patients. There was inadequate sample for assessment in nine cases. Photograph evaluation by reviewers described villi as “definitely” present in 93.1%, 93.6%, and 92.1% of cases and “probably” present in 6.9%, 5.4%, and 7.9% of cases. One reviewer considered villi “definitely not” present in two cases. There was good agreement between the reviewers (Cohen’s kappa values for consensus = 0.78). Microscopic TI changes in patients with normal macroscopic TI appearances. These images were independently evaluated by three gastroenterologists and categorised as “definitely”, “probably”, and “definitely not” depicting villi.

**Results:** Terminal ileum villi photography to document extent of colonoscopy. The endoscopic appearance of the TI was recorded and photographs acquired following instillation of water via the endoscope water channel to flood the visual field and illustrate villi. These images were independently evaluated by three gastroenterologists and categorised as “definitely”, “probably”, and “definitely not” depicting villi.

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**Are variable stiffness colonoscopes really superior? Results of a post hoc analysis**

B. H. Hayee, D. S. Rawbotham, V. Saxena, A. McNair. Queen Elizabeth Hospital, Woolwich, London SE18 4QH, UK

**Introduction:** The use of variable stiffness colonoscopes (VSCs) is reported to improve intubation time, completion rates and reduce the perception of pain during the procedure. In its unstiffened state, the VSC (Olympus PCF-240AL) is significantly less stiff than a conventional colonoscope (CC; Olympus PCF-240S) and at maximal stiffness, it is just as stiff, but only at its distal end.1, 2 The evidence that the VSC is superior to conventional colonoscopes is limited.

**Aims and Methods:** We sought to determine whether our experience with the use of VSC reproduced the results of other studies. As part of a larger trial of sedation regimens for colonoscopy, we gathered data for post hoc analysis of caecal intubation rates, completion times and patient discomfort using a visual analogue scale (VAS) for colonoscopy with a CC and a VSC. All operators involved in the study had confirmed caecal intubation rates in excess of 90%.

**Results:** 169 examinations were performed (97 females); 82 with the VSC. There was no significant difference between operators, or between males and females for all parameters studied. Additional sedative was required in 19 examinations (9 females) in the first 105 procedures and in 31 (13 females) in the subsequent 85. The adjusted completion time (19.96 ± 14.80 minutes, p = 0.20). No significant difference was found for the VSC over the CC in terms of completion rates (94% vs 92%, p = 0.24), intubation times (30.08 ± 30.93 minutes, p = 0.72), VAS assessment by endoscopist (23.77 ± 25.40, p = 0.64), by nurse (23.63 ± 23.18, p = 0.91) or by patients after the procedure (20.69 ± 22.42, p = 0.64).

**Conclusions:** These results demonstrate no statistical or clinical superiority for VSCs over CCs for colonoscopy in adult patients.


**Colonoscopy performance after 190 consecutive procedures: Does type of instrument matter?**

R. P. Arasaradnam, D. P. Hurlstone.1 Wansbeck Hospital, Ashington & School of Clinical Medical Sciences, University of Newcastle upon Tyne; 2Department of Gastroenterology, RHH & NGH, Sheffield Teaching Hospitals, UK

**Background:** The BSG has set out guidelines as to the expected level of competence an endoscopist should strive to achieve. This is vital given the variation in practice throughout the UK as published in the first National Audit in 2002. However, one issue which did not come to light was the variation in types of instruments used and how this may impact on colonoscopic performance.

**Aim:** To determine if colonoscopic performance including caecal completion rate, analgesic dose and sedation practice is affected by variation in instrument.

**Methods:** 190 consecutive procedures performed by a single endoscopist were analysed prospectively. The first 105 procedures were performed using a Olympus CF 240 variable stiffness scope. Subsequent 85 procedures were performed using a Fujinon EC-450WL scope. Demographic data, dose and type of sedation (Midazolam (Mdz)) used as well as caecal and terminal ileal intubation rates (CIR and TIR) were recorded.

**Results:** See table. Indications for colonoscopy were similar in both groups as were hysterecytome rates (3%). Number of patients with previous colonic resections were almost double (11%) in those examined with the Fujinon instrument. Mean list size was five (range 4–6) patients and the number of therapeutic procedures was eight (8%) in the first 105 procedures and 20 (24%) in the subsequent 85. The adjusted completion rates as well as sedation practise were both highly significant ($\chi^2$, p = 0.001) respectively whilst the adjusted angesic dose used was borderline significant ($\chi^2$, p = 0.05). One immediate complication in the first 105 procedures occurred in a 78 year old lady who developed acute left ventricular failure secondary to severe aortic stenosis. She recovered uneventfully.

**Conclusions:** It is evident that type of instrument does influence colonoscopic performance and sedation practice. Perhaps this factor should be taken into account when assessing individual endoscopists or when comparing data between different units.
Abstract 269 Risk stratification and surveillance

<table>
<thead>
<tr>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>97% (19 months)</td>
<td>90% (12 months)</td>
</tr>
<tr>
<td>Appropriate</td>
<td>1%</td>
<td>5%</td>
</tr>
<tr>
<td>Late</td>
<td>2% (68 months)</td>
<td>5% (41 months)</td>
</tr>
</tbody>
</table>

occurred longer than and nine (3%) were appropriate to the guidelines. The table shows their median surveillance intervals with the respective risk stratification.

There were 95 unnecessary examinations at a direct overspend of £62,518. A further 86 examinations occurred sooner than half the recommended interval (unnecessarily early). Indirect costs are estimated to be exponentially higher.

Conclusion: 92% of surveillance colonoscopies were performed earlier than recommended at significant cost, with 30% of these being unnecessary. These examinations have the potential for unnecessary risk, inappropriate management, and highlights areas where our colonoscopic practice can be improved.

270 UTILITY OF COLONOSCOPY FOR EVALUATION OF PATIENTS WITH IRON DEFICIENCY ANAEMIA

V. Subramanian, K. Dhake, R. C. G. Pollok. Department of Gastroenterology, Cellular and Molecular Medicine, St George’s University of London, UK

Introduction: Occult bleeding from the gastrointestinal tract is an important cause for patients with iron deficiency anaemia without obvious sources of blood loss. Current guidelines suggest that such patients should have endoscopic evaluation of the both the upper and lower gastrointestinal tracts. One of the major reasons for recommending colonoscopic evaluation is to pick up colorectal carcinoma in this population. We aimed to assess the utility of colonoscopic evaluation of patients with iron deficiency anaemia.

Methods: Retrospective audit of all patients who underwent colonoscopy for the sole indication of anaemia at St George’s Hospital in 2003 and 2004. Patients were identified from a computerised endoscopy database and data collected from electronic patient records. IDA was defined as having haemoglobin less than the reference range associated with a low mean corpuscular volume and/or a low ferritin. Significant pathology considered were GI malignancy, inflammatory bowel disease, colonic polyp larger than 1 cm, vascular malformations, bleeding diverticular disease, and bleeding hemorrhoids. ROC curves were constructed for variables of interest and p values were calculated using standard tests of proportions for independent samples.

Results: 145 patients with confirmed IDA, 120 with anaemia but no evidence of iron deficiency were included. There were no differences overall detection of significant lower GI pathology, between patients with IDA (15.2%) and patients with anaemia (12.5%) without evidence of iron deficiency. However colorectal cancer rates were significantly higher among patients with IDA. Levels of haemoglobin, ferritin, and iron were not useful in predicting the overall detection of a significant lower GI pathology in either group.

Conclusions: Patients with IDA are more likely to have colorectal cancer than patients with anaemia without evidence of iron deficiency. Haemoglobin, ferritin, and iron levels do not appear to predict the detection of clinically significant lesions on colonoscopy other than colorectal cancer. Prospective studies are required to confirm these observations.

271 WHY WAIT FOR A COLONOSCOPY? AN EASY CURE

K. Chivers, B. Seunarine, A. Shoaib, P. Basnyat, N. Taffinder (introduced by AW Harris). Colorectal Unit, William Harvey Hospital, East Kent Hospitals NHS Trust, Ashford, Kent TN24 0LZ, UK

Background: Guidelines for surveillance and screening colonoscopy were released in October 2002 by the British Society of Gastroenterology and the Association of Coloproctology of Great Britain and Ireland. They were based on sound evidence of the chance of finding malignancies in patients who have had a cancer in the past, or for those with a family history of bowel cancer. These guidelines were expected to lead to a change in clinical practice.

Methods: Before starting the audit, the process was discussed at, and approved by, the Kent Endoscopy Board and Colorectal Cancer DOG. 4837 patients were waiting for a colonoscopy in our network and a team of researchers reviewed their notes in the light of the BSG guidelines. Over two thirds of the list were waiting for screening or surveillance colonoscopy. Those waiting for diagnostic colonoscopy were excluded from the study. The wait times for an urgent diagnostic colonoscopy were measured before and after the audit.

Results: 2369 (78% of those waiting) did not need to have a colonoscopy according to the guidelines. Those patients were identified and each of the seven hospitals within the network received a booklet identifying their patients who could be removed from the waiting list. This could save the network £1.2 million (assuming £500 per colonoscopy). Patients who were removed from the waiting list were contacted with a standardised letter. This review halved the size of our total waiting list and subsequently the average wait time for an urgent diagnostic colonoscopy fell from 70 days to 33 days.

Discussion: Guidelines can have dramatic impact on avoiding unnecessary investigations and reducing waiting lists. In addition our wait times for a diagnostic colonoscopy fell, with increased compliance with the cancer waiting time targets. Most clinicians were comfortable with the guidelines although some exceptions to the recommended surveillance were accommodated for.

272 HOW MANY ENDOSCOPISTS FULFIL QUALITY ASSURANCE CRITERIA FOR THE BOWEL SCREENING PROGRAMME?

M. C. Allison. Gastroenterology Unit, Royal Gwent Hospital, Newport, South Wales NP20 2UB, UK

Background: Colonoscopists who will participate in the forthcoming screening programme are expected to perform or directly supervise >150 procedures per year, to have an adenoma detection rate of >15%, an adjusted caecal intubation rate of >90% and a lifetime perforation rate for diagnostic colonoscopy of <1:1000. Although the programme will start in England in April 2006 it is not known how many colonoscopists fulfil these requirements. A survey of colonoscopists in Wales was therefore done.

Methods: Questionnaires were sent to all 100 career grade endoscopists believed to be doing regular colonoscopy lists in Wales. Completed forms were returned by post to ensure anonymity.

Results: The response rate was 70%. Seven no longer undertook colonoscopy. Of 63 responding colonoscopists, only nine (14%) could quote their adjusted adenoma detection rate (median 18%, range 10–33%), and 33 (52%) could quote their adjusted caecal intubation rate (median 92%, range 70–96%). Median colonoscopy caseload fell within the range of 101–150 procedures per year. Lifetime perforation rates were given by four respondents, of whom 43 quoted a figure of <1:1000. Overall only 12 colonoscopists (19%) met the required criteria for screening colonoscopists (sufficient caseload with acceptable caecal intubation and perforation rates). Of these, 10 indicated keenness to support a screening programme. To support an FOB based programme in Wales the remaining 10 endoscopists would need to undertake an additional 500 colonoscopies per year. Most of those who failed to meet the required criteria did so through having insufficient caseloads.

Conclusions: The findings cast doubt on whether there are enough colonoscopists ready to support a bowel screening programme in Wales. This deficiency could be rectified by (1) concentrating service provision among fewer endoscopists; (2) better record keeping by existing colonoscopists; (3) better training in colonoscopy; and (4) training colonoscopy nurse specialists. Similar surveys should be done to determine whether such deficiencies exist in other parts of the UK.

273 A TWO TIERED ULCERATIVE COLITIS SURVEILLANCE STRATEGY BASED ON RISK STRATIFICATION OF ULCERATIVE COLITIS PATIENTS

N. Suzuki1, N. Arebi1, M. D. Rutter2, B. P. Saunders1. 1St Mark’s Hospital, London; 2University Hospital of North Tees, Stockton on Tees, UK

Background: Ulcerative colitis (UC) surveillance is offered to patients with pancolitis or at least eight year duration. Additional risk factors for UC dysplasia have been reported in previous studies (table). Further subdivision of UC surveillance patients into high and low risk subgroups would enable a better cancer pick up rate and appropriate allocation of resources. A two tiered surveillance strategy based on patient risk is needed.

Aim: To evaluate the appropriateness of this surveillance strategy, we have conducted an audit of colonoscopies performed on UC surveillance patients.
Abstract 273

<table>
<thead>
<tr>
<th>History</th>
<th>High risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSC, PH of CRC</td>
<td>No PSC, No PH</td>
<td></td>
</tr>
<tr>
<td>PH adenoma</td>
<td>No PH adenoma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Colonoscopy</th>
<th>Active colitis</th>
<th>Quiescent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Scurriture</td>
<td>Minimal scarred</td>
</tr>
<tr>
<td></td>
<td>Tubular/scared</td>
<td>No post inf polyp</td>
</tr>
</tbody>
</table>

| Surveillance freq | 1 yearly with dye spray | 5 yearly |

Method: All the colonoscopies undertaken for UC surveillance (475) between January 2004 and March 2005 were audited.

Results: Seventeen neoplastic lesions were detected. Four of these lesions were considered to be a sporadic adenoma as they were located in unaffected areas. The remaining 13 lesions were found in areas of colitis with a median size of 20 mm (ranging 3–200 mm). Histologically, these lesions showed invasive cancer (2), high grade dysplasia (5), and low grade dysplasia (6). Macroscopically, 7/13 dysplastic lesions had a flat profile; flat elevation (2), completely flat (1) depressed lesion (2), laterally spreading tumour (2). Dye spray accentuated these lesions. The 13 lesions were detected from 11 patients of whom 10 patients belonged to the high risk group.

Conclusion: The risk stratification on UC patients may identify those patients most likely to benefit from colonoscopy surveillance.

Abstract 275

<table>
<thead>
<tr>
<th>Nurse decision, n (%)</th>
<th>Consultant agreement, n (%)</th>
<th>Final outcome, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance</td>
<td>Yes, n (%)</td>
<td>No, n (%)</td>
</tr>
<tr>
<td>Stopped</td>
<td>25 (18)</td>
<td>22 (16)</td>
</tr>
<tr>
<td>Reduced freq</td>
<td>63 (45)</td>
<td>52 (37)</td>
</tr>
<tr>
<td>Increased freq</td>
<td>1 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>No change</td>
<td>49 (36)</td>
<td>44 (32)</td>
</tr>
<tr>
<td>Total</td>
<td>138 (100)</td>
<td>119 (86)</td>
</tr>
</tbody>
</table>

Method: A single nurse practitioner was assigned to screen patients on the polyp surveillance waiting list. This was carried out using the British Society of Gastroenterology (BSG) guidelines (2002). Consultants reviewed the notes of patients where rescoping frequency was altered. They were required to provide a reason for any decision that did not meet the guidelines. All consultants reviewed notes of patients whose surveillance programme was stopped.

Results: Of 235 patients awaiting surveillance colonoscopy, 138 were for polyp surveillance. The table shows the outcomes after this process. There was a change in management in 66% of cases, with the majority of cases having either a reduction in frequency of colonoscopy (37%) or where surveillance was stopped (16%).

Conclusion: Screening of waiting lists for polyp surveillance by a nurse practitioner is feasible. This strategy is useful in appropriately reducing the number and frequency of unnecessary colonoscopies.

Abstract 276

Method: 626 colonoscopists nationally comprising mainly consultant members of the ACPGBI and BSG, and their respective Trainees were sent an online questionnaire. This consisted of clinical case scenarios on colonoscopy surveillance.

Results: 328 colonoscopists responded, of which >75% were consultants performing >10 colonoscopies per month. 60% of colonoscopists surveyed patients after cancer resection or polypectomy. Locally, non-compliance with these recommendations resulted in a significant number of unnecessary examinations. We present results of a national survey into colonoscopic surveillance practice.

Conclusion: Colonoscopic practice throughout the UK is extremely variable. In most cases, surveillance occurs more frequently than recommended by the guidelines. Colonoscopists consider histology very strongly in determining follow up of patients.

Abstract 277

Method: A nurse practitioner is feasible. This strategy is useful in appropriately reducing the number and frequency of unnecessary colonoscopies.

Conclusion: Colonoscopic practice throughout the UK is extremely variable. In most cases, surveillance occurs more frequently than recommended by the guidelines. Colonoscopists consider histology very strongly in determining follow up of patients.

Background: The implementation of NHS bowel cancer screening is a limited resource associated with potentially serious complications. Waiting times are likely to be stretched further with the introduction of screening for bowel cancer. We conducted an audit to assess and identify the appropriateness of those patients who are undergoing a repeat colonoscopy.

Aims: To compare local practice for repeating a colonoscopy against current BSG guidelines and thereby identifying patients who did not require the procedure, whose procedure needed expediting or delaying. In addition to offering best practice, it would potentially reduce the waiting time for a colonoscopy.

Methods: 536 patients were on the waiting list for a colonoscopy. Only 483 case notes were located. Previous endoscopy and histology reports were reviewed and indications for a repeat procedure were matched to the guidelines. An audit proforma was used.

Results: 237 (49.1%) were for polyps, 118 (24.4%) for cancer follow up, 112 (23.2%) for family history, and 16 (3.3%) for inflammatory bowel disease (IBD). No other indications were identified. Of the 483 patients listed only 181 (37.4%) were due to have their repeat colonoscopy at the appropriate interval. 136 (28.1%) were too early, 39 (8.0%) too late and 83 (17.18%) did not require a further procedure. In the remaining 44 patients (9.10%) there was no clear follow up documented or they had failed to keep appointments.

Conclusion: Follow up colonoscopy for polyps was haphazard and that for colorectal cancer often over cautious. The screening of high risk families was usually too frequent by many years. For IBD we found far fewer patients on the waiting list for surveillance than we expected for the size of population served. The financial cost for a colonoscopy is approximately £457 leading to an immediate cost saving of £37,931 by removing the “not indicated” patients from the list.

Abstract 277

<table>
<thead>
<tr>
<th>Year</th>
<th>No of cases</th>
<th>OCCR</th>
<th>DCCR</th>
<th>DACR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>766</td>
<td>66.1%</td>
<td>53.5%</td>
<td>58.6%</td>
</tr>
<tr>
<td>Year 2</td>
<td>731</td>
<td>70.6%</td>
<td>56.5%</td>
<td>63.1%</td>
</tr>
<tr>
<td>Year 3</td>
<td>761</td>
<td>77.0%</td>
<td>63.1%</td>
<td>66.7%</td>
</tr>
<tr>
<td>Year 4</td>
<td>762</td>
<td>77.4%</td>
<td>67.7%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Year 5</td>
<td>858</td>
<td>79.8%</td>
<td>72.0%</td>
<td>77.3%</td>
</tr>
</tbody>
</table>

Conclusion: SBM identified isolated small bowel Crohn’s disease in 10 out of 88 (11%) patients with chronic diarrhoea and normal colonic evaluation. 40% of these cases would have been missed if SBM had been reserved only for those patients with raised inflammatory markers.


279 CAPSULE ENDOSCOPY FOR THE DIAGNOSIS OF CROHN’S DISEASE IN ROUTINE CLINICAL PRACTICE

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Background: The mean time to diagnosis of small bowel Crohn’s disease from onset of symptoms is 1–7 years. Despite a high clinical suspicion, in a subgroup of patients, the diagnosis remains elusive with negative investigations. There is now increasing evidence for the use of capsule endoscopy (CE) in the diagnosis of Crohn’s disease.

Aim: To evaluate the diagnostic yield of CE in suspected Crohn’s disease or recurrence of disease in established Crohn’s patients, undetected by conventional modalities. We also assessed the impact of CE findings on the management of these patients.

Methods: All patients who underwent CE from January 2002 to August 2005 for suspected Crohn’s disease were included in this analysis.

Results: Forty-six patients underwent CE for a clinical suspicion of Crohn’s disease, on a combination of patient history, raised inflammatory markers and inconclusive tests. In 59% (n = 27) of patients, a diagnosis of Crohn’s disease was made after detecting erosions, ulceration and mucosal oedema on CE. In 26% (7/27), CE was able to identify recurrence of disease in the small bowel in patients with an established diagnosis of Crohn’s disease. Prior to CE, 70% (n = 19) of patients had evidence of raised inflammatory markers and 85% (n = 23) of patients had undergone small bowel radiology: 70% normal (16), equivocal (6), abnormal (1). Additionally, five patients had a computed tomographic scan: thickening of bowel wall (3), normal (2). Previous histology of the small bowel was normal in five patients and equivocal in six patients despite the presence of terminal ileal ulceration on endoscopy. 74% of patients with findings of Crohn’s disease on CE underwent a change of management. This was in the form of medical treatment for Crohn’s disease (n = 17) or surgery (n = 3). In three patients, no treatment was initiated due to lack of symptoms at outpatient review, post CE. Conclusion: CE has a high diagnostic yield in patients suspected of a new diagnosis of Crohn’s disease or recurrence in established disease. Findings of CE led to the change of management in the majority of patients suspected of Crohn’s disease.
endosonography contributes to the imaging and potentially the diagnosis of PSC.

281 RELATION OF OBESITY TO LATE ONSET CROHN’S DISEASE

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Introduction: Crohn’s disease (CD) is associated with innate immune (IM) activation. Smoking, its strongest main environmental risk factor is also associated with innate immune activation. Another potent condition associated with IM activation is obesity. In an earlier study we demonstrated that obesity was associated with subclinical bowel inflammation as determined by faecal levels of calprotectin. The main genetic risk factors for CD are associated with early age of onset. It is likely that environmental risk factors are collectively more important with older age of onset. We sought to determine whether premorbid obesity is associated with late onset CD.

Methods: We used a validated questionnaire for recall of premorbid weights. 214 subjects (CD = 100, UC = 114; 53% men) were recruited. The mean age of diagnosis was 38.9 (10–82) years. There was a bimodal distribution at age of presentation and we chose a cut off point of 50 years to define the older age group. 23/100 CD and 38/114 UC subjects were diagnosed aged 50+. 11/38 (29%) of UC and 13/23 (56.5%) of CD had a maximum premorbid BMI=30 (p = 0.03). There was a significant effect modification of obesity by age at diagnosis (p = 0.0076) after adjustment for age, sex, smoking, and age at diagnosis.

Conclusion: A possible association of obesity with late onset CD warrants further investigation. Further work is being undertaken to assess the difference in clinical characteristics of late and early onset CD. It is also possible that obesity associated IBD could be a different entity to other forms of CD.


282 DO THIOPURINE METHYL TRANSFERASE LEVELS GUIDE PRESCRIBING AND MONITORING OF THIOPURINES IN OUR CURRENT PRACTICE?

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Introduction: Thiopurines [azathioprine (AZA) and mercaptopurine (MP)] can cause potentially fatal myelotoxicity. Audit of our practice indicates that, despite postal reminders from our inflammatory bowel disease (IBD) nurse specialist, only 82% of patients taking maintenance thiopurine therapy attend for 3-monthly blood testing. Appreciating the unmet need remains a critical step in the role of thiopurine methyl transferase (TPMT) testing. Our aim was to review whether checking TPMT levels prior to initiating therapy can help guide the safe prescribing and monitoring of thiopurines in our practice.

Methods: All IBD patients taking thiopurines were identified over a six month period (October 04–March 05) and their notes reviewed retrospectively.

Results: Ninety patients were identified, 72/90 (80%) were on maintenance therapy whilst 18/90 (20%) were initiated on therapy during the study period. TPMT levels had been checked in all of the initiation group, compared with 33/72 (45.8%) of the maintenance group. TPMT levels were low in 11/90 (12.2%) patients; four in the initiation group and seven in the maintenance group. The 4 patients in the initiation group with a low TPMT level were all started on low dose AZA (1 mg/kg) compared with 4/7 (57.1%) patients in the maintenance group. In the initiation group one patient with a low TPMT level developed hepatitis while in two patients with normal TPMT levels leukopenia (1) and hepatitis (1) occurred. In the maintenance group one patient with a low TPMT level, who had been started on AZA 2 mg/kg, developed leukopenia, whilst a further three patients with normal TPMT levels developed hepatitis.

Conclusion: TPMT levels did not appear to predict side effects in this small group of patients however it is noteworthy that none of the patients with low TPMT levels initiated on AZA 1 mg/kg developed myelotoxicity and that all episodes of leukopenia/hepatitis were identified by standard blood monitoring. TPMT testing does not abate the need for regular blood monitoring but may identify patients at risk and thus help to guide the safe prescribing and monitoring of AZA/MP.

283 INCIDENCE OF GALLSTONES AND RELATED RISK FACTORS IN CROHN’S DISEASE AND ULCERATIVE COLITIS. A PROSPECTIVE COHORT STUDY

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Background and Aim: Crohn’s disease (CD) has been associated with higher prevalence of gallstone disease (GD) in several retrospective studies, but the main contributing factors to the increased risk have not been well established yet as many may be similar to those in general population (age, sex, BMI). Aim of this prospective study was to evaluate the risk of developing GD in a defined cohort of CD and UC patients and to identify the possible predictors.

Material and Methods: We prospectively evaluated a cohort of 600 patients with inflammatory bowel disease (415 CD, 185 UC), who were free of previous GD at baseline liver ultrasound (US) as compared to 600 age, sex and BMI matched GD-free controls during a median follow up of seven years (range 5–12 years). Both patients and controls were followed up with periodic visits including liver US every 12 months. The incidence of GD was described by Kaplan-Meier plots. Multivariate analysis was used to discriminate among the impact of different variables (including age, sex, BMI, site and duration of disease, number of recurrences, type of medical therapy, number and extent of bowel resections, number and total length of hospitalisations) on the risk of developing GD.

Results: The 12 year incidence of GD was 3.1% in CD patients v 2.1% in UC patients and 1.2% in age, sex, and BMI matched controls. The risk of developing GD was 2.09 (95% CI 1.22 to 3.64) in CD patients and 1.33 (95% CI 0.56 to 3.16) in UC patients as compared to matched controls. On logistic regression analysis, ileo-colonic site of CD (OR 2.14, 95% CI 1.02 to 4.52), disease duration longer than 15 years (OR 4.26, 95% CI 1.64 to 11.1), >3 clinical recurrences (OR 8.07, 95% CI 1.03 to 63.3), ileal resection >30 cm (OR 7.03, 95% CI 2.56 to 19.3), >3 hospitalisations (OR 20.7, 95% CI 4.73 to 90.5), and total number of days in hospital >40 (OR 24.8, 95% CI 7.14 to 86.3) were independently associated with GD in CD.

Conclusion: Our data show that CD pts have a double risk of developing GD compared with age, sex, and BMI matched healthy controls, whereas the risk of GD in UC is similar to the general population. Site of disease, surgery, extent of ileal resections but also number of clinical recurrences, frequency, and duration of hospitalisations are the most important independent risk factors for GD.

284 THE IMPACT OF TWO WEEK REFERRAL INITIATIVE ON THE REFERRAL PATTERN OF PATIENTS WITH SUSPECTED INFLAMMATORY BOWEL DISEASE

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Background: Two week referral guidelines were introduced in the year 2000 to improve colorectal cancer services across the United Kingdom. We believe that since the introduction of these guidelines there is a change in the referral pattern of patients with inflammatory bowel disease (IBD).

Aims: To study the impact of two week referral initiative on the referral pattern of patients with suspected IBD.

Material and Methods: The referral, treatment, and histological details of all newly diagnosed IBD patients between 1999 and 2004 were retrospectively reviewed and analysed.

Results: 227 new patients, 48 in 1999, 36 in 2000, 37 in 2001, 38 in 2002, 27 in 2003, and 41 in 2004 were newly diagnosed to have IBD. Details of diagnosis includes; ulcerative colitis (UC) = 118 (52%), Crohn’s colitis (CC) = 84 (37%), and indeterminate colitis (IDC) = 25 (11%). There was a significant change in the referral pattern following introduction of guidelines. In 1999, 36% of newly diagnosed IBD patients were seen by surgeons compared to 66% in 2002 (p = 0.005), 59% in 2003 (p = 0.04), and 66% in 2004 (p = 0.004). We also examined the primary prescription of drugs for the rectal disease. Seventy eight patients (34.4%) had rectal disease. Among 78, 53 patients had isolated rectal UC, nine had rectal disease due to IDC, and eight had left sided UC. Fifty eight patients received rectal preparations along with or without systemic treatment and 17 received systemic treatment alone. Three patients did not require any treatment due to mild disease. Fifty six per cent of patients who were treated with rectal steroid preparations compared to only 17% of patients seen by gastroenterologists (56% v 17%, p = 0.01).
Conclusions: There has been significant change in the referral pattern of patients with IBD following introduction of two week referral guidelines. More patients were referred to surgeons following the introduction of two week referral guidelines. Surgeons tend to prescribe steroids more often than gastroenterologists do for the rectal disease.

**285** LONG TERM PROGNOSIS IN CROHN’S DISEASE: AN EPIDEMIOLOGICAL STUDY OF PATIENTS DIAGNOSED MORE THAN 20 YEARS AGO IN CARDIFF

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Background: Early studies into mortality associated with Crohn’s disease suggested standardised mortality rates (SMR) significantly higher than the general population, especially in those recently diagnosed. One study recognised a second mortality peak in those diagnosed over 13 years. Recent studies report SMR near normal, but these studies have insufficient follow up to capture a second peak. This study investigates mortality experience of patients diagnosed over 20 years ago, representing the longest follow up to date.

Methods: The Cardiff database of patients with Crohn’s disease was established in the 1970s containing data on all patients diagnosed in Cardiff since 1934. 394 patients diagnosed before 1 January 1985 were traced and their mortality status on 31 December 2004 was established.

Results: Overall SMR is 1.29 (95% CI 1.12 to 1.45) and has not statistically significantly changed since the 1970s. Mortality decreases with increasing age, from 16.95 (95% CI 14.99 to 18.91) for patients aged 10–19 years, to 0.92 (95% CI 0.65 to 1.19) in those over 75 years. Kaplan-Meier analysis of age at death shows patients diagnosed aged 10–26 years have mean age at death of 38.3 years, for those aged 27–52, 63–69 years, aged 53–58, 74.5 years and those over 59 years; 79.3 years.

Discussion: This study represents the longest follow up of a cohort of patients with Crohn’s disease to date. It shows significantly raised SMR, not statistically changed since the 1970s and similar to other chronic conditions. Patients diagnosed younger have worse prognosis than those diagnosed later and a reduced life expectancy compared to the general population.

**286** THE IBD DATABASE: USE AND ACHIEVEMENTS

C. M. Edwards1, C. Roystan2, H. Durbin1, A. Coulson1, K. D. Bardhan (on behalf of the User Group)*. 1 Torbay Hospital, Devon; 2 Rotherham DGH, S Yorks, UK

Background: The Rotherham inflammatory bowel disease database (IBD-DB) has been developed in response to the need for easy access to data on patients with IBD. Two centres from the larger user group have piloted the IBD-DB over the last year for clinical, audit, and monitoring purposes.

Principal difficulties: IT; financial and human resource to support IBD-DB set up and data entry.

Principal gains: Electronic patient record; generation of clinic letters; prescribing record and pharmacy audit; immuno-suppression monitoring; medical and surgical activity; colonoscopy surveillance programme; validated phenotypic description of IBD population.

Results: Preliminary demographic data from the two centres show good agreement (see table). Conclusion: The use of the IBD-DB supports good clinical practice, informs the national evidence base for IBD. Its potential for clinical audit, governance, and clinical research is self-evident. Ten centre data will be available shortly.

**287** HYPNOTHERAPY DECREASES RECTAL MUCOSAL RELEASE OF SUBSTANCE P, HISTAMINE, AND IL-13 IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS

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Introduction: Hypnotherapy is effective for functional GI disorders and has been claimed to improve ulcerative colitis (UC). How hypnotherapy may act is unknown but could involve reductions in mucosal neurotransmitter, mast cell mediator and cytokine production.

Aim: To assess the effects of one session of hypnotherapy on the concentrations of substance P (SP), histamine, TNF-α, and IL-13 in rectal peri-mucosal fluid (RPMF) in patients with active UC.

Methods: For 50 minutes patients with active UC (Baron score > 1) underwent either (1) gut focused hypnotherapy or (2) control session—relaxing music. Autonomic response was assessed by pulse and BP every 15 minutes. A sample of RPMF was collected before and after each protocol by placing a 7 × 30 mm strip of filter paper via a rigid sigmoidoscope against the rectal mucosa for 1 minute until wet. The filter paper was incubated in 1 ml BSA (0.3%), sodium azide (0.01%) and Tween 20 (0.002%) in PBS for 24 hours and SP, histamine, TNF-α, and IL-13 concentrations in the buffer measured by ELISA.

Results: The control protocol did not change any variable. Hypnosis reduced pulse rate by 7 bpm, systolic BP by 2 mmHg, and RPMF concentrations of SP by 81%, histamine by 35%, IL-13 by 54%, reduced pulse rate by 7 bpm, systolic BP by 2 mmHg, and RPMF concentrations of SP by 81%, histamine by 35%, IL-13 by 54%.

Conclusion: Hypnotherapy reduces rectal mucosal release of SP, histamine, and IL-13, but not of TNF-α, in active UC. These changes could provide a basis for a beneficial effect of hypnotherapy in UC.

**Abstract 287**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse rate (bpm)</td>
<td>76 (70–86)</td>
<td>69 (63–83)*</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>125 (116–132)</td>
<td>123 (112–137)*</td>
</tr>
<tr>
<td>Substance P (pg/ml)</td>
<td>54 (16–621)</td>
<td>10 (5–20)*</td>
</tr>
<tr>
<td>Histamine (pg/ml)</td>
<td>26 (15–34)</td>
<td>17 (6–25)*</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>111 (42–252)</td>
<td>140 (65–253)</td>
</tr>
<tr>
<td>IL-13 (pg/ml)</td>
<td>18.7 (5.1–99.1)</td>
<td>9.6 (5.1–27)*</td>
</tr>
</tbody>
</table>

*p < 0.05 from pre-hypnotherapy value. Median and IQR shown.

**288** REGULATION AND AUTOCRINE ACTION OF AMPHIREGULIN AND EPIREGULIN IN HUMAN COLONIC SUBEPITHELIAL MYOFIBROBLASTS

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Background: Human amphiregulin (AR) and epiregulin (EP) belong to the epidermal growth factor (EGF) family and exert their effects as mitogenic stimulators. Recent studies have suggested that AR and EP support reconstitution of the gastrointestinal tissue. However, the local secretion of AR and EP in the intestine remains unclear. Subepithelial myofibroblasts (SEMFs) play a central role in processes involved in inflammation and wound healing in the intestine. In this study, we investigated AR and EP secretion in human colonic SEMFs. Aims: Primary cultures of SEMFs were prepared according to the method reported by Mahida et al. The studies were performed on passages 2–6 of SEMFs isolated from three resected specimens. AR and EP mRNA expressions were evaluated by Northern blotting, and the protein secretion was determined by Western blotting. Cell proliferation of SEMFs was tested for by using a MTT assay.

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Abstract 286

<table>
<thead>
<tr>
<th>Variable</th>
<th>Centre 1 (n = 1102)</th>
<th>Centre 2 (n = 693)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>CD</td>
<td>UC</td>
</tr>
<tr>
<td>Disease (%)</td>
<td>49</td>
<td>41</td>
</tr>
<tr>
<td>Prevalence/100000 (n)</td>
<td>195</td>
<td>165</td>
</tr>
<tr>
<td>Males (%)</td>
<td>53</td>
<td>44</td>
</tr>
<tr>
<td>Median duration (months)</td>
<td>86</td>
<td>109</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>Crohn’s (CD) Colonic (%)</td>
<td>–</td>
<td>37</td>
</tr>
<tr>
<td>CD ileo-colonic</td>
<td>–</td>
<td>33</td>
</tr>
<tr>
<td>CD Ileo-ileal</td>
<td>–</td>
<td>23</td>
</tr>
<tr>
<td>CD perianal</td>
<td>–</td>
<td>7</td>
</tr>
<tr>
<td>Extensive UC (%)</td>
<td>35</td>
<td>–</td>
</tr>
<tr>
<td>On immunosuppression (%)</td>
<td>12</td>
<td>26</td>
</tr>
<tr>
<td>Operated (%)</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td>Mortality (IBD related) (%)</td>
<td>3 (0)</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

*IBD not yet classified: 10% Centre 1; 8% Centre 2.
†Centre 1 current smokers; Centre 2 smoking at presentation.
Results: AR and EP mRNAs were not detected in unstimulated SEMFs by Northern blotting. Among the various kind of cytokines and growth factors, interleukin (IL)-1β, tumour necrosis factor (TNF)-α, and EGF strongly induced AR and EP mRNA expression. In addition, AR and EP induced their own mRNA expressions by themselves. The effects were detected in dose and time dependent manner. These responses were significantly reduced by AG1478, the specific inhibitor of EGF receptor tyrosine kinase. AR and EP secretion were also observed at the protein levels. A Western blot assay demonstrated that AR and EP stimulate the proliferation of SEMFs at concentrations of 1 ng/ml–100 ng/ml to a greater extent as compared to IL-1β. EGF significantly induced AR and EP mRNA expression. In addition, AR and EP secretion were also observed at the protein levels. A Western blot assay demonstrated that AR and EP stimulate the proliferation of SEMFs to a greater extent as compared to IL-1β. EGF significantly induced AR and EP mRNA expression. In addition, AR and EP secretion were also observed at the protein levels. A Western blot assay demonstrated that AR and EP stimulate the proliferation of SEMFs to a greater extent as compared to IL-1β. EGF significantly induced AR and EP mRNA expression. In addition, AR and EP secretion were also observed at the protein levels.

