USE OF THE SIMPLE CLINICAL COLITIS ACTIVITY INDEX (SCCAI) TO DEFINE RELAPSE OF ULCERATIVE COLITIS (UC)

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Background: Several tools exist to assess disease activity in patients with UC. The Simple Clinical Colitis Activity Index (SCCAI; Walmsley RS et al. Gut 1998;43:29–32) is a validated symptom based index (score 0–19) which has a good correlation with more complicated disease activity indices. However the score which defines a relapse has not been determined.

Aims: To determine a) the validity of the SCCAI when self-administered, b) the score that defines a relapse c) the correlation with existing disease activity indices.

Method: UC patients routinely attending hospital completed a 6 point questionnaire, the same questionnaire was later administered by the attendant physician who was blinded to the scoring process. As no gold standard for defining relapse exists the attendant physician made a global assessment of relapse/ remission status using the available clinical, laboratory & endoscopic evidence.

Results: Scores were obtained for 74 presentations; age range 16–79 years, 51% male, 34% relapse rate. The mean patient score was 4.1 (range 0–14) & mean physician score 3.7 (0–14). There was excellent correlation between the scores obtained by the patient & physician (mean difference of 0.38, 95% CI 0.10–0.65). The self-administered SCCAI correlated well with a more complicated symptom & laboratory based activity index (Seo M et al. Am J Gastroenterol 1992;87:971–6) (r=0.77, p<0.01). The receiver-operator curve demonstrates the performance of the SCCAI scores in determining relapse. A score of 5 or more defines relapse with 92% sensitivity, 91% specificity, 85% positive predictive value & 89% negative predictive value.

Conclusions: The SCCAI is a simple tool that can be accurately self administered, correlates well with a more complicated disease activity index, & can be used to define relapse of UC with high specificity & sensitivity.

A RANDOMISED TRIAL OF INTRAVENOUS PAMIDRONATE AND CALCIUM & VITAMIN D IN THE TREATMENT OF OSTEOPOROSIS ASSOCIATED WITH CROHN’S DISEASE

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Introduction: Osteoporosis is recognised as a common complication of Crohn’s disease, affecting 10–42% of patients. Several groups have reported increased levels of bone resorption markers in these patients making the use of bisphosphonates, inhibitors of bone resorption, a potentially useful intervention. Optimum absorption of oral bisphosphonates is only 1–2% and we therefore studied the effect of a bisphosphonate given intravenously (pamidronate) compared to calcium & vitamin D supplements.

Methods: Sixty patients, (30 M, 30 F), with a median age of 44.5 years (range 25–70), all with a T score of -1.5 or less at either the lumbar spine or hip (a value recently suggested as the threshold for intervention) were randomised to receive either a daily dose of 500 mg of calcium with 400 IU of vitamin D alone (Group A, n=28) or in combination with 4 three-monthly infusions of 30 mg of intravenous pamidronate (Group B, n=32) over the course of 12 months. Nine patients in Group A (32%) and 16 patients in Group B (50%) were taking corticosteroids throughout the study. Bone mineral density (BMD) at the lumbar spine and hip were measured by dual x-ray absorptiometry at baseline and after 12 months.

Results: There were significant gains in BMD at the lumbar spine in both treatment groups, Group A =+2.1% ±4.8, Group B=+2.5% ±3.4%, p<0.05. At the hip there was a significant gain of +2.5% ±3.1%, p<0.05 in Group B compared to a gain of +1.1% ±3.7%, p=0.2 in Group A. Four patients refused to complete all four pamidronate infusions, 3 because of side effects, and 1 because of difficulty gaining intravenous access. Three patients were intolerant of the calcium & vitamin D supplements.

Conclusions: Despite a number of our patients taking corticosteroids both pamidronate and calcium & vitamin D supplements were effective in increasing bone density at the lumbar spine, but pamidronate was significantly more effective than calcium & vitamin D at the hip. Both treatments were well tolerated.

CAN LEFT-SIDED ULCERATIVE COLITIS BE TREATED WITH EPIDERMAL GROWTH FACTOR ENEMAS?

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Background: Epidermal Growth Factor (EGF) is a 53 amino acid molecule produced by the salivary glands that stimulates intestinal mucosal cell proliferation. Studies in animals have suggested a role for EGF in wound repair.

Aim: To examine whether EGF enemas are effective in the treatment of active left-sided ulcerative colitis.

Methods: A randomised double blind controlled clinical trial was performed. Outpatients with active left sided ulcerative colitis were either started on mesalazine 1.2gm/day or had the dose increased by 1.2gm/day. They were taught to self-administer enemas which contained either EGF (5 mcg EGF in 100ml) or an inert carrier (control) once a day for 2 weeks. Patients were reviewed at 2 and 4 weeks.

Results: Eight patients received EGF and nine placebo. Both groups had similar baseline characteristics. Six patients in the EGF group and eight in the placebo group were on mesalazine before recruitment to the study. Two patients from the placebo group developed worsening colitis and were withdrawn. After 2 weeks of enema treatment, there were significant improvements in the EGF treated group in symptom score (score 0 or 1 for the absence or presence of liquid stools, nocturnal diarrhoea and visible blood in stools) from median 3 to 1 (p<0.01), diarrhoea from median 5 to 2 motions /24 hours (p<0.05), sigmoidoscopic score (Baron, Br Med J 1:89–92 1964) from median 2.5 to 1 (p<0.05) and histological score (Richards, Br Med J 1:160–165,1960), from median 3 to 2 (p=0.01). These parameters were significantly better in the EGF group than in the placebo group at 2 and 4 weeks (p<0.01 for all). No significant change in these parameters was seen in the placebo group. Seven (87.5%) patients in the EGF group as compared to none in the placebo group achieved remission (i.e. a symptom score of 0) after 2 weeks (p<0.05). At 4 weeks, six patients in the EGF group and one in the placebo group were in remission (p<0.05).

Conclusions: EGF enema is an effective treatment for left sided ulcerative colitis. A dose increase of 1.2gm mesalazine had little effect on colitis activity.

IBD/Colorectal/IBS Free Papers: 001–015
004 DIETS CAN MODULATE THE INFLAMMATORY RESPONSE IN VIVO AND IN VITRO

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Nutritional therapy is recognised as a useful therapeutic modality in IBD. It is as successful as corticosteroids in producing clinical remission (Sanderson, 1987). However, little is known about the way diets achieve this response. The aim of this study was to determine in vivo and in vitro whether diets can modulate the inflammatory response.

In vivo study methods: 12 children with active Crohn’s disease undergoing treatment with a six week course of an exclusive polymeric diet (A110, Nestle, UK), Boost (Mead Johnson, USA) and Ensure plus (Ross Products, Abbott Laboratories, UK). The cells were stimulated with IL-1beta (1ng/ml). After 24 hours the media was collected and assayed for IL-6, IL-8 and TNF-alpha. Results: Using paired data (compared with day 0) a significant reduction (p<0.05) in the serum CRP, ESR, IL-6 and the clinical score (Paediatric Crohn’s disease Activity Index) was made at each visit.

Results: Using paired data (compared with day 0) a significant reduction (p<0.05) in the serum CRP, ESR, IL-6 and the clinical score (PCDAI) was found by day 7. None of the nutritional measures improved before 2 weeks. These data show that the diet had an anti-inflammatory effect which is not a consequence of improved nutrition.

In vitro study methods: Caco2 cells were grown in serum free media supplemented (5%) with different whole protein diets (breast milk, modulin (Nestle, UK), Boost (Mead Johnson, USA) and Ensure plus (Ross Products, Abbott Laboratories, UK). The cells were stimulated with IL-1beta (1ng/ml). After 24 hours the media was collected and assayed for IL-6, IL-8 and TNF-alpha. Results: In Caco2 cells IL-1beta leads to a marked inflammatory response with secretion of IL-6, IL-8 and TNF-alpha. Breast milk and Modulin decreased IL-6, IL-8 and TNF-alpha secretion by 50%. Boost decreased IL-6 and IL-8 secretion but had no effect on TNF-alpha and Ensure plus had no beneficial effect.

Discussion: This is the first time, in vitro, that nutritional therapies have been shown to modulate the inflammatory response in stimulated intestinal epithelial cells. This with our clinical data suggest that diets can have a direct anti-inflammatory effect on the intestinal mucosa the mechanism of which needs to be elucidated.

005 ANTI-INFLAMMATORY EFFECT OF ELEMENTAL DIET IN VITRO DEPENDS ON FATTY ACID COMPOSITION

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Introduction: We have recently reported the direct anti-inflammatory effect of elemental diet (ED) on intestinal tissue affected by Crohn’s disease (CD) in vivo. Replacing the amino acids by whole protein (casein, whey) in organ culture did not abolish the anti-inflammatory properties. We now report on the effect of the fatty acid composition of ED on the ratio of anti-pro-inflammatory cytokines produced in organ culture from IBD tissue specimens.

Methods: Colonoscopy biopsies from 12 patients (CD n=4, Ulcerative colitis (UC) n=8) and 10 patients (CD n=4, UC n=6) were incubated for 24h with elemental diet-sunflower oil (ESU) and elemental diet-safflower oil (EA) respectively. The composition of the rest of ED was identical with commercial elemental diet (E028, SHS, UK). Biopsy tissue was incubated in organ culture by adding ESU and EA to modified Waymouth’s MB705/1 complete media in dilutions of 1:20, 1:10 and 1:5 and medium alone as control. Pro-IL-1beta and anti-inflammatory (IL-1ra) cytokines were measured in supernatant by ELISA. Tissue viability was confirmed by estimating BrdU uptake by immunohistochemistry.

Results: In CD, incubation with ESU increased the ratio of IL-1ra:IL-1beta compared to incubation with medium alone. The medium (interquartile range) ratio with medium alone was 13.7 (9.91–23.60) compared with ratios of 64.17 (26.3–129.50) with 1:5 dilution (p<0.03), 5.57 (1.07–16.75) with 1:10 dilution (p<0.03) and 1.98 (29.80–79.30) with 1:20 dilution of ESU (p<0.03). In UC the same effect of ESU was seen on the IL-1ra:IL-1beta ratio in 1:5 dilution only compared to medium control (88.9 (32.7–157.2) Vs 12.2 (4.1–87.1); p=0.03). In contrast, incubation with ESA in CD did not change the IL-1ra:IL-1beta ratio (media alone 22.77 (16.43–34.05) Vs 1.5 ESA 24.12 (13.49–93.6); p>0.05, no difference with 1:10 or 1:20 dilutions). In vitro, a non-significant decrease, rather than an increase in ratio of IL-1ra:IL-1beta was seen after incubation with ESA in all dilutions.

Conclusion: The anti-inflammatory effect of ED depends on the fatty acid composition. Sunflower oil exhibits in-vitro anti-inflammatory activity, but safflower oil shows no such activity. Recently, anti-inflammatory effect of sunflower oil ingestion on breast inflammation has been reported in a PDA composition alone cannot explain these differences, as safflower oil contains, if anything, more PUFA than sunflower oil.

006 A RANDOMISED CONTROLLED TRIAL OF HIGH VERSUS LOW LONG CHAIN TRIGLYCERIDE WHOLE PROTEIN FEED IN ACTIVE CROHN’S DISEASE

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Background: Polymeric feeds have shown variable efficacy in active Crohn’s disease (CD) with remission rates from 36% to 82%. Meta-analysis of elemental, peptide and whole protein feeds have shown a strong inverse correlation between LCT content of diet and the long chain triglyceride (LCT) content of the feed. We performed a randomised controlled double blind trial in patients with active CD comparing two single whole-protein feeds with LCT supplying 5% or 30% of the total energy.

Methods: Fifty four patients with active CD (CDAI >200, serum CRP >10mg/l) were randomised to a high or low LCT feed for 3 weeks. The total amount of energy supplied by fat and total energy content were identical in the two feeds. Remission was defined as a CDAI<150 and response as a fall in CDAI of 70 points or a fall in CRP to less than 10mg/l. Statistical analysis was by Mann Whitney test.

Results: Overall remission rate by intention to treat was 26% for low LCT feed and 33% for high LCT feed (p=0.8). Response was achieved in 33% in low LCT and 53% in the high LCT feed (p=0.27). A reduction in CRP to less than 10 was achieved in 30% in the low LCT and 33% in the high LCT group (p=0.99). Thirty nine percent (21/54) of patients withdrew before three weeks because of inability to tolerate the diet. Excluding patients unable to tolerate the diet, the remission rates were 46% for low LCT and 45% for high LCT (p=0.99) and the attainment of a CRP <10 mg/l was 38% for the low LCT and 35% for the high LCT diet (p=0.99).

Discussion: This trial has shown no difference in the effect of low and high LCT whole protein feeds in active CD. This apparently strong inverse correlation between LCT content of diet and response in active CD is unlikely to be due to LCT itself and may be due to some other component of high LCT feeds.

007 LONGTERM OUTCOME OF U.C. PATIENTS WITH AND WITHOUT LOW GRADE DYSPLASIA (LGD)

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Longstanding extensive ulcerative colitis (UC) is associated with an increased risk of colorectal cancer (CRC). LGD is believed to predispose to this complication and some authorities advocate proctocolectomy when this is identified. The wisdom of this approach is questionable. Between 1978 and 1990, 160 patients with longstanding extensive UC were recruited for colonoscopic surveillance (Lynch DA, et al. Gut 1993;34:1075–80), 40 of these at some stage developed LGD. At the end of the study 128 remained alive with an intact colon. These patients have since been managed conservatively. We report the outcome of those with and without LGD 10 years later.

Methods: Retrospective cohort study. Outcome of the 160 patients originally recruited was established in 2000 by current note review, death certificate, personal interview, patient questionnaire or general practitioner contact.

Results: Outcome was confirmed in 158 of 160 patients (98.8%). Of the 128 patients alive and with an intact colon in 1990 2 were uncontactable 29 had had LGD (LGD group) and 97 no LGD (control group). Over the following 10 years HGD or CRC developed in 10 patients in the LGD group (10.3%) and in 49 controls (4.1%). Death had occurred in 3/29 (10.3%) LGD (one from CRC) and 13/97 (13.4%) controls.
(one from CRC), 3/29 (10.3%) LGD and 9/97 (9.2%) controls had undergone colectomy. Kaplan-Meier analysis from 1991 to death or surgery showed no difference between the two groups.

**Conclusion:** Prophylactic colectomy is unlikely to benefit patients with LGD.

### 008 IMPACT OF THE TWO WEEK WAITING TIME STANDARD ON THE GASTROENTEROLOGY SERVICE OF A DISTRICT GENERAL HOSPITAL (DGH)

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The two week waiting time standard for suspected gastrointestinal cancers came into effect in July 2000. There are concerns that this may overload already stretched resources leading to a longer wait for routine referrals. Many DGH’s already have well established policies for fast tracking urgent referrals. We have studied prospectively patients referred under the two week waiting time standard (Group I, n=28) with contemporaneous urgent referrals (Group II, n=30), routine referrals deemed urgent by the consultant (Group III, n=30) and routine referrals (Group IV, n=50). We have compared the percentage of malignancies and other serious non neoplastic diseases as well as the waiting times in the four groups.

**Results:** In Group I, 15% of referrals had proven malignancy and a further 25% had serious non-malignant diseases. The average waiting time was 7 days (range 1–18) and 95% of patients were seen within two weeks. In Group II, 8% of referrals had malignancies and 20% had serious non-malignant diseases. The average waiting time was 18 days (range 1–37). In Group III, 15% of referrals had malignancies and 30% had serious non-malignant diseases. The average waiting time was 26 days (range 8–37). In Group IV, 2% had malignancies, and 12% had other serious diseases. The average waiting time was 64 days (range 12–133). The routine waiting time rose by an average of 30 days. The two week waiting time standard is being met at the expense of a substantial increase in the waiting time for routine referrals whilst not necessarily identifying treatable cases of cancer.

### 009 MOLECULAR GENETIC TESTS IN FAMILIAL ADENOMATOUS POLYPOSIS MAY GUIDE MANAGEMENT DECISIONS

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**Introduction:** Familial adenomatous polyposis (FAP) is caused by a germline mutation on the APC gene. Management usually involves a prophylactic colectomy often by the age of 20. The choice of operation is usually a colectomy and ileo-rectal anastomosis (IRA) or a restorative proctocolectomy (pouch). A pouch procedure has a higher morbidity than an IRA but removes the risk of rectal cancer. A restorative proctocolectomy (pouch). A pouch procedure has a

**Aim:** To predict patients at the most risk of duodenal cancer.

**Subjects and methods:** 114 patients with FAP were screened for duodenal adenomas ten years previously to a set protocol using a side-viewing duodenoscope. The site, number and size of polyps were recorded and biopsies were taken. The patients were graded and a staging system described (Spigelman staging, stage I).

**Abstract 10, Table 1 Classification of the severity of duodenal polyposis (Spigelman et al. Lancet 1989;2:783–5)**

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<th>No. of points (pts)</th>
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<td>No. of polyps</td>
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<td>Polyp size (mm)</td>
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<td>Dysplasia</td>
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<td>Stage I, 1–4 pts</td>
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<td>Stage III, 7–8 pts</td>
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<td>Stage IV, 9–12 pts</td>
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**Results:** Six of 114 patients developed duodenal cancer at a median of 6 years (range 2 to 10 years) after entering the study and all died of the disease. Median age at diagnosis was 68 yrs. Four of the duodenal cancers were from eleven patients who had Spigelman stage IV disease 10 years previously (36% risk), one was from 41 original stage III patients (2%) and one was from 44 stage II patients (2%).

**Conclusion:** In this long-term cohort study it is clear that those with Spigelman stage IV disease have by far the greatest risk of duodenal cancer. Selection of patients with this stage of advanced benign duodenal polyposis for pylorus preserving duodenectomy can be justified on the basis of this study.
HYPERPLASTIC POLYPOSIS: PREVALENCE AND CANCER RISK

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Background: WHO defines hyperplastic polyposis (HPP) as ≥30 hyperplastic polyps (HP) throughout the colon and/or ≥5 histologically diagnosed HPs (two ≥1 cm diameter) proximal to the sigmoid colon. HPP is thought to predispose to colorectal cancer. Most HPP patients have many distal HPs, permitting diagnosis by flexible sigmoidoscopy (FS).

Aim: To estimate the prevalence and cancer risk of HPP using retrospective and prospective case series.

Methods: HPP patients were identified after a national call for cases. The UK FS screening trial screened 40,673 asymptomatic people aged 55 to 64 years. All prospectively identified HPP patients had a colonoscopy. This is the largest retrospective and the only prospective HPP case series.

Results: The prevalence of HPP at age 55–64 years was 1 in 3000. 50% of 12 asymptomatic screen-detected cases had at least one associated adenoma and 1 of 7 cases developed cancer within 2 years. Only 75% of associated cancers were located proximally in all series (table 1).

Conclusion: HPP is infrequent, but often associated with dysplasia and a significant cancer risk.

FEELING THE BLUES IN FUNCTIONAL GUT PAIN: MANIPULATING MOOD STATE INFLUENCES THE THRESHOLD FOR OESOPHAGEAL PAIN

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Since functional gut pain has been associated with depressed mood, we tested the possible role of mood state in sensitivity to oesophageal pain. We compared the amplitude of electrical stimulation required for 7 healthy volunteers (5 men; age range, 24–47 years) to detect painful and non-painful sensation in the lower oesophagus, in induced happy and sad moods. A phasic electrical current through bipolar ring electrodes was used for distal oesophageal stimulation. The amplitude was sequentially increased to determine sensory and pain thresholds both at baseline and following the use of mood evocative music to induce happy and sad moods. The sad mood induction successfully increased despondent mood compared to the happy mood induction (p < 0.001). There was no effect of mood induction on sensory threshold but we found that an induced sad mood compared to an induced happy mood significantly reduced the threshold for painful sensation (95% CI for difference, −13.88–−0.12, p < 0.03). This finding suggests that depressed mood may be a factor in the reduction in pain thresholds found in functional gut disorders.

DOES IRRITABLE BOWEL SYNDROME (IBS) PREcede OR FOLLOW INFECTIOUS DIARRHOEA (ID)?

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Introduction: Irritable bowel syndrome (IBS) has been reported to follow infectious diarrhea (ID)⁴⁻⁶. ID affects 9.4 million people per year in England of which only 1 in 6 see a doctor and only a percentage of these have stool cultures. We hypothesised that patients present to their GP with ID and have stool samples taken may be different from the normal population with regard to their pre-existing bowel symptoms.

Aim: To see if there is a difference in the prevalence of functional gastrointestinal disorders (FGID’s) in people with infectious diarrhoea compared to an age and sex matched control group.

Methods: Cases with positive bacterial stool cultures were invited to complete the Rome II modular questionnaire looking at bowel symptoms over the preceding year before their recent gastro-enteritis. The FGID’s looked at were Functional Dyspepsia, IBS and Functional Diarrhoea. Controls were approached from the same general practices as the cases and completed the same questionnaire.

WIND-UP IN THE HUMAN VISCERA: CENTRAL SENSITIZATION CONtributes TO VISCERAL PAIN

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Background: Perceptual wind-up is the progressive increase in pain perception to a train of electrical stimuli of the same intensity when delivered at frequencies>0.3Hz. This phenomenon is mediated by an increase in excitability of spinal neurons (central sensitization) and has been used as a clinical tool to investigate mechanisms of pain, and in particular the role of central sensitization in various chronic somatic pain syndromes.

Aim: To determine whether perceptual wind-up occurs in the viscera.