Conclusions: (1) IL-1β, TNF-α, and EGF were strong inducers of AR and EP in human colonic SEMFs. (2) AR and EP acted as autocrine growth factors for SEMFs and stimulated their proliferation. These results show that AR and EP may play an important role in the mechanism of wound healing in the inflamed intestinal mucosa such as inflammatory bowel disease.

289 PHENOTYPIC SUBGROUP ANALYSES REVEAL AN INTERACTION BETWEEN THE NOD1 INSDEL POLYMORPHISM (INSDEL) AND SMOKING STATUS IN CROHN’S DISEASE


Introduction: The development of IBD is under the influence of genetic (for example NOD2) and environmental (for example smoking) factors. We have reported an association between an insertion/deletion polymorphism (INSDEL) in NOD1(CARD4) and IBD.

Aim: To assess the role of the INSDEL in defining IBD subgroups and to explore the NOD1 gene-gene or gene-environment interactions.

Methods: The INSDEL was genotyped in 335 CD, 306 ulcerative colitis (UC) and 335 controls (HC) (cases reported in the original paper) and data was available regarding the presence of extra-intestinal manifestations (EIMs) from the 556 IBD trios also reported in the original paper.

Associations were analysed using standard statistical methods.

Results: Univariate analyses demonstrated association between INSDEL and ileal (p = 0.007), perianal (p = 0.03), stenotic (p = 0.005), and fistulating (p = 0.004) CD, although these associations were not independent in multivariate analyses. Independent associations with the development of CD under 16 years (p = 0.015) and >25 years (p = 0.002) when compared respectively with those developing disease over the age of 16 and 25 were seen. The INSDEL is found at higher frequency in CD non-smokers than in CD smokers (p = 0.0004). Logistic regression analyses suggest association with smoking status (p = 0.034) and not with age of onset (p = 0.38).

No significant association with any UC phenotype was seen. INSDEL was associated with the presence of large joint arthropathies (RR 1.76), erythema nodosum (RR 1.81), ulcers (RR 2.15) and PSC (RR 2.14) in univariate analyses. Multivariate analyses showed strong association with the presence of any EIM (p = 0.0039) and not with age of onset (p = 0.38).

No significant association with any UC phenotype was seen. INSDEL was associated with the presence of large joint arthropathies (RR 1.76), erythema nodosum (RR 1.81), ulcers (RR 2.15) and PSC (RR 2.14) in univariate analyses. Multivariate analyses showed strong association with the presence of any EIM (p = 0.0039) and not with age of onset (p = 0.38).

Conclusion: The risk for developing CD conferred by the NOD1 INSDEL appears to be greatest in non-smokers. This may reflect, in part, the greater influence of genetic, rather than environmental, risk factors in patients who develop CD at a young age.

290 NORMAL RESPONSES TO SPECIFIC NOD1 ACTIVATING PEPTIDOGLYCAN AGONISTS IN THE PRESENCE OF THE NOD2 FRAMESHIFT AND OTHER MUTATIONS IN CROHN’S DISEASE

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Background and Aims: Both NOD2/CARD15 alleles are mutated in 10% of Crohn’s disease patients, causing loss of functional responses to low dose muropeptide agonists. We hypothesised that NOD2 mutations may also impair NOD1/CARD4 responses, supported by data suggesting NOD2 1007fs/1007fs patients had reduced responses to a putative NOD1 agonist, M-TriDAP (Netea et al. J Biol Chem 2005). Methods: We measured peripheral blood mononuclear cell (n = 8) NOD2 wild type, n = 4 1007fs/1007fs, n = 6 702Trp/1007fs, n = 5 702Trp/702Trp, n = 3 908Arg/1007fs) responses to NOD1 agonists alone (IL-8), and agonist enhancement of lipopolysaccharide responses (IL-1b).

Results: Significant responses were seen with M-TriDAP at 10 nM (as with NOD2 agonists), but only at >100 nM with FK565 and TriDAP. M-TriDAP induced IL-8 and enhancement of lipopolysaccharide IL-1β responses were significantly reduced between NOD2 double mutation carriers versus healthy controls. However there was no difference with FK565 or TriDAP stimulation, or between 1007fs/1007fs cells and other genotypes.

Conclusions: M-TriDAP contains the minimal structures for both NOD1 (D-Glu-mesoDAP) and NOD2 (MurNAc-L-Ala-D-Glu) whereas FK565 and TriDAP contain only NOD1 activating structures. M-TriDAP has dual NOD1/NOD2 agonist activity in primary cells, perhaps due to different intracellular peptidoglycan processing compared to the HEK293 cell system typically used for agonist specificity studies. Responses to specific NOD1 agonists are unaffected by NOD2 genotype. NOD1/1007fs/1007fs crosstalk does not occur.

291 CO-LOCALISATION OF TOLL-LIKE RECEPTORS WITH SIGNALLING MOLECULES IRAK-1 AND NFkB IN COLONIC BIOPSIES OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: We have previously reported abnormalities in mucosa associated bacterial flora in inflammatory bowel disease (IBD) patients as well as the presence of E coli associated with macrophages in the lamina propria of these patients. By looking at signalling molecules IRAK-1 and NFκB we have now investigated the activation status of both epithelial cells and lamina proprial macrophages and compared this with the expression of toll-like receptors (TLR) 2, 4, and 5.

Methods: Snap frozen rectal biopsies were taken at routine colonoscopy from patients with ulcerative colitis (UC, n = 8), Crohn’s (CD, n = 8) and controls with normal colorectal mucosa (n = 8). TLR 2, 4, and 5, signalling molecules IRAK-1 and NFκB expression and macrophages (CD68) were determined using immunofluorescence. Co-localisation was confirmed using confocal microscopy.

Results: In controls, moderate epithelial expression of TLRs 2 and 4 but not 5 was seen. This correlated with a complete absence of IRAK-1 and NFκB. IBD biopsies showed an increase in epithelial expression of TLRs 2 and 4 but not 5 with a corresponding increase in IRAK-1 and NFκB levels. Lamina propria, macrophages showed greater expression of TLRs 2 and 4 in IBD patients compared to controls. Modest amounts of TLR-5 were also seen in this group. Co-localisation of TLRs with IRAK-1 and NFκB in lamina proprial macrophages showed a significant increase in activation compared to that seen in epithelial cells.

Conclusion: The increased expression of TLRs in IBD patients may contribute to the heightened immunological response to bacteria especially those associated with lamina proprial macrophages.

292 HISTOLOGICAL PHENOTYPE OF CARD15 GENOTYPE

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Introduction: The histological features of Crohn’s disease (CD) are varied. The characteristic features of CD are considered to be skin lesions and focal ulceration with transmural inflammation, lymphoid aggregates and granulomas. Pyloric metaplasia is a well recognised feature of CD. The aim of this study was to investigate the relationship between the histological features and CARD15 genotype. CARD15 is expressed in Paneth cells of the small bowel. We therefore investigated whether Paneth cell numbers and distribution were related to CARD15 genotype.

Methods: Forty nine patients with CD and 10 controls who had had terminal ileectomy/right hemicolectomy were included in this study. Archival tissue that had been processed routinely was used for histological analysis. Venous blood was obtained for genotyping of the patients with CD. This study was approved by the local research ethics committees.

Results: Ten CD patients carried two CARD15 mutations, 17 one mutation, and 22 were wild type. CD patients who carried two CARD15 mutations had a significantly greater mean number (6.4) of Paneth cells than controls (2.1) and patients who had none (4.2) or one mutation (5.0) p < 0.001. Paneth cells were found significantly higher up the sides of crypts in patients who carried two CARD15 mutations than controls and other genotypes, p < 0.001. The presence of pyloric metaplasia was...
significantly associated with carriage of at least one CARD15 mutation, p<0.001. There was no association with CARD15 and inflammatory score, lymphoid aggregates, and granulomas.

**Background:** We have found a distinct histological phenotype correlated to CARD15 genotype. The finding of an association between pyloric metaplasia and CARD15 in CD is new and warrants further investigation. The increase in Paneth cell numbers in patients with 2 CARD15 mutations independent of degree of inflammation suggests that CARD15/NOD2 pathway may be involved in Paneth cell regulation.

**293 ASSOCIATION OF THE MDR1 GENE WITH INFLAMMATORY BOWEL DISEASE: A CASE CONTROL AND META-ANALYSIS STUDY**

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**Background:** Allelic variants of the multidrug resistance gene (MDR1/ABC1) which encodes the membrane bound efflux transporter P-glycoprotein 170 (Pgp-170) have been associated with inflammatory bowel disease (IBD), but with conflicting results. Our aim was to examine the association of MDR1 variants in a large British case control sample, and to carry out a meta-analysis of published studies.

**Methods:** The C3435T sequence variant in MDR1/TAP were genotyped in 828 Crohn’s disease (CD) and 580 ulcerative colitis (UC) cases and 285 healthy controls, and their effect on disease heterogeneity was examined. A meta-analysis was carried out of our results and those from eight published association studies of the C3435T variant in IBD, including a total of 1743 cases of UC, 2311 of CD, and 2931 controls.

**Results:** The 2677T allele was significantly increased in British UC cases compared to controls (45.2% v 39.6% p=0.034). In particular, the TT genotype was significantly associated with severe UC (OR 1.90, 95% CI 1.01 to 3.55) and in UC patients receiving steroids (OR = 1.77 95% CI 1.01 to 3.55) and in UC patients receiving steroid therapy alone prior to colectomy. Contrary to recent studies, no significant association was seen with C3435T and UC, (OR 1.08 to 2.88). No significant association was seen with C3435T and UC, (OR 1.01 to 3.55) and in UC patients receiving steroids (OR = 1.77 95% CI 1.01 to 3.55).

**Conclusions:** The meta-analysis we have carried out confirms the association of the C3435T sequence variants in a large British case control sample, and to carry out a meta-analysis of published studies.

**294 PREVALENCE OF CYTOMEGALOVIRUS IN COLECTOMY SPECIMENS FROM ULCERATIVE COLITIS PATIENTS**

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**Aim:** Controversy remains over the importance of cytomegalovirus (CMV) in ulcerative colitis refractory to medical therapy. It has been suggested that the infection rate is as high as 27% in steroid refractory disease (Maconi et al. 2005). Our aim was to determine the prevalence of cytomegalovirus (CMV) in colectomy specimens taken from UC patients.

**Methods:** Forty nine colectomy specimens taken from patients with ulcerative colitis were identified between the years 1990 and 2000. The sections between the UC cases and controls was the lower prevalence of H pylori in UC patients, (p=0.013), but not with CD.

**Results:** cDNA DGGE profiles were generated for every sample indicating an active bacterial colon in UC. Although the MSCs obtained for all paired comparisons were generally high, differences were seen amongst some patient groups.

**Discussion:** Overall, these data suggest that the bacterial communities from a “non-diseased” and a diseased colorectal region of an IBD patient are broadly similar. These results also indicate however that many bacterial species associated with the gut mucosa are active and that differences can be identified in the species that are present and active in these samples.

**295 ACTIVE BACTERIA ASSOCIATED WITH COLORECTAL BIOPSY SPECIMENS**

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**Background:** In order to differentiate between the bacteria merely associated with gut mucosa and those that are active, we have studied the marker bacterial rRNA. This molecule, only present in active bacterial cells, allows us to determine the levels of activity of species associated with diseased and non-diseased regions within patients.

**Methods:** Paired colorectal biopsies were taken for 10 patients with active inflammatory bowel disease (IBD). One inflamed biopsy and one uninfamed biopsy was taken. Nucleic acids were recovered directly from each biopsy. After dividing into DNA or RNA, rRNA was converted to cDNA by reverse transcription. Both DNA (bacteria present) and cDNA (bacteria active) templates were separately amplified using primers specific for phylogenetically informative ribosomal sequences within the Domain Bacteria. Both sets of PCR products were separately amplified using Denaturing Gradient Gel Electrophoresis (DGGE) to form profiles from which mean similarity coefficient (MSC) values were generated.

**Results:** cDNA DGGE profiles were generated for every sample indicating an active bacterial colon in UC. However in the control patient group, 23 (60%) were positive for the marker bacterial rRNA. This molecule, only present in active bacterial cells, allows us to determine the levels of activity of species associated with diseased and non-diseased regions within patients.

**Discussion:** Overall, these data suggest that the bacterial communities from a “non-diseased” and a diseased colorectal region of an IBD patient are broadly similar. These results also indicate however that many bacterial species associated with the gut mucosa are active and that differences can be identified in the species that are present and active in these samples.

**296 DETECTION OF HELICOBACTER SPECIES IN ARCHIVAL HUMAN ULCERATIVE COLITIS TISSUE BY FLUORESCENT IN SITU HYBRIDISATION**

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**Background:** The role of Helicobacter species in human inflammatory bowel disease (IBD) is controversial. This in part is due to differences in techniques used and to lack of definition of disease phenotypes.

**Aim:** To investigate archival paraffin embedded tissue from patients with confirmed ulcerative colitis (UC) for the presence of Helicobacter species.

**Subjects and Methods:** 100 UC patients (65 relapsing, 35 de novo) and 39 controls with a normal colonoscopy, had archival biopsies investigated. The biopsies were taken from throughout the colon. Fluorescent in situ hybridisation (FISH) assays were designed to differentiate H pylori from non-pylori Helicobacter species. The sections were analysed in triplicate.

**Results:** The Helicobacter genus was present in 33 of the 100 patients with UC. Of these, 31 were non-pylori and two were pylori species. However in the control group 23 (60%) were positive for the Helicobacter genus but only nine (23%) were non-pylori Helicobacter and 14 (35%) were H pylori. The only statistically significant difference between the UC cases and controls was the lower prevalence of H pylori in the colitis group (p<0.01). There was no difference in prevalence of non-pylori Helicobacters between de novo presenting and relapsing colitis patients. The distribution of Helicobacter species was predominately in the left side of the colon in both the colitis and control patients. The Helicobacter species were detected on the mucosa and in colonic crypts, in both inflamed and non-inflamed biopsies.

**Conclusions:** Non-pylori Helicobacter species are commonly detected in UC patients and subjects with normal colons. The role of these species in the pathogenesis of UC, if any, remains to be established.
297 FURTHER CHARACTERISATION OF MUCOSA ASSOCIATED ESCHERICHIA COLI ISOLATES FROM CROHN’S DISEASE AND COLON CANCER PATIENTS

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Introduction: We previously reported that E coli isolated from biopsies taken from Crohn’s disease and colon cancer patients displayed enhanced adherence to erythrocytes and intestinal cell lines whilst lacking the conventional markers of bacterial pathogenicity (Gastroenterology 2004;127 80–93). Here we describe further phylogenetic and phenotypic characterisation of these strains.

Methods: For phylogenetic analysis, 21 strains of CD and colon cancer associated E coli (14 adherent and 7 non-adherent strains) were screened for the presence of the chuA, and yjaA genes, and the TSPE4.C2 DNA fragment (Appl Environ Microbiol 2000;66:6555–8). Haemagglutination (HA) and HEP-2 cell adhesion assays were performed using all adherent E coli strains.

Results: All adherent isolates and 2/7 non-adherent isolates were classed into E coli phylogenetic groups D1 or D2, characteristic of virulent extra-intestinal E coli. This grouping was performed on the basis of the presence of the chuA gene required for haem transport in enterohaemorrhagic O157:H7 E coli. Five out of seven non-adherent isolates were classed into E coli phylogenetic groups A1 or B1, characteristic of commensal E coli. 11/14 adherent isolates displayed adherence to HEP-2 cells in a pattern characteristic of diffusely adherent E coli (DAEC). All adherent strains displayed chloramphenicol resistant HA indicative of specificity to cell surface receptors other than DAF (CDS3), possibly CEACAMs. Strong haemagglutinating activity was found in some bacterial supernatants suggesting secretion of a bacterial adhesion factor, possibly on shed microvesicles.

Conclusions: Adherent mucosa associated E coli strains isolated from CD and colon cancer display attributes characteristic of virulent extra-intestinal E coli, and probably represent typical or atypical DAEC.

298 EFFECT OF INFLAMMATION ON GUT FLORA DIVERSITY IN INFLAMMATORY BOWEL DISEASE PATIENTS: 16S RNA SEQUENCE ANALYSIS

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Introduction: Gut mucosa associated flora play a key role in the pathogenesis of inflammatory bowel disease (IBD). 16S rDNA is universally distributed among prokaryotes and is reliable source for deducing phylogenetic relationships.

Aim: The aim of this study was to examine how the mucosal adherent microbial communities differ between inflamed and non-inflamed sites in the GI tract of IBD patients and also between different mucosal sites by large scale 16S rDNA sequencing.

Methods and Results: Mucosal biopsies of the inflamed and non-inflamed sites were obtained from IBD patients and controls undergoing colonoscopy. The 16S rDNA genes from each separate biopsy sample were amplified using a low number of PCR cycles, clone library established and approximately 1000 clones from each library sequenced. Phyotype census was constructed for each sample and total novel phyotype presence calculated. Nonchimeric 16S rDNA sequences were further analysed and phylogenetic groups determined. The bacterial phyotype distribution generated from different mucosal sites in two patients, based on 4000 clone sequences (Fig) revealed increased Bacteroidetes and decreased Proteobacteria in inflamed sites.

Conclusions: 16S rDNA molecular characterisation of the mucosal associated flora demonstrates specific changes at sites of inflammation. Further characterisation may provide insights into pathogenic significance of these changes.

299 INFliximab THERAPY FOR CROHN’S DISEASE CAN BE SAFELY INFUSED OVER ONE HOUR WITHOUT INFUSION REACTIONS

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Background and Aim: Infliximab (chimeric monoclonal anti-TNFα anti-body therapy) is licensed for the treatment of rheumatoid arthritis (RA) and Crohn’s disease (CD). Maintenance therapy is indicated for both refractory and fistulating CD. In both conditions maintenance treatment is prescribed at 8 weekly intervals. A two hour infusion regime followed by a two hour observation period is recommended, meaning patients spend ½ day in hospital every 8 weeks receiving their infusion. Reduced infusion time for the treatment of RA has been studied with good success. The aim of this study was to determine whether reduced infusion time would be tolerated in patients with CD, and to assess the safety within the day care setting.

Methods: Patients who had previously received at least four infusions of infliximab at the standard rate of two hours with no adverse effects and no other excluding factors were selected over a 10 week period. Informed consent was obtained. All patients received pre-medication with intravenous hydrocortisone, followed by a one hour infliximab infusion with a one hour post infusion observation period. Infusion reactions, side effects or delayed hypersensitivity reactions were noted.

Results: Thirteen patients received the one hour infliximab regime compared to 20 who received the usual two hour regime during the study period. Within the one hour infusion group, 9/13 (69%) were receiving concomitant immunosuppressant therapy compared to 18/20 (90%) within the two hour infusion group. No infusion reactions or adverse events were observed in either patient group. No patients reported symptoms of delayed hypersensitivity reactions.

Conclusion: CD patients who had previously received four or more infliximab infusions over two hours with no adverse events tolerated reduced infusion rates of one hour well with no immediate or delayed adverse reactions. Faster infusion rates save time for both patients and health care professionals and facilitate better use of healthcare resources within the day care setting.

300 COMBINATION THERAPY OF INFliximab AND AZATHIOPRINE REDUCES DISEASE PROGRESSION IN CROHN’S DISEASE

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Introduction: The Vienna classification of Crohn’s disease (CD) categorised disease behaviour into a hierarchy of inflammatory, structuring, and penetrating types. 92% of patients have been shown to progress over a 20 year period. Infliximab induces mucosal healing...
and clinical remission; it is unknown whether this drug reduces the progression of disease type. We aimed to examine the impact of episodic infliximab treatment on the progression of disease behaviour in CD.

**Methods:** Seventy three CD (38I) patients who received episodic infliximab were assessed, together with an age and sex matched control group comprising 73 patients who had received azathioprine for at least four months. Both groups had two years' follow up during which disease progression events were identified. Demographic details, disease characteristics, and treatment history were collected. Kaplan-Meier survival curve analysis, the log rank test, and multiple logistic regression were used to test for differences and identify independent variables associated with disease progression.

**Results:** Twice as many patients experienced progression of disease type in the azathioprine (70%) group compared with the infliximab group (58%; p = 0.165). In a second analysis, patients on both azathioprine and infliximab (n = 17) had less disease progression compared to those on azathioprine alone (0.17 v 10.5, p = 0.045). Surgical rates did not differ. Disease progression was also associated with significantly more disease flares (p = 0.017) and higher surgical rates (p = 0.000). Multivariate analysis identified smoking at treatment induction and concomitant usage of corticosteroids as independent predictors of disease progression.

**Conclusion:** Combination therapy with episodic infliximab and azathioprine retards the progression of disease in CD and therefore may alter the “natural” history of this disease. Smoking at treatment induction and concomitant corticosteroid therapy are independent predictors of disease progression. In this short term study, the need for surgery was not affected by infliximab usage.

**302 USE OF PHOTOPHORETIC THERAPY IN THE TREATMENT OF REFRACTORY CROHN’S DISEASE**

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**Introduction:** Crohn’s disease (CD) is an incurable chronic debilitating illness. Despite conventional treatments that include steroids, aminosalicylates, 2nd line immunosuppressants, infliximab, and surgery, management remains difficult with many side-effects. Photopheresis therapy (photopheresis) is a treatment modality that is emerging as a new treatment for CD.

**Aim:** To study the response of patients with refractory CD, who had failed conventional treatments and undergone multiple surgeries, to photopheresis treatment.

**Methods:** Patients with refractory CD were treated with photopheresis in a Therakos cell separator. Ultraviolet A light was used for photoactivation of T cells and macrophages which have been photosensitised by 8-methoxypsoralen. Each treatment session consisted of two photopheresis sessions in two consecutive days. In four patients, treatment sessions were planned for every fortnightly for six months then monthly for another six months. One patient was treated fortnightly for six weeks, then monthly for six months followed by 3 monthly for a year.

**Results:** All five patients treated were male and their mean age was 37.2 years old. One patient withdrew from the treatment due to the long distance he had to travel. The patient on the longer but less intense treatment regime had a partial response. The remaining three patients had good response to the treatment. The response included needing less medication (one patient stopped steroid after being steroid dependent for years), decrease in bowel movement frequency, less abdominal pain, less PR discharge, or improvement in the quality of life. None of the patients had significant side effects.

**Conclusion:** Early experience shows that photopheresis could be effective in the treatment of refractory CD. The treatment is well tolerated. This is the largest cohort of patients with refractory CD treated with photopheresis to date in United Kingdom. A larger formal study will now be undertaken to study the effectiveness of this treatment.
306 AVERSE EFFECTS AND RELAPSE RATE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TAKING AZATHIOPRINE VERSUS 5-ASA AND AZATHIOPRINE

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Introduction: An interaction between AZA and 5-ASA may exist, but the mechanism is unclear. There are limited data looking on the clinical impact of this interaction.

Aims: To assess the effect of 5-ASA treatment in conjunction with AZA on adverse events (AEs) and relapse rate in IBD.

Method: A retrospective study of 223 patients taking AZA for IBD was performed. 95 patients received AZA alone (group I) and 104 received combination of 5-ASA and AZA (group II). In 24 patients it was not known whether AZA was given alone or with 5-ASA (group III). Data were collected on AE while taking AZA, its dose and the TPMT level. In 114 patients, rate of relapse of IBD was compared in groups I and II.

Results: Relapse was defined as symptoms requiring increased medical therapy or surgery while on >3 months of AZA. Patients in whom AZA was withdrawn in <3 months due to AEs were recorded in both groups.

Results: Total frequency of AE was 39% (88/223). AE were more common in group II (48%, 50/104), than in group I (30%, 29/95) (p = 0.05). AEs occurred in 37% (9/24) of group III. In group I patients with AE, TPMT was normal in 18/20 in which it was measured. In group II, TPMT was normal in 23/24 with AE. Low dose AZA (<2 mg/kg) was taken in 19/31 (61%) of group I and 32/50 (64%) of group II. Normal TPMT level and taking low dose AZA did not reduce relapse rate in group II (29/73, 43%) than in group I (12/41, 29%) (p = 0.02). Patients in whom AZA was discontinued in <3 months due to AEs were more common in group II (33%), c.f. Group I (12%). Patients taking AZA and 5-ASA were more likely to suffer relapse or discontinue AZA (due to AEs), than patients who took AZA alone (p = 0.001).

Conclusion: Adverse effects appeared more common in those taking combination treatment. These AE were noted despite patients being on low dose of AZA and with normal TPMT levels. The incidence of relapse was significantly higher in patients taking AZA + 5-ASA. In light of chemopreventive effects of 5-ASA, we would not recommend the combination is not prescribed, rather that lower dose of 5-ASA may be preferable and better tolerated in patient taking AZA.

307 ACCELERATED INFliximab INFUSIONS ARE SAFE AND WELL TOLERATED IN THE TREATMENT OF CROHN’S DISEASE

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Introduction: Infliximab is available in standard and accelerated dosing. Whether accelerated dosing affects clinical outcomes is unknown.

Aims: To assess whether shorter infliximab infusion times are safe and well tolerated in the treatment of CROHN’S DISEASE.

Background: The manufacturer’s instructions recommend that infliximab is administered as a two hour infusion with obs for two hours post infusion. A previous retrospective audit at the LGI of 352 infliximab infusions in 62 patients (average 5.7 infusions/patient) revealed a total of five infusion reactions. Reduced infusion times after 4th dose is standard for RA patients in the Leeds IMID centre (Buch et al. 2004).

Methods: The Leeds IMID centre has been established to provide biological therapies to patients with IBD, RA, psoriatic arthritis, ankylosing spondylitis, and psoriasis. A prospective audit of accelerated infliximab infusion in patients with Crohn’s disease was performed. The infusions were given over the standard two hours then reduced to one hour or 30 minutes as follows:

Results: Between May 2003–Oct 2005 56 patients were treated according to the above regimen (17 male, 39 female; age range 17–84). 38 patients were taking azathioprine or 6MP, 11 methotrexate, one mycophenolate, and six received 200 mg hydrocortisone pre-infusion. Of a total of 116 infusions 58 were completed over one hour and 10

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305 PREOPERATIVE STEROID USE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND RISK OF POSTOPERATIVE COMPLICATIONS: META-ANALYSIS OF OBSERVATIONAL STUDIES

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Introduction: Patients with inflammatory bowel disease (IBD) are frequently treated with steroids. Almost a third of them will require surgery within a year of treatment with steroids. Studies examining postoperative complication risk associated with use of steroids in patients with IBD have yielded conflicting results. The purpose of this meta-analysis was to estimate the risk of postoperative infectious complications following abdominal surgery in patients with IBD on steroids at the time of surgery.

Methods: We searched electronic databases Pubmed, EMBASE, CINHAL, Ovid, Zelac, and Ingenta, and hand searched citations from the reference lists in all the articles identified. Studies were excluded if patients had been on steroids in the month preceding surgery, compared with a control group. Studies that evaluated infectious postoperative complications in the two groups with duration of postoperative follow up of a maximum of 30 days or the hospitalisation period were included in the analysis. Data for calculation of odds ratios (OR) had to be provided or could be calculated from the tables or figures for the study to be included. We used the random effects model to calculate pooled odds ratios and 95% confidence intervals.

Results: All six studies that met the inclusion criteria were observational studies. Pooled analysis showed an increased risk of infectious postoperative complications among patients on steroids (OR 1.60, 95% CI 1.17 to 2.20).

Conclusions: This is the first meta-analysis on risk of postoperative infectious complication in patients with IBD taking steroids. Our data indicate that there is an increased risk of infectious complications following the preoperative use of steroids. This is consistent with data on preoperative steroid use and risk of postoperative complications in other general medical patients.
over 30 minutes. There were four infusion reactions (3.4% of total infusions: three patients with two hour infusions, one in one hour infusion, none in 30 minute infusions). No patient required cessation of IFX therapy.

**Conclusion:** Accelerating IFX infusions according to protocol is safe and well tolerated in the treatment of Crohn’s disease. This allows more patients to be treated per session and improves patient convenience.

**SAFETY OF MODIFIED RELEASE ORAL MESALAZINE 4.8 G/DAY (800 MG TABLET) COMPARED TO 2.4 G/DAY (400 MG TABLET) FOR TREATMENT OF ACTIVE ULCERATIVE COLITIS: ANALYSIS OF COMBINED DATA FROM TWO RANDOMISED, DOUBLE BLIND, CONTROLLED TRIALS**

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**Introduction:** To evaluate the safety of an investigational 800 mg mesalazine dose at 4.8 g/day, compared to that of a currently marketed US 400 mg mesalazine tablet dose at 2.4 g/day for the treatment of mildly to moderately active ulcerative colitis.

**Aims and Methods:** Two randomised, double blind, six week, parallel group studies (ASCEND I & II) were conducted to compare the safety and efficacy of a new 800 mg tablet formulation of modified-release mesalazine (P&G Pharmaceuticals), dosed at 4.8 g/day, to that of a marketed 400 mg tablet (Asacol, USA), dosed at 2.4 g/day, in patients with newly or previously diagnosed mildly to moderately active ulcerative colitis. Safety assessments included adverse events (AEs), physical examinations, vital signs, and clinical laboratory evaluations.

**Results:** In treatment groups, the most commonly reported AEs (headache; flu syndrome; respiratory infections; and digestive symptoms) were similar to the US marketed 400 mg tablet. The majority of AEs were assessed by investigators as mild or moderate in severity. The AE experience was similar across subgroups examined, including age, sex, race, and baseline disease state. Serious AEs were reported in 9 patients (two in the 4.8 g/day group and seven in the 2.4 g/day group), and primarily involved the digestive system (worsening ulcerative colitis signs and symptoms, nausea, vomiting, epigastric pain, cholecystitis, and pancreatitis). Non-gastrointestinal serious AEs assessed as related to mesalazine therapy were nephritis (one patient in the 2.4 g/d group) and pericarditis (one patient in the 4.8 g group).

**Conclusion:** The safety profile of mesalazine 4.8 g/day, administered as an 800 mg tablet, is comparable to the post-marketing and clinical experience of the 400 mg marketed tablet at 2.4 g/d.

**MESALAZINE STARTING DOSE AND TIME TO FLARE AMONG ULCERATIVE COLITIS AND CROHN’S DISEASE PATIENTS**

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**Introduction and Aim:** It has been hypothesised that newly diagnosed inflammatory bowel disease (IBD) patients who start on a higher dose of mesalazine therapy may prolong the time to occurrence of a flare compared to patients who begin with a lower dose. The aim of this study was to quantify the time to flare among IBD patients receiving at or above the median average daily starting dose versus below the median average daily starting dose.

**Methods:** A retrospective cohort study was conducted using data from Saskatchewan Health (Canada). Patients with a 400 mg strength/tablet mesalazine prescription between 1 January 1990 and 31 December 2002 (index date) were followed until the time of a flare. A flare was defined as an interval of >6 months until a subsequent 5-aminosalicylate (5-ASA) prescription at the same dose or a 5-ASA prescription at a higher dose; or a glucocorticosteroid or immunomodulator prescription >4 months after the index date. We identified ulcerative colitis (UC) and Crohn’s disease (CD) patients with a diagnosis >60 days from the index date. Mesalazine patients with a UC or CD diagnosis >60 days to <12 months before the index date and patients with a record of 5-ASA or immunomodulator therapy in the 12 month period prior to the index date were excluded from the study. The median average daily starting dose over the first 100 days following the index date was computed to differentiate between higher starting dose and lower starting dose.

**Results:** 896 UC and CD patients with a 400 mg strength/tablet mesalazine prescription were identified (566 patients were UC and 330 were CD). The median time to flare after the index date was 346 days among patients with UC (n=310) and an average daily starting dose of >1.6 g/day, compared to a median time to flare of 269 days for UC patients (n=256) with an average daily dose of <1.6 g/day (p=0.01). CD patients (n=165) with an average daily starting dose of >1.35 g/day had a median time to flare of 286 days versus 260 days for CD patients (n=165) averaging <1.35 g/day (p=0.02).

**Conclusion:** The results suggest that patients with UC or CD starting mesalazine therapy and receiving a higher average daily starting dose prolong their time to flare occurrence compared to patients with a lower average daily starting dose.

**HIGH DOSE MESALAZINE 4.8 G/DAY (800 MG TABLET) COMPARED TO MESALAZINE 2.4 G/DAY (400 MG TABLET) DEMONSTRATES INCREASED EFFICACY IRRESPECTIVE OF DISEASE LOCATION**

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**Background:** Extent of disease is an important aspect of ulcerative colitis. The purpose of this analysis was to investigate the consistency of the treatment effect across various disease extents. Dosages were set for six weeks. Percentages were calculated as proctitis, proctosigmoiditis, left sided colitis, and pancolitis.

**Methods:** Two prospective, double blind, randomised controlled trials (ASCEND I and II) were pooled and analysed. Patients with mildly to moderately active ulcerative colitis (UC) were randomised to receive either mesalazine 4.8 g/day with an 800 mg tablet or mesalazine 2.4 g/day with a 400 mg tablet for six weeks. The endpoint was the % of patients with moderately active UC who achieved treatment success, defined as complete or partial response based on clinical, endoscopic, and physician assessments. The Crohn Mantel-Haenszel test was calculated after stratifying for trial and baseline disease extent and the Breslow-Day test for homogeneity was used to investigate if the treatment effect was different across the varying disease extents.

**Results:** Of the 448 patients with active moderate UC at baseline, 152 (34%) had left sided colitis, 129 (29%) had proctosigmoiditis, 100 (22%) had pancolitis, and 67 (15%) had proctitis. There were no statistically significant differences for any baseline characteristics of extent of disease between the two treatment groups. Overall treatment success at week 6 observed a statistically significant efficacy benefit for 4.8 g/day regardless of disease extent (p = 0.003). There was insufficient evidence to suggest that the treatment effect was different across each of the disease extent areas (p = 0.965). Patients with left sided disease, (including proctitis, proctosigmoiditis and left sided colitis) demonstrated a significant treatment success in the 4.8 g/day (72%) group versus the 2.4 g/day (59%) p = 0.0132.

**Conclusion:** The treatment differences observed between the 2.4 g/day and the 4.8 g/day groups were consistent across all extents of disease indicating that 4.8 g/day dosing provides an increased efficacy benefit regardless of disease extent. Moderately active UC patients, with left sided disease, demonstrate an increased treatment benefit taking mesalazine 4.8 g/day compared to 2.4 g/day.

**THE EFFECTIVENESS OF CONTINUING THE INDUCTION DOSE OF ASACOL INTO THE MAINTENANCE PHASE: RESULTS FROM THE COMMUNITY SETTING**

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**Aim:** There is anecdotal evidence that maintaining the induction dose may be better than dose reduction to prevent relapse. This study used a naturalistic, retrospective design to compare the outcomes of community based ulcerative colitis (UC) patients maintained on the dose used to induce remission with those whose maintenance dose was reduced.

**Methods:** The medical records from 411 UC patients from 39 geographically dispersed, community gastroenterology practices, within the United States, who had a disease flare between 1999 and 2003 successfully treated with US Asacol (Procter and Gamble Pharmaceuticals, Inc) without requiring steroids were reviewed. The review included the single flare of interest and the subsequent maintenance period of 12 months. Outcome measures examined were...
maintenance of remission post-induction, and % rated “normal” on the physician global assessment of symptom severity (PGA) at final data capture. The primary explanatory variable was the relation between maintenance (M) and induction (I) dose, coded as M=I versus M<1. Other covariates examined were:

- Final induction dose: grouped on g/day, < 2.4, 3.2–4.0, > 4.8
- Extent of disease: proctitis/proctosigmoiditis vs left-sided vs extensive
- Severity of disease: mild vs moderate-severe
- Prior treatment history (PH): 1st flare v subsequent flare without immediately prior maintenance medication v subsequent flare while on maintenance medication.

Results:

Of the 411 patients, 178 (43%) patients had mild starting PGA and 233 (57%) had moderate/severe starting PGA. No variables were significantly (p<0.05) predictive of maintenance of remission. In logistic regression analysis, starting PGA and M=I vs M<1 were significantly associated with final PGA. M=I patients were twice as likely to achieve “normal” final PGA compared to M<1 patients (p<0.01, OR = 2.21, 95% CI 1.36 to 3.58).

Conclusions:

Maintaining the same dose of Asacol used to induce remission significantly increased the likelihood of UC patients receiving a physician’s global assessment of “normal” at one year post-induction.

312 UNDER APPROPRIATE CONDITIONS LYMPHOCYTE APOPTOSIS IS CAUSED NOT ONLY BY INFLIXIMAB AND ADAлимУМБАК BUT ALSO BY ETANЕРЦИНТ IN VITRO

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Background: Apoptosis is considered an important mechanism of action of anti-TNF therapy in Crohn's disease. Infliximab, but not etanercept, has been reported to cause apoptosis in stimulated peripheral blood and lamina propria T lymphocytes in healthy controls and Crohn's disease patients (as detected by annexin-V). We report on the importance of the timing of anti-TNF drug addition on the induction of stimulated peripheral CD4 T lymphocyte apoptosis.

Methods: Peripheral CD4 T lymphocytes were isolated from healthy subjects (n = 4) and stimulated with antiCD3 and antiCD28 antibody. Medium with or without drug was added either simultaneously or delayed for 72 hours. Control antibody was used as a negative control and cisplatin as a positive control. Apoptosis was detected after seven days stimulation using annexin V and topo-3 by flow cytometry. Three anti-TNF agents—infliximab, adalimumab, and etanercept—were used at 10 μg/ml.

Results: Following anti-TNF drug addition to lymphocytes stimulated for 72 hours the apoptosis rates compared to background apoptosis (that is apoptosis of stimulated cells with medium alone added) were 91%, 89%, and 88% for infliximab, adalimumab, and etanercept respectively. With simultaneous stimulation and anti-TNF drug addition lymphocyte apoptosis compared to background was 240%, 212%, and 172% with apoptosis compared to background when anti-TNF drug was added concurrently at the time of stimulation and anti-TNF drug addition lymphocyte apoptosis following synchronous drug addition and stimulation was significant for all three anti-TNF agents (paired t-test p<0.05).

Conclusion: We detected an increase in lymphocyte apoptosis above background when anti-TNF drug was added concurrently at the time of stimulation but not when the addition of the agent was delayed for 72 hours post stimulation. In our in vitro model anti-TNF induced apoptosis is dependent on the degree of lymphocyte stimulation. Under the presence of only infliximab and adalimumab but also etanercept causes lymphocyte apoptosis.

313 SQ31 HAPLOTYPE AND RELAPSE AFTER SMALL BOWEL RESECTION

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Introduction: Crohn’s disease is a relapsing remitting disease. The majority of patients with terminal ileal Crohn’s disease will require surgery and often this will need to be repeated. There are few reliable predictors of outcome after surgery. The c allele of the SQ31 haplotype has been found to be associated with Crohn’s disease. We therefore investigated whether carriage of this allele was associated with more rapid relapse after terminal ileal resection in a cohort of well characterised patients with Crohn’s disease.

Method: Patients who had had ileal resection for Crohn’s disease were genotyped for the c and g allele of the Sq31 haplotype. Results are expressed as wild type gg genotype, heterozygote gc and homozygote cc. Age at first operation and postoperative smoking status were obtained from patient records and direct interview. Duration of follow up if no surgical recurrence and time to second operation was analysed with respect to Sq31 genotype using Kaplan-Meier survival curves.

Results: 172 [111 female, 82 smokers] patients were genotyped for the Sq31 haplotype; 45 were wild-type, 87 heterozygote, and 40 homozygote. There was no difference in survival to second operation between Sq31 genotypes. The detrimental effect of smoking on survival to second operation was maintained between Sq31 genotypes, p = 0.017. There was no difference in age at first operation or number of resections and Sq31 genotypes.

Conclusion: We confirm the association between smoking and shorter time to second small bowel resection. Carriage of the disease associated Sq31 allele is not associated with more rapid or more frequent relapse after small bowel surgery in this cohort of Crohn’s disease patients.

314 SERUM PROTEIN SIGNATURES DETERMINED BY MASS SPECTROMETRY (SELDI-TOF) ACCURATELY IDENTIFIES PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is an idiopathic chronic disease of the gastrointestinal tract with many debilitating sequelae some of which is life threatening. Diagnosis of IBD often depends on invasive testing. Non-invasive serological testing such as ASCA and pANCA are insufficiently specific or sensitive for routine diagnostic use. We aimed to develop a novel diagnostic approaches based on differences in protein signatures in sera obtained from individuals with IBD and controls using surface enhanced laser desorption and ionisation time of flight (SELDI-ToF) mass spectrometry (MS).

Methods: We studied protein signatures from 59 patients with IBD and 64 controls (normal and patients with other inflammatory pathology). Protein signatures were obtained using a CM10 chip (weak cation exchange chip), and analysed with SELDI-ToF MS. Preliminary analysis was performed using ‘p’ value determination of integrated peaks. Statistical and neural network analysis was performed using support vector machine techniques using radial basis function kernels. Significant peaks used for discrimination were selected using both Fisher’s and recursive feature elimination (RFE) techniques.

Results: Comparing IBD and controls using support vector machine SVM analysis with a radial basis function kernel (width 5), limited to two peaks selected by RFE, we obtained an accuracy of 97%, sensitivity of 95%, and specificity of 98%. The same analysis for two peaks chosen by Fisher’s scores resulted in an accuracy of 98%, sensitivity of 98%, and specificity of 98%. The peaks selected by both techniques were also significantly discriminative when used in individual peak analysis.

Conclusions: Using protein signatures of patients with IBD and controls we have developed a model of classification which has high accuracy and is more informative than currently available serological tests. Cross validation and characterisation of discriminant peaks is currently underway.

315 ROLE OF INFLIXIMAB IN DOWNREGULATING MATRIX METALLOPROTEINASE-3 IN CROHN’S DISEASE

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Background and Aims: Excessive matrix metalloproteinase (MMP) induced degradation of mucosal matrix is the final step in the cascade of events leading to tissue injury in inflammatory bowel disease. TNF-α blockade prevents matrix degradation concomitant with inhibition of MMP-3 production in an ex vivo model of gut T cell mediated matrix degradation. On this basis, we investigated the effect of infliximab on the mucosal expression of MMP-3 in Crohn’s disease (CD) patients.

Methods: Six steroid refractory CD patients received 3 consecutive infusions of infliximab administered at week 0, 2, and 6 at a dose of
5 mg/kg. Colonoscopy and ileoscopy were performed immediately before the start of the therapy and 10 weeks later, with collection of multiple biopsies. MMP-3 mucosal transcript expression was studied by in situ hybridisation. Fibroblasts isolated from 6 active CD patients and five controls were stimulated in vitro with infliximab, etanercept or TNF-α. After 24 hours culture, MMP-3 expression was determined by western blotting.

**Results:** All six CD patients responded to treatment, four with a complete response, and two with a partial response. MMP-3 mucosal expression was reduced after 10 week treatment, with a higher decrease in patients who had a complete response. While TNF-α increased MMP-3 production, infliximab inhibited spontaneous MMP-3 production. Etanercept was more effective than infliximab in downregulating MMP-3 production.

**Conclusions:** These findings suggest that one of the way in which anti-TNF-α strategies heal mucosa in CD patients is by directly inhibiting MMP-3 production by fibroblasts.

### Colorectal posters

#### 316 ASSOCIATION OF CLINICAL RESPONSE WITH ELEVATED PLASMA INTERLEUKIN-1 RECEPTOR ANTAGONIST DURING SELECTIVE GRANULOCYTOPHERESIS IN PATIENTS WITH REFRACTORY ULCERATIVE COLITIS

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**Background:** In inflammatory bowel disease (IBD), granulocytes and monocytes/macrophages (GM) are elevated with activation behaviour, prolonged survival, and are found in vast numbers within the intestinal mucosa. They are potential sources of cytokines, other tissue damaging substances and therefore, are suspected to contribute to IBD. The Adacolumn can deplete activated GM, up to 65% of GM and a small fraction of lymphocytes adherent to the column leukocytapheresis carriers. This is followed by an increase in the naive (CD10 negative) fraction of neutrophils in the peripheral blood. This study was to investigate the effect of Adacolumn on plasma concentration of interleukin-1 receptor antagonist (IL-1ra), a potent anti-inflammatory cytokine.

**Methods:** Twenty six patients with chronic or repeated relapses of UC were included. Patients received one Adacolumn session/week for five consecutive weeks. Clinical response was defined as Δclinical activity index (ΔCAI = CAI at entry − CAI at post > 10), while remission was defined as CAI ≤ 4. During the procedure, blood was collected for measuring IL-1α, IL-1β, and IL-1ra.

**Results:** Twenty one of 26 patients responded (19 achieved remission). Plasma from responder patients, but not non-responders showed a significant (p < 0.01) increase in IL-1ra in the Adacolumn outflow (blood return to patients). Further, incubation of blood with the Adacolumn carriers in vitro settings showed that the release of IL-1ra from GM was adhesion dependent. Neither at the column outflow nor during the incubation of blood with the carriers, TNF-α or IL-1β increased.

**Conclusions:** The high level of clinical response in patients who had failed drug therapy reflects that GM might have a major role in the perpetuation of UC. Release of IL-1ra might be another mechanism by which Adacolumn can alter cytokine profiles in the circulation.

#### 317 DOES UNCOMPLICATED COLONIC DIVERTICULAR DISEASE CAUSE SYMPTOMS?

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**Background and Aims:** Colonic diverticular disease (DD) is often found among older individuals with colonic symptoms but it is unclear whether DD causes symptoms in the absence of acute diverticulitis. We now report the effect of psychosocial factors on symptoms in this group.

**Methods:** A questionnaire regarding episodes of abdominal pain, diarrhoea, constipation, and most other colonic symptoms, except for difficulty in passing a stool, was not different among those with DD compared with those with normal colons. In the absence of acute diverticulitis, DD is probably not a major cause of abdominal symptoms.

#### 318 DARK BLOOD ON THE RECTAL MUCOSA: IS IT SINISTER?

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**Background:** Assessment of patients by rigid sigmoidoscopy occasionally reveals dark (transported) blood on the rectal mucosa but not its origin. We felt this was sinister. There is however, no evidence to support this view.

**Aim:** To assess the significance of finding dark red blood on the rectal mucosa.

**Method:** All patients in whom dark blood was seen on the rectal mucosa in the outpatient clinic of one surgeon underwent colonoscopy.

Thirty six patients, (16 M, 20F), mean age 61 years (range 31–87) had dark blood seen on the rectal mucosa. Dark blood was seen in 9 patients with diverticulosis, 12 patients with UC, and 15 patients with colitis. Dark blood was seen in patients with diverticulosis following an episode of acute diverticulitis.

**Discussion:** Dark blood on the mucosa is a significant finding. The underlying pathology is usually a high risk adenoma but 15% of patients have colonic cancer. The cancer or largest adenoma is usually found distal to the splenic flexure but 20% of cases will have synchronous proximal neoplasia.

**Conclusion:** Patients in whom rigid sigmoidoscopy reveals dark blood on the rectal mucosa require prompt, complete colonoscopy with polypectomy as required.
320 DO RADIO OPAQUE TRANSIT STUDIES PREDICT QUALITY OF LIFE IN PATIENTS WITH CHRONIC CONSTIPATION?

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Introduction: Transit marker studies are commonly used to assess severity in chronic constipation but have not been validated for this purpose.

Aim: To determine whether results of transit studies correlate with QOL measurements obtained using validated QOL instruments in patients with chronic constipation.

Methods: 110 out of 163 consecutive patients referred to a dedicated constipation clinic at Durham completed evaluations of QOL and colon transit. Patients met Rome II criteria for idiopathic constipation. Median age was 49 years (range 18–77), 75% were female. Symptom duration: 10.5 years. The Gastrointestinal Quality of Life Index (GIQLI) and Patient Assessment of Constipation–Quality of Life (PAC-QOL) were completed by the patients. A high GIQLI suggests better QOL. A high PAC-QOL suggests poorer QOL. Transit studies performed using a recognised protocol with Sitzmark markers (Konsyl), one capsule on three consecutive days, with an x-ray on the 4th day. Segmental marker counts obtained and results expressed as TSM-out (number of markers passed at day four, ie 72–total remaining) and TSM-centre (the average marker position). The assessments were performed at the first consultation and represented the baseline state before intervention or therapy in clinic. Analysis using Pearson correlation coefficient.

Results: There was no correlation between transit study results and QOL assessments. Correlation coefficients: TSM-centre v GIQLI, r = 0.057; TSM-centre v PAC-QOL, r = 0.036; TSM-out v GIQLI, r = 0.034; TSM-out v PAC-QOL 0.092. There was good correlation between GIQLI and PAC-QOL, r = 0.562 (p < 0.001). Correlations between other pairs were effectively not different to zero.

Conclusion: Transit study results in chronic constipation did not predict quality of life. We have previously shown that they do not correlate with symptoms. This is therefore unlikely that they could be used to assess the severity of constipation. They may still have a use in management to symptoms either. It is therefore unlikely that they could be used to assess quality of life. We have previously shown that they do not correlate with Transit study results in chronic constipation did not predict effect effectively not different to zero.

PAC-QOL 0.092. There was good correlation between GIQLI and PAC-QOL. Correlation coefficients: TSM-centre vs GIQLI, r = 0.057; TSM-centre vs PAC-QOL, r = 0.036; TSM-out vs GIQLI, r = 0.034; TSM-out vs PAC-QOL 0.092. There was good correlation between GIQLI and PAC-QOL, r = 0.562 (p < 0.001). Correlations between other pairs were effectively not different to zero.

Conclusion: Transit study results in chronic constipation did not predict quality of life. We have previously shown that they do not correlate with symptoms. This is therefore unlikely that they could be used to assess the severity of constipation. They may still have a use in management to symptoms either. It is therefore unlikely that they could be used to assess quality of life. We have previously shown that they do not correlate with Transit study results in chronic constipation did not predict effect effectively not different to zero.

PAC-QOL 0.092. There was good correlation between GIQLI and PAC-QOL.
Eighteen patients are now deceased (median survival 50 days, range 6–349).

**Conclusion:** Most patients had a technically satisfactory outcome in this series. Our experience supports a role for colorectal stenting as an important therapeutic option in improving outcome and reducing morbidity in the management of advanced or metastatic colorectal cancer.

**324 NEOADJUVANT THERAPY FOR ADVANCED RECTAL CANCER: RESULTS OF SHORT TERM FOLLOW UP**

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**Introduction:** The outcome of advanced rectal cancer has improved with the introduction of neoadjuvant chemotherapy. Our objective was to evaluate the short term outcome of patients who were treated with neoadjuvant therapy and total mesorectal excision (TME).

**Method:** Thirty five consecutive patients (male 22, female 13; median age 55 years (25–77)) diagnosed with locally advanced rectal cancer were treated with protocol based long course chemoradiotherapy (radiation 4500cGy and 5-fluorouracil) before they were subjected to neoadjuvant rectal excision with total mesorectal excision (TME). All patients were prospectively followed up between April 2000 and September 2005. Data sought include: duration of survival, disease free interval, operative blood loss, tumour stage prior to chemoradiation, histopathological examination of resection margin (R0–no resection margins involved, R1–at least one involved margin), tumour regression grade (TRG 1–4, 1 = complete response, 4 = poor or no response) and tumour recurrence. Statistical analysis was performed with χ² test and Kaplan Meier method using SPSS.

**Results:** Thirty four patients were subjected to low anterior resection while one patient had abdominoperineal resection. Fifteen patients (43%) each had either stage II or III cancers, 5 (14%) had stage IV cancer. Lymph nodes were positive in 19 (54%). The mean operative time was 230 minutes (range 150–300), and mean blood loss was 900cc (range 300–2500). R0 margins were seen in 26 (74%); R1 in 9 (26%). Complete tumour response (TRG 1) was seen in 10 (28%). At median follow up of 14 months (range 1–67), local recurrence was seen in 6 (17%) patients. Mean duration to recurrent disease was 8 months (range 4–60). Positive resection margin (R1) and incomplete tumour regression (TRG 2–4) were adversely associated with local recurrence (range 4–60). Positive resection margin (R1) and incomplete tumour regression (TRG 2–4) were adversely associated with local recurrence (range 4–60). Positive resection margin (R1) and incomplete tumour regression (TRG 2–4) were adversely associated with local recurrence (range 4–60). Positive resection margin (R1) and incomplete tumour regression (TRG 2–4) were adversely associated with local recurrence (range 4–60).

**Conclusion:** Involvement of the resection margin by tumour and incomplete tumour regression may accurately predict recurrent disease in advanced rectal cancer. Factors that result in poor response to chemoradiotherapy should be evaluated further in controlled studies to improve the outcome.

**325 RAMAN SPECTROSCOPIC MAPPING TO EVALUATE THE BIOCHEMICAL CHANGES ASSOCIATED WITH THE DEVELOPMENT OF COLORECTAL NEOPLASIA**

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**Introduction:** Raman spectroscopy is an objective, highly sensitive and specific technique used to assess biological tissues. Point spectroscopic measurements can be used to identify changes in a tissue which may enable differentiation between normal, metastatic, adenomatous, and malignant mucosal colorectal lesions. Raman spectral mapping has potential to demonstrate biochemical changes that are associated with the development of neoplasia across an entire lesion rather than at a single point. The purpose of this study was to determine if Raman spectral mapping can define biochemical changes across a variety of colorectal lesions.

**Methods:** Ten colorectal biopsies were obtained at colonoscopy. Each biopsy demonstrated histological heterogeneity on H&E staining. Spectroscopy was used to measure a range of microscopy slides for mapping studies. Raman spectra were recorded at 50 μm intervals across each specimen, and the data used to create pseudocolour maps representing biochemical changes within the tissues.

**Results:** Pseudocolour maps generated using principal component analysis demonstrated spectral differences in different regions of each specimen. These spectral differences correlated well with the different areas of histological classification within the specimen that had been identified in the heterogenous H&E specimens.

**Conclusion:** Raman spectroscopy allows identification of the biochemical changes across colonic mucosa associated with the development of colorectal neoplasia, and may characterise changes at a molecular level that precede the development of histologically detectable malignancy. In the longer term this may be a useful method of distinguishing malignant and premalignant conditions at colonoscopy to allow targeted endoscopic excision.

**326 MOLECULAR SCREENING FOR HNPCC IN AN IRISH POPULATION**

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**Background and Aims:** Tumours resulting from inherited defects in DNA mismatch repair (HNPCC) exhibit molecular features distinct from sporadic tumours. These features may be used to identify clinically unrecognised syndromic kindreds and to expedite confirmatory molecular diagnosis. We describe a defining pattern of molecular features in families meeting the Amsterdam Criteria for HNPCC and apply this pattern to prospectively identify unrecognised kindreds.

**Methods:** We employed detailed family history, immunohistochemistry for MLH1, hMSH2, hMSH6, microsatellite instability (MSI) testing, and methylation-specific PCR of the hMLH1 promoter to molecularly characterise tumours from individuals belonging to 14 families meeting the Amsterdam Criteria. We subsequently screened a prospective cohort of 100 consecutive tumours for these features. Individuals with molecular features suggestive of HNPCC (with or without fulfilling the Amsterdam Criteria) underwent germline testing.

**Results:** Tumours from 10 of the 14 families meeting the Amsterdam Criteria displayed features consistent with an underlying mismatch repair defect. To date, the causative mutation has been identified for six of these families. Using molecular characterisation as a screening strategy, we prospectively identified nine cases with atypical molecular features. Five of these tumours displayed immunohistochemical loss of MLH1 together with hMLH1 promoter hypermethylation, suggestive of sporadic colorectal cancer. Four individuals with tumours showing a molecular pattern indicative of a potentially unrecognised familial cancer were identified.

**Conclusion:** Characterisation of molecular features indicative of hereditary cancer has the potential to accelerate molecular diagnosis and to detect clinically unrecognised cases of HNPCC.

**327 ALTERATIONS IN THE LEVELS OF OXIDATIVE DAMAGE IN SPORADIC COLORECTAL CANCER**

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**Background:** Oxidative DNA damage can be caused by reactive oxygen species (ROS), and 8-oxo-dG is a key biomarker of oxidative DNA damage. The base-excision repair pathway (BER) is the major pathway for repair of oxidative damage, the mismatch repair (MMR) system being an important backup repair pathway.

**Methods:** Using tissue microarrays and immunohistochemistry, we examined levels and localisation of 8-oxo-dG in matched tumour and normal tissues from 60 sporadic colorectal cancers. Loss of mismatch repair proteins, MLH1 and MSH2 was assessed to determine interactions between BER and MMR pathways.

**Results:** There was no association between 8-oxo-dG and loss of mismatch repair proteins in tumours. Total 8-oxo-dG positivity was significantly elevated in normal mucosa (mean 71.6 (SD 23.3)) compared to tumours (36.4 (37.4)), (p<0.001). Individual levels, both in epithelial and stromal cells were greater in normal than tumour (p<0.001 in each case). Total intensity levels were also significant in each case (p<0.001). The percentage positivity and intensity levels of staining in epithelial and stromal tumour cells was significantly greater in non-metastatic versus metastatic cancers (p<0.05 in all cases).
Conclusions: Increased ROS and inflammation may contribute to the increased levels of 8-oxo dG with subsequent promotion of genomic instability, consequent risk of cancer development, and further neoplastic progression.

328 RADIATION AND CHEMOTHERAPY BYSTANDER EFFECTS IN COLORECTAL CANCER
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Background: Bystander effects occur when an irradiated cell communicates with non-irradiated cells possibly via secreted factors, the non-irradiated cells then displaying characteristics of irradiated cells. Little is known regarding bystander radiation and chemotherapy effects alone and in combination in colorectal cancer.

Design: Using five colorectal cell lines and 5 Gy radiation dosage alone and with SFU, Oxalaplatin or FOLFIRI treatment, the aim of this study was to determine if medium from irradiated cells (at different time points) could cause growth inhibition, apoptosis and cell cycle disturbances in non-irradiated cells. These were monitored at 24, 48, 72, and 96 hours after medium transfer. Growth inhibition was assessed using a crystal violet assay and apoptosis and cell cycle disturbances using propidium iodine and flow cytometric analysis.

Results: Using medium conditioned by cells irradiated with 5Gy alone or chemotherapy alone, a bystander effect caused significant reduction in cell proliferation, rates of apoptosis, and cell cycle disturbances. These bystander effects were more pronounced in late stage colorectal cancer lines using medium from cells treated with both radiation and chemotherapy simultaneously.

Conclusion: Bystander effects may induce secretory signals produced by both irradiated and chemotherapy treated cells. In vivo, this stress response could accelerate genomic instability.

Cell/molecular biology posters

329 MEDIA CONTAINING ENERGETIC SUBSTRATES AFFECT MITOCHONDRIA BIOGENESIS AND INCREASE METABOLISM IN THE C3A HEPATOCELLULAR CARCINOMA CELL LINE

Background: We have previously shown that culturing C3A cells in a medium with high concentrations of lactate (L), pyruvate (P), octanoate (O) and NH₄Cl (N) improved gluconeogenesis, ureogenesis albumin synthesis, and galactose elimination capacity.

Aim: To investigate the mechanism of the LPON pre-conditioning by studying (1) the effect of individual and combined L, P, O, and N on C3A cell metabolism and (2) the effect of pre-conditioning on mitochondrial ultrastructure and function.

Methods: C3A cells were cultured until confluent in minimum essential medium Eagle (MEME) supplemented with 10% foetal calf serum (FCS), L, P, O, and N were added to MEME at different concentrations/ combinations (mM): LP 10/1; N4; LPN10/1/4; LPON10/1/1/4. Cells were preconditioned for 10 days before being incubated with LC1 for 72 hours with substrates to assess their metabolic capacity (gluconeogenesis, ureogenesis, galactose elimination) and oxidative phosphorylation function (redox and phosphate potential).

Results: LP improved glucose metabolism, while N affected both glucose and ureogenesis. The combination of LP and N did not further improve the metabolism while addition of O further increased glucide metabolism. LPON-preconditioned cells cytotoxic NADH/NAD was significantly lower. Ultrastuctural studies showed that, compared to control C3A cells, LPON-preconditioned cells had reduced number but larger mitochondria, with much denser internal mitochondrial membrane proteins. This result was further confirmed by the western blot.

Conclusion: The LPON induced significant ultrastructural and functional changes in mitochondria of C3A cells. This was associated with improvement of cell differentiation markers such as glucogenesesis, galactose elimination, and ureogenesis capacity.

330 POLLUTION DERIVED NANOPISTLES PROFOUNDLY AFFECTS HEPATOCYTE BIOENERGETICS

Background: Air pollution, mostly fuel combustion derived nanoparticles, is responsible for exacerbations of chronic airways disease and early death from cardiorespiratory causes. Blood borne nanoparticles reaching the liver may induce acute phase proteins (risk factors for death from acute coronary syndrome), as seen in populations exposed to air pollution.

Aim: To investigate (1) if NP end up in the liver when delivered in the circulation and (2) the effects of nanoparticles on liver cell metabolism and bioenergetics.

Methods: (1) Wistar male rats were injected with 200 µg nanoparticulate ultrafine carbon black (UfCB) in the tail vein and left for one hour before being sacrificed. The liver was prepared for H&E staining. (2) C3A cells were exposed to increasing concentrations (10–50 µg/ml) of UfCB, CuO, ZnO, or TiO₂ for 24 hours. Dihydroxyacetone was used for studies of intermediary metabolism.

Results: (1) UfCB was found in Kupffer cells in the liver samples. (2) CuO and ZnO induced profound concentration-dependent changes in cell metabolism: at 25 µg/ml, total DHA flux was respectively decreased by 40% and 80% (p<0.05), and by 40% at 10 µg/ml for both nanoparticles (p<0.05). These changes reflected a dramatic reduction in the glycolysis for both nanoparticle types. Gluconeogenesis was increased by 80% in the cells exposed to 25 µg/ml ZnO. These metabolism changes were associated with a decrease in the cytosolic redox potential. The phosphatase potential did not change at 10 and 25 µg/ml of ZnO or CuO. At 50 µg/ml, ZnO and CuO were cytotoxic and cells detached from the culture well, preventing any assessment of bioenergetics. UfCB and TiO₂ induced profound concentration-dependent changes in liver cells at the concentrations studied. These results indicate that CuO and ZnO nanoparticles could have a profound oxidative effect of these particles on liver cells, which merits further evaluation.

Conclusion: Fuel combustion derived nanoparticles such as CuO and ZnO had dramatic effects on liver cell metabolism, probably due to oxidative stress. Thus in the context of high air pollution, if large quantities of nanoparticles reach the liver this could lead to acute phase protein synthesis and increase the risks of death from acute coronary syndrome in susceptible individuals.

331 DEVELOPMENT OF A COLLAGEN-CERAMIC COMPOSITE FOR FISTULA REPAIR
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Background: Tissue adhesives, such as fibrin sealant, continue to be used for treatment of complex anal fistulae despite widely varying success rates. This is partly due to a lack of suitable alternatives and the desire for a relatively simple procedure with low morbidity that avoids more radical surgical intervention. Permacol, a cross-linked porcine dermal collagen implant, has been used for treating small bowel fistulae and tissue bulking and is currently being investigated for perianal fistula repair. Growth factors regulate tissue healing and are likely to enhance fistula repair. Vascular endothelial growth factor (VEGF) is a fundamental regulator of angiogenesis. Stimulaton of angiogenesis with exogenous VEGF dramatically accelerates healing of experimental ulcers. VEGF secretion from porcine fibroblasts is significantly increased by 45S5 bioactive glass (BG).

Aim: To modify Permacol with BG particles to enhance its growth factor induced bioactivity for use in fistula repair.

Methods: 4555 BG particles (0%-1% w/v) were added to a cryogenually milled form of Permacol (Permacol Injection) to produce a composite paste. Colonie myofibroblasts (CCD-18C1) were incorpordated into the composite and cultured. Conditioned culture medium was collected after 24, 48, and 72 hours and the amount of VEGF secreted was measured by ELISA. The amount of collagen bound VEGF was similarly measured at 72 hours after dissolving the composite with collagenase type 1A. Viability of the incorporated cells was determined at 72 hours using an MTT assay.

Results: At 48 hours, the amount of VEGF secreted from the composites containing 0.1% w/v 45S5 BG was significantly increased (2209 pg (5555); p<0.01) compared to 45S5 BG (822 pg (30)). The amount of VEGF secreted at 72 hours was significantly increased from composites containing 0.1% (1720 pg (17); p<0.001) and 0.1%
of transcripts for the TRPV6 transporter with physiological doses of vitamin D.

**Conclusion:**
The robust human small intestinal explant system has been validated using controls, and 5.38 (1.00) in the treated group (p < 0.05) respectively. Consistent with or infiltrating the material may accelerate the healing of fistulae post-operative complications.

**45S5 BG composites might provide a safe filler material for repair of enteric fistulae.**

**Background:**
Investigation of human small intestinal function has been impaired by the lack of a suitable differentiated cell line and by differentiation protocols that are complex and inappropriate for clinical use. We aimed to develop a human small intestinal explant system which could be used to determine transcriptional regulation of gene expression.

**Methods:**
Volunteers undergoing diagnostic upper endoscopy were recruited after giving informed consent for studies, approved by the local research ethics committee. Subjects with various specific disorders were not included. After diagnostic biopsy, obtained, eight mucosal biopsies were taken and placed in pre-oxygenated tissue culture medium. Biopsies in groups of 2–4 were cultured on microporous membrane inserts and treated with either hormone or vehicle control.

**Results:**
Initial experiments were performed after 6 hour exposure to the active hormonal form of vitamin D, 1,25(OH)2D3 (10–8 M), or control. The expression of transcripts for the brush border membrane calcium channel, TRPV6, were standardised to those for the housekeeping gene, GAPDH. TRPV6/GAPDH ratios were 1.50 (0.21) (mean (SEM)) in controls, and 5.38 (1.00) in the treated group (p < 0.001). Wilcoxon signed rank test. 29 out of 30 subjects showed an increase in the median change in expression ratios was 3.1. Similar changes occurred in men and women and were not related to age.

**Conclusion:** A robust human small intestinal explant system has been developed. This was able to show a marked increase by 6h in expression of transcripts for the TRPV6 transporter with physiological doses of 1,25(OH)2D3, it has the potential to study other agents that may regulate gene expression including other hormones and drugs.

**333 COLONIC IRON LOADING REDuces E-CADHERIN EXPRESSION AND ENHANCES PROLIFERATION**

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**Background and Aims:** There is increasing evidence to suggest that the colon has the capacity to directly absorb iron. Previous studies have implicated total body iron and high dietary iron intake as major risk factors for colorectal cancer. Murine studies have shown that high dietary iron can increase colorectal tumour incidence, and tumour multiplicity when administered along with a carcinogen. E-cadherin is an adhesion junction protein known to be repressed in epithelial cancer. In human colorectal cancer leads to increased proliferation and decreased E-cadherin expression.

**Methods:**
Two colorectal carcinoma cell lines SW480 (poorly differentiated) and Caco-2 (well differentiated) were routinely cultured. Cells were subsequently stimulated with either growth medium alone (control) or iron loaded medium. Real-time PCR, western blotting, and immuno-histochemistry was performed to determine mRNA and protein expression and localisation of E-cadherin. The effects on E-cadherin expression was further examined by using a promoter assay. The effect of cellular loading on proliferation was examined using an ATP dependent assay.

**Results:** Iron loading of Caco-2 and SW 480 cells resulted in a significant reduction in both E-cadherin mRNA (37% and 48%, p < 0.05) and protein (30% and 54%, p < 0.05) respectively. Consistent with these results we demonstrated a significant fold repression in E-cadherin promoter activity in both iron loaded Caco-2 and SW-480 cells (p < 0.05). Immunofluorescence for E-cadherin in both cell lines revealed preserved immunoreactivity at cell borders in the control group, however the intensity of staining was markedly reduced in the iron loaded groups. The effect of iron loading was to significantly increase proliferation in both cell lines.

**Conclusion:** Iron loading in well and poorly differentiated colorectal carcinoma leads to increased proliferation and decreased E-cadherin expression. This is likely to increase motility, invasiveness, and ultimately metastasis in colorectal carcinoma.

**334 CANNABINOIDs PROMOTE SURVIVAL OF NORMAL HUMAN COLONIC EPITHELIAL CELLS**

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**Background and Aim:** Important roles for the endocannabinoid system in the gastrointestinal (GI) tract under physiological and pathophysiological conditions have been demonstrated. We have shown that cannabinoids promote colonic epithelial wound closure through the CB1 receptor at nanomolar concentrations, which had no significant effect on proliferation. Previous work has suggested that cannabinoids may act through transcriptional regulation of gene expression.

**Methods:** NCM460 cells express both CB1 and CB2 receptors under normal culture conditions. Proliferation experiments were performed in the presence or absence of synthetic and endogenous cannabinoids (10 nM–10 μM) or vehicle over a five day period.

**Results:** ACPA (CB1 agonist), JWH (CB2 agonist), and metAEA (methanandamide, endogenous CB1/CB2 agonist) had no influence on the proliferation of these cells, even under low serum conditions. However, the CB1 receptor antagonist, AM251 (1–10 μM) alone had a profound antiproliferative effect on these cells. This implies that the activity of cannabinoid receptors is linked to the viability and survival of normal colonic epithelial cells. Further investigations revealed that cannabinoids impact on the enzyme-oxidase (HO-1) expression, a protein thought to be important during restimulation of inflammation.

**Conclusion:** These results support our suggestion that cannabinoids may have therapeutic potential during the healing phase of gastrointestinal inflammation.

**335 PILOT STUDY OF A NOVEL TISSUE ENGINEERED INTESTINAL CONSTRUCT**

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**Background and Aim:** Tissue engineering of the small intestine is a novel discipline. The intestinal unit has been characterised by the demonstration of normal enteric functions in tissue engineered small intestinal segments that have been shown to be able to support normal function in vivo. The development of a bioengineered gut construct is an important step towards the replacement of damaged or diseased gut segments with an engineered tissue equivalent.

**Methods:** PLGA scaffolds were implanted subcutaneously into eight male Lewis rats. After five weeks, a suspension of "organoid units", derived via partial digestion of neonatal rat small intestine, was implanted into the lumen of the scaffolds. Tissue was harvested and underwent histological processing. Immunohistochemistry was performed using antibodies against vascular endothelial growth factor (VEGF), vascular endothelial growth factor receptor 2 (VEGFR-2), fibroblast growth factor basic (bFGF) and fibroblast growth factor receptor 2 (FGFR-2). Stereological techniques were used to quantify the density of positively stained cells.

**Results:** At four weeks post organoid unit implantation, clearly recognisable mucosa and submucosa showing histological features...
similar to small intestine were present on the luminal surface of the scaffold. The scaffold showed evidence of vascularisation and early capillary formation. Densities of VEGF and VEGF-R2 positive cells increased with time post organoid unit implantation while those of bFGF and FGF-R2 remained constant. The yield of the tissue engineering process was approximately four times that documented in the literature.

**Conclusion:** This pilot study demonstrates that it is possible to tissue engineer small intestinal neomucosa using subcutaneously implanted PLGA scaffolds. The yield of the process compares favourably to the published literature. Further work is required to optimise the technique.