Methods: In 8 healthy volunteers (7 male; mean age 32 years), oesophageal and non-dominant hand pain thresholds (PT) to single electrical stimuli were first determined using a standard visual analogue scale (VAS) ranging from 0 to 10. At each site, a train of 20 electrical stimuli (pulse width 500μs) was then delivered at frequencies of 0.1 Hz and 2Hz. Each train was applied at both PT and sub PT (75% of pain threshold) intensities in a randomised manner. The VAS score to the first & the last stimulus of each train at both intensities was recorded. The study was repeated on a separate day to establish reproducibility.

Results: The VAS score for the 0.1Hz train remained unchanged for both the oesophagus and the hand. In contrast, for the 2 Hz train there was an increase in the oesophageal VAS score for both PT and sub PT (Wilcoxon: p<0.01), whilst for the hand the increase in VAS occurred only at PT (0.01). These observations were reproducible in both the oesophagus and the hand (intra-class correlation 0.8 & 0.7 respectively).

Conclusion: The increase in pain perception to a train of stimuli when delivered at 2Hz suggests that wind-up occurs via similar mechanisms in visceral and somatic tissues. However, the absence of wind-up to occur at lower thresholds in the oesophagus in comparison to the hand suggests that the viscera may be more susceptible to develop central sensitization in response to repeated stimulation.

PROSTAGLANDIN E, RECRuits SENSORY NEURONS TO RESPonD TO ACID

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Introduction: Therapeutic and mechanistic studies implicate both acid and mucosal prostaglandins (PGs) as able to cause or enhance dyspepsia. We developed an isolated neuronal preparation to investigate the hypothesis that PGs enhance the response of mucosal nociceptors to acid by neural recruitment.

www.gutjnl.com
Methods: Thoraco-lumbar dorsal root ganglia were dissected from adult Wistar rats after CO₂ euthanasia and the sensory nerve cell bodies liberated using a collagenase and trypsin digest. Cells were incubated on poly lysine/laminin coated coverslips and incubated for 10–16 hours in nerve growth factor-supplemented neurobasal medium before being loaded with the calcium-sensitive ionophore FURA-2. The coverslips were transferred to a perfusion chamber mounted on an inverted fluorescence microscope. Cell activation was identified by spikes in intracellular calcium concentration using computerised image analysis. Cells were perfused with a pH 7.4 HEPES buffer before being exposed to pH 6.1 for 1 minute. After a further 10 minutes at pH 7.4 the perfusate was either continued or switched to an identical buffer containing 10⁻⁴M PGE, for 3 minutes prior to a second 1 minute exposure to pH 6.1.

Results: The number of cells imaged in each experiment was 19±3 (Mean±SEM). Thirty eight percent (58%) of them responded to the first acid stimulus (n=10) with only 33±18% responding to the second stimulus (n=3). Addition of PGE, increased the proportion of cells responding to 45±8% (n=7), representing a rise of 40±17% versus a fall of 37±10% compared to respective baseline stimuli (p=0.03). Precipitation with indomethacin decreased viable cell count by a third but had no effect on the pH response of the surviving cells.

Conclusion: Exogenous PGE2 increases the number of sensory nerve cells that respond to acid by reducing desensitisation and recruiting previously insensitive cells.

Abstract 17, Table 1

The percentage of total costs for ulcerative colitis and Crohns disease is as follows, Inpatient 13% & 43%, Outpatient 19.1% & 12.2%, Investigations 23.5% & 15.4% and Medications 44.4% & 29.4%.

Conclusion: The hospital costs of IBD patients are high. This is particularly relevant with the availability of new treatments, which are expensive but could reduce the inpatient hospital days and avoid surgery and thus prove to be cost effective.

Table 1

<table>
<thead>
<tr>
<th>Costs</th>
<th>UC</th>
<th>Crohns</th>
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<tbody>
<tr>
<td>Inpatient (incl. Surgery)</td>
<td>£175 (1297–2213)</td>
<td>£2738 (1802–3674)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>£2,10 (176–244)</td>
<td>£267 (209–325)</td>
</tr>
<tr>
<td>Investigation</td>
<td>£258 (170–346)</td>
<td>£338 (210–466)</td>
</tr>
<tr>
<td>Medications</td>
<td>£487 (384–590)</td>
<td>£642 (478–806)</td>
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</table>

The economic burden of inflammatory bowel disease (IBD) on society and health care systems is high due their occurrence during the economically productive years and chronic nature. Published literature on the economics of IBD are however limited and this has relevance with the introduction of new expensive treatments such as anti-TNF antibody.
patients (8%), 6 in each group, having a normal QOL. Mean PIS score for the patients was 7.04 ± 0.1. 55% of the UC patients and 75% of the CD patients (p=0.006) were considered well informed (ie. PIQ scores of 7 or more). The mean PIQ for UC patients was 6.5 ± 0.4 vs 7.5 ± 0.2 for the CD group (p=0.001). There was however no correlation seen between the QOL and PIQ scores, both for UC and CD patients (r=0.3).

Conclusion: Most patients with IBD have impaired QOL, inspite of having inactive disease. The level of disease related knowledge appears to be better in patients with CD, though that does not seem to affect QOL.

Results: In the antral mucosa, ADAM17 mRNA expression in patients with H. pylori infection (mean±SEM 0.24±0.07, n=27) was significantly greater (p<0.05) than in uninfected patients with normal mucosa (0.08±0.04, n=16). There was a significant correlation (p<0.05) between the expression of ADAM17 and mononuclear cell infiltration. ADAM17 transcripts in gastric cancer mucosa (0.40±1.0, n=9) were also upregulated (p<0.01) compared with normal mucosa. TIMP3 mRNA expression was greater in gastric cancer mucosa (1.0±0.11, n=7) than in normal mucosa (0.4±1.12, n=11, p<0.01) and H. pylori infected mucosa (0.65±0.11, n=9, p<0.05).

Conclusion: ADAM17 mRNA expression was increased in H. pylori infected mucosa and in patients with gastric cancer. ADAM17 is likely to be important in the inflammation induced by H. pylori and may also be relevant to the development of malignancy. TIMP3 mRNA expression was also upregulated in gastric cancer mucosa. Further studies are required to localise the cellular origin of ADAM17 and TIMP3 in normal gastric mucosa and in gastric cancer.

018 HELICOBACTER PYLORI INFECTION REDUCES SYSTEMATIC AVAILABILITY OF DIETARY VITAMIN C
M. Woodward, H. Tunstall-Pedoe, K.E.L. McColl. Dept of Medicine & Therapeutics, Western Infirmary, Glasgow, Scotland, UK

H. pylori infection is recognized to lower the concentration of vitamin C in gastric juice. The objective of this study was to assess whether this effect of the infection on intragastric vitamin C resulted in reduced bioavailability of the ingested vitamin.

Methods: The study involved 1106 men and women aged 25–74 years recruited from the population of north Glasgow. Their H. pylori status was determined by measuring serum IgG antibody titres to H. pylori. Using a validated ELISA (Bio-Rad Laboratories Ltd., England). Dietary vitamin C intake was calculated from a food frequency questionnaire. Plasma vitamin C concentrations were measured by a fluorometric assay. Correction was made for potential confounding factors such as age, sex, smoking and social status.

Results: Fifty percent of these were H. pylori seropositive. The mean plasma vitamin C concentration in those who were H. pylori positive was only 65% of that in those classified negative (p<0.0001). This was partly explained by the fact that the dietary intake of vitamin C of the H. pylori positives was only 86.5% of that of the negatives (p<0.0001).

Conclusions: H. pylori substantially impairs bio-availability of vitamin C. This, together with the reduced vitamin C intake of H. pylori positive subjects markedly reduces the plasma vitamin C level of infected subjects.

Background: H. pylori is implicated in the pathogenesis of gastric cancer. The cadherin-catenin complex (of which β-catenin is a key signalling component) promotes stable adhesion of epithelial monolayers and is altered in several epithelial cancers, including gastric cancer.

Aim: To assess the effect of H. pylori on cadherin-catenin expression in the HT29 epithelial cell line.

Methods: H. pylori strain 60190 (vacA s1/m1, cagA+) was cocultured with HT29 cells for 24 hours at 37°C. Cells were also incubated with VacA (purified from 60190 by broth culture, precipitation, anion exchange and gel filtration chromatography). Using monoclonal antibodies and confocal microscopy, the distribution of E-Cadherin and β-catenin was studied in two consecutive control experiments. Furthermore, germline mutations in the E-cadherin gene have been described in familial gastric cancer.

Conclusion: Co-culture of H. pylori with epithelial cells leads to perturbation of β-catenin but has no effect on E-cadherin. Modification of β-catenin may be important in the pathogenicity of H. pylori.

020 ADAM17 AND TIMP3 mRNA EXPRESSION IN GASTRIC MUCOSA INFECTED WITH H. PYLORI AND IN GASTRIC CANCER
T. Yoshimura, D.J.M. Tolan, M.F. Dixon1, A.T.R. Axon1, P.A. Robinson, J.E. Crabtree. Molecular Medicine Unit, St. James's University Hospital; Leeds General Infirmary, Leeds, UK

Introduction: ADAM17 (a disintegrin and metalloproteinase) protein is implicated in the shedding of TNFα, TGFβ, L-selectin and the p75 TNF receptor. Our previous work demonstrated that H. pylori induced ADAM17 gene expression in gastric epithelial cells.

Aims: To examine ADAM17 and the specific inhibitor TIMP3 mRNA expression in gastric mucosa of patients infected with H. pylori and patients with gastric cancer.

Methods: Endoscopic antral and corpus biopsies were obtained from 54 dyspeptic patients without any medication and 9 gastric cancer operative sections for semiquantitative PCR and histology. The ratio of ADAM17 and TIMP3 transcripts to that of G3PDH was determined by computer image analysis.

021 “TWO WEEK WAIT” GUIDELINES FOR UPPER GASTROINTESTINAL CANCER - DO THEY WORK?
H.L. Spencer, R. Heeley, M.T. Donnelly (introduced by S.A. Riley). Dept of Gastroenterology, Northern General Hospital, Sheffield S5 7AU, UK

Introduction: National guidelines have recently been introduced with the aim of facilitating the earlier diagnosis and treatment of cancer. In the case of upper GI cancer, there is little published evidence to support the use of these guidelines.

Methods: We performed a prospective audit of all referrals for upper GI cancer under the two week wait guidelines, during the first 2 months the system was in operation at a single teaching hospital. We collected demographic data, clinical details and final diagnoses on all patients. We also collected the same data on all patients who had an upper GI cancer diagnosed during the same period who were not referred by the “2 week wait”.

020 SURFACE EXPRESSION OF β-CATENIN IN EPITHELIAL CELLS
J.R. Bebb1, L. Leach2, J.C. Atherton1 (Division of Gastroenterology & Institute of Infections and Immunity and School of Biomedical Sciences, University Hospital, Nottingham, UK

Background: H. pylori is implicated in the pathogenesis of gastric cancer. The cadherin-catenin complex (of which β-catenin is a key signalling component) promotes stable adhesion of epithelial monolayers and is altered in several epithelial cancers, including gastric cancer.

Aim: To assess the effect of H. pylori on cadherin-catenin expression in the HT29 epithelial cell line.

Methods: H. pylori strain 60190 (vacA s1/m1, cagA+) was cocultured with HT29 cells for 24 hours at 37°C. Cells were also incubated with VacA (purified from 60190 by broth culture, precipitation, anion exchange and gel filtration chromatography). Using monoclonal antibodies and confocal microscopy, the distribution of E-Cadherin and β-catenin was studied in two consecutive control experiments. Furthermore, germline mutations in the E-cadherin gene have been described in familial gastric cancer.

Conclusion: Co-culture of H. pylori with epithelial cells leads to perturbation of β-catenin but has no effect on E-cadherin. Modification of β-catenin may be important in the pathogenicity of H. pylori.
**Results:** A total of 63 patients were referred (26 male, 37 female) under the “two week wait” scheme, and all appointed within 2 weeks. Only 7 (11%) had a final diagnosis of cancer (see table 1).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Alive at 2/12</th>
<th>%Curable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophageal</td>
<td>Dysphagia</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>Anorexia</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Oesophageal</td>
<td>R.U.Q. pain</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Breast</td>
<td>Jaundice</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Weight loss</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Gastric</td>
<td>Weight loss</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>Weight loss</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Of these cancer cases, the mean delay to diagnosis was 7 days (range 2–29 days). All were seen within 2 weeks. 4 were still alive and 3 had died at 2 months follow up. Only 2 patients had had surgery for potentially curable disease. 8 others had underlying malignancy. Only 2 cancers diagnosed during the same period (6 oesophageal, 2 gastric). None of these were operable.

**Conclusions:** Cancer patients can be seen and a diagnosis made within a short period to comply with 2 week wait guidelines. Unfortunately, many of the sinister symptoms highlighted in the guidelines suggest advanced disease. An improvement in outcome has yet to be demonstrated.

**024 QUALITY OF LIFE AFTER HELICOBACTER PYLORI ERADICATION: A LARGE PROSPECTIVE STUDY IN PRIMARY CARE**

S. Verma, M.H. Gaffer. Dept of Gastroenterology, Hull Royal Infirmary, Anlaby Road, Hull, HU13 OEL, UK

**Introduction:** Eradication of Helicobacter pylori (HP) and amelioration of dyspeptic symptoms may improve quality of life (QOL) of patients with various upper gastrointestinal syndromes. This study examines the impact of HP eradication on the QOL of primary care patients maintained on long term H2 receptor antagonists (H2RA).

**Patients and methods:** Patients on long-term H2RA were identified from computerised records of 6 primary care practices. HP status was assessed using a standard serological method. Those who tested positive for HP were offered standard 7 day proton pump inhibitor based triple therapy followed by a urea breath test to confirm HP eradication. Patients were followed up for one year after HP eradication at 6, 24 and 36 weeks respectively with measurements of quality of life, overall feeling of well being, and Gastrointestinal symptom rating score (GSRS), severity of dyspeptic symptoms and subsequent need for acid suppression therapy.

**Results:** 297 HP positive patients participated in this study of whom fifty eight percent had PUD whereas 19% and 10% had non ulcer dyspepsia (NUD) and gastric-oesophageal disease (GORD) respectively. 243(83%) finished the one year follow up with successful HP eradication. This was associated with significant reduction in the amount of H2RA being consumed at the end of one year (p<0.0001) along with significant reduction in symptom scores post eradication (p<0.0001). Overall 67% of the patients documented an improvement in their QOL and 75% reported a feeling of well being post HP eradication.

**Conclusion:** HP eradication in patients on long-term H2RA in primary care results in significant reduction in usage of acid suppression drugs and improvement in overall QOL.

**023 BENEFIT OF HELICOBACTER PYLORI ERADICATION IN THE TREATMENT OF ULCER-LIKE DYSPESIA IN PRIMARY CARE**

R. Stevens, G. Baxter. East Oxford Health Centre, Oxford; ‘Wyth Laboratory, Taplow, UK

**Background:** The role of Helicobacter pylori (Hp) eradication in patients without confirmed ulcer is unclear. The majority of studies have been conducted in secondary care on patients with functional ulcer-like dyspepsia (i.e. confirmed absence of ulcer) with equivocal results. This study, conducted in primary care, examines the role of Hp eradication in a broader group of patients presenting with ulcer-like symptoms (epigastric pain), merely excluding those with confirmed ulcer.

**Methods:** 543 patients from 64 primary care centres in UK and Norway were enrolled into the study. 364 patients were assessed as Hp +ve (by near patient antibody blood test). 181 patients were randomised to receive eradication therapy (lansoprazole 30 mg, clarithromycin 250 mg and amoxicillin 1 g) for 1 week followed by lansoprazole 30 mg od for 3 or 7 weeks according to symptoms. 183 patients received placebo antibiotics and lansoprazole 30 mg od for 4 or 8 weeks. Treatment was double blind. 179 Hp –ve patients received open treatment with lansoprazole 30 mg od for 4 or 8 weeks. Epigastric pain and other Gastrointestinal (GI) symptoms, GI consultations, GI prescriptions and GI investigations were recorded during the treatment period and over a 12-month follow-up phase. Primary efficacy variable was the proportion of patients with relapse during the 12 month follow-up period.

**Results:** 394 patients, with Hp status correctly assigned at baseline (by ‘C-Urea Breath Test), completed the study. The average number of GI consultations and prescriptions was lower in the eradication group compared with the Hp +ve non-eradicated group (p<0.02 and p=0.05 respectively).

**Conclusion:** Hp eradication resulted in a significant reduction in symptomatic relapse in patients presenting with ulcer-like dyspepsia in primary care. This was associated with a reduction in the number of GI consultations and prescriptions over the subsequent 12 months.

**024 HYPNOTHERAPY IS EFFECTIVE IN THE LONG-TERM TREATMENT OF FUNCTIONAL DYSPESIA**

E.L. Calvert, L.A. Houghton, P. Cooper, P.J. Whorwell. Dept of Medicine, University Hospital of South Manchester, M20 2LR, UK

We have shown hypnotherapy (HT) to be highly effective in the treatment of irritable bowel syndrome (IBS), with long term improvements in both symptoms and quality of life. The aim of this study was to assess the efficacy of HT in patients with functional dyspepsia (FD). 79 patients (aged 19 to 65 yrs; 38 male) satisfying Rome I criteria for FD were therefore enrolled into a randomised, controlled, parallel designed study in which they either received HT(n=26; aged 22 to 59 yrs,12 male), conventional treatment of ranitidine 150mg twice daily (C)(n=29; aged 19 to 65 yrs, 15 males), or supportive therapy plus placebo tablet (S)(n=24, aged 21 to 63 yrs; 11 male) for 16 weeks. Symptomatology and quality of life were assessed using questionnaires (visual analogue) at the start and end of the 16 week treatment period (short term effect), and at 9 months follow-up (long-term effect). Although concomitant medication was not allowed during the treatment period, patients were allowed medication during the 9-month follow-up.

**Results:** Although there were similar improvements in total FD symptom score in the short term (% improvement, median (IQR), HT: 59%(26–85%), C:48%(31–64%) and S: 43%(33–67%)); long-term, HT improved total FD score significantly more (73%(26–96%)) than either C(43%(15–57%); p<0.01) or S (34%(24–71%);p<0.02). HT also improved quality of life both in the short and long term (short term: 42%(31–69%), long term 44%(24–69%); more than either C (14%(6–35%);p<0.01, 20%(10–26%);p<0.01) or S (26%(5–66%);p=0.06, 43%(9–60%);p<0.02). Interestingly, during follow-up, 90% and 82% of patients who had received C and S respectively, restarted some form of medication, whilst none of the patients who had received HT restarted medication. The most common medication used were proton pump inhibitors and H2 blockers (C: 52%, S: 28%, respectively).

**Conclusion:** HT is effective in the long-term management of FD. Furthermore, the dramatic reduction in the need for conventional medication provides major economic advantages. This study was supported by Wellcome Trust, UK.
025 IV PROTON PUMP INHIBITORS (PPI) WITH OR WITHOUT ENDOSCOPIC THERAPY PREVENT REBLEEDING AND SURGERY IN PATIENTS WITH PEPTIC ULCER HAEMORRHAGE (PUH)—A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS (RCTs)

V.K. Sharma1, G.I. Leonitiadis2, C.W. Howden3, 1University of Arkansas for Medical Sciences, Little Rock, AR, USA; 2“G. Papamikhaliou” Hospital, Thessaloniki, Greece; 3Northwestern University, Chicago, IL, USA

Acute PUH recurrence remains a common problem despite endoscopic therapy. High dose IV PPI can maintain intragastric pH ≥ 6.0 required for clot-stabilization and hence may offer an effective therapeutic option.

**Aim:** To evaluate the effect of high dose IV-PPIs for the prevention of acute PUH using meta-analysis.

**Methods:** Recursive literature search of RCTs using IV-PPI for the management of acute PUH. Only PPI doses that have shown to maintain intragastric pH ≥ 6.0 were included. IV H2 blockers were considered comparable to, and hence combined with, placebo. RCTs were stratified according to prior endoscopic therapy. Calculation of relative and absolute risk reduction (RRR, ARR) and number needed to treat (NNT).

**Results:** 8 RCTs were used, and 10 without, prior endoscopic therapy were included. 17 used omeprazole; 1 used pantoprazole. After endoscopic therapy, high dose IV-PPI significantly decreased acute re-bleeding (RRR = 47%; ARR = 9.2%, CI = 5.3–13.1; NNT = 11) and surgery (RRR = 46%; ARR = 4.4%, CI = 1.5–7.3; NNT = 23). In patients without endoscopic therapy, high dose IV-PPI significantly decreased acute re-bleeding (RRR = 36%; ARR = 6.5%, CI = 2.7–10.3; NNT = 15) but not surgery (RRR = 22%; ARR = 2.5%, CI = −0.4–5.3; NNT = 41). There was no significant reduction in mortality in either group.

**Conclusions:** High dose IV-PPI with or without endoscopic therapy prevents acute re-bleeding following PUH. Patients with PUH should be started on high dose IV-PPI on admission. Once haemodynamically stable, they should have endoscopy and, if needed, endoscopic therapy. Patient with high-risk endoscopic lesions should be continued on high dose IV-PPI for 72h while those at low risk lesion can be switched to standard dose PPI by mouth.

026 REBOUND MAXIMAL ACID HYPERSECRETION AFTER OMEPRAZOLE PERSISTS TO AT LEAST 11 MONTHS AFTER TREATMENT

D. Gillen, A.A. Wira, K.E.L. McColl, Dept of Medicine & Therapeutics, Western Infirmmary, Glasgow, Scotland, UK

**Introduction:** We have previously reported that there is significant rebound maximal acid hypersecretion in *H. pylori* negative healthy subjects at 1 to 8 weeks after an 8 week course of omeprazole. However, it was unclear whether the phenomenon persisted beyond 8 weeks.