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**336 THE STOMACH AND BCL-2**

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Bcl-2 is a protein produced by the B cell lymphoma/leukaemia-2 gene and is known to block apoptosis. Previous studies have found no change in the Bcl-2 expression in inflammatory gastrointestinal diseases. An immunohistochemical study has been performed using glycol methacrylate (GMA) processing of gastric biopsies to investigate the expression of Bcl-2 in Helicobacter pylori infection. The study has involved endoscopic biopsies from 77 patients (33 normal stomachs and 44 stomachs infected with Helicobacter pylori).

In the normal stomach Bcl-2 expression is limited to the mucosal blood vessels with the particulate expression consistent with a localisation in platelets. Bcl-2 is known to be expressed by megakaryocytes.

The present study has shown that Helicobacter pylori infection is associated with a marked upregulation of Bcl-2 in the mucosal connective tissue. Bcl-2 is associated with lymphoma development in transgenic mice and in humans it is associated with follicular lymphomas as well as some diffuse large cell lymphomas. The upregulation of Bcl-2 in Helicobacter pylori infection would be ideally sited to influence B cell survival resulting in the potential for lymphoma development. It would explain why treatment of the Helicobacter pylori infection with the resultant down-regulation of Bcl-2 is beneficial and may result in the regression of gastric “lymphoma” which has been noted under such circumstances.


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**337 LACK OF ASSOCIATION BETWEEN POLYMORPHISMS OF GSTP1, SOD2 AND GPX2 AND RISK OF OESOPHAGEAL ADENOCARCINOMA: RESULTS FROM A POPULATION BASED STUDY IN IRELAND (THE FINBAR STUDY)**

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**Introduction:** Oxidative stress appears to be important in the pathogenesis of Barrett’s oesophagus (BO) and oesophageal adenocarcinoma (OAC). Genetic polymorphisms of enzymes involved in antioxidant pathways may play a part in determining individual susceptibility to OAC. The aim of our study was to determine if single nucleotide polymorphisms (SNPs) of antioxidant enzyme genes were associated with risk of OAC in a population based setting.

**Methods:** A case-control study is a population based case control study of OAC in Ireland (population 5.5 million). Cases of OAC (n=230) were prospectively enrolled as were subjects with BO (3 cm BE at endoscopy with specialised intestinal metaplasia on biopsy, n=190), and normal population controls (n=230). DNA was extracted from frozen white cell buffy coats. Several SNPs spanning the genes for glutathione S-transferase P1 (GSTP1), superoxide dismutase 2 (SOD2), and glutathione peroxidase 2 (GPX2) were selected to identify the major haplotypes. SNP genotyping was carried out using multiplex PCR and SNaPshot. The χ² test was used to compare genotype and allele frequencies between case and control subjects.

**Results:** Seven informative SNPs were genotyped (2 for GSTP1, 3 for SOD2, 2 for GPX2). All SNPs were in Hardy-Weinberg equilibrium. None was significantly associated with OAC or BO even before Bonferroni correction. Odds ratios (OR) for OAC for individual SNPs ranged from 0.88 (95% CI 0.59 to 1.33) to 1.31 (95% CI 0.84 to 2.04). The χ² test showed no significant association with OAC or BO.

**Conclusions:** SNPs involving the GSTP1, SOD2 and GPX2 genes were not associated with OAC. Further studies aimed at identifying susceptibility genes should focus on different antioxidant genes.

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**338 A ROLE FOR IRON TRANSPORTERS IN OESOPHAGEAL ADENOCARCINOMA**

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**Background:** Iron is essential for cellular metabolism, growth, and cell cycling. Iron has previously been implicated in the malignant progression of Barrett’s oesophagus (BO) to oesophageal adenocarcinoma (ADC). To date there has been no characterisation of the proteins involved in iron transport in the progression of ADC. Thus the aims of this study were to characterise several of the proteins involved in cellular iron import (Divalent metal transporter 1 (DMT1), duodenal cytochrome B (DcytB) and transferrin receptor 1 (TFR1)), cellular iron export (hephaestin (HEPH)) and cellular iron storage (ferritin) in normal oesophagus (NO), gastric mucosa (GM), BM, and ADC.

**Methods:** Perl’s Prussian staining was used to examine cellular iron content. mRNA expression of the iron transporters were determined by quantitative real-time PCR in 18 ADC specimens. Semi-quantitative immunohistochemistry was performed to assess cellular localisation and protein expression.

**Results:** Perl’s staining demonstrated increased intracellular iron in ADC whilst there was no evidence of staining in NO, GM or BM. Cellular iron import proteins DMT1, DcytB and TFR1 were all significantly over-expressed in ADC (p<0.01). These changes were also seen at the mRNA level where DMT1 (p=0.004), DcytB and TFR1 (both p<0.001) were overexpressed. Conversely the iron export protein HEPH was transcriptionally repressed in ADC (p<0.05). Ferritin was overexpressed at both the mRNA (p=0.02) and protein level (p<0.001) in ADC. The transcriptional upregulation of TFR1 and ferritin was also observed in matched samples of Barrett’s metaplasia (p<0.05).

**Conclusions:** Oesophageal adenocarcinoma was associated with increased expression of iron import proteins (DMT1, DcytB, and TFR1) and decreased expression of the cellular iron export protein HEPH. We conclude that this causes iron loading of columnar cells which may represent a mechanism of tumourigenesis.
transactivation of the EGFR, and JNK activation. Leptin may directly contribute to the development of oesophageal adenocarcinoma.

**340 ANALYSIS OF INHERITED MYH MUTATIONS IN BRITISH ASIAN PATIENTS WITH COLORECTAL CANCER**

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**Background and Aim:** Biallelic mutations of the DNA base excision repair gene MYH are known to be associated with multiple colorectal adenomas and colorectal cancer (CRC). This recessively inherited disorder MYH associated polyposis (MAP) is distinct from dominantly inherited familial adenomatous polyposis (FAP). We had previously noted that all four families of British Asian origin out of 115 families on the Wales polyposis register had MAP. We conducted a retrospective study after MREC approval to characterise the contribution of MYH mutations to CRC in this group particularly E466X and Y90X which have not been found in any other ethnic group.

**Methods:** Cases were ascertained through five departments of pathology in the UK. Archived paraffin blocks of tissue of cases with CRC were identified and British Asian cases (n = 120) selected by name, then suitably anonymised and re-examined to ensure analysis of only normal background mucosa prior to analysis. The control group (n = 100) consisted of paraffin blocks from Asian individuals from the same centres with a diagnosis of inflammation without neoplasia. DNA was extracted and PCR amplification enzyme digestion used for analysis of the unique Asian mutations E466X (using Apol), and Y90X (using Rsal) along with the common Caucasian mutations G382D (using BglII) and Y165C (using ARMS PCR). Positive results were confirmed by bidirectional sequencing as well as sequencing of all exons of MYH.

**Results:** One case (1/120) and one control (1/100) sample were found to be heterozygous for the E466X variant in MYH. No case or controls had bi-allelic mutations or any of the other three mutations tested. Sequencing of all exons of MYH did not reveal any second mutations in these two individuals.

**Conclusion:** The allele frequency of E466X in this study is comparable to that of Y165C and G382D in the general British population. There is thus a strong case for initial testing for this mutation in Asian individuals with MAP or CRC with apparent recessive transmission.

**341 A ROLE FOR IRON TRANSPORTERS IN COLORECTAL ADENOCARCINOMA**

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**Background and Aims:** Iron is essential for a number of key cellular processes, including cell cycling. There is increasing evidence to suggest that high dietary iron intake is an important risk factor for colorectal carcinoma (CRC). There are no studies to date which have comprehensively characterised the expression of iron transporters in the progression of CRC. The aim of this study was to characterise the expression of key iron transport proteins within the colon; Divalent metal transporter 1 (DMT1), duodenal cytochrome B (DcytB), transferrin receptor 1 (TFR1), ferritin, hephaestin (HEPH), and ferroportin (FPN).

**Methods:** Enhanced Perl’s Prussian staining was used to examine cellular iron content within CRC. Real-time PCR and western blotting were used to examine mRNA and protein levels in 15 human CRC resections. Semiquantitative immunohistochemistry was used to determine protein levels and cellular localisation in normal human colon and colorectal carcinoma.

**Results:** Perl’s staining showed an increased iron content within CRC, compared to normal colon. Expression studies revealed overexpression of the iron import machinery DcytB, DMT-1, and TFR1 in CRC compared to normal colon. Regarding the export proteins, although FPN was overexpressed at the mRNA and protein levels, HEPH was decreased in the majority of CRC examined. Immunohistochemistry however revealed a displacation of iron reabsorption from iron exporters HEPH and iron importers FPN respectively. This results in increased intracellular iron which is likely to be necessary for tumour proliferation.

**342 CHARACTERISATION OF ISOLATED HUMAN COLONIC CRYPT EPITHELIAL CELLS AND THEIR INTERACTIONS WITH INTESTINAL MYOFIBROBLASTS**

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**Introduction:** Intestinal stem cells are located at the base of small and large intestinal crypts and give rise to distinct subpopulations of epithelial cells. Factors that regulate intestinal stem cell survival, proliferation, and differentiation remain to be characterised. Subepithelial myofibroblasts are likely to be important in regulating stem cell function via secreted factors, including extracellular matrix. We have investigated interactions between the two cell types following isolation.

**Methods:** Crypt epithelial cells were isolated and disaggregated from normal colonic mucosal samples following treatment with ethylene diamine tetraacetic acid and pancreatin. Their viability was assessed using trypan blue and they were also were studied by FACS and immunohistochemistry, before and after co-culture with monolayers of intestinal myofibroblasts. Expression of stem cell specific musashi-1 transcripts was studied by RT-PCR. Data are expressed as mean (SD).

**Results:** The disaggregated crypt epithelial cells were immunoreactive for cytokeratin (specific for epithelial cells) and their viability was 71.2 (15.6)%. They expressed β1 integrin, as demonstrated by significantly increased mean fluorescence intensity (MFI) using β1 integrin specific antibody compared to isotype control antibody (190.3 (109.9) v 11.6 (9.0), p = 0.02). Expression of musashi-1 transcripts was confirmed by RT-PCR (n = 3). Following application to monolayers of myofibroblasts for 10 minutes (and subsequent washing), many (10.4 (8.3) per high power field) cytokeratin positive adherent epithelial cells were seen. After culture with myofibroblasts for three days, cytokeratin positive cells within processes were seen. Stem cell containing, disaggregated human colonic crypt epithelial preparations can be consistently obtained for subsequent studies to investigate their interactions with isolated intestinal myofibroblasts. The latter may facilitate survival of the crypt epithelial cells, including stem cells.

**343 DO PATIENTS APPRECIATE A COPY OF THEIR ENDOSCOPY REPORT? AN AUDIT**

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**Background:** Patient involvement in clinical documentation is increasingly regarded as best practice. This is especially relevant to endoscopy reporting, where subjects may be sedated and thus unable to retain verbal information after their procedure. The endoscopy global rating scale (GRS) includes provision of a patient-focused endoscopy report as a criterion of quality. An example of this practice is reviewed here.

**Methods:** The author routinely provides all endoscopy patients (other than those with a first diagnosis of malignancy) with a copy of their printed report, which is worded in a “patient friendly” manner, upon discharge. To audit this practice, 100 consecutive patients were sent a questionnaire asking their views on this practice.

**Results:** Sixty-eight gastroscopy, 20 colonoscopy, and 12 ERCP patients were sent a questionnaire within four weeks of their endoscopy; 78/100 replied. Of these, 88% had kept a copy of their report. 82% reported being able to understand the report and 82% felt that it had helped “reap” on the findings later on. 71% found the report helpful and 86% found it reassuring. 6% felt it caused anxiety. Out of 42 freetext comments, 76% were favourable and 14% unfavourable.

**Conclusions:** Provision of a patient focussed endoscopy report is easy to do, complies with best practice guidance, and is widely appreciated by patients.

**344 INVESTIGATING DYSPENA: BRINGING NATIONAL GUIDELINES TO A LOCAL LEVEL**

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**Introduction:** Dyspepsia is traditionally been investigated using serology; however NICE (2004) guidelines recommend urea breath testing (UBT) or faecal antigen testing (FAT). This study aims to find the optimal...
A90 GUT abstracts

Aim: To investigate the influence of the service on Consultant referrals, access times, and prescribing costs.

Method: Local guidelines on dyspepsia management were developed by representatives from primary and secondary care from the NICE guidelines. The Nurse Endoscopist disseminated these via mail, education sessions, and visits.

Results: Prior to the Dyspepsia service in 2003 there were 990 referrals to three Consultant Gastroenterologists. Following the start of the dyspepsia service Consultant referrals had dropped to 662, 0.6% to the nurse led dyspepsia service. Data for the first six months of 2005 are 331 referrals to Consultants and 90 to the Nurse Endoscopist. Maximum wait time for the nurse led service is three weeks from referral to endoscopy.

Data: For prescribing costs for 2003/04 were £960,757 and £910,669 for 2004/05 a cost saving of £50,000. (not all attributable to the Nurse Endoscopist as proton pump inhibitor costs have reduced)

Conclusion: The nurse led dyspepsia service reduced referrals to Consultants by 330 per year and overall referrals by 110 (11%) without increasing prescribing costs. Patients receive a fast diagnostic service, average time from referral to endoscopy for the nurse led service, is three weeks with a corresponding improvement in Consultant access times. Under payment by results the service almost pays for itself.

347 THE AGREEMENT BETWEEN GP REPORTED DYSPESIA AND PATIENT FILLED DYSPESIA QUESTIONNAIRE IS POOR FOR “TWO WEEK” ENDOSCOPY REFERRAL

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Objective: NICE referral guidelines for suspected cancer in adults and children recommend urgent specialist referral for endoscopic examination to be carried out within two weeks for patients with predefined alarming symptoms or signs for suspected upper gastrointestinal (GI) cancer. There is concern that these predefined criteria may be subjected to misuse as an alternative route for urgent endoscopy for patients who do not actually fulfil the criteria. Hence, the aim of this study is to determine the agreement between the general practitioners (GP) filled referral form with patient self filled questionnaire.

Methods: Leeds validated dyspepsia questionnaire (SFLDQ v7 (3)) with additional alarming symptoms were sent to all patients referred under the “two week wait” criteria and the data were collected prospectively from July to October 2005. Agreement was assessed by Kappa statistics. Kappa value of less than 0.2 is considered poor agreement and more than 0.6 as good agreement.

Results: Two hundred and eight patients were referred for urgent endoscopy. Nine patients were redirected to urgent outpatient assessment and six patients failed to attend their appointment. Hence 193 patients were available for analysis. Fifty four per cent were female (n = 105) and the median age was 71 years (IQR 62 to 79 years). Sixteen (8%) cancers were found (12 oesophageal, 4 stomach). Normal endoscopy was reported in 99 (51%) patients, reflux oesophagitis in 33 (17%) patients, and peptic ulcer disease in 10 (5%) patients. The commonest three alarming symptoms were persistent dyspepsia above 45 years old (62%), dysphagia (40%), and weight loss (34%). One hundred patients (52%) returned their questionnaire and this subgroup had similar commonest three alarming symptoms as the overall group (67%, 31%, and 36% respectively). The percentage of patients reported these symptoms were 74%, 46%, and 45% respectively. The kappa values were 0.2 for dyspepsia, 0.4 for dysphagia, and 0.65 weight loss.

Conclusions: The agreement for the symptom of dyspepsia is poor. These suggest GP may be using incorrect definition for the diagnosis of dyspepsia. Regular feedback and education to GP may reduce the number of urgent referrals for this commonest alarming symptom.


346 PEPTIC ULCERS ARE BEING UNDERTREATED DUE TO THE LACK OF AVAILABILITY OF SPECIALIST NURSING AND EQUIPMENT OUT OF HOURS: AN AUDIT OF 116 CONSECUTIVE REFERRALS FOR GI BLEEDING


We audited all referrals for acute upper GI bleeding in a central London hospital over six months. We recorded patient demographics and haemostatic therapy used on 116 patients undergoing 143 procedures.
and calculated mortality and re-bleed statistics. Many of these patients were high risk ITU, cardiothoracic, and renal patients reflecting the population of a tertiary referral hospital.

Mortality was 15%. 45% of all procedures were performed using a mobile endoscopy stack, remote from the endoscopy department, either in A&E, ICU, HDU or theatres. Either the patient was too sick to move or the procedure was done “out of hours”. These patients were significantly higher risk than those performed “in hours” and in the endoscopy department (mean Rockall score 3.75 ± 6.09; p < 0.001, Mann-Whitney U test).

Only 6/17 peptic ulcers with stigmata of recent haemorrhage received “dual therapy”; 17% of peptic ulcers re-bleed and this was associated with 50% mortality. Acute variceal haemorrhage was associated with a 25% mortality (2/13) and all variceal bleeders admitted to ICU survived to discharge (3/13). High dose PPI infusion was used appropriately for high risk lesions and patients. Endoscopists found it difficult to utilise haemoclips without trained assistants whereas adrenaline injection and band ligation were frequently and successfully performed.

Unassisted emergency upper GI endoscopy with a mobile endoscopy unit, without trained nurses or thermal therapy is unsatisfactory. The audit has lead to the purchase of a bipolar therapy unit for the mobile stack. Re-bleeding rates will be re-audited once this treatment modality is established. The creation of a dedicated inpatient/emergency endoscopy facility, with nursing support is being discussed.

**349 SELECTION OF PATIENTS WITH UPPER GI BLEEDING FOR EARLY DISCHARGE USING THE BLATCHFORD SCORE**

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**Background and Aim:** Acute upper GI haemorrhage (UGIH) is a common medical emergency. Mortality is between 5–12%, however a large number of patients are at “low risk” and could be safely discharged early if they could be identified. The Rockall score is a validated post-endoscopic score that predicts risk of rebleeding and death. The Blatchford score is a pre-endoscopic score that predicts the need for intervention. We applied both these scores to a retrospective cohort of patients who presented to our trust with UGIH to identify which scoring system would have best identified patients for early discharge.

**Results:** 123 consecutive patients admitted with UGIH were identified. Duration of stay, need for intervention, and mortality was calculated. Blatchford score, pre- and post-endoscopy Rockall scores were calculated. The mean age was 58.6 years (16.6–96.3 years). The mean length of stay in hospital was 5.4 days (0–153 days). A total of 83 patients underwent OGD. 42 patients required an intervention i.e. transfusion (n = 26), endoscopic treatment (n = 12), surgery (n = 1), death (n = 7), re-bleed (n = 8). Negative predictive value (NPV) for need for intervention was calculated and compared against the scores. A Blatchford score of 0 (17% of patients) and < 2 (34%) had NPV of 100% and 95% respectively. Pre-endoscopy Rockall score of 0 (27%) and Post endoscopy Rockall score of < 2 (42%) had a negative predictive value of 90% and 75% respectively.

**Conclusion:** In our population of patients the Blatchford score was superior to the Rockall score in identifying patients who did not need clinical intervention and were thus suitable for early discharge. Had the Blatchford score been applied to this cohort almost 20% of patients could have been safely identified for early discharge without inpatient endoscopy. The score would also have reduced the number of emergency endoscopies by 15%. In light of this audit we now apply the Blatchford score to all UGIH patients and discharge without inpatient endoscopy in those with scores of 0. This change in policy is currently being prospectively audited.

**350 IMPACT OF REFERRAL ASSESSORS ON GASTROSCOPY REFERRALS FOLLOWING GUIDELINE INTRODUCTION**

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**Introduction:** There is evidence that effective dissemination practices are required to ensure that guidelines are followed. Increasing demands on endoscopy services and increasing evidence have led to the development of guidelines for the management of dyspepsia. The All-Wales Dyspepsia Management Guidelines (based on the NICE and SIGN guidelines) were circulated throughout Wales in October 2004.

**Abstract 350**

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**Aim:** The aim of the study was to see whether dissemination and education of referrers via feedback improved quality of gastroscopy referrals received by gastroscopy units.

**Method:** All gastroscopy referrals to three endoscopy units in S Wales were recorded over a period of six months before and six months following the introduction of the All Wales Guidelines. Primary Care Referral Assessors evaluated each referral compared to the current Guidelines. No change was made to the actual referral process. For the six months after publication of the guidelines, the referrer of a guideline incongruent endoscopy request was sent a letter and a copy of the guidelines.

**Results:** Percentages of Guideline congruent OGD dyspepsia referrals for the six months before and after intervention are shown in the table.

**Conclusion:** The results indicate that formative feedback of referrals is effective in increasing the quality of gastroscopy referrals from primary care but has limited impact on secondary care referral practices. As well as improving quality and numbers of referrals meeting guidelines, referral assessing resulted in lower numbers of referrals overall. This novel scheme may be extended to other procedures in order to increase quality and appropriateness of referral practices for primary care.

**351 PARTIAL BOOKING FOR OUTPATIENT GASTROSCOPY: ARE SOME PATIENTS DISADVANTAGED?**

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**Introduction:** Partial booking for appointments is being widely introduced in the NHS to improve convenience of appointments for patients and to shorten waiting lists by reducing non-attendance rates. We hypothesised that the system might disadvantage certain groups of patients, for example non-English speakers or the elderly who might have difficulty in understanding and/or responding to the written instructions they receive from appointments staff.

**Aim:** To compare non-response rates to written invitations to make out-patient gastroscopy (OGD) appointments in different subgroups in an inner city population.

**Method:** Data on response to letters of invitation and on attendance for OGD were collected. 100 responders and 100 non-responders were selected. The responders came from 2004; non-attendance rates for booked OGDs fell from 25% to 10%. There were no differences in response rates to letters of invitation in relation to age or ethnicity. Overall, of non-responders, 63% were males (p < 0.05): this difference related primarily to Caucasians, in whom 77% of non-responders were male (p = 0.01).

**Conclusions:** Partial booking has been associated with marked reductions in waiting times and in non-attendance for OGD. Contrary to our expectations, patients failing to make contact to fix appointments for OGD were mainly English speaking white men. It is reassuring that this system of booking appointments for OGD does not seem to disadvantage either elderly patients or those whose first language is not English.

**352 HOW TO REDUCE INAPPROPRIATE ENDOSCOPIC GASTROSTOMY (PEG) REQUESTS**

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**Introduction:** The NCEPOD Report 2004 Scoping our Practice found that 19% of 719 PEG procedures were “futile” and in 63% there was a definite risk of death as assessed by the consultant treating them. We had noticed a steady increase in requests, many inappropriate, for PEG insertions in our hospital.

**Aim:** To reduce inappropriate PEG requests in our hospital.
Methods: We examined our PEG requests over a 10 year period (1996–2005) using our endoscopy database. We devised an inpatient endoscopy request form to obtain more detailed information if the patient was referred for a PEG. It was emphasised that PEG was an operative procedure and death within 30 days would need to be reported formally. The A5 form was piloted then launched in August 2004. We examined the number of PEG insertions in the 12 months before and after introduction of the new request arrangements.

Results: Between 1996 and 2005, we performed 637 PEG insertions. We inserted 25 PEGs each year in 1996 and 1997, rising to about 90 per year from 2002 onwards. In the 12 months before the introduction of the new request form we had inserted 98 PEGs. In the 12 months after the new arrangements we inserted 51 PEGs, a reduction of 46%. The reduction was maintained beyond the first year.

Conclusion: We were able to successfully reduce inappropriate requests for PEGs by the introduction of a simple and clear request form. The impact of this change in the request procedure has been maintained.

353 THE SCOPE OF INPATIENT ENDOSCOPY PRE-ASSESSMENT
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Background: Assessment of demand and capacity forms part of Inpatient Hospital Services NHS (2003) Guidelines. Since pre-assessment of outpatients has been shown to improve utilisation of lists, we wanted to see if a similar intervention for in-patients would be of value.

Objectives: To assess the feasibility, via a pilot study, of specialist nurse led intervention in prioritisation of referrals, thereby reducing inappropriate procedures and delays due to unprepared patients.

Methodology: Every inpatient request for all endoscopic procedures was assessed by a nurse specialist, discussing any concerns with the gastroenterology consultants or SpR. A check list was placed in the patients’ notes and ward staff were advised on correct preparation. Liaison took place between the referring doctor, waiting list manager, gastroenterology team, endoscopy staff, and the nurse specialist, thus maximising use of slots. A written report of any problems encountered was made by the endoscopist.

Results: In the three months since pre-assessment began in July 05, only four problems have been recorded. Out of 227 inpatient requests, 45 patients (20% of referrals) were pre-assessed as inappropriate or unnecessary and directed to more suitable treatment options.

Discussion: Inpatient pre-assessment for endoscopy is feasible and this study demonstrates the potential for its clinical and economic benefits.

354 EVALUATION OF THE OUTCOME AND EFFECTIVENESS OF DIGITAL DICTATION AND INTERNATIONAL OUTSOURCING OF MEDICAL TRANSCRIPTION IN GASTROENTEROLOGY
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Background: Communication with referring physicians and other medical colleagues has traditionally been accomplished using analogue dictation with subsequent transcription by medical secretaries. The quality and speed of transcription can be variable and at best take up to one week to reach intended recipients. Digital dictation and international outsourcing of transcription has been suggested as being an efficient and cost-effective method.

Objective: To evaluate the clarity, speed, accuracy, safety, and effectiveness of digital dictation and outsourced transcription.

Methods: A pilot project was commenced using an established service provider (ScribeTech UK Ltd, London). Dictation was performed using a digital voice recorder (Olympus DS-330). The anonymous files were downloaded to the hospital server and routed via a secure file transfer protocol (FTP) to a transcription centre in Bangalore, India. Although the standard turnaround time was 24 hours, the system could accommodate the hospital electronic patient record (EPR) (Cerner Corporation, USA). Transcriptions were checked, errors were noted and corrected, and the transcription approved. Transcriptions could be sent by letter or email to multiple recipients.

Results: 574 transcriptions were sent through the system (June 2005–October 2005). Clarity of dictation was excellent in all cases and 100% transcriptions were processed within prescribed times with no files lost. Interface with the EPR was successful. The overall error rate in the transcribed files was 1.9% and the errors were minor.

Conclusion: Digital dictation and international outsourcing of transcription is an effective and viable method. The procedure leads to production of more accurate transcriptions, significantly faster turnaround, and allows dictations to be sent to multiple recipients.

355 HOW ACCURATE IS A CLINICAL ‘‘HUNCH’’ AFTER THE FIRST CONSULTATION IN GASTROENTEROLOGY?
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Background: The NHS is under increasing pressure to cut costs and process patients as quickly as possible. Investigations focused on the initial working diagnosis are likely to be cost effective if the clinical ‘‘hunch’’ is accurate.

Aim: To review the accuracy of the first working diagnosis.

Method: Consecutive new patients referred to Gastroenterology outpatient clinics (NVS, KB, SM) were given a working diagnosis (12 categories) following the consultation. Diagnoses were re-analysed after appropriate investigations and non-parametric analysis was used to evaluate any associations.

Results: Data were available for 154 patients (female = 78 (51%)), 95% of the initial diagnoses were the same as the final diagnosis following a diagnostic work-up (x², 16.93 (n=1) < p=0.05 = 19.6).

Conclusion: Our initial ‘‘hunch’’ in outpatients is accurate in more than 95% of cases. This is very reassuring and suggests that tests can usually be targeted at confirming the diagnosis avoiding unnecessary follow up appointments which may generate further investigations. We acknowledge that there will always be a few patients who are challenging and do not fit into an obvious diagnostic category.

Abstract 355

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Diagnostic categories: 1 = functional dyspepsia; 2 = functional abdominal pain; 3 = functional colonic symptoms; 4 = upper GI neoplasm; 5 = lower GI neoplasm; 6 = hepato-biliary pathology; 7 = pancreatic disease; 8 = inflammatory bowel disease; 9 = gallstones; 10 = GORD; 11 = coeliac; 12 = other.

356 ONE YEAR PROSPECTIVE AUDIT OF GASTROENTEROLOGY REFERRAL DEMAND TO A LONDON DISTRICT GENERAL HOSPITAL
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Background: Effective gastroenterology (GI) service provision depends on an accurate evaluation of demand, capacity, and activity. The understanding of the relationships between these factors is complex. GI demand at our hospital can be divided into inpatient, outpatient, and direct access endoscopy. Matching these factors is vital in assessing the effectiveness of GI service provision.

Methods: Prospective data on outpatient GI referral activity were systematically collected from January to December 2004. Numbers of referrals to Gastroenterology from each GP practice were divided into the following categories: Upper GI (UGI), Lower GI (LGI), Liver (L), Rectal Bleeding (RL), Direct Access Endoscopy (DAE) for upper endoscopy, and Others (O). The number of DAE was compared with total number of outpatient endoscopy procedures. Summary statistics were calculated.

Results: 2362 referrals were made over the year: UGI (714), LGI (510), L (229), RB (49), DAE (740), Other (120). DAE comprised 42% of all upper endoscopies (740/1759). Monthly analysis demonstrated that demand variation was driven by DAE rather than consultant-led outpatient demand for upper endoscopy. Only 306 C13 area urothelial cancer cases were performed suggesting that GP adherence to NICE dyspepsia guidance was poor. GP practice referral variation was marked: DAE
(0–65), total referrals (1–118) despite correcting for the size of the adult list of each practice.

Conclusion: There is marked variation (corrected for the list demographics) in the GP practice referral patterns to GI outpatients and through DAE. Investigation into the reasons for the demand variation may help in reducing demand, and matching with activity and capacity.

357 RATIONALISING THE MANAGEMENT OF BARRETT’S OESOPHAGUS: A DISTRICT GENERAL HOSPITAL AUDIT

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Introduction: The BSG have recently published Guidelines for the Management of Barrett’s oesophagus. It has been our practice to undertake annual endoscopic surveillance on patients with this condition. We conducted an audit on all such patients, with a view to modifying their management in accordance with the BSG Guidelines.

Method: We conducted a retrospective case note audit for all patients in our surveillance programme for Barrett’s oesophagus. Patient details together with the findings from previous endoscopies and histology results were carefully reviewed and recorded on an audit template. Two independent consultants in histopathology reviewed the biopsies of all patients with a previous report of dysplasia. Two separate clinicians independently appraised the appropriate management plan.

Results: A total of 55 patients were subjected to audit review. There was a male predominance (72%). Median age was 66. This group had together experienced a total of 140 endoscopic examinations. However, in only 54% of these procedures had quadrantic biopsies been taken according to BSG Guidelines. In patients deemed to have had adequate biopsies, there were reports of dysplasia in 23% of cases (8%). On formal review, dysplasia was excluded in one patient. In the group of patients with inadequate biopsies, dysplasia was noted in only one report out of 60 (2%). In terms of clinical management, 23 patients (42%) were changed from yearly to two-yearly surveillance. Five patients were placed on six-monthly surveillance, due to the confirmation of low grade dysplasia. Seven patients (13%) had never had an acceptable surveillance examination, due to inadequate biopsy protocol. Eight patients (15%) were withdrawn from surveillance due to age and medical frailty.

Conclusion: In our hospital, the audit revealed a variety of practice, reflecting the lack of previous UK Guidelines. Implementing the BSG Guidelines in our hospital will reduce the number of OGDs being performed. Even following the recommended biopsy protocol, there will still be a decrease in overall samples being sent to histopathology. Audit is a useful tool to modify patient management in this area.

358 THE IMPACT OF THE EUROPEAN WORKING TIME DIRECTIVE ON THE CLASSIC GASTROENTEROLOGY FIRM: END OF AN ERA

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Background: To comply with the European Working Time Directive most units have a full shift pattern consisting of weeks of nights, weeks on the acute Medical Admissions Unit (MAU) interspersed by weeks on the “Gastroenterology Firm” wards. As the workforce hasn’t increased to match the reduction in working hours there are fears relating to training, especially of the SpR grade, and of the care provided to patients by the traditional gastroenterology firm.

Aim: To audit the effect of a full shift pattern on the classical Gastroenterology Firm consisting of a Consultant, a Specialist Registrar (SpR), a Senior House Officer (SHO), and Pre Registration House Officer (PRHO) and to determine its implications in relation to service commitment, teaching and training.

Method: Between 4 February 2005 and 2 August 2005 the following were recorded for all the junior members of the team: night shifts, shifts on the Acute Admissions Unit, annual leave, study leave, recuperation time post nights as well as leave for any reason (for example, paternity leave).

Results: Over a period of six months, there were 129 week days. The Firm was present in its entirety (SpR/SHO/PRHO) in 23.3% of the time (30 days). There were no juniors on 11 days (8.5%). The percentage of the week day time on the wards was as follows: SpR/SHO 15.5%, SpR/PRHO 10.8%, SHO/PRHO alone 7.8%, SHO alone 11.6%, SHO alone 13.2% and PRHO alone 9.3%. The SpR spent 15 nights on the MAU, 3 days of recuperation, 33 days of annual/paternity/sick leave, 4 days of study leave. The SpR had an equivalent of 14 weeks with the consultant for clinics and endoscopy sessions (54% of the time) and the SHO 11 weeks (42%).

Conclusion: The full shift pattern has a detrimental effect on the classic Gastroenterology Firm. Words are understaffed and the SpR, when alone with the PRHO, has to sacrifice endoscopy training sessions. Training is compromised for a number of reasons: the same teaching has to be repeated as different members of the team are present on ward rounds at different times. The SHO and SpR do not get enough exposure on the wards, in clinics, and in endoscopy. We need to reassess these issues with the introduction of the Foundation Programmes and find a solution before training becomes suboptimal.
malignancies (27% v 10.8%; p = 0.16), less stone disease (38 v 52%; p = 0.16) and biliary leaks (7.8 v 0%; p = 0.07) in the HOS compared to the non-HOS. There was a difference in stent insertion (ST) (38.5 v 17%; p = 0.02), but not sphincterotomy/pre-cut (54 v 43%; p = 0.41) or mechanical lithotripsy (0.9). Further analysis of ST suggested de novo ST rather than repeat ST was a risk factor (p = 0.07) for HOS. Post procedure symptoms were a good predictor of HOS (54 v 3%; p = 0.001). Overall, the pancreatitis rate was 4.3% and commonest reason for admission was pain and nausea/vomiting. There were no fatalities.

**Conclusions:** Unexpectedly, age, comorbidity, or presence of a trainee were not predictors of hospitalisation after planned DC-ERCP. Diagnoses such as HPB malignancies and biliary leaks were more prevalent in the hospital. The best predictors. The best predictors of repeat procedure are likely to be a stent (particularly de novo) or post-procedure symptoms. Whereas the former can occasionally be anticipated, the latter cannot. This audit further highlights that for ERCP, it remains difficult to identify patients that would be suitable for a successful day-case procedure.

## 361 DIAGNOSIS AND MANAGEMENT OF SUSPECTED COMMON BILE DUCT STONES IN PATIENTS FIT FOR CHOLECYSTECTOMY: A SURVEY OF FIVE UK REGIONS

E. J. Williams, The Steering Committee, BSG audit of ERCP, British Society of Gastroenterology, 3 St Andrews Place, London, UK

**Introduction:** The role of ERCP is changing with the advent of competing technologies such as endoscopic ultrasound (EUS), magnetic resonance imaging (MR), and laparoscopic common bile duct exploration (LCBD). We aimed to establish how clinicians in English hospitals currently manage patients with suspected common bile duct stones (CBDS).

**Methods:** In 2004, 66 ERCP units from five English regions participated in the BSG audit of ERCP. In a separate questionnaire lead endoscopists were asked how their unit would manage the following: “A fit 60 year old patient with a history of abdominal pain is scheduled for laparoscopic cholecystectomy. Bilirubin = 25 μmol/l, though the patient has never been jaundiced or septic. Alkaline phosphatase is >2 the upper limit of normal. Ultrasound shows a calculous gallbladder and non-dilated common bile duct with no obvious ductal filling defects.”

**Results:** Responses were received from 44/66 (67%) of units. The most likely next investigation for such a patient was MR in 30 (69%), with 10 (23%) recommending ERCP. The remaining 4/44 (9%) of units indicated there was no possibility of LCBDE being used to treat CBD stones in such a patient.

**Conclusions:** Unexpectedly, age, comorbidity, or presence of a trainee were not predictors of hospitalisation after planned DC-ERCP. Diagnoses such as HPB malignancies and biliary leaks were more prevalent in the hospital. The best predictors. The best predictors of repeat procedure are likely to be a stent (particularly de novo) or post-procedure symptoms. Whereas the former can occasionally be anticipated, the latter cannot. This audit further highlights that for ERCP, it remains difficult to identify patients that would be suitable for a successful day-case procedure.

## 363 CLOSTRIDIUM DIFFICILE TOXIN POSITIVE DIARRHOEA IS A PREDICTOR OF MORBIDITY AND MORTALITY RATHER THAN A CAUSAL FACTOR

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**Introduction:** The incidence of clostridium difficile toxin (CDT) associated diarrhoea is rising through the NHS and is now the commonest hospital acquired infection. It is of considerable financial burden to the NHS due to the significant associated morbidity and mortality. University Hospitals Aintree (UHA) is a large teaching hospital, where the incidence of CDT at varies between 30–90 case per month with a general upward trend.

**Aim:** To determine the risk factors for the morbidity and mortality of CDT.

**Methods:** 105 episodes in 87 patients case notes in a three consecutive months period (01/10/04 to 01/01/05) were audited after being identified from the microbiology database of CDT positive stool samples. In all fatalities, the death certificates were used to verify the cause of death.

**Results:** 62% patients were female. The mean age (SD) was 77 (15). 75% of patients were elderly (>65) and 77% had multiple comorbidity. The median length of stay (LOS) was 22 days with 26.4% having LOS>60 days. The mortality was high at 43% (n = 37). Analysis between the patients that lived (LIV) and those that died (DIE) revealed no differences in the male to female ratio, blood parameters of CRP, haemoglobin, white cell and platelet count, antibiotics exposure, immunosuppressant, receipt of suboptimal treatment, or recent hospital admissions (p = 0.05 all). The DIE had an increase frequency of previous diagnosis of CDT (13.6 v 6%) and multiple comorbidities (86.5 v 66.5%; p = 0.3). However, the DIE were older (81.5 v 74.2; p = 0.005) and had a lower serum albumin (25 v 29; p = 0.02). Cardiorespiratory disease (60%) and malignancy (19%) accounted for the majority primary cause of death. CDT was the common primary cause of death only once (2.7%) and as a contributor in 6 (16.2%). The average age of these patients were 83 (range 74–95).

**Conclusions:** CDT is of significant cost to the NHS given the long LOS involved. However, this is probably due to the high prevalence of elderly patients with multiple comorbidities. The surprisingly high mortality in patients with CDT, is likely to be a reflection of the patients general illness (very elderly patients with multiple comorbidities and hypoalbuminaemia) rather than a direct causal effect of CDT itself. This may help explain the increase incidence of this infection given that the NHS is dealing with an increasing aging population.

## 362 USE OF SOLUBLE TRANSFERRIN RECEPTORS IS A VALUABLE, RESOURCE-SPARING TOOL IN IRON DEFICIENCY DIAGNOSIS

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**Introduction:** Anaemic patients, with normal MCV and ferritin, are often overinvestigated with endoscopic procedures. However, the ratio of sTfR/log ferritin is a useful tool in discriminating iron deficiency anaemia (IDA) from other types of anaemia.

**Aims and Methods:** (1) To implement a protocol, using sTfR/log, ferritin ratio and iron status, as a tool in differentiating IDA from other forms of anaemia. (2) To assess the impact of this protocol on the workload of the Endoscopy Unit of a busy DGH and on the overall service delivery. Between June and December 2004, 30 patients referred with normocytic anaemia to our DGH were included in the study. All patients had ferritin and sTfR estimated by the first outpatient clinic visit. The BSG (British Society of Gastroenterology) guidelines for IDA were followed.

**Results:** Of thirty patients studied (mean age 70.3 years), eight had ferritin <30 μg/l, thus had further investigations for IDA. Ten patients had ferritin >100 μg/l, making ID unlikely according to BSG guidelines, and were not candidates for endoscopic investigations. Of the remaining 11 patients with ferritin values between 30 μg/l and 100 μg/l, seven had ratio >2 and were investigated, while one had ratio <1 and was not investigated according to the protocol. Three had ratios between 1 and 2, possibly necessitating investigations if they responded to iron. We found 610 patients on our DGH’s endoscopy register having procedures performed between the indication of ‘anaemia’. If our results above were applied, 154 patient groups to belong to which ID could be excluded using the protocol based on sTfR (a single test costs £8; overall cost: £123,000). This would be suitable for a successful day-case procedure.

**Conclusion:** The use of sTfR/log ferritin is recommended as a first line test in patients with normocytic anaemia and normal ferritin. It can improve patient care by increasing the diagnostic yield of endoscopic tests and spare the inappropriate use of these valuable resources.

## 364 IS CONSCIOUS SEDATION PRACTICED SAFELY IN PATIENTS UNDERGOING COLONOSCOPY?

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**Background:** Diagnostic and therapeutic colonoscopy is a common procedure and requires patients to have conscious sedation. The procedure itself is relatively safe with an overall mortality of less than 1% (http://www.ncepod.org.uk). However, the sedation practice of endoscopists differs significantly and oversedation may be putting patients at excess risk particularly in the elderly (>70 years).

**Aims:** To compare the sedation practices of endoscopists performing colonoscopy at a district general hospital.

**Methods:** All patients undergoing colonoscopy during July and August 2005 were identified retrospectively using the computerised endoscopy reporting database and cross referenced with the endoscopy appointment diary. We considered safe conscious sedation practice as

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infrared doses of 5 mg midazolam and 50 mg pethidine in patients aged under 70 and 2.5 mg midazolam and 25 mg pethidine in patients aged >70 years.

Results: 12 endoscopists performed a total of 273 colonoscopies during the study period. The mean number of colonoscopies per endoscopist was 23 (range 2–64). The patients mean age was 64 (range 18–91); there was no significant difference in the patients’ mean age between endoscopists (average range 58–70); 40% (n = 110) of colonoscopies were performed in patients aged >70 years (mean age 79, range 75–87). The sedation dose was 5 mg midazolam (range 2.5–15 mg) and pethidine 50 mg range (25–100 mg). Using our criteria 43% of all patients (n = 118), 18% (n = 30) in the under 70s and 80% (n = 88) of the >70 years received more sedation than recommended; two patients required intravenous doses of midazolam and/or pethidine to reverse sedation.

Conclusion: Our findings raise concerns regarding our use of sedation in the elderly and following the NCEPOD report on endoscopy changes in practice are required. A further audit will be performed six months after these results are discussed with our colleagues.

Acknowledgements: We thank the endoscopy unit administration staff for their help with data collection.

365 THE TWO WEEK RULE FOR COLORECTAL CANCER: EXPERIENCE OF A NURSE LED FLEXIBLE SIGMOIDOSCOPY CLINIC IN PRIMARY CARE

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Background: A nurse led flexible sigmoidoscopy clinic was established in a primary care setting to meet the increased demand generated by the lower GI two week rule. Aim: To establish a protocol driven clinic in the community that would reduce the time to investigation and facilitate the pathway for patients referred for flexible sigmoidoscopy. Methods: Retrospective study of all patients referred under the lower GI two week rule to the community flexible sigmoidoscopy clinic from March 2004 to June 2005. Follow up was protocol based. Patients diagnosed with colorectal cancer were placed on a fast track pathway for further imaging.

Results: 1000 patients underwent flexible sigmoidoscopy in primary care from March 2004 to June 2005. 96 (9.6%) patients were investigated following referral under the two-week rule for colorectal cancer. The median age was 58 years (22–77). The median time to Flexible sigmoidoscopy was 12 days (4–48). Two patients were referred after an initial outpatient visit and 94 patients were investigated directly in primary care. 27 (28%) patients had a normal study. 24 (25%) patients were diagnosed with significant colonic pathology including nine per cent patients with colorectal cancer. 53 (55%) patients underwent further imaging of their colon either in the form of a colonoscopy or barium enema. 28 patients were referred for outpatient follow up and 11 for other investigations. No complications have been encountered.

Conclusions: A nurse led flexible sigmoidoscopy clinic in primary care can provide a safe diagnostic service for patients referred under the two week rule. The use of protocols enables experienced nurses to refer patients for further investigations and safely discharge patients back to the community.

366 SURVEILLANCE COLONOSCOPY: DO THE BRITISH SOCIETY OF GASTROENTEROLOGY GUIDELINES CHANGE CLINICAL PRACTICE?

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Aim: To assess the implementation of the British Society of Gastroenterology (BSG) guidelines for ‘colorectal cancer screening in high risk groups’ for patients awaiting surveillance colonoscopy at the Endoscopy Unit of a Teaching Hospital over a period of 12 months.

Method: Case note review was performed for patients due to undergo surveillance colonoscopy over 12 months and the BSG guidelines for ‘colorectal cancer screening in high risk groups’ (October 2002) were used to guide patients on the waiting list.

Results: The case notes of 193 patients on the surveillance colonoscopy waiting list from July 2004 to July 2005 were reviewed. The median age (range) was 58 (29–83) and 97 (50.2%) patients were male. We were able to cancel or delay the colonoscopy in 85 (44%) patients, with 48 (25%) patients being removed from the waiting list and 37 (19%) patients having their colonoscopy delayed. In this latter group of 37 patients who either had colonic polyps or a positive family history of colonic carcinoma, surveillance had been arranged earlier than advised by the BSG guidelines. It was also of note that 10 (5.1%) patients had their colonoscopy brought forward and six (3%) patients’ families were referred for genetic advice. The reasons identified for removing patients from the waiting list included: inappropriate polyp follow up, deterioration of general health, and calculation of lifetime colorectal cancer risk lower than 1:10.

Discussion: With the pressure on endoscopy waiting times and the potential impact of colorectal cancer screening, validation of waiting lists using the BSG guidelines may prevent large numbers of patients from having an inappropriate or mis timed colonoscopy.

367 RATIONALISING COLONOSCOPY REFERRALS: AN AUDIT OF COLORECTAL POLYP SURVEILLANCE IN A DISTRICT HOSPITAL

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Introduction: In 2000, the BSG produced guidelines detailing an appropriate follow up strategy for patients found to have adenomatous polyps within the colon. We became aware that a number of patients in our unit had been booked for examinations, which did not accord with these recommendations. In the light of this observation, we conducted an audit of patients waiting for surveillance colonoscopy, in order to review their treatment plan and modify this if appropriate.

Method: We conducted a retrospective case note audit for all patients due to undergo surveillance colonoscopy in the six month period from January 2005 to July 2005. Patient details, together with the findings from previous endoscopies and histology results were carefully reviewed using the BSG guidelines. Two separate observers, drawing from the published BSG Guidelines, independently appraised the appropriate management plan.

Results: A total of 111 case notes were reviewed. Out of this group, 39 patients were being followed up because of previous adenomatous polyps. On applying BSG guidelines, 25 patients (64% of the total) needed a change in their management plan. Nine patients (23%) needed no further follow up. In 11 patients (28%), the endoscopy interval was increased from three to five years. In contrast, four patients were noted to have indications for more frequent surveillance, and one patient had been inappropriately booked for a sigmoidoscopy rather than colonoscopy.

Conclusion: In this six month audit, we changed the surveillance plan in a large proportion of our patients. This produced a considerable saving of endoscopy resources and contributed positively to patient safety, through reducing inappropriate examinations. This accords with similar findings reported from other endoscopy units. We would recommend that such audits be conducted on a regular and repeated basis, to avoid inappropriate referrals and to reduce endoscopy waiting times. This would address past clinical decisions. There is also a challenge to educate all endoscopists in the use of current guidelines.

368 NURSE LED INFLAMMATORY BOWEL DISEASE TELEPHONE HELP DESK: IMPACT ON CLINICAL MANAGEMENT AND PATIENT SATISFACTION


Introduction: The role of nurse specialists in management of inflammatory bowel disease is evolving. There is little evidence that it has an impact on hospital admissions, outpatient appointments or patient satisfaction.

Aims: To evaluate the impact of nurse led inflammatory bowel disease (IBD) help desk on (1) the number of hospital admissions, (2) outpatient appointments, and (3) patient satisfaction from the service.

Method: The study was based in our hospital where the IBD help desk was established in August 2001. The patients who used the service between April 2004 and March 2005 (12 months) were identified from a call log book. The reason for the call and advice given were recorded. If a treatment was initiated on telephone advice it was considered to have saved an outpatient appointment. A comparison of hospital admissions due to inflammatory bowel disease flare-ups was made between the study period and a similar 12 month period (April 2000 to March 2001) prior to the help desk being established. A questionnaire was sent to all patients who used the service during the study period.

Results: 234 patients made 836 calls. General practitioners made 10 calls. There was no reduction in the number of admissions [122 in study
Audit of inflammatory bowel disease clinics: results from two patient satisfaction surveys

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**Background:** British Society of Gastroenterology guidelines for the management of inflammatory bowel disease (IBD) emphasise the importance of considering “patient driven criteria” when auditing quality of care.

**Aims:** To examine patients’ views about IBD outpatient clinics, to identify problems associated with clinic attendance or clinic facilities, and to assess patients’ usage of direct access to hospital care.

**Methods:** Interview based audit (Audit A) of 40 patients attending IBD outpatient clinics in 2005 and questionnaire based audit (Audit B) of 40 patients who attended the same clinics in 2004.

**Results:** Participation rates were high, exceeding 95% in both audits. Interviewees (Audit A) gave a mean score of 8.9 out of 10 (range 6–10) for overall clinic satisfaction, and also valued highly the availability of direct access to hospital-based care (mean score 9.3 out of 10, range 5–10). Longish waiting time at clinic was the most commonly reported problem (47.5%), but most of those reporting this problem (94.7%) indicated that shorter waiting times at the expense of direct access would not be acceptable. High numbers of the interviewees (80%) also indicated that the provision of more information for IBD at clinics would be useful. All questionnaire respondents (Audit B) rated overall satisfaction with outpatient clinics as good or excellent. These patients generally viewed waiting times of 40 minutes or more as unacceptable. Direct access to hospital based care by questionnaire respondents was used most commonly in relation to disease flare-ups (71.4%) and/or to arrange a new appointment (42.9%).

**Conclusions:** Direct access to care was valued very highly and it was used most commonly in relation to disease flare-ups. Overall, patients viewed the IBD clinics positively.


Nurse led methotrexate service for patients with Crohn’s disease: a 12 month prospective audit

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**Background:** We have introduced a dedicated nurse led clinic for methotrexate (MTX) administration. The audit examines the outcomes of patients with Crohn’s disease (CD) who attended a dedicated specialist nurse clinic for treatment, education and clinical review.

**Methods:** A drop-in clinic was established for patients requiring parenteral MTX. A Consultant Gastroenterologist reviewed each patient three-monthly. Protocols for the administration of MTX were developed in conjunction with a multidisciplinary team. Patient held records ensured effective communication between primary and secondary care. Protocols for patient education were adapted from the RCP rheumatology guidelines and approved by the hospital trust board for use in patients with CD. A 12 month audit was undertaken, monitoring patients CD activity index (CDAI), outcomes of therapy and interventions undertaken in clinic. Consultant satisfaction was assessed using a questionnaire. A patient questionnaire was used to assess patients’ perceptions of the service.

**Results:** Eleven patients received MTX. All received IM MTX. 25 mg weekly for 12 weeks, administered and prescribed by a specialist nurse using supplementary prescribing. Of these, six converted to oral MTX and remained well. Four patients required long term parenteral MTX, and doses where adjusted to 15 mg. These patients were taught to self administer. One patient discontinued due to intolerance. At 12 weeks, CDAI had fallen from a mean of 308 to 212, and mean prednisolone dose from 36 mg to 12.5 mg. Consultants reported increased confidence in safe administration and monitoring of MTX. A patient questionnaire reported that a drop in clinic was an acceptable means of review, as they received emotional support from peers. Patients identified that a nurse specialist clinic reduced patient attendance, reduced waiting times, improved continuity, and increased satisfaction with care.
Conclusion: The development of a nurse led MTX clinic for patients with CD has facilitated a significant improvement in the overall quality of patient care.

**373 TRAINEE IN GASTROENTEROLOGY VIEWS ON TEACHING IN CLINICAL GASTROENTEROLOGY AND ENDOSCOPY**

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Introduction: During the 2004 meeting of the British Society of Gastroenterology, there were discussions in the Trainees in Gastroenterology meeting, regarding the quality of teaching. By adopting a flexible timetable, which was made training time a premium.

Aims: The questionnaire gathered data on the extent and quality of teaching, training, and supervision in outpatient clinics, on ward rounds, and in endoscopy by procedure, as well as trainees’ teaching experience, training, and intentions to teach.

Methods: The questionnaire was piloted and tested. The final document was sent out via the Trainees in Gastroenterology office using a private mailing company. All trainees who were in substantive training posts in England and Wales were included, approximately 500 SpRs. Only around 250 questionnaires were received by the trainees because of insufficient postage being franked on the envelopes. 173 forms were returned. In view of the difficulties above, we felt that this was a representative sample.

Results: Of the trainees, 68/169 were never, rarely, or not often taught on ward rounds. 92/168 trainees “never, rarely, or not often” discussed new outpatients with the consultant, and only 13/170 trainees discussed new patients frequently or all the time. Although the quality of teaching was rated as “Quite good—Excellent” by 91/170, it was rated “so-so—very poor” by 79/170. Endoscopic supervision and training was inconsistent, with 76/170 being taught “frequently—all of the time”, and 53 “not often—never” for procedures in which they were still training. Trainees not fully trained in a procedure were being supervised by distant trainers.

Conclusions: Teaching and training in gastroenterology is very variable both in quality and quantity. Of particular concern, supervision for endoscopy is often inadequate or absent. There are many opportunities to improve our teaching and training in gastroenterology.

**374 OPTIMISING TRAINING OPPORTUNITIES FOR A GASTROENTEROLOGY SPR IN A BRITISH DISTRICT GENERAL HOSPITAL**

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Background: The EWTD has reduced training time due to restructuring of on call rotas with compensatory time off. Recognising this we devised a prospective flexible timetable for the single SpR in our hospital to optimise training opportunities within a four consultant gastroenterology team.

Methods: An excel spreadsheet was created, dividing the working week into 10 sessions, covering the full 12 months. SpR absences due to days off, post on call (total: 8), days worked on MAU, SpR training sessions, study and annual leave, and consultant absences were identified and recorded on the spreadsheet in advance. In the available sessions left after taking these factors into account, two clinics, two endoscopy lists, and two ward rounds (one SpR led and one consultant) were booked per week in a flexible manner. At the end of the year the number of days worked in gastroenterology was calculated and the numbers of clinics, endoscopy lists and ward rounds that actually occurred were recorded. The number of clinics, lists, and ward rounds that would have occurred had the SpR followed the previous year’s fixed timetable was also calculated.

Results: In 12 months 131 days (26.2 weeks) were worked by the SpR in gastroenterology. The SpR attended 57 clinics, 48 endoscopy lists, 36 consultant, and 33 SpR led ward rounds. Had the SpR followed a fixed timetable he would have attended 35 clinics, 42 endoscopy lists, 51 consultant led, and 25 SpR led ward rounds. There is a statistical difference between each figure (z test p<0.05).

Discussion: In 12 months only 26 (5 day) weeks were spent doing gastroenterology as a result of the various absences. The EWTD has hence made training time a premium. Training centres, trainers, and trainees need to maximise training opportunities to allow SpRs to gain adequate experience. By adopting a flexible timetable we were able to significantly increase SpR training opportunities in endoscopy by 14%.

**375 ALTERATIONS IN HUMAN DEFENSIN-5 (HD-5) EXPRESSION FOLLOWING GASTRIC BYPASS SURGERY**

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Introduction: Roux-en-Y gastric bypass surgery provides a novel human model to investigate mucosal innate immunity, in which there is loss of gastric acid-mediated protection against orally-acquired microorganisms. We have studied changes in mucosal HD-5, which is an antimicrobial peptide normally produced by Paneth cells.

Methods: Mucosal HD-5 samples were obtained from 18 female patients (24–54 years), from the same segment of jejunum during and after (at endoscopy) gastric bypass surgery. Samples were used for bacterial culture and immunohistochemistry using anti-HD-5 antibody. The number of immunoreactive cells per crypt and villi were determined and expressed as mean (SD).

Results: No bacteria were cultured from any of the perioperative jejunal samples but colonies of bacteria normally present in the pharynx were identified during culture of all postoperative jejunal biopsies (1--100 colonies). Paneth cell numbers per crypt were unchanged after gastric bypass [4.16 (0.71) v 4.24 (0.78)]. However, following surgery, there was an increase in HD-positive intermediate cells per crypt (0.25 (0.41) v 1.12 (0.66), p<0.01), HD-5 staining enterocytes per crypt (0.31 (0.09) v 1.38 (1.10), p<0.01), HD-5 staining material in the crypt lumen (crypt lumens: 5.0 (10.9%) v 68.1 (27.9%), p<0.01) and HD-5 immunoreactivity coating the luminal surface of villi enterocytes (villi enterocytes: 1.5 (0.76) v 6.87 (4.20), p<0.01).

Conclusions: (1) Bacteria normally resident in the pharynx were present in the proximal jejunal mucosa following Roux-en-Y gastric bypass surgery. (2) After gastric bypass, there was increased secretion of HD-5 and an increase in HD-5 expressing intermediate cells and enterocytes in the crypt. (3) The increase in HD-5 expression in the jejunal mucosa following gastric bypass surgery is likely to be secondary to exposure to orally-acquired microorganisms.

**376 A PROSPECTIVE STUDY OF THE PREVALENCE OF EXOCRINE PANCREATIC INSUFFICIENCY IN PATIENTS WITH DIARRHOEA PREDOMINANT IRRITABLE BOWEL SYNDROME USING FECAL ELASTASE-1**

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Introduction: Patients who meet the Rome II criteria for irritable bowel syndrome (IBS) may be found to have other underlying pathologies. Mild to moderate chronic pancreatitis may be under diagnosed. Previous evidence suggests that 20% of patients with IBS may have an abnormal triloin breath test suggesting pancreatic insufficiency. We wished to determine if exocrine pancreatic insufficiency may be present in patients who present with diarrhoea predominant IBS (D-IBS).

Patients and Methods: 294 consecutive patients referred to our unit with diarrhoea predominant IBS (D-IBS) were assessed for evidence of exocrine pancreatic insufficiency using the faecal elastase-1 test (Fel-1). Baseline bowel frequency, stool consistency and weight were recorded. All D-IBS patients were investigated as per the British Society of Gastroenterology IBS guidelines (2000). Those patients with a pathologically low Fel-1 level (<100 μg/g stool) were offered pancreatic supplements and bowel habit and frequency assessed at six months. In this group the pancreas was also imaged using ultrasound or CT.

Results: 294 patients were included (median age 47 years, 84 males). 16 patients had a Fel-1 <100 μg/g stool (5.4%). Eight patients to date have been given pancreatic supplements. In this group the median number of stools per day reduced from 6 to 1.5 (p<0.011). These patients also reported a marked improvement in urgency. There were no changes in weight. Other diagnoses in the remaining patients were D-IBS 80.3% (236/294), coeliac disease 6.1% (18/294), diverticular
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age. There is a preponderance of women particularly for those diagnosed under the age of 35 years.

381 THE NUMBER OF CANCERS ARISING TWO OR MORE YEARS AFTER THE DIAGNOSIS OF COELIAC DISEASE IS SMALL

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Aims: To explore the numbers of cancers occurring in a large coeliac population accrued between 1958 and 2005 in a single centre. Selection bias was minimised because this cohort is representative of those patients seen in routine clinical practice.

Methods: The diagnosis of coeliac disease (CD) was based on small bowel biopsy appearances of severe or total villous atrophy. Extensive efforts were made to identify all patients in the area served by the Derby hospital. Information on cancers arising in the group was obtained during clinical review, analysis of case notes available for all patients and comprehensive searching of the histological data base of the Derby hospitals. Cancers were classified as incident if these occurred two years or more after the diagnosis of CD. Cancers arising before the diagnosis of CD or within two years of the diagnosis of CD were regarded as prevalent. A dedicated weekly clinic for CD run by the author acted as a focus for care and research. Patients were followed prospectively from 1978. Those referred from other secondary care centres were excluded from consideration.

Results: Of 1146 patients with CD 115 (10%) developed malignancies. Of these, 57 were incident tumours while the remainder occurred either before (33) or within two years of the diagnosis of CD (37). A wide variety of cancers was encountered, mostly in small numbers. Of the cancers of interest in relation to CD only three oesophageal tumours were found all of which were incident. Three small intestinal adenocarcinomas were encountered, two prevalent, and one incident. 17 non-Hodgkin’s lymphomas occurred but only six were incident and just five were enteropathy-associated T cell lymphomas (EATL) all of which were incident.

Conclusions: In this large population based cohort study of malignancy in CD the number of cancers arising was very small, particularly two or more years after the diagnosis of CD even for oesophageal and small intestinal tumours which have been associated with CD. For lymphomas, particularly EATL, numbers were also small. These data can be used to reassure patients and their carers that two years after the diagnosis of CD only very small numbers of cancers arise.

382 LONG TERM MORTALITY IN PEOPLE WITH COELIAC DISEASE DIAGNOSED IN CHILDHOOD COMPARED WITH ADULTHOOD: A POPULATION BASED COHORT STUDY

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Introduction: Recent studies have shown that people with coeliac disease have a 30–40% increased mortality rate when compared with the general population. We explored whether the excess mortality in coeliac disease remains many years after diagnosis and if there are differences between those diagnosed in childhood versus adulthood.

Methods: 285 children and 340 adults diagnosed between 1943 and 1983 with coeliac disease in the Lothian region of Scotland were followed until death, loss to follow up or the end of 2004 whichever came first. We calculated cause specific standardised mortality ratios (SMR) by comparing their mortality experience with that of the Lothian population between 1970 and 2004.

Results: We included 21 deaths in children and 174 deaths in adults in our analysis with a median follow up of 34 years and 23 years respectively. All cause mortality more than five years after diagnosis was increased threefold in children (SMR 3.32 95% CI 2.05 to 5.07) compared with only a 38% increase in adults (SMR 1.38 95% CI 1.16 to 1.63). This excess mortality in children was primarily due to an increased risk of accidents, suicides and violence (7 deaths, SMR 3.22 95% CI 1.29 to 6.63), cancer (5 deaths, SMR 3.72 95% CI 1.21 to 8.67) — particularly lymphoma (2 deaths, SMR 21.01 95% CI 2.54 to 76.00) and cerebrovascular disease (2 deaths, SMR 10.03 95% CI 1.21 to 36.00). The modest excess in adults was mainly due to lymphoma (8 deaths, SMR 10.62 95% CI 4.59 to 21.00). These differences persisted after 25 years or more follow up.

Conclusions: Children diagnosed with coeliac disease have a long term threefold increased risk of mortality when compared with the general population. This is in stark contrast to the experience of adult coeliac disease where the increase risk is modest. Reasons why may reflect severity of disease in children and/or, for external causes of death, behavioural change related to having a chronic disease diagnosis.

383 LONG TERM HISTOLOGICAL FOLLOW UP OF PEOPLE WITH COELIAC DISEASE

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Background: Increasing numbers of people are being diagnosed with coeliac disease (CD) for which the only treatment is a gluten-free diet (GFD). There are few studies looking at the long term histological follow up of people with CD.

Methods: All CD patients, with an index small bowel biopsy and one or more sets of follow up biopsies and attending a CD clinic in either of two teaching hospitals, were included in the study. The study took their details entered into a Coeliac Patient Database (CPD). Clinical information is entered prospectively where possible and relevant retrospective data extracted from notes, including histological score (HS) (classified as normal, increased intraepithelial lymphocytes (IELs) only, partial villous blunting (PVB), subtotal villous atrophy (TVA) and total villous atrophy (TVA) and adequate compliance with GFD (good, partial, poor). The primary aim of this study is to look at the length of time to histological remission (HR) in CD patients. Correlation between HS, gender, age, and compliance, was examined by Kendall’s rank, Mann-Whitney U and chi² tests, as appropriate.

Results: Of the 169 patients (125 female, 44 male) mean age at diagnosis was 42.8 (range 0.73–80.32) years with a mean follow up of 6.03 (range 0.13–26.21) years. Median number of sets of biopsies taken was three (range 2–12). Nine (all female) patients had an initial biopsy reported as normal (that is, they had latent CD), 17 with IELs, 31 with PVB, 56 with PVA and 61 with TVA. Of the 160 patients with an initial histological abnormality, 58 (43 female, 15 male) patients had a documented complete HR. Only 28 (48%) remissions occurred within two years, 41 (71%) within five years and the remaining 17 took greater than five years to achieve HR. Overall 129 (81%) of these 160 patients showed either HR or some improvement in their HS at least once, but 26 (16%) showed no change and 5 (3%) a deterioration. There was no association between either gender or age and HR, although there was a significant trend towards faster HR as patients got older (p < 0.01). There was a strong correlation (p < 0.001) between good compliance with a GFD and better HS, but not between age and HS, gender and HS or age and compliance.

Conclusion: Time taken to histological remission even for CD patients with good compliance for GFD may take longer than many clinicians realise, especially in younger patients.

384 90% OF COELIAC DISEASE MAY BE BEING MISSED

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Background: Data from Avon Longitudinal Study of Parents and Children (ALSPAC) suggest that the prevalence of coeliac disease (CD) is 1%. In this study 5470 children randomly selected from a total of 14 000 were screened using Tissue Transglutaminase (TTG) and sIgA endomysial antibodies (EMA). S4 children proved positive for CD. Subsequently, 121 children were diagnosed as having CD. ALSPAC is an anonymous study and hence these children have not been referred for biopsy or told the results. Within Avon all children with suspected or serologically positive CD are referred to just one centre, Bristol Children’s Hospital, for small bowel biopsies for formal diagnosis of CD.

Aims: The aim was to identify children from ALSPAC (date of birth 01/04/1991 – 31/12/1992 and Avon postcodes) who had been formally diagnosed as CD.
Methods: Since 1990, data have been prospectively collected on all children having endoscopic small bowel biopsy for CD. These data and centralised computer and dietetic records within Avon have been analysed to identify children with CD.

Results: Twelve children from Avon diagnosed with CD since 1.4.91 have birthdays concordant with ALSPAC. This gives a prevalence rate of 1/1100. All had symptoms. Four had a family history. At time of diagnosis all were aged over 2 years, three were 5–6 years, six were 5–10 years, and three were aged 10–14 years. Discussion: Based on screening data, 140 children from Avon would be expected to have CD. However only 12 of these children have been diagnosed with CD. This suggests that 90% of children with possible CD may be being missed. The screening data also recorded that children with positive screening tests were lagging behind in growth by nine months. There are other well documented long term health hazards of untreated CD. Our data suggest all children should be screened for CD.


385 RECOGNISING COELIAC DISEASE ON TERMINAL ILEAL BIOPSIES: SHOULD INTRAEPITHELIAL LYMHCYTOSES BE ROUTINELY QUANTIFIED?


Background: Coeliac disease (CD) may cause histological changes throughout the small bowel but is conventionally accepted as being predominantly a proximal lesion. Reports have shown changes of ileal villous atrophy, crypt hyperplasia, or raised intraepithelial lymphocyte (IEL) counts on terminal ileal (TI) biopsy.

Aim: We wanted to assess whether TI histological abnormalities occurred more commonly in patients with CD by comparison to other disease groups.

Methods: TI biopsies were examined from 20 patients with a new diagnosis of CD. The controls comprised of four groups: CD established elsewhere on a gluten free diet (GFD) but with persisting symptoms (n = 25), inflammatory bowel disease (IBD) (n = 44), chronic diarrhoea (n = 44), and polyp surveillance (n = 47). All the biopsies were examined for the presence of villous atrophy, crypt hyperplasia and IEL count per 100 enterocytes (IEL/100EC).

Results: One patient of 20 (5%) with new CD had changes of villous atrophy, crypt hyperplasia, and polyp surveillance of 12.6 IEL/100EC (p < 0.0001). Validating TI villous IEL counts as a test for CD using an IEL/100EC of >25 gives a sensitivity of 45% and a specificity of 97.8% respectively.

Conclusion: IEL should be routinely requested and quantified in TI biopsies. The presence of IEL on a TI biopsy should alert the colonoscopist to the possibility of CD.

386 SURVEY OF THE USE OF SMALL BOWEL FOLLOW THROUGH

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Background: Small bowel follow through (SBFT) has been shown to under diagnose certain conditions. We felt that a large number of the tests requested in our hospital showed normal results and decided to examine our current practice of investigating the small bowel with SBFT.

Methods: We retrospectively identified consecutive small bowel follow through reports from the radiology department. Indications, results and final diagnosis (by other tests or operation) were noted.

Results: We identified 72 patients and retrieved 68 notes. Six of 68 patients had an abnormality diagnosed on SBFT. Indications (figures given in brackets: normal/abnormal test): known inflammatory bowel disease (IBD) (8/2); suspected IBD (16/1); IBS (3/0); abdominal pain (5/0); vomiting (2/0); diarrhoea (4/0); small Bowel Obstruction (SBO) (4/0); anaemia (1/0); iron deficiency anemia (IDA) (3/0); coeliac disease (8/0); malabsorption (1/1); suspected tumour (3/1); unknown (1/0). Abnormal SBFT (6 patients, 9%); two patients with previous radiation exposure for CA endometrium (indications: SBO and suspected tumour respectively), two patients with Crohn’s disease (SBO and polyps), one patient with a Spigelian hernia (suspected ID), one patient with small bowel diverticulitis (malabsorption). Normal SBFT (62 patients, 91%). Missed diagnosis: Three patients with Crohn’s disease. One patient with coeliac disease on small bowel biopsy (abdominal pain). Negative test: normal in all three patients with known IBS. No patient with coeliac disease had any evidence of small bowel lymphoma. Diarrhoea, abdominal pain, and vomiting were not associated with positive SBFT result.

Conclusion: We will consider our investigation modalities for the small bowel. SBFT is a valid investigation for SSBO. In all other patients another modality, such as capsule endoscopy, is more appropriate.


387 ARE GASTROINTESTINAL SYMPTOMS A PREDICTOR OF NSAID INDUCED SMALL BOWEL INJURY? A PILOT STUDY


Background: The use of non-steroidal anti-inflammatory drugs (NSAIDs) has been associated with small bowel (SB) injury. The spectrum of NSAID induced enteropathy varies from minor punctate haemorrhages to erosions, ulcers, and diarrhoea like strictures. The frequency of these lesions in relation to symptoms is yet to be defined.

Aim: To assess the prevalence of SB injury in patients taking long term NSAIDs and the role of gastrointestinal (GI) symptoms in predicting the presence of NSAID induced enteropathy.

Methods: Patients with arthritis and on NSAIDs (>3 months duration), were enrolled in this pilot study. Patients with obstructive symptoms or previous GI surgery were excluded. The presence of GI symptoms and ingestion of all drugs were noted. All patients underwent capsule endoscopy (CE) (Given Imaging, Yoqneam, Israel) after ingestion of two sachets of Kleen Prep and an overnight fast. The images were read by a gastroenterologist who was blinded to the presence of symptoms and type of NSAID. Lesions seen were classified as red spots, erosions, or ulcers.

Results: Twenty two patients were included in this pilot analysis (12 males), average age 58 years (range 38–75 years). Nine patients were asymptomatic, with heartburn (6) or abdominal pain (3). In addition, four patients were on aspirin 75 mg and three patients were on proton pump inhibitors (PPI). Complete examination of the SB was achieved in all patients without complications. One patient underwent Roth net placement of CE due to chronic opiate intake. Evidence of SB injury was seen in 36% of patients with NSAID enteropathy detected by CE (p < 0.1). 75% of patients who were on aspirin in addition to other NSAID’s and 67% of patients on a PPI had evidence of erosion in the SB.

Conclusion: NSAID induced enteropathy is common in chronic NSAID users. Small bowel injury detected by capsule endoscopy is poorly correlated with patient symptoms. May 21, 2021.
Conclusion: Serological testing before gastroscopy would have recognised 92% of patients with CD (46/50). The four cases that were seronegative would still have been diagnosed if a D2BX was performed in high risk groups. We would recommend serological testing for CD in low risk group patients prior to gastroscopy, in our series we would have avoided D2BX in 832 patients without missing a case of CD.

Nutrition posters

389 TIMING OF PERIOPERATIVE PARENTERAL NUTRITION SUPPORT AND CLINICAL OUTCOME

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Introduction: In our Institution we provide parenteral nutrition (PN) for patients with intestinal failure such that they can not be fed adequately by other means who are either severely malnourished (BMI < 18.5 or > 10% weight loss) or who have eaten very little for > 5 days and/or are unlikely to eat for the next 5 days. We sought to investigate the merits of the latter indication in patients who were not severely malnourished with postoperative ileus.