**Aim:** To determine the duration of rebound maximal acid hypersecretion after omeprazole.

**Methods:** 9 *H. pylori*-negative healthy subjects were studied with pentagastrin-stimulated maximal acid output (MAO) studies at 1, 2, 4, 6, 8 weeks and 11 months after an 8 week course of omeprazole 40mg/day.

**Results:** All values are means; all values after treatment are significantly elevated over that before treatment at p<0.004.

<table>
<thead>
<tr>
<th>Time after treatment</th>
<th>Pre-R</th>
<th>1 week</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>11 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAO (mmol h⁻¹)</td>
<td>29.0</td>
<td>38.6</td>
<td>43.8</td>
<td>42.1</td>
<td>36.8</td>
<td>36.3</td>
<td>33.7</td>
</tr>
<tr>
<td>%↑ in MAO</td>
<td>41.1%</td>
<td>58.7%</td>
<td>43.2%</td>
<td>30.0%</td>
<td>32.0%</td>
<td>19.6%</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion:** The MAO is still significantly elevated at a median of 11 months after a 2 month course of omeprazole 40mg/day. This prolonged acid hypersecretion may have implications for withdrawal of treatment with this drug.

**Conclusion:** Significant rebound maximal acid hypersecretion after omeprazole persists until at least 11 months after treatment.

027 OESOPHAGITIS, A RISK FACTOR FOR OESOPHAGEAL CANCER

J.A. Todd1, T. Weston1, D. Steinke2, D.A. Johnston3, J.F. Dillon4. 1Peterborough District Hospital, Peterborough, PE3 6DA; 2Ninewells Hospital & Medical School, Dundee, DD1 9SY, UK

**Background:** Barrett’s oesophagus is regarded as being a risk factor for oesophageal adenocarcinoma. The presence of heartburn has recently been described as being a risk factor for oesophageal adenocarcinoma. No data currently exists to our knowledge on the risk of oesophageal adenocarcinoma in patients with oesophagitis.

**Method:** Using the Tayside endoscopy database, patients with a normal oesophagus and those with oesophagitis at their first endoscopy in the period 1975–1985. Those with Barrett’s oesophagus were excluded. They were followed up to the end of 1995, using the Scottish Cancer Registry to identify those who had developed oesophageal carcinoma more than one year after their initial endoscopy.

**Results:** There were 14901 patients with a normal oesophagus and 3397 with oesophagitis. 49.5% of those with a normal oesophagus and 47.9% of those with oesophagitis were male (p=0.09). Those with a normal oesophagus were younger than those with oesophagitis (50.4 ± 52.7 years, p<0.0001). The crude odds ratio for oesophageal carcinoma for those with oesophagitis as compared to those with a normal oesophagus was 3.02 (1.40–6.50, p=0.0031). The age and sex adjusted odds ratio for oesophageal carcinoma for oesophagitis was 2.89 (1.34–6.25, p=0.0067).

**Conclusions:** Patients with oesophagitis are at three times greater risk of developing oesophageal carcinoma than those with a normal oesophagus at endoscopy, more than one year after their initial endoscopy.

028 ONE YEAR FOLLOW-UP OF ARGON PLASMA COAGULATION (APC) ABLATION OF BARRETT’S EPITHELIUM (BE)

K.K. Basu, R. Bale, K.P. West, J.S. de Caestecker. University Hospitals of Leicester NHS Trust, Leicester, UK

**Introduction:** The aim of BE ablation is to reduce malignant potential which is related to BE extent. APC is effective for ablation but the long-term effects are unclear.

**Aim:** To assess the effects of APC therapy on BE ablation after 1 year.

**Methods:** Following APC therapy of BE (≥ 3cm containing specialised intestinal metaplasia), patients were maintained on high dose proton pump inhibitor (PPI) therapy, (acid suppression documented by 24 hour oesophageal pH studies), and re-endoscoped after a mean of 13.7 months, range 12–19 months. BE extent was recorded and 2cm interval quadrantic jumbo biopsies taken at the previous levels of original BE area to look for “buried” glands.

**Results:** 15 patients, mean age 56.1 years (range 29–79 years), previously treated with APC to achieve ≥ 90% macroscopic BE clearance were followed-up. Their initial mean BE length was 4.7cm (range 3–7 cm) versus 1.5cm (range 0–4 cm) at 1 year. 7 patients had recurrent BE; in 4 this amounted to > 50% of the original area. 3 of these 4 had reduced their omeprazole dose from 20mg twice daily to 20mg once daily during follow-up. All other patients remained on high dose PPI. “Buried” BE glands were seen in 7 out of 144 (4.9%) biopsies at completion of APC and in 5 of 107 biopsies (4.7%) at follow-up in 5 patients. No dysplasia was seen.

**Discussion:** About half the BE patients had recurrent BE at follow-up after successful APC ablation. This was most marked in patients who had reduced their acid suppression dose. “Buried” BE persists over 1 year post APC therapy but the incidence is unchanged. Patients should not reduce PPI dosage after APC ablation of BE.

029 CLINICAL OUTCOME AND LONG-TERM SURVIVAL FOLLOWING RADICAL OESOPHAGECTOMY IN THE ELDERLY

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**Background:** Oesophagectomy is considered an especially high-risk procedure in elderly patients. The aim of this study was to compare the early clinical outcome and subsequent survival of patients aged 70 years or over with that of patients younger than 70 years.
A NEW APPROACH TO THE TREATMENT OF INOPERABLE CARCINOMA OF THE OESOPHAGUS: LASER AND RADICAL CHEMORADIATION THERAPY

L.B. Lovat1, C.H. Bridgewater2, T. Evans1, S.M. Thorpe3, G.M. Blackman1, S.G. Brown1, J. Tobias1. National Medical Laser Centre, Royal Free and University College School of Medicine, University College London, Meyoer Institute of Radiotheraphy, The Middlesex Hospital London, UK

Background: Most patients with oesophageal cancer are elderly and present with advanced local disease. Even when surgically fit, the MRC OE02 trial suggests that median survival is only 17 months in patients treated with neo-adjuvant chemotherapy. Dysphagia induces malnutrition, which can further worsen prognosis. Other approaches are urgently needed, particularly for those who are not surgical candidates. We present our initial experience using endoscopic relief of dysphagia followed by chemohormotherapy.

Methods: Fifteen patients (10 male), median age 71 (range 47–82), who were inoperable due to locally advanced oesophageal cancer were treated with endoscopic thermal laser therapy to relieve dysphagia followed by chemoradiation. Twelve had squamous cell cancer were treated with endoscopic thermal laser therapy to relieve dysphagia followed by chemoradiation. Twelve had squamous cell cancer were treated with endoscopic thermal laser therapy to relieve dysphagia followed by chemoradiation.

Results: After laser therapy and prior to commencing radiotherapy, 13 patients were able to tolerate semi-solids or a normal diet for withholding surgery.

Conclusions: With careful selection early clinical outcome and long-term survival following radical oesophagectomy are equivalent in both younger and older patient groups. Survival is dependent solely on wall thickening or full restoration of wall layers. The accuracy of EUS for T/N staging of all cancers of the oesophagus and gastro-oesophageal junction was determined (n=133). Films on patients who had received neo-adjuvant chemotherapy (n=25) were reviewed in a blinded fashion for: presence of mass lesion; changes in residual mass morphology and echogenicity; restoration of wall layer pattern and presence of mitotic activity. Aims: To assess the prognostic value of an endoscopic ultrasound (EUS) finding of locally advanced (T4) oesophageal carcinoma compared with a similar cohort with EUS staged T3 tumours.
Introduction: Colonoscopy is acknowledged as the gold standard for examining the colon. The goal of colon cancer prevention is interrupting the adenoma-carcinoma sequence and effective management of polyps requires complete colonoscopy with complete polyp removal, retrieval and histological assessment to enable appropriate follow up. As part of the IBNC prospective audit of 8902 colonoscopies, the prevalence and management of polyps was assessed.

Results: Polyps were diagnosed in 2014/8902 (22.6%) of the colonoscopies. Polyps were the sole diagnosis in 130/8902 (14.7%) of the colonoscopies. In 48/8902 (0.9 %) colonoscopies, polyps were reported in the presence of obvious cancer, and in 621/8902 (7.0%) polyps occurred in the setting of other disorders. The caecum was successfully intubated in 1670/2014 (82.9%) colonoscopies whereas in 54/84 (64.3%) colonoscopies where polyps were associated with cancer. No answer regarding intervention was given in 59/2014 (2.9%) of colonoscopies. Where polyps were reported, there was no attempt at polypectomy in 126/2014 (6.5%).

All polyps were judged completely removed in 1401/2014 (69.6%) colonoscopies and incomplete removal was recorded in 331/2014 (16.4%). In 1239/2014 (61.5%) of cases information on polyp retrieval was not answered. Retrieval of all polyps was reported in 465/2014 (23.1%) of colonoscopies where polyps were discovered and complete retrieval was recorded in 310/2014 (15.4%).

Conclusion: Currently, colonoscopy is incomplete in almost 1/5 patients with polyps and it is likely that a significant number of proximal polyps remain undetected. A small but significant number of polyps are either left in situ or only partly removed, and retrieval is often incomplete. It is likely that improved performance will require a program of intensive training and repeated audit cycles.

Intercollegiate National-BSG Colonoscopy

Introduction: Colonoscopy is acknowledged as the gold standard for examining the colon. A caecal intubation rate of >90% is the recommended target for practising colonoscopists. As part of the IBNC audit caecal intubation rate was recorded in 8902 colonoscopies. In addition, commonly used method(s) for identifying the caecum were recorded (transillumination, tri-reflective, appendicular orifice, ileo-caecal valve, terminal ileum intubation, finger indentation of right
Results: Caudal intubation was reported in 6864/8902 (77.1%) colonoscopies. If terminal ileum intubation or ileo-caecal valve visualisation are considered as the only reliable methods for identifying a complete procedure, the ‘adjusted’ caecal intubation rate falls to 5085/8902 (57.1%). Methods used for identifying the caecum included: transillumination 2364/6864 (34.4%), tri-radiate fold 4809/6864 (70.1%), appendiceal orifice 2942/6864 (42.9%), ileo-caecal valve 1368/6864 (19.9%), right ileal fossa indentation 3057/6864 (44.5%) and screening 42/6864 (0.6%). The most common reasons for incomplete colonoscopy were “patient discomfort” and “looping of the colonoscope”.

Discussion: Currently, the caecal intubation rate falls far short of the recommended 90%. In addition, caecal intubation is often recorded in the absence of positive identification of the ileocaecal valve. Colonoscopists should be aware of the best methods for identifying the caecum. Failure to complete colonoscopy is most often ascribed to patient discomfort and looping and formal training and assessment in colonoscopy is required to reduce the number of technique-related failures.

**ENDOSCOPY IN PRIMARY CARE: A SURVEY OF STRUCTURES, SERVICES AND STANDARDS**

J. Gibson, P. Evans, J. Featherstone, J. Galloway, R. Spence, P. Willoughby. Endoscopy Subcommittee PCSG

Background: Long hospital waiting lists and savings from fundholding have contributed to an increase in endoscopy services in primary care. Concerns about safety, supervision and cost effectiveness have been voiced but the DH has also floated ideas about intermediate care endoscopy units, throughput, case mix, endoscopists' experience, supervision and CME, waiting times, complications, equipment and reporting standards.

Method: PC endoscopy units were identified via the Primary Care Gastroenterology and appeals in GP journals. A postal questionnaire was sent seeking details about the history of primary care endoscopy unit, throughput, case mix, endoscopists' experience, supervision, audit and CME, waiting times, complications, equipment and reporting standards.

Findings: 27 (96%) of 28 units identified replied. 13 provided both OGD and lower GI examinations, 6 OGD only, 8 lower GI only. The units had been in existence on average for 5 years (range 2–18 years). Services were provided by a total of 41 GPs and 68 nurse assistants. The average experience of endoscopists was 11 years. 96% of units undertook audit. Average “urgent” waiting time was 1–2 weeks; “routine” 3–4 weeks (range 1–6 weeks).

Total procedures performed by all units, to date 34,959: of these, 24,195 were OGD and 10,764 lower GI. Total annual throughput for OGD (12 units) 4,506 and lower end (10 units) 1,305.

Conclusions: Local PC endoscopy units were identified via the Primary Care Gastroenterology Subcommittee PCSG.

**“WAITING LIST INITIATIVE” COLONOSCOPY LISTS: ARE THEY VALUE FOR MONEY? A REVIEW OF THE INITIAL 12 MONTHS EXPERIENCE**

A. Douglass, P. Cann. South Cleveland Hospital Endoscopy Unit, Middlesbrough, UK

Trusts have been under increasing pressure to reduce waiting times for all specialities. In Gastroenterology, one solution has been to provide extra ‘out of hours’ sessions, which rely upon the goodwill of medical & nursing staff involved and raise a considerable extra cost. The first year waiting list initiative (WLI), in our unit, has been to direct the resource towards the open access Colonoscopy (OAC) service, but selecting patients 45 years or older. This was driven by the need to move forwards and meet the “2 week rule” requirement.

Results: Over the first 12 months (Feb 98–Jan 00), 44 additional lists were performed on Saturday mornings. 256 of the 263 patients endoscoped failed to attend. 256 (97%) of 263 patients had ‘dual pathology’. 6 (2%) (out of 43) had haemorrhoids requiring injection at the time. We count, therefore, 45 (17%) as having a “useful” procedure. The estimated cost, in extra salaries alone, was £29,000. This means about £650 per “useful” diagnosis. The OAC waiting time has fallen to half of the peak level before the WLI, despite a steady referral load.

**WORKLOAD AND DYNAMICS OF A DGH OUTPATIENT CLINIC: BALANCING THE BOOKS**

H.C. Mitchison, M. Rutter, G.D. Bell. Dept of Gastroenterology, Sunderland Royal Hospital, Sunderland, UK

Background: Maintaining GI outpatient (GOP) targets and keeping clinic size manageable, requires the number of new patients (NP) plus follow up patients (PUP) to be balanced by clinic discharges. Royal
College of Physicians Guidelines (RCPG) on a) consultant OP workload and b) SpR training recommend 15–20 “units” per clinic (i.e. 6–8 NP or 15–20 FUP) for consultants and no greater than 0.75 this number for SpRs.

Methods: In our DGH (population served 330,000), we prospectively categorised GP patients by diagnostic/symptom group for 6 months. Retrospectively we examined workload plus compliance with a) RCGP and b) the Patient’s Charter.

Results: The 2 consultants averaged 3 clinics per week, the single SpR two. There were 587 true NPs plus 246 NPs who were endoscoped and then seen in GP (ENP). The NP+ENP/FUP and NP/FUP ratios were 3.7 and 2.5 respectively. In total 604 patients were discharged. Of 2209 patients receiving appointments, 210 did not attend. The numbers receiving 1, 2, 3, 4 and 5 appointments were 1889, 227, 39, 12 and 8 respectively. The discharge rates for IBG (n=425) and Liver Disease patients (n=237) were low at 3% and 10% compared with those with functional bowel symptoms (41%) or reflux (41%). In these latter two groups of NP 32% were discharged at their first GP visit. Despite both Consultants and the SpR working unacceptably high “units” per clinic, 25% of patients were kept waiting over 30 minutes beyond their appointment time.

Discussion: The study reveals how the balance between NP and FUP in an under staffed GOP was maintained. Prompt discharge of these diagnostic categories was essential to provide adequate time for the long-term care of chronic conditions such as IBG and liver disease. We would have required a further 3.2–5.9 GOP sessions per week to meet RCGP. We have now appointed a third consultant but experience already suggests a fourth consultant will be needed to meet service and training requirements.

IS AGE 45 AN APPROPRIATE CUT OFF POINT FOR OPEN ACCESS ENDOSCOPY?

P. Mairs, P. Wheeler.

This retrospective study looks at cumulative experience from a district general hospital in the south east of England in order to determine if the present age cut off for open access endoscopy in patients with dyspepsia of 45 could reasonably be increased to 55 without the risk of missing any gastric malignancies.

Methods: Since 1995 all endoscopies carried out on the endoscopy unit at the above hospital have been entered into the computerised database for reporting and audit. This database was searched to determine how many patients were being diagnosed with gastric cancer at endoscopy. The age range of patients being gastroscoped was analysed. To ensure that no patients were overlooked if for example their malignancy was diagnosed at open operation or for some reason they had not been entered onto the database a separate analysis was made of the hospital pathology department database. Over the period January 1995 to April year 2000: 6951 patients underwent gastroscopy. 5824 of these were aged over 55 years.

Results: No patients aged less than 50 were diagnosed with any malignancy (Cancer of gastric antrum and/ or body, cancer of the cardia, cancer of the oesophagus). In the study period a total of 7 patients aged between 50 and 55 were found to have a cancer of the gastric cardia or lower oesophagus. Notes were available on four of these and all had presented with symptoms of reflux and weight loss. Two had presented with dysphagia. A shift in the age range for open access endoscopy from 45 to 55 would not have missed one malignancy of the gastric antrum or body in the 5 year period studied. This would be in keeping with previous data. Those patients in whom malignancies were found were invariably aged greater than 50 and would have been candidates for open access endoscopy on the basis of alarm symptoms. All had cancer of the cardia or distal oesophagus. Provided guidelines emphasize the importance of alarm symptoms then it seems reasonable to lift the age cut off for open access endoscopy to 55.


ENDOSCOPIC ULTRASOUND IN THE MANAGEMENT OF GASTROINTESTINAL SUBMUCOSAL TUMOURS

E.F. Shen1, J. Plevris1, I.D. Penman1. Western General Hospital, Royal Infirmary, Edinburgh, UK

Introduction: “Submucosal” tumours (SMT) in the upper gastrointestinal tract (UGI) may be hard to evaluate. Endoscopic ultrasound (EUS) can provide high quality information about the nature of SMT and assist in their management.

Aims: To assess the use of EUS in the evaluation and management of UGI SMT.

Methods: We evaluated 41 consecutive patients who were referred with UGI SMT for EUS. All examinations were performed by one of two experienced endoscopographers.

Results: The average age of the patients was 62.2yrs, 54% were female. The indications for endoscopy were; UGI bleeding 22%, dysphagia/abdominal pain 27%, dysphagia 12%, and unspecified 12% and presumed co-incidental finding in 27%. Most patients were referred for EUS with a presumed diagnosis of a gastrointestinal stromal tumour (GIST). The pre-EUS diagnosis, however, did not correlate with the EUS diagnosis in 51% of patients (table 1). Pathological correlation was possible in 41% of patients. EUS diagnosis was confirmed in all these patients. Based on EUS findings 13 patients underwent resection. Pathology confirmed EUS findings in these patients. None of these lesions was malignant. Three patients underwent EUS follow up and the rest were felt not to require further endoscopic or EUS follow up.

Abstract 42, Table 1

<table>
<thead>
<tr>
<th>EUS diagnosis</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIST</td>
<td>13</td>
<td>32%</td>
</tr>
<tr>
<td>Inflammatory Polyp</td>
<td>6</td>
<td>15%</td>
</tr>
<tr>
<td>Ectopic pancreas</td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Normal/ No lesion</td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Vascular lesion</td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Lipoma</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Carcinoid</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>15%</td>
</tr>
</tbody>
</table>

Conclusion: EUS can assist more accurate diagnosis of SMT, increase physician certainty, and facilitate the management process.

SUBSTITUTION OF ENDOSCOPIC ULTRASOUND (EUS) FOR ERCP: IMPLICATIONS FOR SERVICE DEVELOPMENT AND TRAINING

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Background: Endoscopic ultrasound (EUS) provides an accurate, safe and rapid method for visualizing the biliary tract. EUS obviates the risks of pancreatitis and inappropriate intervention associated with ERCP. The growing number of centres utilizing EUS raises the question of whether the risks associated with diagnostic ERCP can be justified. Consequently, previous assumptions about numbers presenting for ERCP must be questioned.

Aim: To determine the proportion of cases referred for ERCP that could be diverted to EUS imaging.

Methods: During the six months to October 2000, patient referrals for ERCP (n=417) were triaged with respect to the likelihood of therapeutic intervention being required. Those without jaundice, fever or, biliary pathology previously identified by trans-abdominal ultrasound/CT, underwent EUS (n=81, 19%) with conscious sedation. In two further cases CBD stones identified at EUS were confirmed. In two further cases, EUS failed to identify the CBD (both normal on subsequent ERCP). In two further cases CBD stones identified at EUS were removed at ERCP. No complications occurred with EUS.

Results: The indications for EUS were: (a) Raised LFT’s/pre-liquefaction, n=21; (b) Acute pancreatitis, n=16; (c) Post-cholecystectomy RUQ pain, n=10; (d) RUQ pain and raised LFT’s, n=8 (e) RUQ pain, other tests normal, n=16 and (f) Abnormal LFT’s, n=10. In two cases, EUS failed to identify the CBD (both normal on subsequent ERCP). In two further cases CBD stones identified at EUS were removed at ERCP. No complications occurred with EUS.

Conclusion: EUS is a safe and effective method for imaging the biliary tree. Approximately one-fifth of cases referred for ERCP can be assessed by EUS, raising the question of whether the risks associated with potentially diagnostic ERCP’s can be justified. Further research, in light of case-number recommendations for centre
recognition, the greater use of EUS imaging will have profound implications on ERCP tuition and increases the need for centres offering training in EUS.

044 ENDOSCOPIC MRI IN SUSPECTED OESOPHAGEAL CANCER

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Background: The current gold standard for pre-operative staging of oesophageal cancer, endosonography (EUS), has limited accuracy for TNM staging. MR endoscopy (Endo-MR) allows simultaneous visual information and high definition cross-sectional imaging using endovacuatory coil mounted on a MR compatible endoscope. Preliminary experience has shown that Endo-MR is particularly useful for local staging of oesophageal and rectal carcinoma.