Methods: Patients were grouped according to the number of days they had been without nutrition (0-5, 6-10, and >10 days). Clinical outcomes following the introduction of PN were recorded. Patients with severe malnutrition were excluded (BMI < 18.5 or > 10% weight loss).

Results: Sixty five patients were studied (55% female, median age 69 years). See table of results.

<table>
<thead>
<tr>
<th>Days without nutrition</th>
<th>PN days*</th>
<th>Recovery of GI tract (days)*</th>
<th>Organ failure</th>
<th>Length of stay (days)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 days (n = 18)</td>
<td>9 (6-16)</td>
<td>7 (6-14)</td>
<td>2 (11%)</td>
<td>33 (25-51)</td>
<td>1 (5.5%)</td>
</tr>
<tr>
<td>5-10 days (n = 28)</td>
<td>7.5 (5-10)</td>
<td>6 (5-9)</td>
<td>2 (7%)</td>
<td>27 (17-49)</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>&gt;10 days (n = 19)</td>
<td>8.0 (4-11)</td>
<td>7 (4-9)</td>
<td>2 (11.5%)</td>
<td>31 (21-56)</td>
<td>1 (5.5%)</td>
</tr>
<tr>
<td>Total (n = 65)</td>
<td>8.0 (5.5-10.5)</td>
<td>7 (5-10)</td>
<td>6 (9%)</td>
<td>30 (21-53)</td>
<td>5 (8%)</td>
</tr>
</tbody>
</table>

*Median and interquartile range.
†Not significant.

Results: 137 patients were studied (53% female, median age 69 years). 28 patients (20%) had a BMI < 20 kg/m² and 32 patients (23%) had >10% weight loss during the preceding 3-6 months. All patients had a MUST score > 2; 22 (16%) had a MUST score of 5-6. The median duration of PN was eight days (interquartile range 6-14) and the median time to tolerance of solid food or enteral tube feeding was seven days (IQR 5-12). These outcomes and the incidence of septic complications were not influenced by nutritional status. The incidence of organ failure was significantly higher in those with a BMI < 20 kg/m² (29% v. 12%; p = 0.03) and those with a MUST score of 5-6 (32% v. 12%; p = 0.02). Those with >10% weight loss tended to have a higher incidence of organ failure (25% v. 12%; p = 0.08). The median length of stay was 33 days (IQR 22-56) and was not influenced by nutritional status. It was overall mortality rate was 12%, which was significantly higher in those with a BMI < 20 kg/m² (29% v. 8%; p = 0.004) and a MUST score of 5-6 (32% v. 9%; p = 0.003). Those with >10% weight loss tended to have a higher mortality rate (22% v. 10%; p = 0.07).

Conclusion: These results demonstrate that malnutrition is a common cause, MUST criteria are useful in identifying high risk patients and should be incorporated into clinical practice.

390 IMPACT OF NUTRITIONAL STATUS ON CLINICAL OUTCOME FOLLOWING MAJOR ABDOMINAL SURGERY

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Introduction: Malnutrition is common, under-recognised and has a detrimental impact on clinical outcome. We sought to investigate the incidence and consequences of malnutrition in a population of perioperative patients requiring parenteral nutrition (PN) support.

Methods: Nutritional status was assessed by body mass index (BMI), percentage weight loss, and Malnutrition Universal Screening Tool (MUST) score. Clinical outcomes including duration of PN, recovery of gut function, septic complications, organ failure, length of stay, and inhospital mortality were recorded.

Results: 128 patients were treated with subcutaneous infusion of 0.9% saline +/- magnesium over a 10 year period. 16 of these (38%) required conversion to intravenous fluid administration (+/- electrolytes or macronutrients) within three months of starting and were judged to have failed treatment. Reasons for failure included intolerance (68%) due to discomfort, poor absorption or haemotoma, dehydration (13%), and death from unrelated causes (6%). The remaining 26 patients (62%) were compared with 12 patients successfully treated in Centre B. Of the 26 patients successful treated in Centre A, 12 (46%) continued treatment for >12 months and four (15%) continued for >60 months. Median treatment duration was 10.5 months (range 1-107 months). Treatment was discontinued due to dehydration (43%), corrective surgery (31%), no further requirement (13%), or death from unrelated causes (13%). 20% of patients resumed exclusive enteral support, 15% required IV fluids +/- electrolytes and 15% required IVN. Subcutaneous fluid infusion was ongoing in 38% of patients. Median treatment length in Centre B was five months (range 2-46 months). 64% of patients underwent surgical repair after a median of 3 months (range 2-8 months) and 84% were able to return to exclusive enteral support.

Conclusion: Subcutaneous fluid infusion is a useful treatment modality in the management of patients with moderate intestinal failure both as a long term measure to maintain fluid balance and as a bridge to definitive surgical treatment. It can be considered as a viable alternative to long term intravenous fluid replacement and magnesium supplementation in patients with high intestinal losses and overall negative fluid balance.
ONE YEAR EXPERIENCE OF NASOJEJUNAL FEEDING USING THE TIGER TUBE

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Introduction: Nutritional support is vital to improving the clinical outcomes in patients in the intensive care unit. Enteral nutrition should be administered early and aggressively, thereby reducing the need for parenteral nutrition (TPN). Nasogastric (NG) feeding may not be tolerated due to gastroapensis, small and large bowel ileus associated with drugs and/or surgery.

Aims: We hypothesised that if NG feeding was not tolerated by 24 hours then a self-propelling Tiger Tube (TT) would be placed and NJ feeding commenced reducing TPN requirements.

Methods: We prospectively monitored patients with NG feeding intolerance pre- and post TT placement. (NG tube was also left in situ for aspirate assessment). Abdominal x ray was performed six hours after TT placement to confirm location and feeding regimen commenced.

Results: See table.

Conclusion: The TT was easily placed aided by prokinetics (90%). All tubes were placed by the nurse/doctor at the bedside and did not require endoscopic placement. Massive savings have resulted from reduced TPN use, reduced associated morbidity associated with TPN and its complications and finally reduction in endoscopic episodes. No complications were associated with the use of Tiger Tubes.

PEGGING MORTALITY DOWN A STRUCTURED APPROACH TO PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT

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Objective: To examine whether the pathway for percutaneous endoscopic gastrostomy (PEG) placement established following a project funded by Clinical Effectiveness has had an impact on 30 day post placement mortality.

The structure:

- Procedure specific request card with clinical indication
- Formal assessment of suitability of patient for procedure by Gastroenterology SpR
- MRSA prophylaxis for all patients pre procedure.

Methodology: A comparison was made between the 30 day mortality rates recorded in the 1999–2001 audit and the results obtained from a two year retrospective audit ending August 2005.

Results: Thirty day post placement mortality had dropped from 13.6% in 2001 (66 PEGs placed) to 6.1% in 2003 (65 PEGs placed). A year on year decrease in the mortality rate can be demonstrated, as the mortality rate for 2004 was 8%.

Conclusion: A structured approach to PEG placement has resulted in a significant decrease in post placement mortality.

THE KELLETT DRAINAGE ACCESS NEEDLE: AN AID TO IMPROVING COMPLETION RATES IN PEGS AND PEJS

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Background: The Kellett Drainage Access needle (Cook Europe) is a 20 cm needle with a 5 Fr outer sheath. It is used by radiologists for access to deep cavities. Its length and slimness can make it helpful in percutaneous endoscopic gastrostomy (PEG) and jejunostomy (PEJ) placement, if difficulty is encountered in accessing or puncturing the gut lumen, although fluoroscopic guidance may also be required. A review is presented here.

Methods: An 18 month casenote review of all PEGs and PEJs done by the author. Fresenius 15Fr PEG kits were used in all cases. For PEGs, the Kellett needle was used in place of the Frensenius needle if there was difficulty accessing or puncturing the stomach, after which the procedure was completed in the usual manner. For PEJs, the Kellett needle was adapted routinely. Fluoroscopy was used in each case if necessary.

Results: PEGs: out of 52 cases, five were done with the Kellett needle, 3/5 under fluoroscopic guidance. PEJs: nine cases were done, all under fluoroscopic guidance. All PEGs and PEJs done with the Kellett needle were completed successfully with no procedural complications. Thus in this review, all patients requiring an artificial feeding prosthesis had successful placement of a PEG or PEJ.

Conclusion: The Kellett needle is a useful accessory which can improve completion rates in endoscopic placement of artificial feeding prostheses.

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: INDICATIONS, MORTALITY, AND RISK FACTORS. A DISTRICT GENERAL HOSPITAL EXPERIENCE

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Background: Percutaneous endoscopic gastrostomy (PEG) has been the preferred method for long term feeding in patients who cannot eat but otherwise have a functionally intact gut. Although it has been widely used for more than 25 years, and is considered safe and technically simple, yet PEG has been associated with a significantly high early mortality.

Aim: We aim to present the results of our experience looking at the outcome, indications, and the characteristics that predicted adverse outcome in a cohort of patients treated in our unit.

Methods: Records of 101 patients who underwent PEG were reviewed retrospectively. Demographic data, indications, pre-existing medical conditions, and death at 30 days and three months were obtained. Other factors that were suggested to predict outcome by previous studies were also recorded. When a comparison between groups was made the χ2 test was used.

Results: The indications for PEG in our series were acute Stroke (70%) other neurological disorders (15%), dementia (7%), and others (8%). The average age of patients was 75 years, and the average time from admission to the date of procedure was 24 days. The mortality rates at 30 days and three months were 24% and 40.6% respectively. Other results are presented in table.

Conclusion: The early mortality in patients who undergo a PEG procedure remains significant. Referrals continue to increase, and there is no clear guidance when it comes to patient selection. Despite the evidence against, we are still performing PEG in patients with dementia.

We have demonstrated an increase in 30 days mortality in older patients, in those with elevated WCC, and who had recent pneumonia.
These factors should be considered when making decision about timing of PEG.

OUTCOMES OF INAPPROPRIATE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE REFERRALS IN A DISTRICT GENERAL HOSPITAL

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Background: The demand for percutaneous endoscopic gastrostomy (PEG) feeding has increased over the last few years. However, some referrals are deemed inappropriate, after assessment by the Nutrition Support Team (NST). The decision to withhold PEG feeding relies on assessment of prognosis, risks and benefits to the patients, and quality of life judgements.

Aims: To determine morbidity/mortality of those patients not accepted for PEG placement.

Methods: The records of patients, who were deemed inappropriate for a PEG tube, were reviewed noting the underlying diagnosis, comorbidity, and reason(s) for refusal. The clinical nurse specialist reviewed all these patients and the cases were discussed with and/or reviewed by a consultant gastroenterologist.

Results: Between January and December 2004, 32 out of a total of 104 referrals (32%) for a PEG tube were felt to be inappropriate (female, 23; median age 81 years (range 22–95 years)). The referral to decision time was seven days (mean; range 3–36 days). The commonest underlying diagnoses were cerebrovascular accident (CVA) (53%) and dementia (19%). 15 patients died (47%) within two weeks of referral; eight died from a lower respiratory tract infection, seven from a CVA. Outcome data was available on five patients who were deemed medically unfit. Eight patients had died before review by the NST. Eight patients (25%) successfully converted to oral feeding by the time of assessment and one was discharged.

Conclusion: One third of referrals for PEG placement do not undergo the procedure either due to active refusal by the NST, or due to the natural history of the underlying condition causing death or recovery within a few days of referral. Where the NST declined a PEG, those patients died quickly and the PEG would not have altered the outcome.

LONG TERM PEG-J FEEDING: A SINGLE CENTRE EXPERIENCE

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Introduction: The use of percutaneous gastrostomy (PEG) feeding has increased significantly in recent years. A proportion of patients require feeding distal to the pylorus (for example, in recurrent aspiration or diabetic gastroparesis). We have evaluated all consecutive patients in whom jejunal extension tubes (PEG-J) tube were inserted over a nine year period between May 1996 and April 2005 (Fresenius Freka intestinal 9Fr through Fresenius Freka 15Fr gastrostomy).

Methods: Data were collected regarding patient demographics, indication, length of PEG-J feeding, re-intervention, and patient outcome for all patients in whom PEG-J tubes were inserted at our institution.

Results: PEG-J tubes were inserted in 26 patients (12 male, mean age 43 years, SD 17) for recurrent aspiration (14), gastroparesis (5), recurrent vomiting (5), duodenal obstruction (1), and entero-cutaneous fistula (1). Patients were fed for a total of 31.9 years (mean 1.2, SD 1.2). Tubes had to be replaced on 40 occasions (mean 1.54 per patient, SD 1.0). The indications for replacement were external displacement (24), displacement into stomach (13) and blockage (3). The majority of tube failures occurred in a small number of patients (65% in six patients, 10 patients requiring no repositioning or replacement). PEG-J tubes lasted for a mean of 183 days (SD 52). Eight patients continued with PEG-J feeding at the end of the study. Five patients died while being fed via PEG-J (46, 74, 466, 533, and 774 days after insertion). The reasons for ceasing PEG-J feeding were death (5), recovery (4), patient preference (3), repeated displacement (3), surgical jejunostomy (2), and persistent aspiration (1). From November 2002, external connectors were superglued after one patient repeatedly disrupted his tube with no statistically significant effect on PEG-J longevity.

Discussion: This is the largest UK series to date of long term feeding via PEG-J tube. It is useful for patients requiring long term post-pyloric nutrition. Although there is a significant risk of tube failure requiring repositioning or replacement, the majority of carefully selected patients require one or fewer re-interventions.

REDUCING PEG MORTALITY RATES BY NURSE LED PRE ASSESSMENT AND PLACEMENT

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Background: Prior to nurse led assessment, the 30 day mortality for percutaneous endoscopic gastrostomy (PEG) at this hospital was unacceptable, high at 30%. All patients referred for a PEG had to be deemed appropriate by two clinicians without a set pre-assessment protocol.

Aims and Objectives: To reduce the 30 day PEG mortality by instituting a nurse led pre-assessment proforma for patients referred for (PEG) insertion, aligned with nurse PEG tube assisted placement.

Methods: A total of 66 patients were assessed over a two year period. No patients were excluded from the study. All patients were assessed by a dedicated nurse in order to ensure continuity. The pre-assessment proforma was devised specifically for this study and includes discussion with a variety of healthcare professionals to ensure a multidisciplinary decision is made.

Results: Forty one PEG placements were recommended out of the 66 assessed. The 30 day mortality rate significantly reduced over the two years of the study using the pre-assessment proforma and when a dedicated endoscopist and nurse assistant placed the PEGs to less than 5%.

Conclusions: This process has demonstrated that assessing all patients considered for a PEG with good clinical guidelines, evidence based practice, and multidisciplinary decision can reduce both mortality and morbidity rate and improve the quality of treatment for this complicated group of patients. Aligned to this in our unit the practice of a dedicated nurse aiding PEG placement appears to be extremely safe.

DEMENTIA AND HOME ENTERAL TUBE FEEDING IN THE UK: THE REALITY OF CURRENT PRACTICE

B. J. M. Jones. Russells Hall Hospital, Dudley. Presented on behalf of the British Artificial Nutrition Survey committee (BAPEN), UK

Introduction: In the UK, chronic neurological diseases are the commonest indication for home enteral tube feeding (HETF) and gastrostomy insertion for which the ethics of consent are often controversial. Recent evidence suggests that dementia is a poor indication for enteral nutrition, with no improvements in quality of life, aspiration pneumonia or survival.

Aim: To determine the prevalence and characteristics of dementia and HETF in the UK.

Methods: Analysis of data from the British Artificial Nutrition Survey (BANS) for 2004 (British Association for Parenteral and Enteral Nutrition).

Results: In 2004, of 5656 new BANS HETF registrations, 221 (4%) in 107 centres had dementia. Point prevalence of dementia was 254/82 18 260 (3.2%) in 167 centres and period prevalence was 735/21 677 (3.4%) in 181 centres. The predominant age of new patients was 71–90 years (74%). The indication for HETF in dementia was “swallowing difficulty” in 59% and “to improve nutritional status” in 36%. HETF was by gastrostomy (89%), nasojejunal tube (11%), and jejunostomy (0.5%). HETF was provided in a nursing home in 81% with only 15% at home. 61% were bed bound and 98% totally dependent. Commercial homecare companies supplied equipment and feeds in 81% cases. Mortality one year after commencing HETF was at least 48% although follow up underreporting may have led to over recording of survival.

Conclusions: A substantial number of demented patients receive HETF in the UK. They are characterised by total dependency and nursing home placement in majority of cases. It is possible that HETF is being offered to earlier cases of dementia with some residual cognitive function and that HETF can not be avoided in these patients but the majority appear to have very poor quality of life with high mortality. We have no data on whether nutritional status or clinical outcomes were improved by HETF. There is still insufficient evidence of benefit in favour of HETF for dementia. Protected by copyright.
Results: There were 121 patient years of experience, 55% female, median age 40 (range 3–73). Median duration of HPN was 218 days (18–3881). Indications were Crohn’s disease (35%), vascular (11%), dysmotility (10%), other (44%), but between 1st and 3rd quintiles Crohn’s became a less common indication (44% v 28%, NS). Overall mortality was 13.6% and HPN related mortality 1.1%. Complication rates (episodes per patient year) were: line sepsis 0.35, line occlusion 0.25, central venous obstruction 0.03, endocarditis 0.02, cholestasis (2/3 of bilirubin, ALP >GT with 1–5 fold elevation) 0.17, Line sepsis and occlusion were more common in the 1st than 3rd quintile (0.6 v 0.26%, NS) and 0.53 v 0.18% respectively, p = 0.07. No cases of endocarditis occurred in the third quintile. 31% patients had double lumen catheters, one for HPN and the other for vascular access if peripheral access was limited. Direct and indirect 1-year reduction in the proportion with Crohn’s disease on HPN is consistent with other experience and probably reflects a reduction in surgery performed on poorly nourished patients. Many received HPN in preparation for definitive surgery. Mortality and line complications are comparable to the best series, and cholestasis less common. The trend to fewer line complications in the 3rd quintile cannot be accounted for by any change in practice. Double lumen catheters for HPN have an acceptable complication rate if strict management protocols are followed.

401 CONSUMPTION OF GLUTEN FREE FOODS AND MACRONUTRIENT INTAKES IN PATIENTS WITH COELIAC DISEASE

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Background and Aim: Management of coeliac disease (CD) relies on strict adherence to a gluten free (GF) diet. In the UK, GF foods are available on prescription for patients with CD to provide basic staples to help achieve an adequate energy and carbohydrate (CHO) intake and aid compliance to a GF diet. Little is known however about the consumption of GF foods in the UK, their contribution to the GF diet and whether the macronutrient intake among patients with CD is optimal. The aim of this study was to accurately assess intakes of energy, fat, CHO, and GF foods in patients with CD and compare intakes with the National Diet and Nutrition Survey (NDNS) 2002 and dietary guidelines, DOH, 1991.

Methods: Adults with established CD (diagnosed >2 years), confirmed by biopsy, who demonstrated histological improvement on a GF diet were recruited from out patient clinics and Coeliac UK. Diet was assessed through a 10 day weighed food intake. Diet records were analysed using a nutrient database to which the composition of manufactured GF foods were manually added. Dietary intakes were compared with the NDNS, 2002 and dietary reference values for macronutrients, DOH, 1991.

Results: Forty nine patients were recruited, 42 completed the study, 10 males, 32 females, mean age 55 years (25–71 years). Mean body mass index was 24.5 kg/m². Diet records showed strict compliance to a GF diet in 41/42. Gastrointestinal symptoms were absent in the study period. Mean index was 24.5 kg/m². Diet records showed strict compliance to a GF diet. Little is known however about the consumption of GF foods in the UK, their contribution to the GF diet and whether the macronutrient intake among patients with CD is optimal. The aim of this study was to accurately assess intakes of energy, fat, CHO, and GF foods in patients with CD and compare intakes with the National Diet and Nutrition Survey (NDNS) 2002 and dietary guidelines, DOH, 1991.

Discussion: The 15 year reduction in the proportion with Crohn’s on for HPN and the other for vascular access if peripheral access was limited. Direct and indirect 1-year reduction in the proportion with Crohn’s disease on HPN is consistent with other experience and probably reflects a reduction in surgery performed on poorly nourished patients. Many received HPN in preparation for definitive surgery. Mortality and line complications are comparable to the best series, and cholestasis less common. The trend to fewer line complications in the 3rd quintile cannot be accounted for by any change in practice. Double lumen catheters for HPN have an acceptable complication rate if strict management protocols are followed.

402 RISK FACTORS FOR THE DEVELOPMENT OF BARRETT’S OESOPHAGUS: A CASE CONTROL STUDY

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Background: The main risk factor for Barrett’s oesophagus (BO) is chronic gastro-oesophageal reflux disease (GORD). It is not clear why some patients with GORD develop BO and some only develop oesophagitis. We hypothesised that BO may be associated with a familial predisposition to metabolica and cancer.

Methods: 221 patients with BO (>3 cm in length) and 276 patients with oesophagitis (controls) were asked to complete two questionnaires. One measured symptoms of GORD, potential aetiologic factors and demographic data. The second took a detailed family history, including the number of first degree relatives and their history of cancer.

Results: 149 (67%) BO and 174 (63%) controls responded. 130 (59%) BO and 141 (51%) controls completed the questionnaire fully. 116 BO were age, sex, and ethnicity matched with controls, 68 males. BO median age 67 (range 38–85), controls 65 (range 40–88). Univariate analysis revealed that BO was associated with a history of frequent acid regurgitation (p = 0.03) and a family history of BO (p = 0.03). There was an inverse relation in BO with ever smoking (p = 0.04). No educational attainment (p = 0.06), cancers per first degree relative (p = 0.09), body mass index, alcohol intake, duration of GORD symptoms (all p > 0.1) did not reach statistical significance. Forward stepwise logistic multivariate regression analysis revealed that BO was associated with frequent acid regurgitation odds ratio 1.9 (95 CI 1.1 to 3.5) (p = 0.03), no educational attainment 2.2 (1.3 to 4.0) (p = 0.007) and cancers per first degree relative 9.9 (1.7 to 57.7) (p = 0.01).

Conclusion: Frequent acid regurgitation, no educational attainment and a history of cancer within first degree relatives are independently associated with BO. The association of BO with a family history of BO and cancer in first degree relatives raises the possibility of an inherited predisposition to metaplasia in BO.

403 BARRETT’S OESOPHAGUS IN PATIENTS PRESENTING WITH SYMPTOMS UNRELATED TO GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Barrett’s oesophagus (BO) is a manifestation of severe gastroesophageal reflux disease (GORD) and predisposes to oesophageal adenocarcinoma (OAC). Many patients who present with OAC are found to have BO associated with the tumour and it is thought that BO remains undiagnosed in many patients throughout their lives. If so, BO may be an incidental finding in many patients.

Aim: To determine the proportion of patients newly diagnosed with BO in whom endoscopy was done for symptoms unrelated to GORD.

Methods: All endoscopies performed in the hospital are entered prospectively into a database (Micromed), which was examined retrospectively, looking for endoscopic diagnosis of BO and the symptoms that prompted the endoscopy.

Results: From 01/01/1998 to 31/12/2004, 14 170 endoscopies were performed on 12 966 patients at our hospital. There were 221 patients with a new diagnosis of BO. 11 patients with oesophageal cancer were excluded. These patients were divided into two groups: group 1 with symptoms of GORD (heartburn, reflux, abdominal pain, or dysphagia) and group 2 in whom endoscopy was performed for other indications.

Conclusions: Almost half of patients with BO present with symptoms unrelated to GORD. This supports the hypothesis that in many patients, BO remains unrecognised throughout their lives.

404 DIAGNOSIS AND MANAGEMENT OF BARRETT’S OESOPHAGUS: RESULTS OF THE UK NATIONAL BARRETT’S OESOPHAGUS REGISTRY (UKBOR) ENDOSCOPIST QUESTIONNAIRE

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Background: Criteria and techniques employed for the diagnosis of columnar lined oesophagus (CLO) have changed over the last decade. Guidelines for both diagnosis and management of CLO exist, but are

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<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
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<tr>
<td>(n = 132)</td>
<td>(n = 89)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61.5</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>87 (66)</td>
</tr>
<tr>
<td>Mean length of BO (cm)</td>
<td>4.6 (n = 125)</td>
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<tr>
<td>Hiatus hernia present (%)</td>
<td>51 (39)</td>
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www.gutjnl.com
Methods: A questionnaire was designed on behalf of the UK National Barrett's Oesophagus Registry (UKBOR) to examine consistencies in the diagnosis and management of CLO and its complications. Questionnaires were sent to the lead endoscopists of 41 centres spread throughout England, Scotland, and Wales. All centres currently register patients with CLO. WNB with NBI.

Results: Fifteen patients with Barrett's oesophagus were evaluated (mean age 57 years, 13 males). Mean length of Barrett's segment was 3.6 cm (range 1.7–7.7 cm). With WNB, striking contrast was observed between squamous and columnar mucosae. Three distinct mucosal patterns (1, tubular/villous/linear; 2, circular; and 3, distorted) and two microvascular patterns (1, regular-fine face-like network and 2, irregular-dilated, tortuous) were seen. A total of 93 biopsies were taken. All areas with tubular/villous/linear pattern showed specialised intestinal metaplasia (SIM) in histology. Both sensitivity and specificity of tubular/villous/linear pattern to detect SIM were 100%. One area had distorted pattern with irregular microvessels-biopsies showed high grade dysplasia. Six areas had circular pattern-pattern-biopsies showed columnar mucosa with no SIM in all cases.

Conclusion: Using HRME with NBI we described the non-dysplastic and dysplastic features in Barrett's epithelium. Further randomised controlled studies are required to prove the efficacy of this technique in the surveillance of patients with Barrett's oesophagus.
Conclusions: OE33 cells express Ob-R in surface epithelial cells noted at the stages of dysplasia and cancer. Confirmed by immunohistochemistry with marked upregulation of Ob-R.

Discussion: The effect of leptin on Barrett's epithelial cells requires further study. Therapeutic manipulation of leptin receptor signalling might provide a novel mechanism for the prevention or treatment of oesophageal adenocarcinoma.

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play a role in Barrett's carcinogenesis via activation of the retinoid signalling.

Methods: A 3T3 cell line stably expressing a RARE-SEAP reporter was generated to assay retinoic acid (RA) activity. These cells were treated with one or both of All trans retinoic acid (ATRA) or LCA compared to serum-free medium as the control. The expression levels of retinoid target genes were determined in dysplastic Barrett's cell lines (G ihtert and Gohtert) by real-time PCR.

Results: RA signalling induced by LCA and ATRA in combination were synergistic (p = 0.024; p = 0.018) (see figure). This synergistic effect was confirmed in two immortalised Barrett's cell lines by examining the expression of the ATRA response gene p21. ATRA and LCA in combination resulted in a threefold increase in p21 mRNA expression compared to addition of either LCA or ATRA alone (p < 0.01).

Discussion: These data suggest that LCA may induce RA activity in Barrett's oesophagus. This could have physiological significance in view of the known role of RA in cell growth and differentiation.

409 EPITHELIAL CELLS OVEREXPRESS THE LEPTIN RECEPTOR DURING MALIGNANT PROGRESSION IN BARRETT'S OESOPHAGUS

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Introduction: Obesity is a recognised risk factor for oesophageal adenocarcinoma. The reason for the link between excessive weight and cancer is unclear. We hypothesised that leptin receptor (OB-R) might be overexpressed in metastatic or neoplastic oesophageal epithelium during carcinogenesis. This would provide a mechanism whereby obesity related hyperleptinaemia might exert a direct growth promoting effect on oesophageal mucosa, potentially favouring malignant progression. Leptin has been shown to stimulate proliferation of various epithelial cell lines expressing OB-R.

Methods: mRNA abundance of OB-Rb (main functional OB-R isoform) was determined by quantitative PCR performed on cDNA generated by reverse transcription of RNA extracted from endoscopic biopsies. Values were normalised relative to H-HPRT housekeeping gene. Product was confirmed by agarose gel. Normal gastric fundus expresses OB-Rb and was used as positive control. Immunohistochemistry for OB-Rb was performed on formalin fixed biopsies and used to detect cyclin A in the setting of dysplasia.

Results: OB-Rb is expressed at very low level in the normal squamous oesophagus but exhibits progressive expression during malignant progression at levels significantly in excess of the healthy stomach (see table: mean values (SD), p < 0.001 ANOVA). Epithelial cell staining was confirmed by immunohistochemistry with marked upregulation of OB-R in surface epithelial cells noted at the stages of dysplasia and cancer.

Methods and Results: Expression of cyclin A at the luminal surface is a marker of progression to AC. Detection of cyclin A positivity in endoscopic brushings could be used as a first step to stratify BO patients with a high risk of progression. A large clinical study is still required to confirm these findings.

410 CYCLIN A IMMUNOCYTOLOGY AS A RISK STRATIFICATION TOOL IN BARRETT’S OESOPHAGUS SURVEILLANCE

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Background: The incidence of oesophageal adenocarcinoma (AC) is increasing rapidly. Endoscopic surveillance of patients with Barrett’s oesophagus (BO) using biopsies for histopathological assessment is prone to sampling bias, is not cost effective and interpretation of dysplasia is subjective. Alternative methods for surveillance are direly needed. We have previously demonstrated that surface expression of a proliferative marker, Mcm2, is a marker of progression. However, it lacked specificity for detection of patients at risk.

Aims: To determine whether cyclin A, which detects a proportion of proliferating cells, would be more specific.

Methods: Archival specimens (30 squamous esophagus (SE), 12 gastric antrum (GA), and 9 duodenum (D2), 62 BE/E – dysplasia, 16 AC) were stained for cyclin A. In addition, nine patients with 3–13 years follow up who developed AC were compared with 18 controls matched for age and length of follow up who did not progress. Endoscopic cytological brushings were taken from a prospective cohort (24 SE, 93 BE/E – dysplasia, and 36 AC) and scored blind as cyclin A positive or negative.

Results: There was no surface expression of cyclin A in control samples (NE, GA, D2) and its expression at the surface of BE samples correlated with the degree of dysplasia (p = 0.016). In the case control cohort, patient with biopsies expressing cyclin A at the surface were more likely to progress to AC than those who did not (odds ratio 10.0, 95% confidence interval 1.5–64.2). The sensitivity and specificity of cyclin A expression in brushings for the detection of high grade dysplasia (HGD) and cancer patients were 97.9% and 61.2% respectively. The associated negative predictive value was 98.2%.

Conclusion: Expression of cyclin A at the luminal surface is a marker of progression to AC. Detection of cyclin A positivity in endoscopic brushings could be used as a first step to stratify BO patients with a high risk of progression. A large clinical study is still required to confirm these findings.

411 EVIDENCE FROM BARRETT’S CARCINOGENESIS THAT CYP26A1 IS IMPLICATED IN CANCER

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Background: Retinoic acid (RA) is an important signalling molecule for Anterior-Posterior (AP) patterning in embryogenesis. Tight control of intracellular RA levels results in an anterior shift in endoderm gene expression and induction of the caudal gene CdxA. CYP26A1 is the major RA catabolising enzyme responsible for maintaining exquisite control over cellular RA concentrations.

Hypothesis: We hypothesised that alterations in RA signalling may have a role in differentiation status in Barrett’s carcinogenesis.

Aims: In this study we have investigated the role of RA and CYP26A1 on Barrett’s metaplasia and associated dysplasia and adenocarcinoma.

Methods and Results: Using retinoic acid response element (RARE) reporter cells we demonstrated that non-dysplastic Barrett’s cell lines (BAR, GhERT) and non-dysplastic Barrett’s tissues has the highest levels of RA bioactivity, which decreased progressively with the degree of dysplasia in cell lines (Ghert, GhERT), and patient tissues (p < 0.05). The degree of RA bioactivity was inversely correlated with CYP26A1 gene levels. Functionally, overexpression of CYP26A1 in Ghert cells increased proliferation as determined by their cytometric DNA profile, CholordU and IododU incorporation and an MTT assay. An in vitro matrigel assay demonstrated that cells overexpressing CYP26A1 were more invasive (p < 0.01). The increased invasion is likely to be due to alterations in matrix metalloproteinase expression (upregulation of
MMP-3, down-regulation of TIMP-1 and TIMP-3 (p<0.05) which were demonstrated by quantitative RT-PCR. Using an organotypic culture system we also demonstrated that CYP26A1 gene overexpressing cells are "dedifferentiated" as shown by co-localisation with a stem cell marker Oct-4. Pathway arrays showed induction of c-myc and EGFR expression in these CYP26A1 overexpressing cells.

Discussion: Overexpression of CYP26A1 causes intracellular RA depletion and drives the cell into a highly proliferative, undifferentiated, and invasive state with induction of other known oncogenes. These data suggest a previously unknown role for this gene in cancer.

412 HELICOBACTER PYLORI AND CAG A STATUS IN OESOPHAGEAL ADENOCARCINOMA, BARRETT’S OESOPHAGUS, AND REFUX OESOPHAGITIS

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Introduction: Helicobacter pylori (H pylori) appears to reduce the risk of oesophageal adenocarcinoma (OAC), possibly by causing gastric hypochlorhydria. We set out to compare the prevalence of H pylori infection (detected by Cag A strains) in normal controls and reflux oesophagitis (RO), Barrett’s oesophagus (BO), and OAC patients from throughout Ireland.

Methods: In this population based case control study, data were collected about potential lifestyle and environmental risk factors and a 30 ml blood obtained. Using standard serum, IgG antibodies to H pylori and CagA were measured in 253 population controls, 208 OAC, 215 BO and 229 RO patients by Western Blot (Helico Blot 2.1, Genelabs Diagnostics, Singapore).

Results: H pylori seropositivity was less common in OAC (OR 0.51 (95% CI 0.34 to 0.78)), BO (OR 0.40 (95% CI 0.26 to 0.61)) and RO patients (0.30 (95% CI 0.19 to 0.47)) compared to controls. OAC, BO and RO patients were also less likely than controls to be CagA positive, OR (95% CI): 0.58 (0.39-0.88), 0.55 (0.36-0.83), and 0.59 (0.38-0.91), respectively.

Conclusions: H pylori seropositivity, and to a lesser extent, Cag A positivity were less prevalent in patients with RO, BO, and OAC than in normal controls. H pylori infection may reduce OAC risk by a mechanism other than induction of gastric hypochlorhydria.

413 EXPRESSION OF TISSUE INHIBITORS OF METALLOPROTEINASES AND TARGET PROTEASES DURING BARRETT’S CARCINOGENESIS

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Introduction: A multi-step pathway for oesophageal adenocarcinoma (AdCa) proceeds from squamous epithelium (SqEp) via Barrett’s metaplasia (BM) to dysplasia and cancer in the setting of reflux disease. These processes involve remodelling of tissue architecture and fundamental changes to extracellular matrix (ECM). Regulation of the ECM is under the influence of the matrix metalloproteinases (MMPs) and their natural tissue inhibitors (TIMPs), a system of molecules that have roles in ECM homeostasis, inflammation, angiogenesis, and metastasis.

Methods: The aim of the present study was to define expression profile of TIMPs (1 to -4) and selected MMPs (-3 and -8) at different points in the cancer pathway. Oesophageal biopsies were measured in 253 population controls, 208 OAC, 215 BO and 229 RO patients by Western Blot (Helico Blot 2.1, Genelabs Diagnostics, Singapore).

Results: H pylori seropositivity was less common in OAC (OR 0.51 (95% CI 0.34 to 0.78)), BO (OR 0.40 (95% CI 0.26 to 0.61)) and RO patients (0.30 (95% CI 0.19 to 0.47)) compared to controls. OAC, BO and RO patients were also less likely than controls to be CagA positive, OR (95% CI): 0.58 (0.39-0.88), 0.55 (0.36-0.83), and 0.59 (0.38-0.91), respectively.

Conclusions: H pylori seropositivity, and to a lesser extent, Cag A positivity were less prevalent in patients with RO, BO, and OAC than in normal controls. H pylori infection may reduce OAC risk by a mechanism other than induction of gastric hypochlorhydria.

414 IMPACT OF THE "TWO WEEK RULE" AND ROUTE OF DIAGNOSIS ON OUTCOME OF OESOPHAGEAL CANCER

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Background: The UK National Cancer Plan aimed to improve patient outcomes by raising awareness of “alarm symptoms” and establishing a two week waiting time standard for fast track specialist assessment. In this study we aimed to establish the impact of our Rapid Access Upper GI Cancer Service (RAUGICS) on patient outcomes and to assess whether patients continuing to access care via traditional routes are at a disadvantage.

Methods: (A) Using hospital IT systems, a cancer service database and casenotes, we audited outcome of all oesophageal cancer (O-Ca) diagnosed during two 2 year periods, one before (PRE-) and one after (POST-) the implementation of the RAUGICS system. Data for tumour stage, age, operability, and 2 year survival were obtained. (B) In the post “two week rule” (TWR) period, route of diagnosis of cancer was designated as: RAUGICS (preferred route, n = 3008 referrals), traditional open access endoscopy (OAE), outpatient clinic (OPD), emergency admission (E&O). We audited Barrett’s surveillance (BarS; n = 420 referrals).

Results: (A) Pre versus post RAUGICS periods: Cases: 72 v 95; Mean age: 68 v 68; Surgery (curative intent): 38% v 26%; 2 year survival: 19.4% v 24.2% (AdenoCA: 22.5% v 25.4%; squamous cell CA: 16.1% v 25%). All non-significant. (B) Route of diagnosis: 2 year survival: RAUGICS 18%; other routes (OAE, OPD, A&E): 30%; and BarS 50%. BarS detected CA at a rate of 0.49% per annum (6.5% of all AdenoCA cases in the population).

Conclusions: Major service reorganisation took place to ensure fast-track assessment of patients with alarm symptoms. Overall survival for O-Ca has not improved significantly. Cases of cancer continue to be diagnosed by traditional routes but these selected cases have a better outcome than those in the RAUGICS system overall, suggesting earlier stage disease diagnosed “by chance” in patients without obvious alarm features. The current fast-track system selects mainly patients with late-stage disease and a poor outcome. Cancers detected via BarS have superior survival but represent only a minority of tumours diagnosed. Prompt palliation is a worthwhile outcome of the TWR but a screening programme is needed if survival is to improve for O-Ca.


415 A LARGE SERIES, RESECTION CONTROLLED STUDY TO ASSESS THE VALUE OF RADIAL EUS IN RE-STAGING OESOPHAGEAL CANCER AND PREDICTING SURVIVAL FOLLOWING NEOADJUVANT CHEMOTHERAPY

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Background: The utility of EUS post neoadjuvant chemotherapy for esophageal cancer is not established. Superior survival for O-Ca may yield useful staging and prognostic information but information on its true clinical value as compared with CT is limited.

Methods: We prospectively studied 109 patients with esophageal cancer; 99 undergoing surgery. All had EUS and helical CT imaging before and after neoadjuvant chemotherapy and results were compared with pathological staging of resected specimens. Tumour response was assessed by reduction in maximal tumour depth at EUS and correlated with patient survival.

Results: There was no difference in T and N stage accuracies between EUS and CT following neoadjuvant chemotherapy. Multivariate analysis showed a reduction in maximal tumour depth by >50% at EUS to be associated with longer survival (relative risk=0.48, p<0.05). EUS responders had a median survival of 38 months compared to 30 months for non-responders (p<0.05). The identification of lymphadenopathy at radial EUS was not predictive of survival.

Conclusion: This large series study demonstrates the staging accuracy of CT and non-biopsy EUS in the setting of neoadjuvant chemotherapy for
esophageal cancer to be equivalent and poor. Endosonography may contribute useful clinical information in respect of potential survival.

416 LOCAL RISK FACTORS FOR SQUAMOUS CELL OESOPHAGEAL CARCINOMA IN A SOUTH ASIAN COMMUNITY
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Background: Squamous cell carcinoma of the esophagus is the 8th most common cancer in women and the 5th most common cancer in men in South Asia. Tobacco is not only smoked but is also chewed in various forms (nasswar and paan) extensively in South Asia as well as by South Asian communities living abroad. Naswar is a crude form of chewing tobacco where as paan is a quid of pipi betel leaf containing areca nut, lime, condiment, sweeteners, and sometimes tobacco. Studies have linked the use of these products with oral and pharyngeal carcinomas however, no work examining their role in oesophageal carcinoma has been done.

Methods: The aims of this study were to identify the risks associated with oesophageal carcinoma in a South Asian population with a particular focus on paan consumption. Biopsy proven primary cases of squamous cell carcinoma of the esophagus from three major tertiary referral centres were recruited for the study. Controls were pair matched for age, gender and hospitals, excluding subjects with a past or present history of any type of malignancy. Variables that were statistically significant in univariable analysis were further examined through multivariable conditional logistic regression.

Results: There were 91 cases and 364 controls with a male to female ratio of 1:1. The average age was 54 years (age range: 22-90). People with oesophageal carcinoma were at 11 times higher odds of being users of paan with tobacco (95% CI 5 to 24). Other significant associations were paan without tobacco (OR 3.6), naswar (OR 3.4), and smoking (OR 2.5), after adjustment for other covariates. No significant associations were identified between subethnic groups and oesophageal carcinoma.

Conclusion: This study identifies independent associations of paan (with or without tobacco), naswar and smoking with squamous cell oesophageal carcinoma. These findings are of public health significance in South Asian communities.

417 SIMVASTATIN INDUCES APOPTOSIS AND INHIBITS PROLIFERATION IN OESOPHAGEAL ADENOCARCINOMA CELLS BY INHIBITING ACTIVATION OF EXTRACELLULAR SIGNAL RELATED KINASE (ERK) AND AKT
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Background: The incidence of oesophageal adenocarcinoma (OAC) is rapidly increasing in the western world. Statis are widely used in obese or without tobacco), naswar and smoking with squamous cell oesophageal carcinoma. These findings are of public health significance in South Asian communities.

Methods: The effects of simvastatin, lovastatin, and pravastatin on the LT4 level was measured by ELISA.

Results: All three statins inhibited proliferation in a similar dose dependent manner. This effect was partially dependent on farnesylation and the availability of mevalonate. Simvastatin increased apoptosis by 40%. Statins significantly enhanced the antiproliferative effect of the COX-2 inhibitor NS-398, but did not enhance the effects of cisplatin and 5-fluorouracil. The effects were associated with significant inhibition of serum-induced phosphorylation of extracellular signal-related kinase (ERK) and Akt but did not affect p38 MAP kinase or JNK phosphorylation. Statins did not affect levels of membrane associated Ras and Rho, or Ras activity.

Conclusion: Statins inhibit proliferation and induce apoptosis in OAC cells, and further enhance the antiproliferative effects of COX-2 inhibition. Statins inhibit the ERK and Akt pathways, which are involved in proliferation and cell survival, but this is not due to inhibition of membrane associated GTPases. Statins may have beneficial effects in Barrett’s oesophagus and further study is warranted.

418 DIETARY FISH OIL LOWERS MUCOSAL PGE2 LEVELS DURING OESOPHAGEAL ADENOCARCINOGENESIS
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Background: There is evidence that n-3 (omega-3) fatty acids can inhibit carcinogenesis, perhaps through suppression of prostaglandin biosynthesis. Using a previously developed animal model of oesophageal adenocarcinoma we have compared the effects of dietary fish oil versus corn oil on prostaglandin E2 (PGE2) levels during the early stages of carcinogenesis.

Methods: Oesophagealjejunostomy was performed on 24 male Sprague-Dawley rats which were then given a diet providing 15% energy from fat. Twelve were fed a diet based on corn oil (high in n-6 fatty acids) and 12 on a diet based on fish oil (high in n-3 fatty acids). Twenty one animals survived 10 weeks post-surgery, at which point they were sacrificed and gastroesophageal tissues were harvested. Mucoasa from the distal oesophagus was assayed for PGE2 levels and lipid peroxidation. Gastric tissue was analysed for fatty acid profile and serum CRP levels were also measured.

Results: Animals fed on fish oil had significantly higher levels of tissue n-3 fatty acids than those fed corn oil (5.46% vs 0.31%, p<0.001). There was less fish PGE2E2 levels of fish oil compared to corn oil (PGE2E2 levels during the early stages of carcinogenesis. This effect was partially dependent on farnesylation and the availability of mevalonate. Simvastatin increased apoptosis by 40%. Statins significantly enhanced the antiproliferative effect of the COX-2 inhibitor NS-398, but did not enhance the effects of cisplatin and 5-fluorouracil. The effects were associated with significant inhibition of serum-induced phosphorylation of extracellular signal-related kinase (ERK) and Akt but did not affect p38 MAP kinase or JNK phosphorylation. Statins did not affect levels of membrane associated Ras and Rho, or Ras activity.

Conclusion: Statins inhibit proliferation and induce apoptosis in OAC cells, and further enhance the antiproliferative effects of COX-2 inhibition. Statins inhibit the ERK and Akt pathways, which are involved in proliferation and cell survival, but this is not due to inhibition of membrane associated GTPases. Statins may have beneficial effects in Barrett’s oesophagus and further study is warranted.

419 NSAIDS INDUCE LTB4: A POSSIBLE MECHANISM BY WHICH NSAIDS PREVENT OESOPHAGEAL CANCER
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Background: There are 4000 deaths per annum from oesophageal cancer and it has a five year survival rates in the UK of under 10%. Oesophageal cancer commonly arises from Barrett’s oesophagus. NSAIDs appear to reduce incidence of this cancer. This may be by substrate diversion from the cyclooxygenase pathway to the lipoxgenase pathway producing LT4, a PPARα ligand. We have investigated the hypothesis that:

2. Enhanced LT4 causes regression by ligand activation of peroxisome proliferators activated receptor (PPARα).

Aims: [1] To establish LT4 synthesis in organ culture from normal oesophageal tissue, Barrett’s oesophagus, and oesophageal adenocarcinoma.[2] To assess if NSAIDs increase LT4 synthesis in these three tissue types.

Methods: Samples from oesophageal squamous epithelium, Barrett’s oesophagus, or oesophageal adenocarcinoma were placed in organ culture (RMPI 1640), 10% FCS, 95% O2/5% CO2, 37°C with or without indomethacin 10-6 M and 10-4 M. After 24 hours LT4 was measured in culture medium by ELISA.

Results: LT4 levels are higher in oesophageal adenocarcinoma than in Barrett’s oesophagus and oesophageal squamous epithelium. The mean LT4 level was 15.2 (4.1) (mean (SEM)) pg/mg in oesophageal squamous epithelium, 20 pg/mg (4.8) in Barrett’s oesophagus and 28.4 (7.1) pg/mg in oesophageal cancer (n=6, not significant). Indomethacin caused a concentration dependent increase in LT4 synthesis. The addition of indomethacin 10-6 M and 10-4 M resulted in mean LT4 levels of 170 pg/mg (87.4) and 321 pg/mg (8.1) in squamous epithelium and 294 (89.6) and 543 (121.3) in Barrett’s oesophagus and 450 pg/mg (6.2), and 720 pg/mg (7.4) in oesophageal cancer.
Conclusions: Oesophageal mucosa is capable of synthesizing LTB4. Indomethacin causes a substantial significant increase in synthesis in all the above oesophageal epithelium, sufficient to affect PPAR activity substantially.

420 CHEMICALS FORMED FROM THE GASTRIC ACIDIFICATION OF SALIVARY NITRITE INFLUENCE OESOPHAGEAL AND GASTRIC FUNCTION
J. J. Manning, A. Wirz, K. E. L. McColl. University Department of Medicine, Western Infirmary, Glasgow, UK

Introduction: Saliva contains high concentrations of nitrite derived from the enterosalivary recirculation of nitrate and its reduction by buccal bacteria. Acidic gastric juice converts the nitrite to varying proportions of nitrous acid and nitric oxide determined by vitamin C availability, Nitrite and nitrous acid relax the stomach, lower oesophageal sphincter (LOS), and oesophageal body. Neuronally generated NO contributes to the pathophysiology of GORD, playing a major role in upper gastrointestinal motility.

Aim: To determine whether luminal administration of NO or nitrous acid alters oesophageal or gastric function.

Method: Fifteen Helicobacter pylori negative healthy volunteers were studied on three separate days. A manometry catheter was placed across the lower oesophageal sphincter (LOS) after a meal, to record oesophageal, LOS and gastric pressure and transient lower oesophageal sphincter relaxations (TLOSRs). Two pH probes were placed in the oesophagus to record reflux events. On each day one of three solutions was infused for one hour into the region of the LOS. (1) Control solution of hydrochloric acid pH 1.0 (HC1), (2) HCl plus nitrite ie: nitrous acid, and (3) HCl plus nitrite plus ascorbic acid to generate NO. Solutions were randomised and double blinded.

Results: The NO solution gave a significantly increased oesophageal acid exposure, 62.2%, compared to both control, 37.5% (p<0.03) and nitrous acid, 36.6% (p<0.002). The frequency of TLOSRs was also significantly increased by the NO solution (5.2/hour) compared to both control (3.5, p<0.01) and nitrous acid (3.1, p<0.0001). There was also evidence of impaired oesophageal clearance of acid refluxate following the NO infusion. Intragastric pressure was 3.4 mmHg lower in the nitrous acid group during the meal (p<0.03) compared to the control.

Conclusion: Luminal chemicals formed from the acidification of salivary nitrite influence both oesophageal and gastric motility and may play a role in the aetiology of gastric and oesophageal disorders.

421 ENDOSCOPIC PROGRESSION OF GASTRO-oesophageal reflux disease over seven years
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Background and Aim: Some authors feel that non-erosive reflux disease (NERD), erosive oesophagitis and Barrett’s oesophagus (BO) represent different stages of gastro-oesophageal reflux disease (GORD), which can progress over time. Others have suggested that these entities which tend to remain unchanged. We aim to determine whether the endoscopic severity of GORD progresses over time.

Methods: A prospectively collected database (Micromed) of all upper GI endoscopies (OGD) performed in the hospital was retrospectively examined, looking for disease progression.

Results: From 01/01/98 to 31/12/04, 14 170 OGDs were performed on 12 750 patients (48% male, mean age 58 years). 882 patients had more than one OGD. Of 739 patients initially without oesophagitis (277 of whom had reflux symptoms), 134 (18%) developed oesophagitis at the second endoscopy (mild 71 (54%), moderate 45 (34%), severe 15 (11%), after a mean time interval of 134 days. BO developed in two patients. The mean age of the 134 patients was 60 years. Thirteen patients (9%) were using a proton pump inhibitor (PPI) at the first OGD, 38 at the second (28%). Of 143 patients with oesophagitis at the first endoscopy (mild 85 (59%) moderate, 37 (26%) severe 21 (15%), oesophagitis resolved in 118 (83%) and remained unchanged in 20 (14%) but progressed in five (3%) (2 developed moderate oesophagitis, 1 severe oesophagitis, 2 developed BO and 1 developed a cancer). The five patients who progressed had a mean age of 56 years and a time interval between OGDs of 753 days. Only one of the patients was taking a PPI at either first or second OGD. The 138 patients in whom oesophagitis did not progress had a mean age of 62 years, a mean of 630 days between OGDs. 19 (14%) were using a PPI at the first OGD, 38 (28%) at the second.

Conclusion: Although the grade of oesophagitis remains stable in the majority of patients, it does progress in a small number, with oesophagitis progressing to more severe oesophagitis, BO or cancer in 3% of patients.

422 THE ORACLE (OESOPHAGEAL REFUX AND CHANGE IN LIFESTYLE EVALUATION) STUDY
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Background: Gastro-oesophageal reflux disease (GORD) is highly prevalent in the Western population. It has a significant effect on the sufferer’s physical health and health related quality of life (HRQOL). An ideal intervention should aim to improve both the symptoms and HRQOL. Lifestyle recommendations as treatment for GORD so far lacks strong scientific support.

Aim: To study in depth the effects of a patient targeted dietary advice and lifestyle intervention on the symptoms and HRQOL of the patient.

Methods: Patients with ongoing symptoms of GORD and Savary-Miller grade 1 or less oesophagitis on gastroscopy were screened and suitable subjects randomised. Subjects in arm 1 were met by the researcher for 30 minutes, leaflets provided and advised on standard lifestyle recommendations. Subjects in arm 2 met the researcher and then a dietician. A patient specific dietary intervention with special focus on weight loss was provided. The GORD questionnaire was used as the measuring tool. The main outcome measures were GORD symptom scores (GSF, GSb), eating related scores (ESF and ESb), and sleep related score (PSL). An increase of 9 or more at six months is considered significant.

Results: 2450 patients were screened over a period of 18 months. 180 patients were suitable and randomised. 110/180 (61%) were female. The GSF score increased by 19.5 and 24, the GSb score increased by 14 and 22, the ESF score increased by 9 and 18, the ESb score increased by 6.9 and 15.8, and the PSL score increased by 13.7 and 24 in the arms 1 and 2 respectively.

Discussion: There was a significant increase in all the scores except the ESB in arm 1. The increase in scores in arm 2 was seen in all outcome measures, was significant and more pronounced. However the increase in scores compared to arm 1 did not attain statistical significance.

Conclusion: A structured dietary and generic lifestyle advice given by a professional improves GORD symptoms and HRQOL in the sufferers. The intervention provided was pragmatic and could be replicated in the primary care setting. A further study with longer follow up to assess the sustainability of the improvement in score is needed.

423 MODERATE–SEVERE REFUX OESOPHAGITIS HEALING RATES AT EIGHT WEEKS WITH FULL DOSES OF ESOEMPRAZOLE, PANTOPRAZOLE, LANSOPRAZOLE, AND OMEPRAZOLE
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Introduction: Several large studies have compared reflux oesophagitis (RO) healing rates of esomeprazole versus pantoprazole, lansoprazole, and omeprazole. Data versus rabeprazole are not available. Patients with moderate to severe RO (LA Grades C and D) demonstrate higher failure rates at week 4 and 8 than those with RO Grades A–B. To investigate PPI efficacy in this difficult-to-treat group, this analysis pooled data from previous studies to determine healing rates in patients with LA Grades C & D only.

Aims and Methods: Patients with confirmed RO (LA Grades A–D) were enrolled into three randomised, controlled, multicentre studies of similar design. Patients received either esomeprazole 40 mg od (E40), pantoprazole 40 mg od (P40), lansoprazole 30 mg od (L30), or omeprazole 20 mg od (O20) for up to eight weeks. Crude healing rates for Grades C & D were pooled and differences assessed using a χ² test.

Results: The percentage of patients with moderate to severe RO who were healed after four or eight weeks treatment was significantly greater with E40 compared with either P40, L30 or O20 (see table).

Conclusion: Esomeprazole 40 mg provided significantly better healing of RO Grades C & D than pantoprazole 40 mg, lansoprazole 30 mg, and omeprazole 20 mg at both 4 and 8 weeks. Esomeprazole is therefore the PPI of choice in healing patients with moderate/severe RO.

424 MODERATE–SEVERE REFUX OESOPHAGITIS: REMISSION RATES AT SIX MONTHS WITH LOW DOSES OF ESOMEPRAZOLE, PANTOPRAZOLE, AND Lansoprazole

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Introduction: The efficacy of low dose esomeprazole (20 mg) has been compared with low doses of pantoprazole (20 mg) and lansoprazole (15 mg) in two large studies.1 Patients with moderate to severe RO (LA Grades C & D) demonstrate higher failure rates at six months than those with RO Grades A and B. To investigate PPI efficacy in this difficult-to-treat group, this analysis pooled data from previous studies to determine remission rates in patients LA Grades C and D only.

Aims and Methods: Patients with confirmed RO (LA Grades A–D) were enrolled into two randomised, controlled, multicentre studies of similar design. Patients received either esomeprazole 20 mg od, pantoprazole 20 mg od, or lansoprazole 15 mg od for up to six months. Life table estimates of the percentage of patients in remission at 6 months were calculated for Grades C and D only.

Results: The percentage of patients with moderate to severe RO who remained in remission after six months treatment was significantly greater with esomeprazole 20 mg compared with either pantoprazole 20 mg or lansoprazole 15 mg (see table).

Conclusion: Esomeprazole 20 mg provided significantly better control of RO Grades C & D than either pantoprazole 20 mg or lansoprazole 15 mg at six months. Esomeprazole provides predictable efficacy in maintaining remission in patients with moderate to severe RO.


425 DOES LAPAROSCOPIC ANTIREFLUX SURGERY IMPROVE QUALITY OF LIFE IN PATIENTS WHOSE GASTRO-OESOPHAGEAL REFLUX DISEASE IS WELL CONTROLLED WITH MEDICAL THERAPY?

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Background: Both medical therapy and laparoscopic anti-reflux surgery (LARS) have been shown to improve quality of life in gastro-oesophageal reflux disease (GORD). While patients with poor symptom control or side effects on medical therapy might be expected to have improved quality of life after surgery, no study has examined whether patients well controlled on medical therapy who choose to undergo surgery (patient preference) might also experience improved quality of life.

Aim: To determine if LARS can improve quality of life in GORD patients even if their symptoms are well controlled on medical therapy.

Method: Between October 1998 and September 2003 all patients undergoing LARS were asked to complete three quality of life questionnaires preoperatively, while on medical therapy, and six months following LARS. Two questionnaires were generic, Short Form 36 (SF-36) and Psychological General Well-Being Index (PGWB); one was disease specific, Gastrointestinal Symptom Rating Scale (GSRS). The indication of patient preference for LARS was clearly identified in all patients prior to surgery.

Results: Completed questionnaires were received from 44 patients who underwent LARS for patient preference: 36 male, 8 female; mean age 42 (15–66) years. Preoperative quality of life scores while on medical therapy were significantly improved six months following LARS: SF-36 median physical composite scores 52 and 54 (p=0.05) and mental composite scores 51.5 and 56 (p<0.05); PGWB median total scores 77 and 90 (p<0.0001); GRSR median total scores 2.13 and 1.70 (p<0.001) and reflux scores 2.25 and 1.00 (p<0.0001).

Conclusion: LARS can significantly improve quality of life in GORD patients whose symptoms are well controlled on medical therapy. Such patients, therefore, should be considered for LARS.

426 A RANDOMISED TRIAL OF LAPAROSCOPIC TOTAL FUNDOPICATION VERSUS POSTERIOR PARTIAL FUNDOPICATION FOR GASTRO-OESOPHAGEAL REFLUX DISEASE BASED ON PREOPERATIVE OESOPHAGEAL MANOMETRY

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Aims: To assess (1) whether tailoring the operative procedure to preoperative oesophageal motility had any bearing on the results of fundoplication, whether performed by 360˚ or 270˚ laparoscopic fundoplication, and (2) whether there was any difference in outcome between total and partial fundoplication.

Methods: Prospective randomised trial. Preoperative motility assessed by oesophageal manometry (HRM) demonstrates the segmental anatomy of the oesophagus and predicts the success of liquid bolus transport more accurately than conventional manometry. No significant differences were reported in heartburn, regurgitation, dysphagia, post-prandial fullness, gas bloat inability to burp, increased flatus, diarrhoea, or abdominal pain at any of the postoperative intervals. Chest pain was more common at one year in the 360˚ group (p=0.03). There were eight failures on postoperative pH test: three in the 360˚ and five in the 270˚ groups. Patients in the ineffective motility group did not suffer any more dysphagia postoperatively than those in the normal motility group, whether they underwent a total or partial fundoplication.

Conclusions: (1) any differences in the symptomatic outcome of laparoscopic total or partial fundoplication appear minimal. (2) Tailoring the fundoplication to preoperative oesophageal motility has no scientific or clinical basis.

427 OESOPHAGEAL SOLID BOLUS TRANSIT: STUDIES USING CONCURRENT VIDEOFLUOROSCOPY AND HIGH RESOLUTION MANOMETRY

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Introduction: The efficacy of oesophageal solid bolus transit is less efficient than that of liquids in health and disease. The biomechanics of oesophageal function are complex and current investigations do not collect data that fully addresses the relationship between motor function and bolus transport. A recent study has shown that high-resolution manometry (HRM) demonstrates the segmental anatomy of the oesophagus and predicts the success of liquid bolus transport more accurately than conventional manometry.
Aims and Methods: Concurrent HRM and videofluoroscopy were performed to study solid bolus transport. 18 healthy volunteers were studied while swallowing 10 ml liquid barium and 10 mm diameter barium marshmallow bolus in a supine posture. HRM and videofluoroscopy data was analysed separately and in a blinded fashion. The characteristics and coordination of oesophageal peristalsis on HRM were assessed and related to the success of solid bolus transport.

Results: Oesophageal clearance of liquid and solid bolus was 88\% and 65\% of swallows respectively (p<0.005). For successful swallows, peristaltic velocity was slower (p<0.05) with solid than liquid bolus; contraction pressures were higher (p<0.05) and the pressure gradient across the GOJ was greater (p<0.01).

Conclusion: In healthy subjects bolus properties alter the pressure and velocity profile. When bolus escape occurs it is usually between the proximal and mid-oesophageal segments. Coordination between segmental contractions appears to be more important to the success or failure of solid bolus transport than contraction pressure.


E428 EOSINOPHILIC OESOPHAGITIS, AN EMERGING CAUSE OF DYSPHAGIA

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Background: Eosinophilic oesophagitis (EO) in adults is a recently described but under recognised condition. EO is characterised by intermittent and often painful dysphagia which may become persistent as the disease progresses. It is predominantly seen in men and a small proportion of these patients have atopic predisposition. Endoscopic appearances vary from small calibre, multi-ringed to a normal looking oesophagus. The average time to diagnosis from the first presentation of the symptom is usually in terms of years. This is mainly due to lack of awareness of the condition and the reluctance to biopsy an otherwise normal looking oesophagus. Diagnosis is made by detection of ≥20 eosinophils per high power field in the oesophageal biopsies. Treatment with corticosteroids (topical or oral) or leukotriene antagonist (Montelukast) has been successful in resolving symptoms in majority of patients.

Methods: We have identified 11 cases of eosinophilic oesophagitis (EO) who presented to our unit with recurrent attacks of dysphagia of long duration between 2002 and 2005. The mean age of the patient was 45.09 years and 10/11 patients were males. Three patients had atopic predisposition with hay fever, asthma and eczema respectively. Endoscopic appearances varied from ringed oesophagus in two patients, small hiatus hernia in three, schatzki ring in one, and normal looking oesophagus in five patients. Random biopsies over a length of 10 cm were taken in all and the diagnosis was confirmed by histological demonstration of eosinophils >20 per high power field. Eight patients have been treated with oral corticosteroids and three patients with montelukast. Six patients have reported subjective improvement in the symptoms and others at present are under review.

Conclusions: The recognition of EO as an underlying cause of recurrent dysphagia is steadily increasing. High clinical and endoscopic vigilance along with histological assessment is the key to the diagnosis of this condition. We would recommend oesophageal biopsies to look for EO in all patients presenting with recurrent dysphagia in the absence of any other obvious cause.

A REVIEW OF PATIENTS WITH ACALASIA CARDIA AND MEGAOESOPHAGUS: A SINGLE CENTRE EXPERIENCE

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Introduction: Megaoesophagus is defined as an oesophagus measuring 8 cm or larger on the barium swallow examination in patients with achalasia cardia. Its existence defines a late stage of achalasia cardia and therapy will include an oesophagectomy or pneumatic dilatation in the management. The former carries a high morbidity and mortality especially in centres with low patient load.

Method: We reviewed retrospectively all patients with achalasia cardia from January 2000 to December 2004 and identified 10 patients with megaoesophagus who subsequently underwent pneumatic dilatation.

Results: The average presenting age is 52 (SD 15) (range 20–73) years with four males and six females, out of which five were Malays, three were Chinese, and two Indians. The duration of illness before diagnosis was 7 (SD 5) (range 1–16) years. All patients had dysphagia, regurgitation, and weight loss. All 10 patients demonstrated oesopatrisis but interestingly eight patients failed lower oesophageal sphincter (LES) intubation during standard oesophageal manometry due to coiling of the catheter. Failure to elicit failure of relaxation of the LES translates as a high technical failure of manometry (80\%) in the diagnosis of achalasia cardia. A confident diagnosis of achalasia cardia was made on barium swallow all 10 cases (100\%). All 10 patients underwent pneumatic dilatation. Eight patients required only single dilatation. However two patients required two dilatations. The durability of the 12 pneumatic dilatations was 27 (SD 13) (range 4–44) months with good symptomatic relieve and an objective post-procedural weight gain of 10 (SD 6) kg over a period of 3–12 months. There was no complications noted past procedure.

Conclusions: In advanced cases of achalasia cardia, barium swallow is superior to manometry for obtaining the diagnosis. Pneumatic dilatation is a safe procedure with good durability and symptomatic improvement in patients with megaoesophagus.

Neurogastroenterology/motility posters

A430 INDUCING A VIRTUAL LESION IN THE HUMAN SWALLOWING MOTOR CORTEX

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Background: Cortical control of swallowing is bilateral but displays inter-hemispheric asymmetry, with dominant (D) and non-dominant (ND) projections. However, the precise relationship between these D and ND pathways remains unclear. 1 Hz repetitive transcranial magnetic stimulation (rTMS) can transiently suppress brain excitability non-invasively (a virtual lesion) with effects on peripheral function. Until now, a virtual lesion has not been applied to bilateral systems such as swallowing.

Aims: We assessed the effects of a 1 Hz rTMS induced virtual lesion on the excitability of D and ND swallowing motor cortex (SMC) and compared this to hand MC.

Methods: Seven healthy adult volunteers (four male, age range 25–46) had EMG excitability measurements from the pharynx and the hand in response to TMS before and up to 60 minutes post 1 Hz rTMS. Real and sham rTMS paradigms (600 pulses over D SMC) were applied at 120\% of pharyngeal resting motor threshold and randomised to separate days.

Conclusions: The recognition of EO as an underlying cause of recurrent dysphagia is steadily increasing. High clinical and endoscopic vigilance along with histological assessment is the key to the diagnosis of this condition. We would recommend oesophageal biopsies to look for EO in all patients presenting with recurrent dysphagia in the absence of any other obvious cause.

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Conclusions: An rTMS induced virtual lesion can induce differential interhemispheric suppression and excitation of SMC. These compensatory changes may be relevant to mechanisms of recovery after dysphagic stroke, a likely consequence of the bilateral innervation pattern for swallowing.

431 A COMPARISON OF SELECTIVELY ATTENDED VISCERAL AND SOMATIC PAIN

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Background: Visceral and somatic pain differ in several key aspects—visceral pain is described as ill defined and diffuse and results in divergent coping strategies to somatic pain (quiescence as opposed to escape). These differences in perception must be reflected in differing cortical patterns of activation. We have used a paradigm of attentional modulation to study the differences in activation in selectively attended visceral and somatic pain.

Methods: Twelve healthy, pain-free, right-handed subjects were recruited for the study. Simultaneous electrical pulses and auditory tones lasting six seconds were delivered to the subjects during a whole-brain functional scan acquisition. The electrical catheter was placed into the retromental fossa and cranial and onto the lower abdomen for the scan. Subjects were instructed to attend to and count either the auditory tones or electrical pulses. Electrical pulses and auditory tones were delivered at either 2, 3.5, or 4.3 Hz thereby varying the cognitive demand of the tasks. Pain intensity, unpleasantness and tone/pulse count were recorded after each stimulus.

Results: Pain intensity and unpleasantness were well matched for the two sensory modalities. Selective attention to both modalities resulted in activation in sensory-discriminative (secondary somatosensory cortex), affective (anterior insula, rostral-cingulate cortex), and cognitive (mid-cingulate cortex) regions. Subtraction analysis (selectively attended visceral pain minus somatic pain and vice versa) identified greater activation during visceral pain in the right thalamus, right hypothalamus, mid-cingulate cortex, bilateral cerebellum, and the right anterior insula (during the 4.3 Hz condition alone). There were no areas of greater activation during somatic pain.

Conclusions: Selectively attended visceral pain results in greater activation of affective (right anterior insula), autonomic (right hypothalamus), and attentive (mid-cingulate) regions compared with matched selectively attended somatic pain.

432 THE EFFECT OF PRE-STUDY ANXIETY STATE IN MEASURING THE MAGNITUDE OF SENSITISATION IN A HUMAN MODEL OF VISCERAL PAIN HYPERSENSITIVITY

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Background: Patients with stress or anxiety at the time of gastrointestinal injury/inflammation (for example, gastroenteritis) have a higher risk of developing subsequent irreversible bowel syndrome (IBS), but the mechanisms are uncertain. We have previously shown that oesophageal pain thresholds (PT) are inversely correlated with anxiety scores.1 In addition, we have shown that distal oesophageal acidification induces sensitisation of spinal dorsal horn neurones leading to the development of pain hypersensitivity (PH) in the non-acid exposed proximal oesophagus (PO) and chest wall (CW).2 The effect of anxiety on modulating the magnitude of sensitisation to oesophageal acid has not been studied.

Aim: To determine whether the magnitude of PH after oesophageal acidification correlates with pre-study anxiety state.

Methods: In 14 healthy volunteers the Spielbergber State Anxiety Inventory (SAI), a validated measure of state anxiety, was completed. PT to electrical stimulation (in milliamperes, mA) were determined in the PO and CW. The SAI was over 30 than below (r = 0.953, 95% CI = 0.997 to −0.448; p = 0.01 v = −0.001, 95% CI = −0.665 to 0.663; p = 0.99).

Conclusions: Increased baseline anxiety state is associated with a greater reduction of oesophageal PT after acid infusion. There may be a role for anxiety in modulating the sensory responses to injurious stimuli in the gut. Future studies with larger numbers and more objective physiological measures of stress and anxiety may more help to understand the mechanism by which anxiety influences post injury gut sensitisation.


433 EFFECTS OF REPEATED EXPERIMENTAL OESOPHAGEAL ACIDIFICATION ON PAIN THRESHOLD REPRODUCIBILITY IN HEALTHY SUBJECTS

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Introduction: Distal oesophageal acid has been shown to sensitise oesophageal mucosa both at the site of acid infusion (peripheral sensitisation) and also proximally away from the site of acid exposure (central sensitisation). Decreasing the interval between infusions potentiates this response but the long term effects of distal oesophageal acid infusions on oesophageal mucosal sensitivity to acid is unknown.

Aims: To determine the duration and magnitude of response of oesophageal sensitisation to both a single and repeated acid infusions in healthy volunteers.

Methods: (1) Duration: In eight subjects oesophageal pain thresholds (PT) to electrical stimulation were recorded at baseline and hourly following a 30 minute distal oesophageal acid infusion. If by the end of the study day the PT had not returned to baseline the subject returned the next day for further PT measurements. (2) Magnitude: 10 subjects underwent a repeat acid infusion two weeks after the first infusion and baseline and post acid oesophageal PT were compared between visits. Data from 36 subjects who have previously undertaken ≥1 acid infusion were also analysed to investigate whether the number of acid infusions accounts for an individual’s magnitude of sensitisation.

Results: (1) In six subjects the oesophageal PT had returned to baseline within nine hours of the acid infusion. In two subjects their PT remained reduced at the end of the experimental day, but had reverted to baseline when reassessed the next morning. (2) No difference in magnitude of effect on PT was seen with the first acid infusion compared with the second (p = 0.61 ANOVA) in all 10 subjects. Of the 36 subjects’ data, 31 sensitised to acid on their latest visit while five subjects did not. Logistic regression analysis showed that the number of acid infusions increased by 1 then the probability of sensitising to a subsequent acid infusion reduced by 4%, accounting for the magnitude of sensitisation. However, this result is not significant (odds ratio 0.96, 95% CI 0.68 to 1.37).

Conclusions: Acid induced oesophageal sensitisation is temporary and normalises within 24 hours in healthy subjects. Repeated distal oesophageal acid infusions do not alter the magnitude of sensitisation provided a two week period occurs between visits. Further studies with more frequently repeated acid infusions are warranted to assess changes in the magnitude and duration of oesophageal sensitisation, which reflects the role of frequent acid reflux that occurs in patients with GORD.

434 INVESTIGATING THE FUNCTIONAL PROPERTIES OF THE SOMATOSENSORY CORTEX DURING EXPERIMENTAL VISCERAL PAIN USING MAGNETOENCEPHALOGRAPHY

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Background: The somatosensory cortex has been inconsistently activated in pain studies and the functional properties of subregions within this cortical area are poorly understood. To address this we used magnetoencephalography (MEG), a brain imaging technique capable of recording changes in cortical neural activity in real-time, to investigate the functional properties of the somatosensory cortex during different phases of the visceral pain experience.

Methods: In eight participants (4 male), 151-channel whole cortex MEG was used to detect cortical neural activity during 25 trials lasting 20 seconds each. Each trial comprised four separate periods of 5 seconds in duration. During each of the periods different visual cues were presented, indicating that period 1 = rest, period 2 = anticipation, period 3 = pain and period 4 = post pain. During period 3, participants...
Postprandial gallbladder emptying and small intestinal transit in coeliac patients: A distinct effect of gluten free diet?