Aim: To study endo-MR prospectively in patients with suspected oesophageal cancer.

Method: Endo-MR was attempted in 11 patients (7 male, median age 61 yrs (range 30–78 yrs), using prototype MR endoscope (diameter 13 mm, biopsy channel 2.8 mm, umbilical cord length 5 meters) and 0.5 T MRI machine. Propofol was used for sedation in 9 patients. EUS and operative pathology findings were available in 3 and 5 patients respectively (after reporting of Endo-MR) and 2 patients are awaiting EUS.

Results: Symptoms included dysphagia in 6 patients. Histology findings included: invasive cancer (7), dysplasia (2) and glycogenic acanthosis (1 patient). All patients tolerated endo-MR well with no complications, but one patient failed to be intubated. Endo-MR findings on TNM staging (shown below) and tumour size matched well with known coeliac disease. Only 3 lesions (27.2%) identified were within reach of the standard endoscope (2 adenomas, 1 stromal tumour), all other lesions were located in the proximal jejunum.

Conclusions: The overall yield of push enteroscopy for small bowel neoplasia was 4.6%. In contrast to other reports, patients with small bowel tumours were significantly older than the general population referred for enteroscopy. In our series small bowel tumours were more common in patients undergoing investigation of malabsorption or with coeliac disease than those with anaemia or occult gastrointestinal bleeding.

046 THE WIRELESS ENDOSCOPE: FIRST CLINICAL TRIALS IN PATIENTS GI BLEEDING

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Background: Current endoscopic methods to image the small bowel are limited in patients with obscure GI bleeding (negative gastroscopy and colonoscopy), push-enteroscopy fails to find the source in up to 60%. Improved methods are required to visualise the entire small bowel which are less invasive and better tolerated.

Methods: A new wireless capsule endoscope (Given®M2A video capsule system) was used to assess 6 patients with obscure or uncontrolled GI bleeding after ethical committee approval had been given. The patients were fasted overnight and swallowed the capsule endoscope with a glass of water.

Case 1: Female aged with Hereditary Haemorrhagic Telangiectasia (HHT) and a transfusion requirement of 4 units/year despite hormonal therapy and endoscopic treatment. Capsule endoscopy (CE) revealed several telangiectasias in the stomach, duodenum and proximal jejunum. 2 large bleeding lesions were seen in the jejunum and ileum.

Case 2: Male aged 59 with HHT and a transfusion requirement of 5 units/month unresponsive to hormonal therapy or endoscopic treatment. CE revealed 8 moderately sized angiodysplasias in the duodenum and proximal jejunum. Good views of the large bowel to sigmoid colon revealed 3 further telangiectasias not seen on a recent colonoscopy.

Case 3: Male aged 16 with a past episode of melaena presented with an episode of melaena, Hb 9 with normal endoscopy, colonoscopy and Meckel's scan. CE revealed no abnormality although various images were obtained from the stomach to caecum.

Case 4: Male aged 78 with HHT and a transfusion requirement of 3 units/month despite treatment hormonal and endoscopic therapy. CE revealed multiple angiodysplasias affecting the proximal small bowel.

Case 5: Male aged 79 with HHT and a transfusion requirement of 4 units/month. Multiple telangiectasias, including one actively bleeding in the stomach, were seen at CE and subsequently treated endoscopically.

Case 6: Male aged 65 with recurrent anaemia and melaena. CE revealed bleeding erosive gastritis probably due to aspirin ingestion.

Conclusion: CE provides good views of the GI tract. The CE was easy to swallow, completely painless and preferable to conventional endoscopy. Results have been helpful in directing the management in these patients.

045 DETECTION OF SMALL BOWEL NEOPLASIA AT PUSH ENTEROSCOPY

M. Priest, A.J. Morris. Dept of Gastroenterology, Glasgow Royal Infirmary, Glasgow, UK

Introduction: Push enteroscopy is of proven value in detecting proximal small bowel disease. The diagnostic yield for small bowel neoplasia, in an unselected population referred for this procedure, has not been reported. We have undertaken a retrospective review of all push enteroscopies carried out in a single referral practice, over a 4 year period, to identify the clinical, pathological, and enteroscopic features of patients with small bowel neoplasia.

Results: 410 procedures were performed on 388 patients (146 male, 242 female). Small bowel neoplasia were detected in 18 (4.6%) patients respectively (after reporting of Endo-MR) and 2 patients are awaiting EUS and operative pathology findings.

Abstract 44, Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Endo-MR-TN stage</th>
<th>EUS-TN stage</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T1Nx</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>T1N0</td>
<td>T1N0</td>
<td>T1N0</td>
</tr>
<tr>
<td>3</td>
<td>T4Nx</td>
<td>-</td>
<td>T4N0</td>
</tr>
<tr>
<td>4</td>
<td>T1N0</td>
<td>T1N0</td>
<td>T1N0</td>
</tr>
<tr>
<td>5</td>
<td>T4Nx ( poor image)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>T1N0</td>
<td>T1N0</td>
<td>T4N0</td>
</tr>
<tr>
<td>7</td>
<td>T4N1</td>
<td>-</td>
<td>T4N1</td>
</tr>
<tr>
<td>8</td>
<td>T1N0</td>
<td>T1N0</td>
<td>T1N0</td>
</tr>
<tr>
<td>9</td>
<td>T3N0</td>
<td>T2N0</td>
<td>T1N0</td>
</tr>
<tr>
<td>10</td>
<td>T4N1</td>
<td>-</td>
<td>T4N1</td>
</tr>
</tbody>
</table>

Conclusion: Endo-MR is safe and well tolerated. Endo-MR findings correlate well with EUS and operative pathology.

047 ENDOSCOPIC MANAGEMENT OF BLEEDING PEPTIC ULCERS IN A LARGE UK TEACHING HOSPITAL

S. Mahadeva, M. Lynch, D. Mawer, S. Babu, M. Hull. Division of Gastroenterology, St. James's University Hospital, Leeds, UK

Background and methods: Single centre RCTs suggest that endoscopic haemostasis (EH) can reduce rebleeding, surgery and mortality in patients with bleeding peptic ulcers. In order to determine whether such RCT results are applicable in general, we retrospectively examined endoscopic practice in a large UK teaching hospital over a 3 year period (1997–99). Patients were identified from an endoscopy database and the clinical records reviewed.

Results: 872 patients were identified with upper GI haemorrhage. 179 (21%) had an endoscopic diagnosis of bleeding peptic ulcer. 154 (86%) medical records were available for review. 72 (47%) patients...
had stigmata of bleeding at initial endoscopy (adherent clot, visible vessel or active bleeding). 56 (78%) patients had EH (75% Adrenaline, 25% Adrenaline plus other). 20/56 patients had active bleeding at endoscopy compared with 0/16 in the group that did not receive EH. The re-bleeding rate in the group which had EH was 36% (11/32 Adrenaline only, 9/14 Adrenaline plus other), compared with 31% if EH was avoided. Of the EH group that re-bleed, 10 patients had a further attempt at EH (4 late required surgery), 8 patients went immediately for surgery and 2 died within 24 hours. Amongst those that rebled without prior EH, 2 had EH (1 required surgery later), 2 had surgery immediately and 1 died early. In total, 15/72 (21%) patients with stigmata of peptic ulcer bleeding required surgery. The mortality rate (<30 days) in patients with stigmata of recent bleeding was 16%, while overall mortality for all bleeding peptic ulcer patients was 14%.

Conclusion: Only 78% of patients with stigmata of bleeding peptic ulcer had EH at initial endoscopy. The re-bleeding rate following EH was higher than available RCT data. Endoscopic management (such as repeat EH for re-bleeding) performed in experienced centres in the setting of a RCT requires validation in individual endoscopy units.

Aims and methods: This study aimed to directly measure the pH profile of the proximal stomach. Ten healthy subjects underwent dual pH electrode pull through studies under fasting and then postprandial conditions. The pH catheter was positioned in the stomach and then withdrawn by 1 cm increments. The pH at each catheter position and the distance of the step-up to oesophageal pH was measured in each subject.

Results: Under fasting conditions the pull through studies revealed a stable intragastric pH throughout the stomach, median pH 1.5 (range 0.7–1.9). When the pull through studies were repeated after the meal the extent of food related buffer varied throughout the stomach. Postprandially the cardia remained highly acidic compared to the body of the stomach, median pH 1.4 (range 0.9–5.0) vs median pH 4.6 (range 2.0–6.7) (p<0.001). After the meal the pH step-up from gastric to esophageal pH was noted to be a median of 2 cm (range 3–10). Under fasting conditions the pH step-up was noted to be a median of 1 cm (range 0.9–5.0).

Conclusions: The cardia region of the stomach experiences meal stimulated acid secretion but escapes the buffering effect of meals. After a meal an area of high acidity (equivalent to fasting pH) was recorded at electrode positions just below the pH step-up point. The presence of this unbuffered pocket of acid immediately below the gastro-oesophageal junction is likely to be an important factor in the pathogenesis of gastro-oesophageal reflux disease.

A050 PATTERN OF PRESCRIBING LONG-TERM H2 RECEPTOR ANTAGONISTS IN PRIMARY CARE: ROLE OF HELICOBACTER PYLORI INFECTION. A CROSS SECTIONAL SURVEY

S. Verma, M.H. Gaffier. Dept of Gastroenterology, Hull Royal Infirmary, Anlaby Road, Hull HU13 OEL, UK

Background: Dyspepsia is a common problem in the community requiring patients to be maintained on long-term acid suppression. Nonetheless the prevalence of Helicobacter pylori in this subgroup of patients has never been assessed before.

Aim: This cross sectional survey was designed to assess the indications/costs for prescribing long-term H2 receptor antagonists (H2RA) in general practice with particular reference to Helicobacter pylori (HP) infection.

Patients and methods: Six large primary care groups (PCG), in the Humberside area were studied. Patients who met the entry criteria were invited for an interview and serological determination of their HP status.

Results: 1034 (1.5%) patients were on long term H2RA. Peptic ulcer disease (PUD) was the commonest indication for prescribing (36%) followed by Non ulcer dyspepsia (NUD) (25%). Gastro-oesophageal reflux disease (GORD), 18%. In 82% of the patients treatment with H2RA therapy followed a previous endoscopic or radiological investigation. Only 27 (2.5%) patients had had their HP status checked within the last 6 months. Of the 471 patients who eventually had their HP serology tested, 271 (57%) were HP positive. Fifty eight percent of the HP positive patients had PUD while the majority of HP negative patients had either GORD (32%) or NUD (29%). The duration of therapy was significantly longer in the HP positive patients (8.3 ± 0.3 vs 6 ± 0.8, p < 0.00001), especially those with PUD. The mean symptom score was also significantly higher in the positive patients (7.1 ±0.2 vs 6±0.2, p<0.0008).

Conclusion: A significant proportion of patients in primary care are on long term H2RA, imposing a considerable financial drain on the NHS resources. Approximately two thirds of these patients will be HP positive, and amongst them the largest group will comprise of patients with PUD. Since these are the patients most likely to benefit from HP eradication, stringent attempts should be made to identify them.

A051 NON-INVASIVE HP TESTING VERSUS ENDOSCOPY WITH HP TESTING FOR DYSPEPSIA


Introduction: There is interest in using non-invasive H. pylori (H.P.) testing in place of endoscopy for investigating dyspepsia.

Aim: To compare by prospective randomised trial HP breath test versus endoscopy plus H. pylori testing in dyspepsia.

Patients and methods: The study involved 708 consecutive patients (mean age = 36 years, range 17–75) (53% males) referred for investigation of upper GI symptoms. Patients with sinister symptoms...
or taking NSAIDs were excluded. Epigastric pain/discomfort was the predominant symptom in 53% and heartburn/reflux in 29%. The patients were randomised in double blind fashion to "C-urea breath test (BT) or endoscopy with HP testing (E). All HP positives were given triple therapy and the negatives treated according to symptoms ± endoscopy findings. Outcome was assessed by an independent investigator at 1 year.

**Abstract 51, Table 1**

<table>
<thead>
<tr>
<th>Outcome at one year</th>
<th>Breath test</th>
<th>Endoscopy (n=332)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Glasgow Dyspepsia Score</td>
<td>5.6</td>
<td>5.4</td>
</tr>
<tr>
<td>% attending GP since randomised</td>
<td>37%</td>
<td>33%</td>
</tr>
<tr>
<td>% attending hospital since randomised</td>
<td>6.2%</td>
<td>6.2%</td>
</tr>
<tr>
<td>Patients’ concern about missed pathology</td>
<td>104</td>
<td>105</td>
</tr>
<tr>
<td>Patients’ satisfaction with management</td>
<td>5.3</td>
<td>5.3</td>
</tr>
</tbody>
</table>

**Results:** One year follow-up was 83%. HP prevalence was 48% in the BT group and 51% in the E group and eradication rates at one year 84% and 79% respectively.

The above scores remained similar when patients subanalysed according to predominant symptom or HP status on presentation. Of the 356 patients randomised to BT, only 24 (6.7%) were referred for subsequent endoscopy showing no abnormality in 17, mild oesophagitis in 5, DU in 1 and failed examination in 1. Of the 352 patients randomised to endoscopy, no pathology was identified which required treatment other than HP eradication or symptomatic management.

**Conclusion:** This large, randomised prospective study indicates that BT is as effective and as safe as endoscopy in this patient population and should be the investigation of choice on account of its lower cost and less invasive nature.

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**GASTRIC SECRETION OF AMOXICILLIN AND METRONIDAZOLE IS INCREASED BY PRONASE, A LUMINAL MUCOLYTIC**

P.V. Sherwood, J.L.D. Wibawa, N. Jordan, D.A. Barrett, P.N. Shaw, R.C. Spiller. Deps of Gastroenterology and Pharmacological Sciences University Hospital, Nottingham; Dept of Biomedical Sciences, Hallamshire University, Sheffield, UK

**Introduction:** Reduced gastric mucous thickness has been associated with enhanced Helicobacter pylorus eradication rates. Furthermore the addition of the mucolytics pronase and N-acetyl cysteine to antibiotic regimens has also been shown to be beneficial.

**Aim:** To use a rat model to investigate the impact of pronase on mucus thickness and gastric antibiotic secretion.

**Methods:** Fasted male rats were anaesthetised. At laparotomy a cannula was inserted via a duodenal incision into the gastric lumen, which was washed and then filled with 1.5 mL of 0.9% saline or 20 mg/mL pronase solution. Gastric acid secretion was inhibited by i.v. histamine. 2 hours, plasma was sampled and gastric luminal contents were aspirated and replaced with fresh solution. Samples were analysed by narrow-bore HPLC. Gastric mucous thickness was measured using histology.

**Results:** Pronase reduced mean gastric mucous thickness from 162 to 30 μm (p < 0.001), reduced coverage from 100 to 60% and caused some fissuring of the epithelial cell layer. There was a 66% increase in gastric clearance of metronidazole (control = 0.087 ± 0.014 μM/min, pronase = 0.145 ± 0.041, n = 17, p = 0.005). Gastric clearance of amoxicillin increased four-fold (control = 0.029 ± 0.0019, pronase = 0.0120 ± 0.0038, n = 16, p < 0.001). However there was a 40% reduction in the gastric clearance of clarithromycin (control = 0.129 ± 0.031, pronase = 0.082 ± 0.018, n = 15, p = 0.003).

**Conclusions:** Pronase damages the gastric mucous layer and epithelial integrity suggesting that these are barriers to the gastric transfer of amoxicillin and metronidazole. This may account for the improved eradication rates with pronase. Gastric mucosal damage reduces the clarithromycin secretion rate, suggesting that a different transport process is involved for this larger, more lipophilic molecule.

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**VALIDATION OF A RISK STRATIFICATION IN ACUTE UPPER GASTROINTESTINAL HAEMORRHAGE**


**Aim:** Acute upper gastrointestinal hemorrhage has an incidence of approximately 100 per 100,000 per year and an event related mortality of up to 14%. Accurate identification of risk of mortality prior to endoscopy would allow focused treatment of high risk patients.

**Method:** Over a 3-year period, all consecutive patients admitted to our institution with acute upper GI haemorrhage were prospectively stratified and followed up. Patients were stratified into the highest risk group for which they possessed at least 1 putative risk factor (high risk: recurrent bleeding, persistent tachycardia (>100/min), history of oesophageal varices, systolic BP <100mm Hg, coagulopathy, thrombocytopenia, postural hypotension (>20mm Hg) without taking negative chronotropes; intermediate risk: age >60 years, haemoglobin <11g/dl, co-morbidity, melena, alcohol (excessive recent or chronic), NSAIDs, previous GI bleed or peptic ulceration, abnormal LFTs, postural hypertension (>10mm Hg), systolic BP >20mm Hg below patient’s normal; low risk: none of the aforementioned factors).

**Results:** 1349 episodes occurred during the study period (incidence of 100 per 100,000 per year). 2-week mortality was 84 (6.2%) overall with 66 (11.8%) of 561 high risk, 18 (2.5%) of 717 intermediate risk and 0 (0%) of 71 low risk. This was significantly stratified in the high risk group than intermediate (p<0.007) or low risk (p=0.002). Significantly more high risk than intermediate risk patients rebled (250 vs 16), underwent surgical intervention (27 vs 9), required transfusion (239 vs 234) and required central venous moni-toring (130 vs 0) (all p<0.001). None of these end-points occurred in low risk patients.

**Conclusions:** This risk stratification was easily applied prior to endoscopy by junior medical staff at a single institution. It identified groups at particularly high and low risk of mortality and other adverse end-points following haemorrhage. It is simple and rapidly applied and might be useful both to hospital physicians and general practitioners, allowing more intensive management of those at highest risk and, potentially, outpatient management of those at lowest risk.

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**ASSESSING CYCLIN D1 & p53 AS MARKERS OF MALIGNANT POTENTIAL IN BARRETT’S OESOPHAGEAL ADENOCARCINOMA USING TISSUE MICROARRAYS**

B.C. Oates, J.R. Dunn, F. Campbell, F. Fielding, A.I. Morris, A. Ellis, J.K. Field, A.J.M. Watson, Royal Liver University Hospital, Molecular Genetic & Oncology Unit, Clinical Dental Sciences, University of Liverpool, UK

**Background/aims:** Molecular markers of malignant potential may help to identify risk-highest individuals leading to more efficient and effective surveillance programmes in Barrett’s Oesophagus. Our aims were to see if tissue microarray technology could be used to a) determine p53 expression in the Barrett’s / carcinoma sequence and b) see if the cell cycle regulator, cyclin D1, has a prognostic significance.

**Patients/methods:** We have constructed microarrays using paraffin embedded tissue at several different stages of cancer development in 114 patients (95 men, 19 women) who had undergone resection over the last 10 years for Barrett’s oesophageal adenocarcinoma (BOA). Tissue cores of squamous epithelium, gastric epithelium, Barrett’s intestinal metaplasia (BIM), different grades of dysplasia, BOA and positive lymph nodes for each patient were taken wherever possible. The tissue microarrays were stained using p53 and cyclin D1 antibodies.

**Results:** For p53 we found positive stained cores in 1.6% of histological normal epithelium (2 of 122), 6.7% of BIM (3 of 45), 56% of dysplasia (42 of 75), 43.1% of BOA (44 of 102) and 49.1% of positive lymph nodes (20 of 57). For cyclin D1 we found positive stained cores in 100% of BIM (46 of 46), 93.3% of dysplasia (70 of 75), 88.9% of BOA (88 of 99) and 79.6% of positive lymph nodes (43 of 54).

**Conclusions:** As p53 positive staining does not significantly precede the onset of dysplasia it is not a clinically useful marker of malignant potential in patients with Barrett’s oesophagus. This data

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IMPORTANCE OF METAPLASTIC SUBTYPES AND TREATMENT OUTCOMES FOR THE ROLE OF ENDOSCOPIC ULTRASOUND (EUS) IN...
Most patients underwent more than one treatment modality and the vast majority had advanced disease at presentation. Five-year survival was 20% in patients undergoing resection. Other treatment modalities did have long-term survivors, but these were small in number.

The table summarises the outcomes of the various primary treatment modalities.

<table>
<thead>
<tr>
<th>Number</th>
<th>Mean age</th>
<th>30 day mortality</th>
<th>1-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>522</td>
<td>74.6</td>
<td>36%</td>
</tr>
<tr>
<td>Ablation</td>
<td>242</td>
<td>76.1</td>
<td>12%</td>
</tr>
<tr>
<td>Dilatation</td>
<td>425</td>
<td>73.4</td>
<td>19%</td>
</tr>
<tr>
<td>Infusion</td>
<td>374</td>
<td>72.8</td>
<td>18%</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>571</td>
<td>71.2</td>
<td>2%</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>135</td>
<td>61.8</td>
<td>4%</td>
</tr>
<tr>
<td>Resection</td>
<td>1125</td>
<td>63.8</td>
<td>10%</td>
</tr>
</tbody>
</table>

The data from this audit confirms the poor outlook for patients presenting with cardio-oesophageal cancer, but may provide a baseline for future changes in health care delivery for upper GI cancer in the UK.

Aims: The aim of this large retrospective study is to identify where improvements can be made in the diagnosis of adenocarcinoma and to identify the potential for making earlier diagnosis.

Methods: All upper GI adenocarcinomas diagnosed in South Tees Health District (population ~350,000) were identified from the computerised pathology database. The pathology and GP records were then reviewed and analysed using Epilinfo.