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Background: Gallbladder (GB) motility and small intestinal transit time (SITT) have been reported to be altered in coeliac disease (CD) and to normalise during gluten free diet (GFD), but these parameters have always been studied separately and in response to "artificial" liquid meals. Our aim was to assess GB motility and SITT simultaneously and in response to a physiologic solid meal in CD patients studied before and during GFD.

Methods: We measured GB motility using ultrasonography and SITT using a validated H2 breath test in 17 CD patients studied twice, before (n = 17) and during (n = 10) GFD, and in 24 healthy volunteers. Patients and controls were studied after following ingestion of a physiologic solid meal (kcal 539; 1 fried egg, butter, tea, sugar, bread, and baked beans).

Results: GB fasting volume and postprandial residual volume were significantly higher in CD than in controls (mean (SEM): 32 (4) ml v 14 (1) ml, p = 0.0002 and 9 (2) ml v 2 (0.3) ml, p = 0.01, respectively). T ½ GB emptying and emptying rate were similar in CD and controls. SITT was longer in untreated CD (238 (21) min) than in controls (169 (16) min, p = 0.013). After 12 months GFD, GB fasting volume was unchanged (22 (3) ml during v 27 (5) ml before GFD) and GB residual volume was significantly smaller during (3 ± 1 ml) than before GFD (16 (5) ml, p = 0.047). T ½ GB emptying was reduced (8 (0.5) min v 31 (6) min, p = 0.004) and GB emptying rate was increased during GFD by comparison with basal diet (–0.06 (0.01) ml/min v –0.02 (0.03) ml/min, p = 0.0034, respectively). SITT remained unchanged during (232 ± 20) min and before GFD (228 (22) min). Endomysial-Ab were negative and duodenal histopathology improved in CD during GFD, but Marsh II lesion persisted in all.

Conclusion: Postprandial GB emptying and SITT measured under physiological conditions in response to a solid meal are altered in CD patients. GB emptying, but not SITT, revert to normal during GFD, an effect mirroring incomplete histopathological recovery.

GI physiology posters

Endoscopic placement under sedation does not affect pH monitoring by the Bravo system

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Introduction and Aims: The Bravo system is designed to provide catheter-free, intrasophageal pH measurements over 48 hours. Early observations suggested that oesophageal acid exposure is less during the first than the second 24 hour period.1, 2 This study examined whether endoscopic placement under sedation had effects on pH measurement directly or indirectly through a reduction of activity or oral intake.

Methods: Fifty six consecutive patients (median age 48 (35–61) years) referred for pH monitoring were studied. The Bravo capsule was placed using a standard gastroscope under moderate sedation (midazolam 3–5 mg, fentanyl 0–50 μg) on an afternoon list and measurements began one hour after the procedure. “Reflexogenic” test meals (1000 kcal) were provided to 12/56 patients throughout the study. Acid exposures during the 3, 6, and 24 hours after endoscopy on the first day were compared to the same time periods on the second test day.

Results: Complete 48 hour pH data were available for 47 (85%) patients (incomplete recording/patient error (n = 8), early detachment (n = 1)). Pathological acid exposure (≥4.2%/24 hour) was recorded on at least one day in 34/47 (74%) patients. Acid exposure was similar after endoscopic placement on day 1 than the same period on day 2 (at 3 hours 8.7 (SD 1.4)% v 7.3 (1.6)%), p = 0.28, at 6 hours 8.8% (1.8)% v 8.0% (1.5)%, p = 0.71). Moreover pH measurement during the first 3 hours after endoscopy was not significantly different to that during any other time period (p = 0.58 by ANOVA). Acid exposure was also comparable in the postprandial periods (11.5 (1.6)% v 11.2 (1.5)% and during the first and second nights/supine periods (7.5 (1.4)% v 6.9 (1.5)%). The results were the same in the subset of patients that received set meals. Provision of set meals had no significant effects on pH measurements.

Conclusions: Endoscopic placement of the Bravo capsule under moderate sedation had no impact on pH recordings. Providing patients with set meals did not alter the reproducibility of pH measurements. The interpretation of pH recordings obtained by the Bravo system need not take the effects of endoscopy on acid reflux into account.


Identifying phenotypic variations in CCK induced gastric emptying delay in man

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Background: Ingested nutrients release cholecystokinin (CCK) which acts via CCK1 receptors on the vagus nerve to delay gastric emptying and limit meal intake. However, the invasive methods required to measure gastric emptying in previous studies have hitherto prevented their use in population studies.

Methods: Fifty-six consecutive patients (median age 48 [35–61] years) referred for pH monitoring were studied. The Bravo capsule was placed using a standard gastroscopy under moderate sedation (midazolam 3–5 mg, fentanyl 0–50 μg) on an afternoon list and measurements began one hour after the procedure. “Reflexogenic” test meals (1000 kcal) were provided to 12/56 patients throughout the study. Acid exposures during the 3, 6, and 24 hours after endoscopy on the first day were compared to the same time periods on the second test day.

Results: Complete 48 hour pH data were available for 47 (85%) patients (incomplete recording/patient error (n = 8), early detachment (n = 1)). Pathological acid exposure (≥4.2%/24 hour) was recorded on at least one day in 34/47 (74%) patients. Acid exposure was similar after endoscopic placement on day 1 than the same period on day 2 (at 3 hours 8.7 (SD 1.4)% v 7.3 (1.6)%), p = 0.28, at 6 hours 8.8% (1.8)% v 8.0% (1.5)%, p = 0.71). Moreover pH measurement during the first 3 hours after endoscopy was not significantly different to that during any other time period (p = 0.58 by ANOVA). Acid exposure was also comparable in the postprandial periods (11.5 (1.6)% v 11.2 (1.5)% and during the first and second nights/supine periods (7.5 (1.4)% v 6.9 (1.5)%). The results were the same in the subset of patients that received set meals. Provision of set meals had no significant effects on pH measurements.

Conclusions: Endoscopic placement of the Bravo capsule under moderate sedation had no impact on pH recordings. Providing patients with set meals did not alter the reproducibility of pH measurements. The interpretation of pH recordings obtained by the Bravo system need not take the effects of endoscopy on acid reflux into account.

Aims: To develop a non-invasive technique in order to define the range of responsiveness of gastric emptying delay to a CCK releasing meal in healthy adults and to determine the effect of CCK; receptor antagonism on the responsiveness to the meal.

Methods: Thirty three healthy volunteers consumed multiple test meals comprising either, 500 ml water alone, half strength or full strength CCK releasing meal, labelled with $^{13}$C acetic acid. Gastric emptying was expressed as the cumulative ratio of exhaled $^{13}$CO$_2$ to $^{13}$CO$_2$ over 45 minutes. The effects of the CCK receptor antagonist, dexloxiglumide were also studied.

Results: Compared to water, half strength and full strength meal delayed gastric emptying by 26% (3.5) and 50% (2.8), respectively (mean % decrease in gastric emptying (SEM), p<0.005). Within the study group, there was up to 95% difference in CCK responsiveness between individuals. Dexloxiglumide inhibited the effect of the CCK releasing meal by 50%.

Conclusion: A wide range of interindividual responsiveness in CCK induced gastric emptying delay exists in the presence of good intrasubject repeatability. Since gastric emptying delay is a major determinant of meal volume ingested, individuals who are less sensitive to CCK releasing meals are likely to be able to tolerate greater meal volumes. This is therefore a likely factor in calorie consumption and a risk factor in obesity development.

437 MRI STUDIES OF BLOOD FLOW THROUGH THE SUPERIOR MESENTERIC ARTERY

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Introduction and Aims: Chronic ischaemia of the small intestine is uncommon. It is hypothesised that this may be related to the nature of flow in the superior mesenteric artery (SMA) and the dynamic response to calorific load. To investigate this, SMA blood flow was studied during fasting and following ingestion of a controlled calorific load.

Method: Flow in the SMA was assessed in 18 healthy volunteers (11 male, 7 female, average age 36) by 1.5 Tesla magnetic resonance (MR) imaging. ECG gated, flow sensitive (phase contrast), sequences were acquired with high temporal resolution (21 frames per heartbeat) over the cardiac cycle. Images were obtained after overnight fasting and 30 minutes after ingestion of a 600 kcal Scandishake milkshake. A period of 30 minutes post-prandial was chosen as it coincides with peak flow (as determined from previous Doppler flow studies). Velocity fields in the SMA were monitored throughout the cardiac cycle and mean flow calculated throughout diastole.

Results: At 30 minutes post-prandial, mean diastolic flow was 3.7 times that of the fasted value (n=18, SD 2.2, range 0.8–9.8). During systole, flow disturbances, indicative of high velocity flows, were seen in 15 subjects post-prandially. This phenomenon was also seen in two of these 15 subjects after fasting.

Discussion and Conclusions: (1) Diastolic flow in the SMA increases markedly in response to calorific load. (2) The velocity of blood in the SMA during systole is sufficient to cause instabilities in the flow; the resulting loss of MR signal prevents the quantitative interpretation of velocity data at these high flows. (3) For most subjects, flow during systole is undisturbed following fasting. (4) The change in flow regime over these timescales may have important effects on wall shear stress, endothelial cell morphology, and risk of atherosclerosis.


Pathology posters

440 BAX PROTEIN EXPRESSION IN GASTRIC CANCER: CLINICOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

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Background: Reduced pre-apoptotic Bax protein expression has been identified in various human malignant tissues but little is known about its expression and its relationship with the biological behavior of human gastric cancer. The aim of our study was to examine the expression of bax protein in gastric cancer and precancerous lesions and correlate it with clinicopathological features and prognosis.

Methods: The expression of bax protein was studied by immunohistochemistry, using monoclonal antibodies, in a total of 48 paraffin embedded blocks of patients (30 males, mean age 67 years) who underwent gastrectomy due to gastric cancer. Bax expression patterns was graded as follows: negative, very weak, weak, less than 5% of cells stained, weak, 5–20% of cells stained, moderate, 20–50% of cells stained, intense, >50% of cells stained. The results were correlated with survival and clinicopathological data.

Results: Nineteen (39%) cases were positive for Bax protein staining which was mainly located in the cytoplasm of tumor cells. In 11/19 cases the staining was very weak. A wide range of interindividual responsiveness in Bax expression was not correlated with age, sex, tumour size, or depth of invasion. A negative immunostaining reaction was significantly correlated with lymph node metastasis (p<0.05), intestinal type gastric cancer (p<0.05), and with poorly differentiated neoplasms (p<0.05). In adjacent precancerous lesions, Bax was expressed in 81% of specimens with atrophic gastritis, 54% of specimens with intestinal metaplasia and 33% of dysplastic cases (p<0.001 compared with atrophy). Mean follow up of patients was 54 months. Median survival was 31 months in cases with positive bax expression and 22 months in patients with low bax protein expression. Negative expression of bax was associated with decreased survival.

Conclusion: Negative Bax protein expression in gastric cancer correlates with aggressive tumour characteristics. Positive bax protein expression is associated with favourable prognosis.

441 THE ROLE OF MATRIX METALLOPROTEASE-7 IN REDEFINING THE GASTRIC MICROENVIRONMENT IN RESPONSE TO GASTRIN AND H PYLORI

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Background: Epithelial organisation depends on interactions between epithelial and subepithelial cells including myofibroblasts. Gastrin activates these interactions is likely to be important in responses to injury, inflammation, and the progression to cancer. In the gastric epithelium, MMP-7 is increased in infection with Helicobacter pylori; there is also stromal cell expansion. Similar changes occur in patients with high plasma gastrin concentrations due to either pernicious anaemia (PA) or multiple endocrine neoplasia (MEN)-1 syndrome.

Methods: We investigated the role of MMP-7 as a signalling molecule between epithelial cells and a key stromal cell type, the myofibroblast. Media from primary human gastric epithelial cells either infected with H pylori or treated with gastrin released active MMP-7.

Results: In media from primary human gastric myofibroblasts, 2-dimensional gel electrophoresis and mass spectrometry identified MMP-7 acts as an epithelial derived signal to increase the density of myofibroblasts in gastric tissue. It is a key stromal cell type, the myofibroblast. Media from primary human gastric epithelial cells either infected with H pylori or treated with gastrin released active MMP-7.

Conclusion: MMP-7 acts as an epithelial derived signal to increase the density of myofibroblasts in gastric tissue. It is a key stromal cell type, the myofibroblast. Media from primary human gastric epithelial cells either infected with H pylori or treated with gastrin released active MMP-7.

442 IS BILE CYTOLOGY HELPFUL IN THE DIAGNOSTIC WORK UP OF PATIENTS WITH BILIARY STRICTIONS? A DISTRICT GENERAL PERSPECTIVE


Introduction: Identifying pancreaticobiliary malignancy in patients who present with a biliary stricture can be difficult. In the absence of EUS reliance upon imaging modalities and pathological specimens is
required. Biliary cytology and/or brushings at ERCP have a low sensitivity but a high specificity. Some studies suggest that utility is higher in cholangiocarcinoma than pancreatic cancer. Identifying malignant cells at cytology reduces the need to perform more invasive tissue sampling techniques before commencing of oncological therapy.

**Aims:** To determine the usefulness of biliary cytology and/or brushings in patients with biliary strictures in a district general setting.

**Patients and Methods:** Over the period January 2002 to December 2003 there were 119 patients diagnosed with pancreatobiliary tumours (73 pancreatic) and discussed at the upper GI multidisciplinary team meeting. Retrospective notes audit identified patients in whom biliary cytology and/or brushings were taken and this was correlated with findings from surgical resection or biopsy. Bile cytology samples were examined by two dedicated pathologists.

**Results:** Twenty three of these patients had 27 pathological samples taken; 19 by ERCP and eight via PTC. 13 patients had both biliary and bile aspiration samples, seven had just aspiration samples, and seven had aspiration samples only.

Sensitivity for a malignant report was 17.4% increasing to 43.5% if malignant/suspicious reports and specificity was 100%. Negative predictive value was 23.5%. Brushings and aspiration was superior to either alone and aspiration alone was superior to brushings alone (specificity 60%, 42%, and 16% respectively).

**Conclusion:** Positive cytology clearly aids management of these patients whereas a negative sample adds little reassurance. Combining aspiration with brushings gives the highest sensitivity and specificity.

**443 DETECTION OF GASTROINTESTINAL MALIGNANCY BY FLUORESCENCE LIFETIME IMAGING OF UV LASER INDUCED TISSUE AUTOFLUORESCENCE**

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**Background:** There is increasing interest in fluorescence imaging to help the early detection of malignancy in the GI tract. Fluorescence lifetime imaging (FLIM) is a novel wide-field imaging technique based on the decay kinetics of fluorescence at each point in the image field. Imaging fluorescence lifetimes can potentially improve the specificity of fluorescence based widefield imaging techniques and enhance their ability to discriminate between malignant and normal tissue. We present unique preliminary data from ex vivo imaging of GI malignancies obtained using a prototype FLIM system.

**Methods:** Unfixed macroscopic tissue samples were obtained from surgical specimens from oesophagus, stomach and colon immediately following resection for malignancy. Tissue autofluorescence was induced by exciting the samples en face with a pulsed UV (355 nm) Nd:YVO₄ laser and a set of wide-field fluorescence lifetime images recorded for areas macroscopically diagnosed as containing normal and cancerous mucosa. Tissue samples were subsequently fixed in formalin and the FLIM images compared with the histopathology findings.

**Results:** There was a marked change in the lifetime characteristics of malignant oesophageal, gastric, and colonic tissue compared to normal epithelium. For the majority of malignant lesions, the lifetime of the autofluorescence was shorter than that of the contiguous corresponding normal mucosa.

**Discussion:** FLIM generates inherent contrast between malignant and non-malignant GI tract tissue. Wide-field images can be updated at near video rate. These promising early data suggest FLIM has the potential to become an endoscopically deployable tool in vivo to help identify areas of early cancer.
induce activation of NF-κB and augment the expression of its driven transcription targets particularly IL-8 and IL-B.

Methods: A growing body of studies elucidated the effect of numerous phytochemicals in chemoprevention process in cancer. Hence, the objective in this study was to assess the effect of six dietary ingredients on the bile induced NF-κB activity in oesophageal cancer OE33. IL-8 and IL-B mRNA expression were particularly utilised as surrogate of induction of NF-κB activity, since the link between them has been previously demonstrated.

Results: Of the six agents validated, curcumin (from turmeric), vitamin C, resveratrol (from red wine), and EGCG (green tea extract) seemed to be effective at blocking NF-κB activity, as determined by the specific expression of IL-8 and IL-B utilising Real-time PCR. In some cases, this completely abrogated bile induced NF-κB activity. Furthermore, to investigate these phytochemicals mode of action in oesophageal cancer cells, their impact on the level of reactive oxygen species as inducers of NF-κB plus the exerted effect on GFP tagged p65 construct in conjunction with a confocal microscope to monitor cellular localisation are carried out at present.

Conclusion: As NF-κB activity appears to be linked to neoplastic progression in Barrett’s patients, some of the dietary phytochemicals may have a role in oesophageal cancer chemoprevention.

DURING ACID REFLUX, LUMINALLY GENERATED NITRIC OXIDE FROM DIETARY NITRATE LEADS TO NITROSATIVE STRESS WHICH IS MAXIMAL IN THE OESOPHAGUS

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Background: The mutagen responsible for the rising incidence of adenocarcinoma of the gastric cardia and distal oesophagus is unknown. In healthy volunteers, we have previously demonstrated that high concentrations of nitric oxide are generated from dietary nitrate, leading to in situ formation of N-nitroso compounds. In these subjects without reflux, this luminal nitrosative chemistry is maximal in the proximal region of the stomach.

Aim: To examine the influence of gastro-oesophageal reflux on the anatomical location of this in situ nitrosative stress.

Methods: Seventeen H pylori negative patients with Barrett’s oesophagus were studied. A segmented silastic tube containing the secondary amine morpholine was attached to a 4 channel pH catheter and passed naso or oesophageally. The tube wall has the same physical properties as the epithelial lipid membrane. Subjects then drank 2 mol of 15N enriched potassium nitrate. On one visit they were studied in the absence of acid reflux, and on the other reflux was stimulated posturally and pharmaceutically. The tube was removed after 2.5 hours and each segment analysed for markers of nitrosative stress.

Results: In the absence of acid reflux, nitrite and N-nitrosomorpholine were detected in the gastric sections, with concentrations maximal proximally. During reflux, 80% of nitrosative stress occurred in the oesophageal sections. A linear relationship existed between the duration of acid reflux and the proportion of stress occurring in the oesophagus (p<0.001). The N-nitrosomorpholine measured was enriched with 15N, indicating it was derived from the administered nitrate via nitric oxide production.

Conclusion: Acid reflux results in proximal migration of the area of nitrosative stress induced by dietary nitrate via nitric oxide production. The presence of nitrosative stress in a region already damaged by inflammation and metaplasia may contribute towards carcinogenesis at this site.

LONG TERM SURVIVAL OF OESOPHAEGAL AND GASTRIC CANCER PATIENTS TREATED SURGICALLY AT A DISTRICT GENERAL HOSPITAL

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Background: Survival following gastric/oesophageal cancer surgery is poor. In recent years, advances have been made in surgical techniques and chemoradiotherapy, as well as changes in the coordination of cancer services with the aim to improving mortality.

Aim: To identify patients who have survived in excess of seven years following gastric/oesophageal cancer surgery and factors that may have contributed to prolonged survival.

Methods: The pathology database was analysed for patients who were treated for gastric/oesophageal cancers between 1992 and 1998, and were matched against hospital patient administration system for survival. The surgical pathology was reviewed and staged according to TNM classification.

Results: 129 patients who were diagnosed with gastric/oesophageal cancer were identified between 1992 and 1998. Of these nine had survived to the present day (7%). Only five of the surviving nine patients had diagnostic CT scans prior to surgery. Many of the patients had advanced stage disease, three had nodal metastases, and one had pathologically involved surgical resection margins.

Conclusion: Surprisingly, many of the survivors is this series had poorly differentiated tumours of advanced stage. Exceptional longevity following gastric/oesophageal cancer surgery is not limited to those with well differentiated early stage disease.
(p<0.0001). High grade tumours represented 87% of the raised AFP group vs 31% in the normal AFP group (p<0.0001).

Conclusion: AFP is a marker of aggressive disease in a subset of NET patients. It is associated with both histologically aggressive and clinically progressive disease. These patients are three times more likely to show radiological tumour progression and high grade histology compared to those with normal AFP levels. A prospective analysis of AFP alongside changes in disease state will allow us to determine the role of AFP as a clinical parameter for monitoring tumour behaviour in NET patients.

451  BIOMARKERS OF THE IMMUNE RESPONSE IN PRIMARY COLONORECTAL CANCER

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Aim: The object of this project is to characterise lymphocytes in colorectal cancer (CRC), to identify subpopulations that reflect immune activation or suppression. Our aim is to validate the methods used so that they may be used in future early vaccine trials to assess the effect of such trials on the immune microenvironment of this disease.

Methods: We recruited 34 patients undergoing surgery for CRC. Lymphocytes were harvested from blood (PBL) and tumour (TIL). Flow cytometry and immunohistochemistry was used to detect subpopulations within TIL by identifying 18 markers for T cell homing and two of immune suppression (CD25 and Foxp3). To assess function, cells were stimulated and the supernatant was tested in cytokine ELISA.

Results: Using flow cytometry, the average number of CD4+CD25+TIL was 19.9% (range 2–31) compared to 5.6% (0–27.9) for PBL (p=0.1972). Immunohistochemical staining for Foxp3 was positive in samples obtained from 14 patients. Expression of homing markers differed between PBL and TIL, with the proportion expressing CCR6 higher (p<0.0001). Using flow cytometry to calibrate TIL input numbers enabled more accurate measurement of functional status. TIL released both interferon-γ and IL-10, associated with positive and negative antitumour responses respectively, but at levels lower than PBL.

Conclusions: We have confirmed the presence of immunosuppressive cells in CRC; however, there is not an increase in expression when compared to PBL. The percentage expression of the chemokine receptor CCR6 is higher in TIL when compared to PBL. Subpopulations within TIL expressing particular cell surface markers may contribute differently to the immune microenvironment, and work is currently going on to isolate these cells and determine their functional properties. The methods we have developed to assess the immune response at the tumour site can be used to analyse the effect of future vaccine trials.

452  CONFOCAL MICROSCOPY: A NOVEL METHOD TO ASSESS ABERRANT CRYPT FOCI IN APCMIN/+ AND APCMIN/−(PPARα−/−) MICE

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Background: Peroxisome proliferator-activated receptor α (PPARα) is expressed at low levels in colon tumours. APCmin/+ mice fed with methylclofenapate (a PPARα ligand) have 50% less tumour burden in the small intestine and colon than control. Recent studies showed that aberrant crypt foci (ACF) are the earliest morphological lesion detectable in colorectal cancer and that they may lead to cancer. However, the relationship between PPARα and ACF formation is not known. Dissection microscopy is the most common method used for quantifying ACF. However it is time consuming and requires a great deal of skill to obtain a good preparation.

Aims: (1) To determine whether confocal microscopy is a viable method for identifying ACF in scientific practice. (2) Examine the role of PPARα in colon carcinogenesis using APCmin/+ and APCmin−/− (PPARα−/−) mice.

Method: Confocal microscopy was performed on ulcerative colitis (UC) and FAP mouse models using a Cell-", version 5.0.50.1 software. ACF were clearly identified in APCmin/+ and APCmin−/− mice and the number of ACF per unit area was counted. The lateral resolution of normal colon was determined using the "vizio" probe. The "vizio" probe is a simple and quick method of accessing ACF, with the potential of refining experiments so that mice can be studied serially. PPARα role in colon carcinogenesis may be to inhibit the formation of ACF rather than their progression. Greater understanding of PPARα dependent genes may enable the pathogenesis of colon cancer to be further understood.

453  IS THE FULL BLOOD COUNT RELEVANT IN THE DIAGNOSIS OF COLORECTAL CANCER?

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Introduction: The national cancer 31 and 62 day waiting time targets are driving the diagnosis of colorectal cancer by a straight to test policy. We have looked at the full blood count (FBC) of proven cancer cases to see whether it is relevant to referral and diagnosis.

Method: The FBC at diagnosis of proven colorectal cancer was correlated to the patient gender and site of tumour, retrospectively over 18 months.

Results: 143 patients were included with a mean age of 67 years (male) and 74 years (female). The tumours were located on the left side in 96, including 68 rectal or rectosigmoid, and on the right side in 47. Mean haemoglobin (Hb) was 12.7 g/dl in males (n=85) (lab ref 13.0–18.0 g/dl) and 12.0 g/dl in females (n=58) (lab ref 12.0–16.0 g/dl) and was below the lower limit of normal in 48% (male) and 50% (female). Mean Hb was 92.3% of normal for rectal cancers v 82.5% for non-rectal cancers (p<0.001), and was below the lower limit of normal in 32.4% v 64.0% (rectal v non-rectal; p<0.001). Mean Hb was 79.6% of normal in right sided v 91.3% of normal in left sided cancers (p<0.01) and was below the lower limit of normal in 70.2% v 38.5% (right v left sided; p<0.001). In multiple regression analysis, after first adjusting for sex, the mean difference in Hb associated with non-rectal compared with rectal cancers was −1.6 g/dl (SEM 0.3 g/dl).

Conclusion: Non-rectal cancer patients, particularly those with right sided lesions, are significantly more likely to have a greater degree of anaemia at presentation. However, this observation may not determine the referral, investigation or management of patients suspected to have colorectal cancer. Irrespective of haemoglobin, such patients should be referred via the two week rule pathway.

454  COLON CANCER RATE IN PATIENTS WITH A WELL RECOGNISED CAUSE OF IRON DEFICIENCY ANAEMIA IN THE UPPER GI TRACT

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Background: Upper and lower GI tract investigations are mandatory in most patients with iron deficiency anaemia (IDA). BSG guidelines indicate that only the presence of coeliac disease or malignancy encountered at OGD precludes lower GI tract evaluation. This is based on inconsistent results from studies suggesting that colon cancer may be uncovered even in a cause for IDA is found at OGD. It could be argued that such cases merely reflect the background prevalence of colon cancer.

Methods: We conducted a retrospective analysis of 408 patients with iron deficiency anaemia. We defined the cause of IDA by exclusion and/or reduced serum ferritin concentrations. All patients had undergone OGD and were then divided into two groups. The first comprised 73 patients with an upper GI tract lesion that could feasibly account for IDA (gastric/duodenal ulceration, severe oesophagitis, severe haemorrhagic gastritis-duodenitis, and vascular lesions). The second comprised 335 patients whose upper GI tract was normal, or contained minor lesions, considered unlikely to cause IDA (mild gastritis, duodenitis or oesophagitis, Barrett’s oesophagus, and hiatus hernia). In the two groups we defined the prevalence of colon cancer in subsequent lower GI tract evaluation.

Results: Colonoscopy or double contrast barium enema studies were completed in 278/408 (68.1%) patients.

Conclusion: Colon adenocarcinoma was present in 31 patients. Cancer was located in the right hemi-colon in 80.6% of cases. In 49 patients with a well recognised cause of IDA in the upper GI tract who underwent lower GI tract evaluation, colon cancers were only present in one case (2%). This isolated case had a chronic gastric ulcer and a proximal transverse adenocarcinoma. Conversely, in patients with upper GI tract lesions
sufficient to account for IDA, colon cancer was present in 30 cases (13.1%), (p=0.05). In summary the prevalence of colon cancer is very low in patients with an upper GI tract lesion sufficient to account for IDA.

455 DO 31/62 DAY CANCER TARGETS WORK FOR PATIENTS WITH LIVER METASTASES?

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Introduction: NHS Cancer Plan (2000) requires trusts to achieve “62 days” (urgent GP referral to first treatment) and “31 days” (decision to treat to first treatment) targets and stipulates specialist teams of clinicians and cancer nurse specialists should care for all patients with cancer. Patients with liver metastases are an unknown primary or often fall outside specific cancer multidisciplinary team meetings (MDT) and are at greater risk of missing targets. This study was aimed to determine if patients with liver metastases met these targets.

Methods: Patients with diagnosis of “liver metastasis” on outpatient abdominal ultrasound in August 2004–August 2005 were identified and notes and computerised records were reviewed retrospectively.

Results: Thirty nine patients (17 males, median age 73 years, range 51–91 years) had liver metastases on ultrasound, five with alternative diagnoses including hepatoma (3), multiple liver abscesses (1), and focal nodular hyperplasia (1). Primary cancer was known at diagnosis in six patients, was diagnosed within 31 days in nine patients, and beyond 31 days in 11. No further tests were done in six patients, no primary was diagnosed despite investigations in two. 25 patients were referred for treatment including symptom control, one refused treatment, and no treatment was offered to eight. Other treatment included radiotherapy (2), curative chemotherapy (2), chemo ablation (1), palliative chemotherapy (6), palliative procedures (6). Only 19/34 (56%) patients met the 31 day target and 16/34 (47%) met the 62 day target. 64% of patients were discussed in cancer MDT, 59% were seen by cancer nurse specialist.

Conclusions: Patients with liver metastases have complex pathways with worse clinical outcome. Approximately half the patients failed the 62 day and 31 day target; a third did not have access to MDT nor support of a cancer nurse specialist. This highlights the need for streamlining cancer pathways for patients with liver metastases so they may benefit from advances in cancer therapy.


Radiotherapy posters

456 INTEGRATED FDG PET/CT IN THORACIC OESOPHAGEAL AND GASTRO-OESOPHAGEAL JUNCTION CARCINOMA: A PICTORIAL REVIEW

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Thoracic oesophageal and gastro-oesophageal junction (GOJ) cancers, in common with many other malignant tumours, usually have a high rate of glucose metabolism which enables their detection with 18F-labelled fluoro-2-deoxy-D-glucose (FDG). Integrated positron emission tomography/CT (PET/CT) combines functional imaging with accurate anatomical localisation and is emerging as a powerful technique for the assessment of patients with these cancers.

Endoscopy and biopsy of suspicious areas remains the cornerstone for establishing the diagnosis of oesophageal carcinoma. Small volume primary disease is not reliably detected on FDG PET particularly at the gastro-oesophageal junction where normal physiological uptake may occur. Integrated FDG PET/CT may have a role in the detection of severe dysplasia associated with Barrett’s oesophagus.

In staging disease, endoscopic ultrasound remains the method of choice for assessing the primary site and adjacent para-oesophageal nodes. Integrated FDG PET/CT provides, however, the most comprehensive single stage tool for detecting disease and can lead to more appropriate selection of patients for surgical resection. In patients with advanced disease undergoing neo-adjuvant chemotherapy, integrated FDG PET/CT is potentially useful for monitoring treatment response.

Between March 2004 and September 2005 the authors have conducted 76 integrated FDG PET/CTs for staging these tumours and correlated findings with surgery and the clinical course. Drawing from this data, the exhibit will outline the contribution of integrated FDG PET/CT in the management of thoracic oesophageal and GOJ cancer with several illustrative cases.

457 3D VIRTUAL REALITY COLONOSCOPY AND TARGETED OPTICAL COLONOSCOPY: THE LIGHT AT THE END OF THE TUNNEL?

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Introduction: V3D-colon (Viatronix) is a validated CT application which generates a primary 3D virtual reality image of the colon.

Aim: To compare findings on V3D (VRC) with gold standard optical colonoscopy (OC) in symptomatic patients.

Method: 100 patients attending GI outpatient requiring colonoscopy agreed to participate in a study comparing VRC with OC. Colon cleansing was undertaken using a standard preparation with dilute barium and gastrografin added to the preparation protocol. Air in the VRC was performed with 4 sensor CT gantries and parallel imaging using the V3D-colon software engine. Contrast tagged stool and fluid were removed electronically. The 3D VRC image was used as the primary diagnostic image with 2D colography available for problem solving. Polyps >5 mm in diameter were considered significant.

Results: Pancolonscopy was completed in 99 VRC examinations and 92 OCs. VRC demonstrated >99% of the mucosal surface with colonoscopists reporting a mean estimate of 88% surface visualisation. Both techniques revealed two rectal and one hepatic flexure cancer. Eleven polyps >5 mm were discovered in nine patients. One of these polyps was found on OC in the single patient who failed VRC and a 15 mm polyp missed on OC was found after unblinding (sensitivity for both VRC and OC was 91.6%). Two of three cancers and all the benign polyps >5 mm were present in the left-sided colon and rectum. Diverticulosis was reported in 39 VRC and 30 OC examinations. Significant extracolonic findings were reported in 29 patients. One OC patient experienced bradycardia.

Conclusion: 3D VRC is a major development in minimally invasive colonic imaging with sensitivity comparable to OC. In symptomatic patients, a case can be made for VRC followed if necessary by immediate targeted colonoscopy.

458 HIGH FREQUENCY MINI PROBE EUS IS A VALID PREDICTOR OF DISEASE ACTIVITY IN ULCERATIVE COLITIS ADOPTING MODIFIED TSUGA SCORES: FIRST VALIDATION DATA WITH RELAPSE PREDICTION

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Background: In ulcerative colitis (UC) colorectal wall parameters using 20 MHz EUS can be classified into four discrete subgroups (Ts 1-IVb). Our group have previously shown 20 MHz EUS to be a useful adjunctive activity index parameter. In UC prognosis is dependent on the severity of mucosal inflammatory change where accurate assessment of disease activity is required to optimise medical therapy. Relapse prediction using conventional endoscopic, histopathological and clinical criteria has proven unreliable.

Aims: (1) To evaluate the validity of Ts EUS criteria in UC as compared with standardised measures of clinical, endoscopic and histopathological severity. (2) To assess the relapse rates in patients fulfilling baseline Ts class III/IV criteria.

Methods: Segmental colorectal 20 MHz imaging using water +/- Tseng balloon acoustic coupling was performed in 200 patients. Endoscopic EUS criteria were then compared to the endoscopic Baron score, a laxity score, and Matts histopathological grade. Baseline indices were then repeated at “acute” presentation; otherwise 6, 12, and 18 months post index assessment.

Results: Rectum: K coefficient between Tsuga criteria I/II and Matts grade 1/2 was 0.78 (95% CI 0.67 to 0.89), 0.57 (95% CI 0.46 to 0.68), and 0.48 (95% CI 0.34 to 0.62) for Tsuga class IIIa/b, IVa/b, and Matts grade 3a/b and 4 respectively. Colon imaging showed a Kappa coefficient between Tsuga class I/II and Matts grade 1/2 of 0.76 (95%
High frequency ultrasound is a valid adjunctive "tool" for the transmural assessment of the colorectal wall in ulcerative colitis. This technique may aid in the initial diagnosis, and ongoing chronic management of disease.

**Conclusions:** High frequency ultrasound is a valid adjunctive "tool" for the transmural assessment of the colorectal wall in ulcerative colitis. This technique may aid in the initial diagnosis, and ongoing chronic management of disease.

**459 THE RADIOLOGY OF ABDOMINAL TUBERCULOSIS**

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Abdominal TB can involve any part of the GI tract, including the peritoneum, hollow and solid organs and the lymphatics. Although the high level of pulmonary TB seen during the last two centuries has declined, the number of cases of abdominal TB in the UK has risen due to a number of factors. The major reasons are HIV infection, and the subsequent development of AIDS, and the emergence of multidrug resistant TB. In addition, an increase in the immigrant population, thought to have an 80-fold higher incidence of non-pulmonary TB compared to the indigenous population, has produced a renaissance in abdominal TB.

Major diagnostic hurdles include the non-specific nature of the presenting symptoms and the unwillingness of the clinician to make the diagnosis of abdominal TB. It remains a disease primarily of the young, with a peak incidence in the third and fourth decades of life. Patients can suffer pain, fever, weight loss, anorexia, jaundice, or a change in bowel habit, and often investigated for a possible malignancy. In the majority of cases, radiological investigations are vital in correctly diagnosing mycobacterial infection in the gastrointestinal tract.

We present four cases of abdominal TB in young Somalian males referred to the department of gastroenterology with abdominal pain and constitutional symptoms suspicious of intra-abdominal malignancy. The cases include the following diagnoses: abdominal tuberculous adenopathy, gastric outflow obstruction secondary to pyloric stenosis, Potts disease of the spine, and two cases of tuberculous involvement of the pancreas. Radiological images, including plain radiographs, ultrasonographic images, computed tomography, and magnetic resonance imaging are included to illustrate the role of radiological investigations in the diagnosis of abdominal tuberculosis.