Results: The total number of patients identified was 618 (for the period April 1991–January 2000); to date 102 patients’ notes have been analysed. 94% were adenocarcinoma of which 26% were oesophageal and 74% were gastric. 6% were squamous carcinoma (mis-coded on the pathology computer). The M:F ratio is 63.5:36.5 and the mean age is 70.2 years (range 43–91). The symptoms at time of diagnosis consisted of (i) anaemia/weight loss/dysphagia in 55.2% (ii) epigastric pain in 31.3% (iii) dyspepsia/reflux/heartburn in 9.4% and (iv) haematemesis/malena in 4.2%. Of the 96 patients with adenocarcinoma 55% had AST between the 1st GP consultation and diagnosis and in 57% this was initiated at the 1st visit. Overall the GP suspected a cancer diagnosis in 24% of cases. For those treated prior to gastroscopy the mean time from 1st GP consultation to diagnosis was 17.1 weeks compared to 9.2 weeks in those given no treatment. Of the 43 patients who had no AST prior to the diagnostic investigation only 1 (2.3%) had a previous OGD within 3 years of diagnosis, whereas of the 53 who had been prescribed AST prior to the diagnosis 18 (34%) had had a previous OGD (p=0.001). Overall, 27% of the cancers had had a previous upper GI investigation within 3 years of the diagnostic investigation, of which 73% were OGD and 23% were barium studies. 40% had had a previous upper GI investigation more than 3 years from the diagnostic OGD.

Conclusion: Although this is preliminary data, it shows that 41% of patients did not have alarm symptoms at diagnosis. Also 55% of patients were treated with AST prior to the diagnostic OGD increasing the mean time from 1st GP consultation to diagnosis from 9.2 to 17.1 weeks. It seems likely that 34% of cancers were not diagnosed at the time of their first investigation and therefore the potential for improving the detection of EGC is significant.

Gastrin mediated expression of p53 in AGS GASTRIC CANCER CELLS
J.P. Cotton1, S.D. Oglesby1, A.M. Thompson1, J. F. Dillon1. Deps. of Molecular and Cellular Pathology, and Surgery and Molecular Oncology, University of Dundee, UK

Introduction: Gastrin is an important trophic hormone for malignant and normal gastric mucosal, and the trophic action of gastrin has been shown to act in an autocrine and paracrine manner in cell culture. Animal models of gastric carcinogenesis have implicated the overexpression and mutation of p53 in response to hypergastrinemia. p53 mutations are common in gastric cancer. Does gastrin have an effect on p53 in human tumours?

Methods: AGS Gastric cancer cells were obtained from ECACC, and grown in Ham’s F12 medium supplemented with 10% FCS. For time course experiments cells were plated out onto 100mm tissue culture plates, and grown to 50% confluence, cells were treated with 0.2µg/l Gastrin 17 (Sigma) in serum free and serum supplemented medium. Cells were harvested at 0, 6, 12, 24, and 48 hours. For dose response experiments cells were treated with 0.1µg/l 0.2µg/l, 0.4µg/l, 0.6µg/l, and 1.2µg/l and harvested at 24 hours. Cells were lysed with a urea based lyss buffer, protein concentration estimated, and separated using SDS PAGE electrophoresis. Protein was transferred to a nitrocellulose membrane overnight. The membrane was probed with DO-1 (anti-p53) and Ab1 (anti-p21) and detected using ECL. For RT PCR, total RNA was extracted using a total RNA extraction kit (Qiagen), reverse transcription (RT) performed using superscript RT (Qiagen), and cDNA amplified using Hotstar Taq (Qiagen) with DO-1 (anti-p53) and Ab1 (anti-p21) and detected using ECL. For Western blot analysis, cells were treated with 0.2µg/l LPS in the intestinal lumen.

Results: Gastrin caused an increase in p53 expression peaking at 12 hours, no alteration in p21 levels were noted. This occurred in a dose response with a maximal expression of p53 at a concentration of 0.6µg/l. RT-PCR detected a product for Gastrin but not for the Gastrin receptor. Summary: Gastrin seems to have a relationship with p53 expression and may be implicated in generating a fertile field for carcinogenesis to occur.

A 9 YEAR RETROSPECTIVE STUDY OF UPPER GI ADENOCARCINOMA. HOW MANY CANCERS ARE WE MISSING
S.J. Panter1, H. O’Flanagan2, M.G. Bramble1. ‘Endoscopy Centre, South Cleveland Hospital, Middlesbrough and Centre for Health Studies, University of Durham; NoREx, Middlesbrough, UK

Background: The detection rate of Early Gastric Cancer (EGC) in the UK remains low despite the widespread availability of gastroscopy. Previous research has suggested that treatment with acid suppressing medication (AST) prior to gastroscopy can lead to cancers being missed at endoscopy.

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Conclusion: Although this is preliminary data, it shows that 41% of patients did not have alarm symptoms at diagnosis. Also 55% of patients were treated with AST prior to the diagnostic OGD increasing the mean time from 1st GP consultation to diagnosis from 9.2 to 17.1 weeks. It seems likely that 34% of cancers were not diagnosed at the time of their first investigation and therefore the potential for improving the detection of EGC is significant.

ABSENCE OF TOLL LIKE RECEPTOR 4 (TLR4) EXPLAINS ENDOTOXIN HYPORESPONSIVENESS IN HUMAN INTESTINAL EPITHELIUM
S. Naik, L. Meijer, S. Pettersson, E.J. Kelly, L.R. Sanderson.

Introduction: The Toll protein in Drosophila regulates dorsal ventral patterning during embryogenesis and participates in antibacterial and antifungal host defense. Mammalian homologs are termed Toll like Receptors and in humans, six have been cloned (TLR1–6). They are characterised by extracellular leucine rich repeats and a cytoplasmic domain similar to the Interleukin 1 receptor. Both TLR2 and TLR4 recognise various bacterial cell wall components including lipopolysaccharide (LPS). This results in activation of the NFkB pathway. Peripheral blood lymphocytes (PBLs) express both TLR2 and TLR4. We hypothesise that the expression of TLR 2 and TLR4 in human intestinal epithelial cells differs to PBLs because of the abundance of LPS in the intestinal lumen.

Methods: Epithelial cells were isolated from Caco-2 cells (a human intestinal carcinoma cell line), fetal gut explants and small bowel resection specimens using Hanks/EDTA solution. Peripheral blood lymphocytes (PBLs) were used as positive controls. RNA was isolated by TRizol method. Standard RT-PCR examined TLR2 and TLR4 mRNA expression. NFkB expression was determined using a luciferase reporter assay.

Results: TLR2 mRNA was highly expressed in PBLs and was present in all human intestinal epithelial cells. TLR4 mRNA was detected only in PBLs. TLR4 is not present in epithelium from children with inflammatory bowel disease. In Caco2 cells significant NFkB activation in response to LPS only occurred in the presence of TLR4.

Conclusion: TLR2 mRNA, but not TLR4 mRNA, is present in normal human intestinal epithelial cells. TLR4 is not directly involved in inflammation of the epithelium. Although TLR2 is normally present in the epithelial cell, it plays a limited role in inflammation. It may be activated in conditions where bacterial cell wall components within the intestine are pathologically high.

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INCREASED EXPRESSION OF PRO-IL-18 BY
INTESTINAL EPITHELIAL CELLS INFECTED WITH
CRYPTOSPORIDIUM PARVUM

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Dept of Adult & Paediatric Gastroenterology, St Bartholomew’s & The Royal
London School of Medicine; Faculty of Medicine, Univ. Sussex, UK

Introduction: Cryptosporidiosis is an important cause of diarrhoea
world-wide. The causative organism, C. parvum, is an intracellular
parasite that infects the gastrointestinal epithelium. The development of a
Th1-mediated immune response and in particular enhancement of IFN γ production is critical in the control of the parasite. Epithelial cells may function as immune sensors of infection by producing cytokines including the Th1 inducing cytokine IL-18. We therefore explored the potential of C. parvum to modulate IL-18 production by enterocytes using an established in vitro model of infection.

Methods: HCT 8 and Caco-2 cells were grown to confluence in 24 well plates and infected with either viable or heat-inactivated purified C. parvum sporozoites (0.05–2x10⁶ sporozoites/well) in some experiments. Cells were pre-treated with IL-18 (2–200ng/mL) for 24h prior to infection. Forty eight hours after infection protein expression of mature and pro-IL-18 in cell lysates of infected and uninfected cells was determined by Western blotting using an anti-IL-18 antibody. IL-18 mRNA expression was also quantified by competitive RT-PCR in infected and uninfected cells 24h post-infection. Infection in IL-18 pre-treated cells was quantified by immunofluorescence microscopy using an anti-C. parvum antibody and compared to untreated controls.

Results: Forty eight hours post-infection pro-IL-18 protein expression was increased in infected cells compared to uninfected control cells or cells inoculated with heat-inactivated parasites and this increase was related to initial parasite inoculum. No concomitant rise in the expression of mature IL-18 was observed. IL-18 mRNA induction paralleled the increase in pro-IL-18 protein expression. At 24h post-infection a 30 fold increase in IL-18 mRNA was observed in infected HCT 8 cells compared with uninfected control cells or cells infected with heat-inactivated sporozoites. Infection was inhibited in IL-18 pre-treated cells, maximal inhibition was 31.1% ± 7.1% (p<0.001).

Discussion: Our findings indicate that C. parvum may induce both expression of IL-18 mRNA and pro-IL-18 by enterocytes, and that recombinant IL-18 may inhibit infection in an vitro model. Production of mature IL-18, which is dependent on the activation of caspase 1 does not occur. We speculate that C. parvum infection in vivo may activate caspase 1 in enterocytes by an unknown mechanism resulting in production of mature IL-18. (RCPG is a Welcome Trust Training Fellow).

THE PROBiotic ON BACTERIAL TRANSLOCATION AND SEPTIC MORBIDITY IN ELECTIVE SURGICAL PATIENTS

C.E. McNaught, N.P. Woodcock, C.J. Mitchell, J. MacFie. The Combined Gastroenterology Unit, Scarborough Hospital, North Yorkshire, UK

Aims: Bacterial translocation occurs in surgical patients and may account for postoperative sepsis. Many factors are thought to influence the prevalence of translocation, one of which is the luminal density and composition of the gut microflora. The aim of this study was to assess the impact of the probiotic Lactobacillus plantarum 299v (Proviva) on the incidence of bacterial translocation and septic complications in elective surgical patients.

Methods: In this prospective trial, surgical patients awaiting major GI resection were randomised to receive an oral preparation containing Lactobacillus plantarum 299v (Proviva) or the placebo on the day of surgery. Bacterial translocation was assessed by the culture of mesenteric lymph nodes and serosal biopsies. Nasogastric aspirates were taken to establish gastric colonisation with enteric organisms. All septic morbidity was documented.

Results: 129 patients were entered into the study.

<table>
<thead>
<tr>
<th></th>
<th>Proviva Group</th>
<th>Control Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F Ratio</td>
<td>39:25</td>
<td>36:29</td>
<td></td>
</tr>
<tr>
<td>Median age (QQR)</td>
<td>68 years (58-74)</td>
<td>69 years (58-77)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Bacterial translocation</td>
<td>7 patients (11.8%)</td>
<td>7 patients (11.8%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Gastric colonisation</td>
<td>6 patients (11.0%)</td>
<td>8 patients (15%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Septic complications</td>
<td>7 patients (11.8%)</td>
<td>10 patients (15.3%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Conclusions: Lactobacillus plantarum 299v administration in elective surgical patients does not alter bacterial translocation rates or subsequent septic morbidity. The use of a preoperative probiotic had no effect on the incidence or nature of gastric colonisation.

ELECTIVE SURGICAL PATIENTS

S. Lewis, M. Egger, P. Sylvestre, S. Thomas, Dept of Gastroenterology, Addenbrooke's Hospital, Cambridge; MRC Health Services research Collaboration, Dept of Social Medicine, Bristol; Dept of Surgery, Bristol Royal Infirmary, Bristol, UK

Early enteral feeding after gastrointestinal surgery may be of benefit, however, a period of starvation (‘nil by mouth’) is still routine practice. We performed a systematic review of the effectiveness of early enteral feeding. Systematic review and meta-analysis of randomised trials comparing any type of enteral feeding within 24 hours of surgery with management by ‘nil by mouth’ in elective gastrointestinal surgery. Three electronic databases were searched, reference lists checked and letters requesting details of unpublished trials sent to pharmaceutical companies. Anatomostic dehiscence, infection of any type, wound infection, pneumonia, intra-abdominal abscess, length of hospital stay and mortality. 11 studies met the inclusion criteria. Feeding directly into the small bowel was used in the intervention group in six of the studies and oral feeding in five. Early feeding reduced the risk of anastomotic dehiscence (RR 0.53, 95% CI 0.26 to 1.07, P=0.077), the risk of any type of infection (RR...
0.72, 95% CI 0.53 to 0.98, P=0.036), and the mean duration of hospitalisation (reduction by 0.84 day, 95% CI 1.33 to 0.36 day, P=0.001). Risk reductions were also seen for wound infection, pneumonia, intra-abdominal abscess and mortality but these were not statistically significant (P>0.10). The risk of vomiting was increased among patients fed early (RR 1.27, 95% CI 1.01 to 1.61, P=0.045).

Early feeding appears to be of benefit. An adequately powered trial is required to confirm or refute the benefits seen in small trials.

THE EFFECT OF GLUCAGON-LIKE PEPTIDE-2, EPIDERMAL GROWTH FACTOR AND GLUTAMINE ON INTESTINAL GROWTH

P. Kitchen1, A. FitzGerald, N. Mandir1, M. Ghatei2, S. Bloom2, J. Walters, A. Forbes1, R. Goodlad3. St Mark’s Hospital, ICSM, ICRF, UK

Background: Glucagon-like peptide 2 (GLP-2), epidermal growth factor (EGF) and glutamine (gln) stimulate growth of the intestine in the total parenteral nutrition (TPN) rat model. However, in this model the interaction of GLP-2 with EGF or gln has not been investigated.

Aims: To determine whether EGF or gln has a synergistic effect on growth of the intestine with GLP-2.

Methods: Rats were established on TPN. The treatment groups were as follows; 20 mcg/day of GLP-2, 20mcg/day of EGF, 20mcg/day of GLP-2 plus EGF, 2% gln, and 2% gln plus 20mcg/day of GLP-2. The small intestine and colon were weighed. Tissue was obtained of GLP-2 plus EGF, 2% gln, and 2% gln plus 20mcg/day of GLP-2. The small intestine and colon were weighed. Tissue was obtained of GLP-2 plus EGF, 2% gln, and 2% gln plus 20mcg/day of GLP-2.

Results: The mean (±SEM) small intestinal weight (g) in the TPN, GLP-2, EGF, GLP-2/EGF, gln and gln/GLP-2 groups were 1.7(±0.05), 3.1(±0.02), 3.8(±0.04), 1.9(±0.13) and 2.8(±0.11) respectively (all P<0.01 compared to TPN group, except gln group). The mean (±SEM) colonic weight (g) for the above groups were 0.44(±0.01), 0.45(±0.02), 0.72(±0.02), 0.75(±0.03), 0.50(±0.03) and 0.50(±0.04). Two way ANOVA without interaction demonstrated a significant effect by gln on colonic weight (P<0.05).

Conclusion: GLP-2 and EGF have additive effects on growth in the small intestine. Furthermore gln does not augment the growth of the intestine stimulated by GLP-2. However there is a modest effect of gln on colonic growth.

TNF-α INDUCES β-CATENIN/TCF MEDIATED TRANSCRIPTION: OPPOSING ACTIONS OF MAPK AND NF-κB PATHWAYS

I. Perry1, C. Tselepis1, B.T. Cooper1, H.T. Igba1, J.A.Z. Jankowski1, D.A. van Heel1, D.P. Jewell1, A.H. Carey1. ‘Wellcome Trust Centre for Human Genetics and Gastroenterology Unit, University of Oxford, UK’, ‘Oxagen Ltd, Abingdon, UK

Introduction: Human/mouse chimeric monoclonal antibodies directed against tumour necrosis alpha (TNFα) is becoming an established treatment for steroid resistant and fistulising Crohn’s disease (CD). Although the efficacy has been shown in clinical trials, the financial implications often limit its use and there is little data regarding the impact in clinical practice.

Aims: We therefore aimed to audit the clinical effectiveness of the use of Anti TNF-α (Infliximab, Centocor, USA) in the treatment of Crohn’s disease and other gastrointestinal conditions in our institutions.

Methods: We prospectively audited the use of Infliximab in both Crohn’s disease (CD) and other gastrointestinal conditions in our institutions. Data was collected regarding demographic and disease details, and the indication for treatment was confirmed. Clinical disease activity was assessed by the Harvey-Bradshaw index and blood was taken for inflammatory parameters, complement fractions C3 and C4 and double stranded DNA. All patients received an infusion of Infliximab at a dose of 5mg/Kg over 4 hours. The patients were then followed prospectively for 12 weeks and categorised as to whether they had responded or not. If they had responded they were followed until relapse or the end of the 12-week period. A response was defined as improvement in well being with a reduction in steroid dose.

A068 NOVEL POLYMORPHISMS IN THE BETA 7 INTEGRIN GENE (ITGB7): FAMILY BASED ASSOCIATION STUDIES IN IBD

D.A. van Heel1, D.P. Jewell1, A.H. Carey1. ‘Wellcome Trust Centre for Human Genetics and Gastroenterology Unit, University of Oxford, UK’, ‘Oxagen Ltd, Abingdon, UK

Background: Linkage studies from five groups worldwide have confirmed the presence of an inflammatory bowel disease (IBD) susceptibility locus on chromosome 12q. ITGB7, a positional candidate gene within this region, is involved in lymphocyte homing to the gut and retention of intra-epithelial lymphocytes. Monoclonal antibodies to alpha 4 beta 7 integrin have been shown to ameliorate colitis in animal models. No polymorphisms in ITGB7 had been reported and therefore we screened this gene in order to identify markers to test for association. In order to overcome potential false positive results from a case control study, polymorphisms were genotyped in IBD families and the transmission disequilibrium test (TDT) was used to assess association.

Aims: To screen ITGB7 for polymorphisms, and carry out association testing of common or functional polymorphisms in IBD families.

Methods: Genomic sequence was obtained for the whole gene and polymorphism region by direct sequencing of the products of inverse PCR and PCR between exons. PCR fragments covering all 16 exons and 1.7kb of 5’ promoter region were designed and analysed for polymorphisms in 24 individuals by denaturing HPLC (Transgenomic Wave). Samples showing heterozygote traces were sequenced to verify the SNP. PCR-RFLP assays were designed for each SNP and allele frequencies were tested in 90 healthy controls. Common alleles (frequency >= 10%) and potentially functional polymorphisms were genotyped in 567 trios from 464 IBD families. A permutation based association test was used to calculate association independent of linkage (Aspex).

Results: 14 SNPs were identified and two common intronic and two amino acid changing SNPs were genotyped. Data were available from 102 multiply affected families and 362 simplex families containing 254 ulcerative colitis (UC), 13 indeterminate colitis and 300 Crohn’s disease (CD) trios. No significant TDT results were obtained with any SNP for the IBD, UC or CD phenotype.

Conclusion: The ITGB7 gene is unlikely to be involved in IBD susceptibility and therefore future studies on chromosome 12 should focus on other positional candidate genes.

A069 AUDIT OF ANTI-TNF-α ANTIBODIES IN CLINICAL PRACTICE

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Introduction: Human/mouse chimeric monoclonal antibodies directed against tumour necrosis alpha (TNFα) is becoming an established treatment for steroid resistant and fistulising Crohn’s disease (CD). Although the efficacy has been shown in clinical trials, the financial implications often limit its use and there is little data regarding the impact in clinical practice.

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**Results:** 29 patients received infusions of Infliximab between February 1999 and September 2000. There were 16 females and 13 males with a median age of 35 years (17–68 years). Indications for administration were chronic active steroid resistant CD in 21 patients, fistulating Crohn’s disease in 4, resistant pyoderma gangrenosum in 1, refractory pouchitis in 1 and refractory coeliac disease in 2. 15 of the CD patients have undergone colectomy and 11 were established on immunosuppressives at the time of the infusion. The median dose of Infliximab was 303mg (range 200–500mg) and the only adverse event was headache in 3 patients. Follow up is currently available in 23 patients. Of the 23 patients 14 (61%) had a response when assessed at 4 weeks post infusion. Of the 9 that did not respond, 3 had surgical resections and 6 were managed medically. Of the 14 that responded when assessed at 12 weeks 1 had a surgical resection and 3 more had relapsed. The frequency of perianal disease was significantly lower in the group that responded when compared to those that did not (p<0.05). There were no other differences between the groups.

**Conclusions:** The response rates to Infliximab in our group are comparable to those seen in clinical trials. Despite the cost it remains a useful adjunct to treatment in this otherwise difficult group of patients. Our data suggests that patients with perianal disease respond less well than those patients with out.

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**NEUTROPHIL DEFICIENCY DURING ACUTE INFLAMMATION IN INFECTIOUS BOWEL DISEASE**

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**Hypothesis:** In Crohn’s disease (CD) and ulcerative colitis (UC) there is a reduced neutrophil influx during the acute inflammatory response. This may be due to a deficiency in the mediators of acute inflammation.

**Aim:** i) To assess neutrophil migration into cantharidin induced skin blisters. ii) To assay mediators of acute inflammation in the blister fluid.

**Methods:** Patients with inactive CD (n=14; 5 male; av. 49.8 years (S.D. 20.5)) and inactive UC (n=11; 6 male; av. 45.1 years (S.D. 12.1)), and non-inflammatory controls consisting of medical students (C) (n=16; 12 male; av. 22.5 years (S.D. 3.0)) were recruited. Cantharidin (0.1% in 25μl acetone) was applied to 0.8cm skin blisters. i) To assay mediators of acute inflammation in the blister fluid. ii) To assay neutrophil migration into cantharidin induced skin blisters.

**Results:** Inflammation was assessed at 4 weeks post infusion. Of the 9 that did not respond, 3 had surgical resections and 6 were managed medically. Of the 14 that responded when assessed at 12 weeks 1 had a surgical resection and 3 more had relapsed. The frequency of perianal disease was significantly lower in the group that responded when compared to those that did not (p<0.05). There were no other differences between the groups.

**Conclusions:** The response rates to Infliximab in our group are comparable to those seen in clinical trials. Despite the cost it remains a useful adjunct to treatment in this otherwise difficult group of patients. Our data suggests that patients with perianal disease respond less well than those patients with out.

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**ASSOCIATION BETWEEN THE LOW PRODUCING INTERLEUKIN-10 ALLELE AND ULCERATIVE COLITIS IN PATIENTS UNDERGOING COLECTOMY**

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**Background:** Interleukin-10 (IL-10) is an important immunoregulatory cytokine. IL-10 gene knock-out mice develop a chronic enterocolitis. Recent studies have demonstrated that inter-individual differences in IL-10 production are in large part genetically determined. A number of polymorphisms in the promoter region of the gene have been identified and the A to G polymorphism at position -1082 has been associated with increased IL-10 production in vitro.

**Aims:** To assess the hypothesis that the IL-10 -1082 promoter region polymorphism is associated with susceptibility to UC, a case-control association study was performed in well defined UC patients who had undergone colectomy.

**Methods/results:** Genotyping for the single nucleotide polymorphism at position -1082 (A to G) in the IL-10 promoter region was performed in 127 patients who had undergone colectomy for UC and 198 anonymous blood donors. Disease diagnosis and extent were confirmed by histology of the resected colon. All individuals were genotyped by 5’-nucleotide polymerase chain reaction (PCR) using the PE Biosystems Taqman allelic discrimination system using primers and fluorescent probes.

**Abstract 71, Table 1**

<table>
<thead>
<tr>
<th>IL-10 -1082 Genotype</th>
<th>N</th>
<th>AA</th>
<th>AG</th>
<th>GG</th>
<th>Allele A Carriage</th>
<th>Allele A Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>127</td>
<td>35</td>
<td>70</td>
<td>22</td>
<td>82.7%</td>
<td>55.1%</td>
</tr>
<tr>
<td>Controls</td>
<td>198</td>
<td>43</td>
<td>98</td>
<td>57</td>
<td>71.2%</td>
<td>46.5%</td>
</tr>
</tbody>
</table>

Carriage of the low producing allele (A) was significantly associated with UC (p=0.02; Odds ratio = 1.93 (95% CI 1.1–3.4; chi-squared 5.5).

**Conclusions:** This study in well defined patients support the hypothesis that individuals genetically predisposed to produce less IL-10 have an increased susceptibility to UC.

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**TRANSPORT OF MICROPARTICLES ACROSS HUMAN COLON MUCOSA IN VITRO**

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**Introduction:** Transepithelial transport of microparticles across the intestinal mucosa has been studied in animal models, but there is scant data in humans. Peyer’s patches in the small intestine are specialized to transport microparticles, but there is little information on microparticle transport in the colon mucosa. It is generally thought that colonic microparticles are not permeable to large sized particles.

**Aim:** To demonstrate microparticle transcytosis in cultured human colon mucosa, normal and inflamed with or without lipopolysaccharide (LPS).

**Methods:** Sigmoid colon biopsies from eight ulcerative or Crohn’s colitis patients and 8 normal were cultured in modified Waymouth’s medium with or without LPS of E.Coli 055:B5 (50µg / ml). After 3 h of incubation in a modular incubator with 95% O2 and 5% CO2 at 37°C, flat-bottomed wells were loaded with 5.68 X 10^6 particles per 0.1 ml. Organ culture was maintained for further 21 h and tissue viability was assessed by BrdU uptake. Fluorescent microparticles were located in 15 µm cryostat sections stained with propidium iodide under epifluorescence and confocal laser scanning microscope. In TEM, location of particles in the cytoplasm was determined. Statistical analysis was done by SPSSPC+ and groups were compared by non-parametric tests.

**Results:** BrdU uptake in dividing cells confirmed viability of explant tissues in short-term organ culture up to 24 h. Serial optical sections by confocal laser scanning microscope showed that particles were located in the epithelium and lamina propria. Number of particles (per mm²) transcytosed was normal with or without LPS were (mean±SE): 28 ± 4 vs. 36 ± 5, p= NS. In IBD, number of particles...
transcytosed without vs. with LPS were (mean ± SE): 84 ± 11 vs. 232 ± 35, p <0.001. The number of transcytosed particles in IBD were significantly more (p <0.01) compared to normal with or without LPS.

**Conclusion:** We have shown for the first time microparticle transport across human colon mucosa. Particles as large as 2 μm were transported in situ. More particles were transported across inflamed colon mucosa compared with normal mucosa. LPS augmented particle transport in inflamed mucosa only. The implication of such inert particle transport in terms of amplification of inflammation requires further study. The results also indicate the potential for particulate drug delivery to the colon.

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**AN AUDIT OF OPPORTUNISTIC SCREENING OF PATIENTS PRESENTING WITH LOWER GI SYMPTOMS IN A SINGLE-HANDED GP PRACTICE OVER AN EIGHT YEAR PERIOD**

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In recent years, this single handed general practice has referred patients for fibroptic sigmoidoscopy as an initial investigation when they have presented with symptoms suggestive of a lower gastrointestinal cause, including iron deficiency, or with a strong family history (FH) of colon cancer. The referral indications have been very similar to the present colon cancer referral guidelines. Following sigmoidoscopy, a decision was made about the need for further assessment. The overall outcome was recorded. The audit reviews the data of 175 referrals over 8 years, 1992–99 inclusive. The ages ranged from 20–90 years (mean 58). For 95% of all the patients the duration of symptoms to the time of presentation to the GP was less than 12 weeks (mean 6 weeks). The main reasons for referral were: rectal bleeding (27%), culture negative diarrhoea lasting a minimum of 6 weeks (37%) and abdominal pain (22%). Alternating constipation and diarrhoea occurred in 18% but only 3% of asymptomatic patients were considered on account of a FH despite a newsletter being sent to all patients in the practice. Of these 175 patients having a sigmoidoscopy examination, 58 had a subsequent barium enema and 24 a colonoscopy. Carcinoma was found in 8 patients (4.5%) and colonic polyps in 21 (12%) and 2 of these the dysplasia was severe. Twelve (7%) patients had colitis +/- proctitis whilst the overall result was considered normal in nearly 50% of those examined. Five of those with carcinoma and 6 of those with polyps were under the age of 60 whilst 5 of those with colitis were over 60. The overall numbers referred for sigmoidoscopy from this practice were readily manageable by the local endoscopists and were comparable numerically to those undergoing upper GI endoscopy over the same period.

General practitioners should therefore be encouraged to refer within the new cancer guidelines and to take the advantage of opportunistic limited colon assessment in those presenting with symptoms.

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**INTERCOLLEGIATE-BSG NATIONAL COLONOSCOPY (INBC) AUDIT: EVALUATION OF THE PRESENCE OF ABNORMAL FINDINGS WITH THE INDICATION FOR COLONOSCOPY**

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**Introduction:** Colonoscopy is acknowledged as the gold standard for examining the colon. Demand for colonoscopy continues to increase for diagnosis, therapy and surveillance. As part of the INBC audit, the primary indication for the colonoscopy and the diagnosis reported following the procedure were recorded. Abnormalities included polyps, diverticular disease, colitis, tumour, previous colorectal resection, strictures, angiodysplasia, melanosis coli, foreign body and “other”. A comparison was made between indications and outcomes in 8902 colonoscopies.

**Results:** Diagnosis was the sole indication in 4333/8902 colonoscopies. The most frequent diagnostic indications are shown with the number of abnormal colonoscopies. Diverticularis has been separated from other diagnostic categories. Solely therapeutic colonoscopies were abnormal in 176/189 (93.1%). The most common indication with findings of cancer was bleeding.

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**THE EPIDEMIOLOGY OF DISTAL HYPERPLASTIC POLYPS IN THE UK POPULATION**

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**Background:** Hyperplastic polyps (HP) have always been considered unimportant lesions with no malignant potential. Consequently there has never been a proper description of their epidemiology in living subjects.

**Aim:** To accurately describe the prevalence, sex and age distribution of distal HPs in an asymptomatic UK population.

**Method:** 40,673 individuals aged 55 to 64 years had a flexible sigmoidoscopy (FS) as part of the UK FS screening trial. Subjects investigated with lower gastrointestinal endoscopy during the last two years, a history of inflammatory bowel disease, colorectal dysplasia or family histories of colorectal cancer were excluded. All polyps above the distal 5cm of the rectum smaller than 1cm diameter were recorded, removed and sent for histopathological assessment. Polyps 1cm or larger were removed at a later colonoscopy. Polyps in the distal rectum less than 3mm diameter were recorded but not included in the analysis of results.

**Results:** 19.1% of 20,518 males and 11.3% of 20,155 females had one or more histologically confirmed distal HPs (male: female ratio = 1.7:1; 95% ci 1.6–1.8; p<0.001). 84.2% HPs were <4mm in diameter, 14.5% were 5–9mm and 1.2% (>9mm) were >10mm. The mean diameter was 3.4mm. The majority of distal HPs were located in the rectum (59.3%). 79.0% were sessile, 15.0% pedunculated and 2.3% flat or depressed. Males were more likely than females to have multiple distal HPs (43.4% vs 34.2%; risk difference = 9.1%; 95% CI for risk difference 6.6–11.7%; P<0.001). The prevalence of HPs varied significantly in size, location or morphology. Neither prevalence, size, location or multiplicity changed with age in either sex.

**Conclusion:** Distal HPs are common. They occur more frequently and are more likely to be multiple in males than females. Most people have their full complement of distal HPs by 55 years.

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**FLAT COLORECTAL NEOPLASMS; THE INCIDENCE IN THE UK POPULATION**

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**Background:** Flat and depressed colorectal adenomas/cancers have been described in the Japanese literature for almost 15 years, and has never been a proper description of their epidemiology in living subjects.

**Method:** To clarify the incidence and clinical importance of flat neoplasms in a Western population, 364 consecutive patients undergoing routine colonoscopy were assessed over a 6 month period (May–Oct 2000). All examinations were performed by two experienced Colonoscopists (BPS/NS) using standard Olympus video-colonoscopes. Dye spray was performed using 0.1% indigo carmine when suspicious areas were seen. Macroscopically Kudo’s classification for flat adenomas was used and the histological diagnosis of dysplasia was based on the WHO system.
Results: Total colonoscopy (adjusted) was achieved in 95% of patients. Indications for colonoscopy were: bleeding (62), polyp surveillance (52), change in bowel habit (34) and others (216). In total 416 polyps were found in 170/364 patients with 9 cases of advanced cancer. Of these 25 were classified as flat (6%) and 391 polypoid (94%). 354/416 could be assessed histologically (21 flat; 336 polypoid). All flat lesions were neoplastic (adenomatous) while 39% of the polypoid lesions were non-neoplastic (inflammatory/hyperplastic). Of the neoplastic lesions severe dysplasia was found in 3% of the polypoid lesions and in 50% of flat& depressed lesions.

Abstract 76, Table 1

<table>
<thead>
<tr>
<th>Mild/mod.</th>
<th>Severe/Dublet A</th>
<th>(Non-neoplasms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypoid</td>
<td>97% (195/202)</td>
<td>3% (7/202)</td>
</tr>
<tr>
<td>Flat elevated</td>
<td>100% (17/17)</td>
<td>0</td>
</tr>
<tr>
<td>Flat &amp; depressed</td>
<td>50% (24/48)</td>
<td>50% (24/48)</td>
</tr>
</tbody>
</table>

Conclusion: In this study the macroscopic incidence of flat adenomas during the procedure was 6% and the incidence to the all adenomatous lesions was 9.4%. According to our result, flat elevated lesions may have the similar characteristics as polypoid lesions in terms of malignancy. On the other hand, as flat and depressed lesions had a high incidence of malignancy, Colonoscopists should be more meticulous in detecting especially flat and depressed lesions.

FAMILIAL COLONRECTAL CANCER: OUTCOME OF COLONOSCOPIC SURVEILLANCE IN DOMINANT FAMILIES WITH AND WITHOUT HEREDITARY NONPOLYPOSIS COLONRECTAL CANCER MICROSATellite INSTABILITY

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Introduction: Hereditary nonpolyposis colorectal cancer (HNPCC) is an important dominantly inherited predisposition to colorectal cancer (CRC). It is caused by mutations in DNA mismatch repair genes, which are characterised by microsatellite instability (MSI) in tumours. It has been proposed that there are other important genetic predispositions to CRC.

Aims: Assess the outcome of colonoscopic surveillance in dominant CRC families stratified according to their MSI status.

Methods: Individuals with a family history of CRC are stratified according to their empirical lifetime risk of developing CRC and offered colonoscopic surveillance if the risk is \( \geq 1 \) in 10. CRC pedigrees may be due to non-HNPCC genetic predispositions (MSI-H) in tumours. It has been proposed that there are other important genetic predispositions to CRC.

Aims: To determine the brain intracellular pH (pHi) in patients with chronic hepatic encephalopathy (HE): a \(^{1}P\) MR spectroscopy (MRS) study

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Aim: To determine the brain intracellular pH (pHi) in patients with chronic HE non-invasively, using \( \text{In vivo} \) \(^{1}P\) MRS.

Patients: 82 patients (46 M; 36 F), with biopsy-proven cirrhosis of mean (range) age 52 (31–77) yr and 30 aged-matched controls were...
studied. 11 subjects had no evidence of neuropsychiatric impairment, 37 had evidence of minimal HE and 34 had overt HE.

Methods: Unlocalised spectra were acquired from the entire head in 48 patients (TR 5s; 64 averages). Spectra from the basal ganglia (BG) were acquired in 34 patients, using a 3-D CSI technique (TR 5s; 2048 averages). $p$H values were calculated from the chemical shift difference with the inorganic phosphate (P) and phosphocreatine (PCr) resonances. The %P, PCr and $p$JNTP signals relative to the total $p$H signal and peak area ratios of P, and PCr relative to $p$JNTP were also measured.

Results: There were no $p$H differences between patients and volunteers in $p$H MR spectra from the whole head or BG. There was no correlation between $p$H and the severity of HE or Child score. There was no change in spectra from the whole head, but in BG spectra, there was a significant increase in mean $p$H/NTP ($p=0.02$) and PCr/NTP ($p=0.009$). The mean $p$SP and $p$PCr were also increased ($p=0.06$; $p=0.05$). When the patients were classified according to the severity of HE, those with overt disease had a higher mean $p$H/NTP and %P ($p=0.03$; $p=0.01$), compared to controls.

Conclusion: Our results suggest that there are detectable bioenergetic abnormalities in patients with minimal and overt HE and that any $p$H change, related to mitochondrial dysfunction, is probably a secondary, rather than a primary phenomenon.

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### 081 HEMODYNAMIC CONSEQUENCES OF PRECONDITIONING IN LIVER ISCHAEMIA-REFUX INJURY

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**Background:** Ischaemic preconditioning (IPC) may increase tolerance of the liver to ischaemic insults of surgery. IPC may be mediated via nitric oxide (NO). The hemodynamic changes of IPC have not been correlated to NO metabolism.

**Material and Methods:** Sprague Dawley rats were subjected to 45 mins lobar ischaemia followed by 2 hr reperfusion (IR). L-arginine or L-NAME were administered to stimulate or block NO synthesis. Study groups (n=6) had, (1) sham laparotomy, (2) IR, (3) IPC with 5 min ischaemia and 10 min reperfusion before IR, (4) L-arginine before IR, (5) L-NAME + IPC before IR. Hepatic tissue oxygenation was measured by near infrared spectroscopy (NIRS) and hepatic microcirculation (HM) by laser doppler flowmeter (LDF). Liver function tests and nitrates were analysed. Differences between groups and confidence intervals were established using analysis of variance (ANOVA) with Bonferroni test, and paired student's t test.

**Results:** IR injury produced significant reduction in HM (31.6% of preischaemic value, $p=0.00$ vs baseline). IPC improved the HM (49.5%, $p=0.02$ vs controls) upon reperfusion. IPC improved hepatic oxyhemoglobin and cytochrome oxidase (both $p<0.05$ vs controls). NO stimulation and blockade did not influence HM or hepatic tissue oxygenation. IPC as well as L-arginine treatment significantly increased nitrates and decreased liver enzymes. L-NAME administration with IPC prevented the rise in nitrates and decrease in liver enzymes.

**Conclusion:** IPC resulted in improvement of HM and hepatic tissue oxygenation following IR, but the effect may not be solely mediated by nitric oxide.

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### 082 REPEAT OESOPHAGEAL AMBULATORY pH MONITORING—IS IT WORTHWHILE? A RETROSPECTIVE ANALYSIS OF 6000 PATIENTS

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**Introduction:** Patients who have undergone oesophageal pH studies are re-referred for a variety of reasons, after varying time intervals. The aim was to determine if repeating the pH study was likely to alter the diagnosis.

**Patients and methods:** Data was reviewed from adult patients who were studied between January 1985 and June 2000. Over 6000 patients have had pH tests, of which there were 211 patients with two or more studies. As therapeutic interventions potentially alter the underlying pathology, only the 111 patients who had no therapy at any stage were included. Both initial and repeat referrals and subsequent diagnoses, were stratified and analysed. The total percentage of reflux (pH<4) time (TPR) and DeMeester score were examined. The initial TPR was also compared to the repeat studies.

**Results:** Patients diagnosed initially as normal (TPR<5.78 or DeMeester score<14.7) were unlikely (p=0.05) to have their diagnosis changed if their DeMeester score was less than 5.8 (average score 2.0 with SD 1.9). Non-intuitively, the TPR could not predict (p<0.05) whether an initial diagnosis of normal would change. In those initially diagnosed with gastro-oesophageal reflux disease (GORD), TPR and DeMeester score were not predictive (p<0.05). There was a poor correlation between the initial and repeat TPR, even in those whose initial diagnosis was confirmed by the second test (correlation coefficient $R^2$=0.008). There was no consistency of TPR either, in specific groups where throughout the diagnosis was GORD ($R^2=0.016$) or where throughout the diagnosis was normal ($R^2=0.025$).

**Conclusion:** There is a high degree of intra-patient variation in TPR, in interval repeated studies. In those initially diagnosed as normal, surprisingly TPR is not predictive however a DeMeester score below 5.8 is a relative contra-indication to performing a repeat pH study.

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### 083 THREE-HR POSTPRANDIAL pH MONITORING IS USEFUL IN EXCLUDING GASTRO-ESOPHAGEAL REFLUX DISEASE IN SYMPTOMATIC PATIENTS

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**Introduction:** Currently ambulatory 24hr oesophageal pH monitoring is the gold standard for the diagnosis of gastro-oesophageal reflux disease. This long period of oesophageal intubation is unpleasant. Thus the aim of this study was to determine if a 3hr postprandial study would be as sensitive as the 24hr study.

**Patients and methods:** Two hundred symptomatic patients (86 male, 114 female, average age 56yrs 3 months) were studied. A 3hr postprandial period was analysed and compared to a standard ambulatory 24hr oesophageal pH monitoring (Synectics Medical). A positive test was defined as >5.78% of the total period of pH<4. The De Meester score was also calculated from the 24hr study, with a score $>14.72$ regarded as positive.

**Results:** The 3hr post prandial oesophageal pH correlated well with the complete 24hr study (r=0.885, p<0.001), and the De Meester score (r=0.82, p<0.001). When only supine periods during the 3hr test was examined this again correlated well with the complete 24hr study (r=0.885, p<0.001), and the De Meester score (r=0.796, p<0.001). The negative predictive value of the 3hr study was 92% when compared with the 24hr test, and 88% when compared with the De Meester score.

**Abstract 83, Table 1**

<table>
<thead>
<tr>
<th>3hr pH vs 24hr pH</th>
<th>3hr pH vs De Meester score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative predictive value</td>
<td>92%</td>
</tr>
<tr>
<td>Positive Predictive value</td>
<td>65%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>88%</td>
</tr>
<tr>
<td>Specificity</td>
<td>75%</td>
</tr>
</tbody>
</table>

**Conclusions:** The 3hr post prandial study is a sensitive test for the detection of gastro-oesophageal reflux disease, and a negative 3hr test is useful in excluding disease in symptomatic patients.

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### 084 CLINICAL ROLE OF OESOPHAGEAL MANOMETRY

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**Background:** Although several modalities are available to investigate oesophageal motility disorders, most gastroenterologists regard manometry as the gold standard. Manometry is increasingly available in district general hospitals but the clinical utility of the investigation in this setting remains unclear.
Aims: To evaluate the outcome and usefulness of oesophageal manometry in a district general hospital setting.

Methods: Data on 100 consecutive oesophageal manometry procedures performed in Neath General Hospital between September 1998 and December 1999 (14 months) were analyzed, taking into account the referral pattern, indications, and results. Manometry was performed using the Synectics Polygraph with polygram software and a Gaelic triple solid-state transducer catheters.

Results: There were 46 male, 54 female patients, average age 52.8 years, range 15–81 years. Referrals were from six hospitals in southwest Wales and were from—surgeons (51 patients), physicians (47) and paediatricians (2). The indications for referral were gastro-oesophageal reflux (pre-operative assessment before fundoplication) (58), dysphagia (28), chest pain (12) and epigastric pain (2). Manometric diagnoses were made using standard pre-defined criteria and were as follows: normal (41), non-specific motility disorders (NSMD) (38), achalasia (15), diffuse oesophageal spasm (4) and scleroderma (2). Of the 58 patients who had undergone manometry as a pre-operative assessment of oesophageal motility before fundoplication, 27 (47%) were abnormal. Twenty-five (43%) had NSMD and 2 (3%) had achalasia. Forty-eight of these pre-operative cases were combined with 24 hour pH recording, which confirmed acid reflux in 35 (73%).

Conclusion: Our experience reflects the published evidence that the use of manometry is changing. It is now more commonly used for assessment before anti-reflux surgery and for dysphagia, and the use in the assessment of chest pain is declining. Our findings confirm the importance of eliminating significant motility disorders (particularly achalasia) to avoid inappropriate anti-reflux surgery.

085 REFLECT SYMPTOM REPORTING AND ACID PERFUSION TESTING IN SCLERODERMA

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Gastroesophageal reflux disease causes significant morbidity in scleroderma (SSc) yet the reliability of reflux symptoms in the diagnosis is unclear. Acid perfusion testing (APT) has produced conflicting results regarding acid insensitivity in SSc patients. The aim of this study was to assess the value of reflux symptom reporting in predicting acid reflux in SSc and to assess the diagnostic value of acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACG diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associated acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-assocaied acid reflux. Patients complaining of heartburn and/or acid regurgitation and who fulfilled the ACR diagnostic criteria for SSc were recruited. Acid suppression was discontinued for at least 3 days prior to assessment. Reflux symptoms were quantified using a scoring system and acid perfusion testing in SSc-associ...
H. Pylori (HP), Intragastric (IG) PH and Helicobacter Pylori Infection and the Beneficial Effect of Rabeprazole 20 mg in Future of Acid

Background: The gastric cardia is variably exposed to acid before and after a meal. The factors that determine this exposure are unknown but the presence of acid at the cardia increases the pathogenic mechanisms.

Methods: 41 EO patients (mean age = 46y; sd = 13; 54% men; 90% white) underwent dual probe pH testing. The distal probe was positioned in the gastric body/antrum; the proximal probe 5 cm above the OG junction. Patients underwent repeat pH testing at 1 (n=12) and 12 months (n=9) on therapy with lansoprazole 30mg once daily.

Results: Although, IG acid suppression with lansoprazole in HP+ subjects was significantly better (p<0.001), OAE or change in OAE was not different between the two groups at either 1 or 12 months post-therapy (P > 0.05).

Conclusions: Although HP+ GORD patients are significantly older and have higher IG pH than those who are HP−, they have numerically more OAE. This may be due to effects of age, HP infection, or both on the lower oesophageal sphincter.

Results: For heartburn relief in all patients, rabeprazole 20 mg once daily effectively relieved both daytime and nighttime symptoms on Day 1 and throughout the first week, with this treatment effect maintained at week 4. Similar findings were noted in those patients reporting prior ineffective relief with either omeprazole or lansoprazole, with their symptomatic response equaling the all-patient population at week 4.

Summary: Rabeprazole 20 mg demonstrated symptom relief on Day 1 of therapy, even in patients reporting prior ineffectiveness with other PPIs.

Rabeprazole 20 mg in Future of Acid Suppression Therapy (F.A.S.T.) Trial: Acute Heartburn Relief in Patients Refractory to Omeprazole and Lansoprazole

Background: Clinical effectiveness of rabeprazole 20 mg once daily in symptoms associated with endoscopically confirmed erosive esophagitis was studied in the F.A.S.T. Trial, including patients who had reported ineffective relief with prior proton pump inhibitor (PPI) therapy.

Methods: An open-label multicenter, clinical trial of 2449 efficacy evaluable patients diagnosed with erosive GERD was conducted. Within this group, 290 omeprazole recipients and 212 lansoprazole recipients reported prior ineffective relief in the 3 months prior to study entry. After recording baseline daytime and nighttime heartburn at enrollment, patients used an interactive telephone response system within 36 hours to report symptoms for the first 7 days of therapy and at week 4. 4-point Likert scale responses were recorded (0=no symptoms; 3=severe symptoms). Complete relief was computed daily as the percentage of baseline symptomatic patients with a score of 0 divided by all reporting patients who had been symptomatic at baseline.

Results: 55.4% of patients with Complete Relief

Baseline (Mean) | HP+ (n=10) | HP- (n=11) | P
---|---|---|---
Age (y) | 55.4 | 42.8 | 0.007
% time oesophageal pH < 4.0 | 17.5 | 11.6 | 0.12
# reflux episodes > 1min | 215 | 190 | 0.6
 Mean pH | 8.4 | 5.7 | 0.3
% time IG pH > 4.0 | 3.0 | 2.1 | 0.005

Daytime Heartburn

<table>
<thead>
<tr>
<th>Day</th>
<th>All patients</th>
<th>Prior Lanso ineffect relief</th>
<th>Prior Lanso ineffect relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64.0 70.8 75.3 76.7 78.2</td>
<td>80.0 81.1 81.1</td>
<td>54.1 66.9 70.0 73.5 72.0 74.1 75.5 81.0</td>
</tr>
<tr>
<td>2</td>
<td>69.2 78.1 80.9 82.3 83.8</td>
<td>85.8 85.7 85.7</td>
<td>57.4 62.7 72.7 72.5 74.2 75.0 77.3 82.3</td>
</tr>
<tr>
<td>3</td>
<td>62.0 78.1 71.9 74.3 72.8</td>
<td>82.9 76.8 84.4</td>
<td>62.0 78.1 71.9 74.3 72.8</td>
</tr>
</tbody>
</table>

Conclusions: Although HP+ GORD patients are significantly older and have higher IG pH than those who are HP−, they have numerically more OAE. This may be due to effects of age, HP infection, or both on the lower oesophageal sphincter.

Background: Despite research on the potential link between H pylori infection and gastro-oesophageal reflux disease, there is to date no formal systematic review evaluating the overall picture.

Objectives: To evaluate the role of H pylori in reflux disease through a systematic review of the literature.

Selection criteria: Cohort and case-control studies comparing prevalence of H pylori in reflux disease with controls. Randomised, quasi-randomised and cohort studies comparing the effect of H pylori (presence or absence) on oesophagitis and or reflux symptoms.

Data collection and analysis: Two reviewers independently assessed trial quality. Data was extracted from eligible trials on a standardised form by a single investigator that was checked by a second investigator.

Preliminary results: Twenty three studies were included in the systematic review, which evaluated 2665 patients and 1730 controls. H pylori prevalence was 37% in reflux and 46% in controls. Following successful H pylori eradication in 531 patients with duodenal ulcer, heartburn symptom had decreased from 162 patients at baseline to 132 patients at a mean follow-up period of 18 months. In 257 patients with reflux oesophagitis evaluated at 3–57 months, no significant difference in terms of amount of proton pump inhibitors required to maintain remission, dyspepsia scores, and mean reflux values was found between H pylori positive and H pylori negative patients.

Conclusions: Preliminary results, subject to further statistical refinement, do not suggest a protective role for H pylori in reflux disease. The value of eradication in patients with gastro-oesophageal reflux remains open.

HECILOBACTER PYLORI INFECTION AND THE MANAGEMENT OF GASTRO-OESOPHAGEAL REFLUX DISEASE: A SYSTEMATIC REVIEW OF THE LITERATURE

A.S. Raghunath, S. Childs, A.P.S. Hungin. Centre for Health Studies, University of Durham, UK

Background: Despite research on the potential link between H pylori infection and gastro-oesophageal reflux disease, there is to date no formal systematic review evaluating the overall picture.

Objectives: To evaluate the role of H pylori in reflux disease through a systematic review of the literature.

Selection criteria: Cohort and case-control studies comparing prevalence of H pylori in reflux disease with controls. Randomised, quasi-randomised and cohort studies comparing the effect of H pylori (presence or absence) on oesophagitis and or reflux symptoms.

Data collection and analysis: Two reviewers independently assessed trial quality. Data was extracted from eligible trials on a standardised form by a single investigator that was checked by a second investigator.

Preliminary results: Twenty three studies were included in the systematic review, which evaluated 2665 patients and 1730 controls. H pylori prevalence was 37% in reflux and 46% in controls. Following successful H pylori eradication in 531 patients with duodenal ulcer, heartburn symptom had decreased from 162 patients at baseline to 132 patients at a mean follow-up period of 18 months. In 257 patients with reflux oesophagitis evaluated at 3–57 months, no significant difference in terms of amount of proton pump inhibitors required to maintain remission, dyspepsia scores, and mean reflux values was found between H pylori positive and H pylori negative patients.

Conclusions: Preliminary results, subject to further statistical refinement, do not suggest a protective role for H pylori in reflux disease. The value of eradication in patients with gastro-oesophageal reflux remains open.

A BENEFICIAL EFFECT OF H PYLORI ERADICATION IN REFUX PATIENTS IN THE COMMUNITY

R.C. Stuart, C. Craig, C. Morran, H. Burns, K. Harden, A. Power, D. Walsh, A.J. Morris. ACID1 Study Group, Digestive Diseases Centre, Glasgow Royal Infirmary, UK

Theoretical concerns have been raised about H pylori eradication in patients with reflux disease. The effect of H pylori eradication in patients in general practice with reflux is not known. These patients...
A POTENTIAL NEW INDICATION FOR PROTON PUMP TREATMENT OF UNEXPLAINED CHEST PAIN: A
on maintenance therapy and may be beneficial in reducing prescribing
ation does not adversely a

H pylori
was determined using
H pylori
eradica-

Cough
and 19 patients had an abnormal motility profile (11 patients
chronic cough mean age 57.5 years (range 37 to 76), mean cough
oesophageal dysmotility.

It has been reported that the chronic cough of patients with proven
Gastric acid, providing a barrier to acid reflux into the
Gaviscon Advance (GA) form strong, buoyant alginate rafts on

Introduction:

overlapped, 4 of this overlap group had no reflux symptoms). Cough

Methods:

over an 18-month period, 40 patients (21 female) with
chronic cough mean age 57.5 years (range 37 to 76), mean cough
oesophageal manometry has identified a subgroup of chronic cough

Abstract 92, Table 1

<table>
<thead>
<tr>
<th>Heartburn</th>
<th>Osophagus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved ≥3</td>
<td>H pylori eradicated</td>
</tr>
<tr>
<td>32.7%</td>
<td>21.7%</td>
</tr>
<tr>
<td>Deteriorated ≥3</td>
<td>7.9%</td>
</tr>
<tr>
<td>Unchanged</td>
<td>59.4%</td>
</tr>
<tr>
<td>Drug therapy 1 year post Rx</td>
<td>35.6%</td>
</tr>
<tr>
<td>% off therapy</td>
<td>2.7%</td>
</tr>
<tr>
<td>% change to PPI</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: *H pylori* eradication in the community is of benefit in
patients on therapy with uninvestigated heartburn. *H pylori* eradica-
tion does not adversely affect patients with endoscopic oesophageal
on maintenance therapy and may be beneficial in reducing prescribing
costs.

A POTENTIAL NEW INDICATION FOR PROTON PUMP INHIBITORS: CHRONIC COUGH ASSOCIATED WITH OESOPHAGEAL DYSMOTILTY

M. Dakkak1, J.A. Kastelik2, G.K. Buckton1, C.M. Smith1, A.H. Morice1.
1Dept of Gastroenterology, Hull Royal Infirmary; 2Academic Dept of Medicine, University of Hull, Hull, UK

It has been reported that the chronic cough of patients with proven
gastrooesophageal reflux (GOR) may respond to proton pump inhab-
tors (PPI), but less is known about those cough patients who have
oesophageal dysmotility.

Methods:

Over an 18-month period, 40 patients (21 female) with
chronic cough mean age 57.5 years (range 37 to 76), mean cough
duration of 9.3 (0.16 to 50) years underwent oesophageal manometry
and 24-hour pH monitoring. 31 patients had reflux symptoms while 9
did not. Patients with abnormal results received standard doses of
PPI. GOR was diagnosed if pH below 4.0 was recorded in 3.5% or
more of total time. Dysmotility was diagnosed when more than 30%
of non-transmitted oesophageal peristaltic waves were recorded
during 10 wet swallows.

Results:

10 patients had normal results, interestingly 9 of those
had reflux symptoms. 22 patients had positive 24-hour pH monitoring
and 19 patients had an abnormal motility profile (11 patients
overlapped, 4 of this overlap group had no reflux symptoms). Cough
responded well to PPI therapy in 19 patients (86.4%) with positive
pH recording and 14 patients (73.7%) with abnormal motility profile.

Conclusions: The absence of reflux symptoms does not exclude
abnormal oesophageal motility or abnormal 24-hour pH recording.
Oesophageal manometry has identified a subgroup of chronic cough
patients with manometric abnormalities who respond to PPI therapy.
A randomised trial is needed to verify these pilot results.

TREATMENT OF UNEXPLAINED CHEST PAIN: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF AMITRIPTYLINE

P.I. Lim, S.A. Lewis1, R.G.P. Watson, B.T. Johnston, Dept of Gastroenterology, Royal Victoria Hospital, Belfast; 1Dept of Anaesthetics, Ulster Hospital, Dundonald, UK

Background: 10–20% of patients undergoing coronary angiography
for investigation of chest pain have no significant coronary artery
stenoses. Visceral hypersensitivity plays an important role in the
pathogenesis of unexplained chest pain (UCP). Tricyclic antidepress-

Aim: To determine the effects of low dose Amitriptyline on the
frequency of chest pain, oesophageal sensitivity and quality of life
of patients with UCP.

Methods: Thirty-nine patients with UCP were entered into the
study following baseline assessment of psychosocial profile, quality
of life, oesophageal manometry, oesophageal sensitivity and 24-hour
ambulatory oesophageal pH monitoring. Patients were randomised
in a double-blind fashion to Amitriptyline 25 mg nocte (21 patients), or
placebo (18 patients) for 4 weeks. Daily records of chest pain
frequency and severity were maintained for 2 weeks prior to entry and
for the duration of the trial. Intra-oesophageal balloon distension was

Results: Sixteen patients in each of the 2 treatment groups
completed the study. There was no difference in mean age, gender,
baseline psychosocial profile, quality of life scores, oesophageal man-
ometry, oesophageal sensitivity and pH monitoring between the 2
groups (p>0.05). Patients on Amitriptyline showed no significant
improvement in chest pain frequency (p=0.66) or severity (p=0.71)
when compared with patients on placebo. Oesophageal sensory and
pain thresholds of patients on Amitriptyline were not significantly
altered (p=0.98 and p=0.54) when compared with patients on placebo.
Patients on Amitriptyline had no improvement in their SF-36 scores
(p>0.05) when compared with placebo patients.

Conclusions: Low dose Amitriptyline does not improve the
symptom of chest pain or quality of life of patients with UCP. Visceral
sensitivity in these patients is not altered by low dose amitriptyline.

IN VITRO REFLUX RESISTANCE IN ALGINATE RAFTS

I.G. Jolliffe, F.C. Hampson, R. Campbell, P.W. Dettmar. Reckitt Benckiser
Healthcare (UK) Ltd., Danson Lane, Hull HU8 7DS, UK

Introduction: The anti-reflux products Liquid Gaviscon (LG) and
Gaviscon Advance (GA) form strong, buoyant alginate rafts on
contact with gastric acid, providing a barrier to acid reflux into the
oesophagus. The objective of this study was to compare the in vitro
performance of LG and GA in tests designed to be representative of
the forces involved in reflux into the oesophagus. Rafts were forced
to extrude or rupture through an orifice similar in cross sectional area
to the relaxed lower oesophageal sphincter and resistance to reflux was
measured with a Texture Analyser.

Methods: Rafts were formed by adding a maximum dose of product
(20ml of LG or 10ml of GA) to 150ml of 0.1M HCl at 37°C,
inside a cylindrical forward extrusion cell fitted with a base disc giving
an extrusion orifice of either 10, 15 or 20mm diameter, in a beaker.
After stabilisation for 30 minutes, resistance to reflux by extrusion was
tested by a plunger fitted to the Texture analyser. Resistance to reflux
by rupture was tested by a 9mm diameter cylindrical rod fitted to the
Texture analyser. Typical weights and volumes of rafts were also
measured.

Results: The force required to extrude GA through a 10mm or-
ifice (3.0Kg) was significantly greater than that required for LG
(2.3Kg). The force required to extrude both products decreased with
increased orifice size, but at the largest orifice size (20mm) there was
no significant difference. The force required to rupture GA rafts
(47.4g) was significantly greater than that required for LG rafts
(25.2g). GA rafts typically had weights of 20–25g and volumes of
30–42ml. LG rafts typically had weights of 30–35g and volumes of
90–100ml.

Discussion: Rafts of GA are more resistant to simulated reflux
than those of LG, either by an extrusion or a rupture mechanism. GA
products are a more dense gel, and also the LG raft contains much more
CO2. The same alginate dose (1g) thus creates a buoyant but weaker
raft in LG, which may be less likely to suppress reflux than the
stronger GA raft.

Conclusion: Gaviscon Advance performs better than Liquid
Gaviscon in in vitro tests designed to assess the ability of alginate
products to resist reflux.
096 PSYCHOSOCIAL PROFILE, OESOPHAGEAL FUNCTION AND QUALITY OF LIFE OF PATIENTS WITH UNEXPLAINED CHEST PAIN

P.L. Lim, S.A. Lewis1, R.G.P. Watson, B.T. Johnston. Dept of Gastroenterology, Royal Victoria Hospital, Belfast; Dept of Anaesthetics, Ulster Hospital, Dundonald, UK

Background: 10%-20% of patients undergoing coronary angiography for investigation of chest pain have normal coronary arteries. Oesophageal dysfunction, psychiatric abnormalities and visceral hypersensitivity are possible aetiologic factors. Despite a good prognosis, most patients continue to experience chest pain with impaired functional status and quality of life.

Aims: To compare the psychosocial profile, oesophageal manometry, oesophageal sensitivity and quality of life of patients with unexplained chest pain (UCP) with those of healthy age and sex-matched controls (HC). To determine the incidence of gastro-oesophageal reflux disease in UCP patients.

Methods: Sixty-one patients with UCP and 19 HC were recruited. All subjects completed the Hospital Anxiety and Depression (HAD) Scale, Interview Schedule for Social Interaction (ISSI) and Short Form-36 (SF-36) quality of life questionnaires. Subjects then underwent oesophageal manometry and intra-oesophageal balloon distension. 24-hour ambulatory oesophageal pH monitoring was performed on UCP patients.

Results: UCP had higher mean anxiety (8.7 vs 4.7, p<0.001) and depression (4.7 vs 1.5, p<0.001) scores. 21/59 (36%) of UCP had abnormal HAD scores (p<0.001). Their mean ISSI ADAT score was higher (8.2 vs 6.6, p=0.02) but mean AVAT, AVSI and ADSI scores were not significantly different from those of HC. All the SF-36 scores were lower in UCP (p<0.01). 11/48 (23%) of HC had abnormal oesophageal manometry (p<0.05). UCP had lower sensory (11.2 ml vs 17.9 ml, p<0.001) and pain thresholds (15.3 ml vs 20.5 ml, p=0.002) on intra-oesophageal balloon distension. 26/48 (54.2%) of UCP had positive pH studies.

Conclusions: UCP patients have a higher tendency to anxiety and depressive disorders but have good social support. Their quality of life is impaired due to continuing chest pain. The incidence of oesophageal dysmotility is not significantly different from that of healthy controls. However, UCP patients show evidence of visceral hypersensitivity and have a high incidence of gastro-oesophageal reflux disease.

097 DOES PNEUMATIC DILATATION AFFECT THE OUTCOME OF LAPAROSCOPIC CARDIOMYOTOMY?


Background: Controversy surrounds the use of laparoscopic cardiomyotomy as the primary treatment of achalasia or as a second-line treatment following the failure of non-surgical treatment. Laparoscopic cardiomyotomy may be technically more difficult following pneumatic dilatations and the aim of this study was to compare the outcome of primary laparoscopic cardiomyotomy to that performed following failed pneumatic dilatation.

Methods: Laparoscopic cardiomyotomy was performed in 7 patients following a median of 4 pneumatic dilatations (group A) and in 5 patients as their primary treatment (group B). Outcome was measured using manometry, modified DeMeester symptom scoring system and a quality of life questionnaire.

Results: There were no significant differences between groups A and B in sex, age, preoperative modified DeMeester score or mean barrier pressure. Six of 7 group A patients had evidence of peri-oesophageal and submucosal fibrosis at surgery, but this was not detected in group B patients. Operative time was slightly longer in group A patients. There was no difference in complication rates (a primary haemorrhage in group A and an oesophageal perforation in group B) and both groups had a significantly improved modified DeMeester score at 6 weeks and at long-term follow up (median 26 months). Eleven of 12 patients would choose laparoscopic cardiomyotomy as their primary treatment if newly diagnosed with achalasia.

Conclusions: Laparoscopic cardiomyotomy is safe and effective as a primary or second-line treatment following previous pneumatic dilatations in patients with achalasia.

098 LAPAROSCOPIC CARDIOMYOTOMY FOR ACHALASIA

G.M. Tierney1, P.C. Bornman, I.J. Beckingham1. Groote Schuur Hospital, Observatory 7925, Cape Town, South Africa; ‘Queen’s Medical Centre, Nottingham, UK

Introduction: Laparoscopic cardiomyotomy is an accepted treatment for achalasia. It has advantages over the standard surgical approaches of thoracotomy and laparotomy. This series compares patients treated with laparoscopic cardiomyotomy de-novo with those who had undergone previous failed balloon dilatation.

Methods: Twenty-two patients underwent a single anterior cardiomyotomy for achalasia. Twelve had previously undergone minimum of 2 (range 2–7) balloon dilations. Ten patients had no previous treatment.

Results: Mucosal tears were seen in 4 patients in the previously dilated group, there were none in the de-novo group. In those patients with no previous treatment there was no requirement for post-operative dilatation. In the previously dilated group, 2 patients required further dilatation. Operative time was significantly longer (median 150 mins vs 120 mins, p<0.05 Mann-Whitney) in the previously dilated group, despite the fact that this group had fewer simultaneous anti-reflux procedures. Post-operative stay was significantly reduced in the non-dilated group (median 2 v 4 days, p<0.05 Mann-Whitney).

Conclusion: Laparoscopic cardiomyotomy provides relief from the symptoms of achalasia even in patients who have undergone previous balloon dilatation. However, there is a significant increase in complications, operative time and post-operative stay in those patients who have undergone previous balloon dilatation. This series supports the concept that the best first line treatment for achalasia is laparoscopic cardiomyotomy.

099 QUALITY OF LIFE AFTER LAPAROSCOPIC ANTI-REFLUX SURGERY

J.M. Blazey1, R. Harling1, M.H. Thompson1. Division of Surgery, Bristol Royal Infirmary, Bristol; Dept of Surgery, Southmead Hospital, North Bristol NHS Trust, UK

Laparoscopic treatment of gastro-oesophageal reflux disease (GORD) has largely replaced open surgery. This study compared the impact of laparoscopic anti-reflux surgery on quality of life (QL) compared to chronic proton pump inhibitor therapy. Prospective clinical data of 53 consecutive patients (33 men, mean age 48) undergoing laparoscopic anti-reflux surgery and 25 patients (18 men, mean age 49) on proton pump inhibitors for more than 12 months awaiting surgery were compared along with questionnaires validated for use in patients with GORD. Three patients required revisional surgery (2 for recurrent reflux). 41 patients, (77% response rate) who had undergone fundoplication and 20 (80% response) patients on medical therapy returned questionnaires. After fundoplication, patients reported significantly fewer digestive problems interfering with daily activities, sleep and eating (p<0.001) than patients receiving proton pump inhibitors. Fewer patients with worry and anxiety (p < 0.001) were also reported. Overall QL scores from patients who had undergone fundoplication were significantly better (p < 0.0001) than scores from patients awaiting surgery. These data show that laparoscopic fundoplication is an effective procedure that controls reflux and produces a good QL. Quality of life data contribute to informed decision making for patients with GORD.

100 DEOXYCHOLIC ACID AND APOPTOSIS IN OESOPHAGEAL CARCINOMA CELL LINES

J.A. Todde1, D.A. Johnston1, J.K. Hillott. 1Peterborough District Hospital, Peterborough, PE3 6DA; 2Nenehills Hospital & Medical School, Dundee DD1 9SY, UK

Background: Previous studies have demonstrated that bile acids can damage oesophageal mucosa. However the concentrations of bile acids that were used, are not normally seen in the oesophagus in gastro-oesophageal reflux disease. The aim of this study was to assess if physiological concentrations of bile acids can damage oesophageal cells.

Method: OE21 (oesophageal squamous carcinoma) and OE33 (oesophageal adenocarcinoma) cell lines were used. Cells were grown to 50% confluence using serum supplemented RPMI 1640 medium.
They were exposed to 0, 5, 10 and 100 micromoles/l of deoxycholic acid (DCA) for 24 hours at pH 7.4. The ability to cause cellular damage was assessed by the induction of apoptosis. The induction of early apoptosis was detected by FACS scanning using Annexin V FITC and Propidium Iodide.

**Results:** There was a significant effect on early apoptosis seen in OE21 cells (p<0.03, Friedman’s test). The most marked effect was seen at 5 micromoles/l of DCA, the median percentage of cells in early apoptosis increasing from 1.65 at 0 micromoles/l to 2.60% at 5 micromoles/l of DCA. There was also a significant effect of DCA seen on early apoptosis in OE33 cells (p<0.041, Friedman’s test). The most marked effect was seen at 100 micromoles/l of DCA. The median percentage of cells in early apoptosis increased from 1.90% at 0 micromoles/l to 3.10% at 100 micromoles/l of DCA.

**Conclusions:** Physiological concentrations of deoxycholic acid cause damage oesophageal cells at pH 7.4. Bile acid induced damage may have an important role in the complications of gastrooesophageal reflux disease, especially when oesophageal pH is greater than 4.

**101 THE ROLE OF ANTRODUODENAL DYSMOTILITY IN GASTRO OESOPHAGEAL REFLUX DISEASE AND BARRETT’S COLUMNAR LINED OESOPHAGUS**

R.M. Navaratnam, A. Watson, M.C. Winslet. University Dept of Surgery, Royal Free Hospital, London NW3 2QG, UK

**Aims:** Antroduodenal dysmotility has been implicated in the pathogenesis of duodenal reflux (DGOR), which in turn is thought to be particularly pertinent in the delivery of bile to the distal oesophagus. The role of alkaline reflux and its implication in GOR and its sequelae is well recognised. Non invasive assessment of antral dysmotility, utilising electrogastrography (EGG) and antral ultrasound (AS), in GORD is well documented, there are however no previous comparative studies with Barrett’s CLO.

**Methods:** A prospective study group of 7 asymptomatic control patients, 15 patients with Barrett’s CLO (mean age 60, no evidence of high grade dysplastic changes, 4 patients with short segment Barrett’s CLO) and 30 patients with varying grades of endoscopic oesophagitis (mean age 52, 5 patients with grade IV Savary Millar changes, the remainder had grade I - 11 changes) was undertaken. Each patient underwent initial preprandial EGG and AS analysis, followed by a standardised test meal (500 Kcal) and subsequent post prandial EGG and AS analysis for an identical time period.

**Results:** Our results reveal that the mean pre and post prandial frequencies for all patient groups fall within normal limits ie slow wave activity is greater than 70 % in all patient groups. However, the degree of antral dyssmotility (both pre and post prandial values) was more marked in the Barrett’s CLO and GORD group respectively in comparison to the control group (p = 0.001). In addition, postprandial frequencies were delayed in the Barrett’s CLO group in comparison to the GORD group (p = 0.08). Increased antral dysmotility was identified in 30% of the Barrett’s CLO group in comparison to GORD patients and asymptomatic controls.

**Conclusion:** This study suggests that antroduodenal dysmotility is more marked in a Barrett’s CLO patient group in comparison to a GORD and an asymptomatic control group. This may partly explain the increased presence of bile in the oesophageal refluxate in Barrett’s CLO patients and be associated with their recognised increased morbidity.

**102 IS MUCOSAL SENSIVITY A RELIABLE PREDICTOR OF DISEASE SEVERITY IN BARRETT’S COLUMNAR LINED OESOPHAGUS?**

R.M. Navaratnam, A. Watson, M.C. Winslet. University Dept of Surgery, Royal Free Hospital, London NW3 2QG, UK

**Aims:** The metaplastic epithelium in Barrett’s columnar lined oesophagus (CLO) has both premalignant potential and reduced sensitivity to long standing acid reflux. The role of alkaline reflux and its particular implication in Barrett’s CLO and its sequelae, oesophageal adenocarcinoma is well recognised, however, there are no studies acknowledging the sensitivity of the metaplastic epithelium to alkaline reflux.

**Methods:** A prospective study group of 8 asymptomatic control patients, 22 patients with Barrett’s CLO (mean age 64, no evidence of high grade dysplastic changes, 5 patients with short segment Barrett’s CLO) and 40 patients with varying grades of endoscopic oesophagitis (GORD) (mean age 51, 9 patients with grade IV Savary Millar changes, the remainder had grade I - 11 changes) was undertaken. Perfusion of the recognised endoscopic abnormality, following the placement of a fine bore nasogastric tube with 3 different solutions of 30 ml 0.1M hydrochloric acid, 30 ml 0.1 M sodium bicarbonate and 30 ml normal saline was undertaken. The patients were unaware of the composition of the solutions and were asked if the infusion of the above solutions induced heartburn and if so, to grade it on a scale of 0 (asymptomatic) - 3 (severe symptoms). Symptom onset, was also noted and calculated with a score of 1 for immediate heartburn, 2 for intermediate and 3 for late onset symptoms.

**Results:** Using the independent t test, mucosal sensitivity in the Barrett’s CLO group was reduced to both acid and alkaline infusion in comparison to asymptomatic controls (p < 0.001) and reduced to acid infusion alone in comparison to the GORD patient group (P < 0.001). Symptom onset was delayed in the Barrett’s group in comparison to the GORD and asymptomatic groups respectively.

**Conclusion:** The reduction in mucosal sensitivity in Barrett’s CLO to both acid and alkaline perfusion, may explain why a significant number of patients with this condition present de novo with severe disease or an occult malignancy.

**103 ACID SUPPRESSION IN BARRETT’S OESOPHAGUS: DEMOGRAPHIC AND CLINICAL FEATURES AS PREDICTORS OF ADEQUACY**

M.J. Gibbons, R.G.P. Watson, B.T. Johnston. Dept of Medicine, The Queen’s University of Belfast, Belfast BT12 6BA, Northern Ireland, UK

Barrett’s oesophagus (BO) is a premalignant condition. Recent evidence suggests that a reduction in oesophageal acid exposure promotes differentiation and limits proliferation in Barrett’s mucosa. The aim of this study was to determine the value of demographic and clinical features in the identification of those patients with BO demonstrating an inadequate response to acid suppression. Patients with BO were recruited from routine endoscopy lists and outpatient clinics. Inclusion criteria included a Barrett’s segment of at least 3cm with specialised intestinal metaplasia on biopsy. Demographic and clinical features were recorded including time interval from diagnosis, smoking and alcohol history, length of Barrett’s segment, presence of dysplasia or neoplasia and presence of mucosal inflammation on biopsy. Twenty-four hour oesophageal pH monitoring was performed on maintenance acid suppression therapy when rendered asymptomatic (reflux <=x1/month) to determine the adequacy of treatment. Thirty-three subjects were recruited. Seventeen (51%) had abnormal acid exposure despite acid suppression therapy.

**Abstract 103, Table 1**

<table>
<thead>
<tr>
<th>Normal pH</th>
<th>Abnormal pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=16</td>
<td>n=17</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>9:7</td>
</tr>
<tr>
<td>Mean age</td>
<td>56.4</td>
</tr>
<tr>
<td>Smoking history (%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Alcohol history (%)</td>
<td>11 (69%)</td>
</tr>
<tr>
<td>Median duration (IQR)</td>
<td>3 (1-3)</td>
</tr>
<tr>
<td>Median length (cm) (IQR)</td>
<td>6.75-9.25</td>
</tr>
<tr>
<td>Low grade dysplasia (%)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>Mucosal inflammation (%)</td>
<td>14 (88)</td>
</tr>
</tbody>
</table>

A significant number of Barrett’s patients are undertreated yet no single demographic or clinical feature predicts inadequate therapy. The use of pH monitoring would ensure adequate acid suppression is achieved.

**104 SYMPTOM REPORTING AND THERAPEUTIC REQUIREMENTS IN BARRETT’S OESOPHAGUS**

M.J. Gibbons, R.G.P. Watson, B.T. Johnston. Dept of Medicine, The Queen’s University of Belfast, Belfast BT12 6BA, Northern Ireland, UK

Patients with Barrett’s oesophagus (BO) are relatively insensitive to oesophageal acid exposure. Consequently they may be undertreated with the risk of ongoing oesophagitis, stricture formation and possibly malignant transformation. The aim of this study was to assess the reliability of reflux symptom reporting as a guide to the adequacy of acid suppression.
suppression therapy in BO and to determine therapeutic requirements in refractory cases. Patients with BO of 3 cm or greater in length and specialised intestinal metaplasia on biopsy were recruited from endoscopy and outpatient lists. Maintenance acid suppression was noted with current reflux symptom status using a scoring system for heartburn and acid regurgitation with total minimum and maximum scores of 0 and 6 (0 = no symptoms, 6 = daily symptoms). Twenty-four hour ambulatory oesophageal pH monitoring was then performed on treatment. In those subjects with normal pH profiles acid suppression was increased by double dose increments with repeat pH monitoring at each increment until oesophageal acid exposure was normalised or a maximal dose allowed was reached. Thirty-three patients were recruited. Twenty-three (70%) were maintained on standard once daily maintenance doses of acid suppression with the remainder on varying doses. Seventeen (51%) had an abnormal pH profile despite acid suppression therapy. Acid suppression doses were not significantly different between the groups. However, frequency of therapy differed significantly with twice daily dosing more common in the normal group (p = 0.01). Median reflux symptom scores did not differ between normal and abnormal (1 vs 0, p = 0.42). There were 6 BE patients (3 day old mice). Human inflammation in 5/6 TSP-1 null mice. The metaplasia was less marked PAS-positive, mucin-secreting columnar-epithelium with minimal however, there were focal distal histopathological appearances of a phenotype in BE patients. Nuclear staining was also witnessed in certain sections,Three withdrew before normalisation and 1 had refluxatory reflex at maximal dosing. Symptom reporting is minimal in BO and does not reflect treatment success. Twice daily dosing is more effective than once daily and in the majority of resistant cases only modest dose increments are required.

Transforming growth factor-β (TGF-β) is important for oesophageal embryological development and cell differentiation. Dysregulation of TGF-β2 receptor (TßR-2) expression is implicated in oesophageal carcinogenesis. Mice null for TGF-β or Thrombospondin-1 (TSP-1, a TGF-β activator) may have altered cell differentiation in the distal oesophagus (J. Lawler, Cell 93, 1998). TGF-β null mice also have elevated levels of Th-2 cytokines and we have shown a Th-2 phenotype in BE patients.

Methods: The gut was harvested from TSP-1 null (n=6) and control mice (n=6) and control mice (n=6) and examined histopathologically. Acanth blue and PAS stains for mucins, and immunohistochemistry for cytokeratin 8/18, were performed. Total TGF-β was examined by RT-PCR and active TGF-β immunohistochemically. Endoscopic biopsies from patients with normal oesophageal, oesophagitis and BE were analysed for TGF-β mRNA levels by competitive RT-PCR. Protein levels of TSP-1 and TGF-β were analysed (Western blotting and ELISA) and tissue localisation of TGF-β isoforms and receptors were examined (immunohistochemistry).

Results: Genotyping of tail-DNA confirmed mice identities. Total oesophageal TGF-β levels were unchanged but active TGF-β levels were reduced in the TSP-1 null mice. There was no macroscopic BE. However, there were focal distal histopathological appearances of a PAS-positive, mucin-secreting columnar-epithelium with minimal inflammation in 5/6 TSP-1 null mice. The metaplasia was less marked proximally compared to distally in 3 day old mice (n=4). Acanth blue and PAS studies revealed a reduction in TGF-β mRNA levels in BE compared with uninflamed or inflamed squamous oesophagus (4.0±10^5, 10.2±10^5 8.9±10^5 molecules/µg RNA respectively, p<0.05). TSP-1 protein levels were similar for all tissues. Surface epithelium showed a progressive reduction in TGF-ß1 staining in squamous oesophageal oesophagitis and BE, (p<0.05). TßR-1 and TßR-2 staining was also reduced in BE (p<0.001).

Conclusions: The role of oesophageal levels of TGF-β in the aetiopathogenesis of BE merit further investigation.

ALTHERATION OF PHASE II DRUG DETOXIFYING ENZYME LEVELS IN BARRETT’S METAPLASIA COMPARED TO NORMAL OESOPHAGEAL EPITHELIUM

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Background: The pathogenesis of Barrett’s oesophagus and the subsequent development of oesophageal adenocarcinoma are topical due to the marked increase in cases of oesophageal cancer. Phase II detoxifying enzymes, including GSTs (Glutathione S-transferases), AFAR (Aflatoxin B1 Aldehyde Reductase) and AKR (Aldoketoreductase) protect the mucosa from carcinogens which can cause oxidative damage to cells. Therefore a reduction in these anti-oxidant enzymes can increase the risk of carcinogenesis.

Aims: To discover whether the levels of GST, AFAR and AKR alter due to metaplasia in oesophageal tissue as compared to normal tissue. GST alpha, mu, pi and microsomal GST were studied, along with AFAR and AKR.

Method: Paraaffin-embedded sections were analysed immunohistochemically for expression of different phase II enzymes, using specific polyclonal antibodies. Biopsy specimens from Barrett’s tissue and normal oesophageal tissue were compared with an equal number of specimens from normal oesophageal and gastric mucosa. The slides were examined microscopically and allocated a visual score representing the density of staining.

Results: Expression of the GST enzymes was generally lower in Barrett’s tissue compared to normal oesophageal tissue. Conversely, AFAR and AKR appeared to be expressed to a greater extent in Barrett’s tissue. Nuclear staining was also witnessed in certain sections, though with no definite pattern.

Conclusion: Barrett’s Metaplasia involves the reduction of certain GST enzymes. This alteration is critical as it would render the Barrett’s tissue more prone to neoplastic transformation, due to reduced protection against carcinogens. The nuclear staining also suggests GSTs may act as transcription factors, recruited at times of stress to enhance the resistance of cells against damage.

EXPRESSION OF COX-2 LINKS BARRETT’S METAPLASIA, DYSPLASIA AND ADENOCARCINOMA IN THE OESOPHAGUS

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Background: Barrett’s oesophagus is a pre-malignant condition and progresses in a step-wise fashion to adenocarcinoma. The factors leading to this progression are far from clear. Increased cox-2 expression has been shown to be tumorigenic in in-vitro studies. Furthermore, epidemiologic studies have shown an inverse association between aspirin consumption and the risk of oesophageal cancer.

www.gutjnl.com
Aims: To investigate the expression of cox isoforms in Barrett’s metaplasia, dysplasia and adenocarcinoma.

Method: Oesophageal biopsies from a retrospective sample of patients with Barrett’s oesophagus were obtained. Paraffin embedded sections were stained with monoclonal antibodies for cox-1 and cox-2. A semi-quantitative assessment was made.

Results: Constitutive expression of cox-1 was seen but no significant difference in the pattern of expression was observed within the subgroups. There was a clear progressive increase in cox-2 expression at the deep glandular level from normal to Barrett’s (p=0.006) to dysplasia (p=0.03) to adenocarcinoma (p=0.03). The table shows the mean (SE) cox-2 expression at the surface (a) and deep glandular (d) level:

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Cox-2 (a)</th>
<th>Cox-2 (d)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0.20 (0.20)</td>
<td>0.00 (0.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Barrett’s</td>
<td>0.17 (0.17)</td>
<td>1.00 (0.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>0.80 (0.37)</td>
<td>1.80 (0.2)</td>
<td>0.11</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>1.44 (0.29)</td>
<td>2.11 (0.42)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusion: The progressive increase in cox-2 expression particularly at the deep glandular level may play an important role in the metaplasia to carcinoma sequence in Barrett’s oesophagus.

109 PALLIATION OF OESOPHAGEAL CARCINOMA: A 10-YEAR AUDIT OF CLINICAL PRACTICE

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Background: The majority of patients with oesophageal carcinoma are not suitable for surgical resection and instead require palliative treatment. The aim of this study was to evaluate the indications for non-operative management and the outcome following palliation in a specialist unit.

Methods: 657 patients with oesophageal carcinoma have undergone surgical evaluation in this unit from 1/6/90 to 1/6/00. Staging investigations included thoraco-abdominal CT, endosonography from 1997 and a detailed fitness evaluation. 278 patients underwent subtotal oesophagectomy with curative intent with the remaining 379 patients (58%) requiring palliative treatment modalities.

Results: The median age of palliative patients was 73 years (range 27–97) with a male to female ratio of 1:6:1 and a predominance of adenocarcinoma (n=201) versus squamous cell carcinoma (n=178). Reasons for declining surgery were distant metastases (n=83), unresectable loco-regional disease (n=167) and poor fitness (n=129). 78% (133) of patients with unresectable loco-regional disease had squamous cell carcinoma; 5=3.2; 2df, p<0.001. 13% had no active treatment whilst the initial treatment was an endoprosthesi in 25%, external beam radiotherapy, brachytherapy or chemotherapy in 60% and argon beam in 2%. These were evenly distributed amongst the three patient subgroups although many patients ultimately had multiple treatments. The median survival for all patients from the time of diagnosis was 196 days (range 1–2394 days). Patients with distant metastatic disease had a significantly worse survival (median 168 days) compared to those with unresectable loco-regional disease (median 186 days) and those considered unfit (median 249 days), log rank=16.73; 2df, p=0.0002.

Conclusions: Patterns of dissemination and imoperability vary according to histological subtype. Patients selected for palliation are heterogeneous with different survival characteristics and this must be recognised in trials of palliative therapy.

110 CONTINUING RISE IN INCIDENCE OF OESOPHAGEAL ADENOCARCINOMA IN ENGLAND AND WALES

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Background: In the US and several other western countries the incidence of oesophageal adenocarcinoma (AC) has been rising rapidly. No recent data has been reported from England and Wales. The present study is based on the data from the whole population of England and Wales between 1971–1993 released by Office of National Statistics.

Methods: 99280 cases of oesophageal cancer registered by regional cancer registries were analysed. Age-adjusted incidence rates of AC (ICD-O codes 8140–8380) and squamous cell carcinoma (SCC) (ICD-O codes 8050–8080) were calculated using European Standard Population. Rates were corrected for the proportion of cases with no histology in the early 1970s and no sub-site specification throughout the study period.

Results: Age adjusted incidence rates per 100000 AC increased from 1.49 and 0.42 in 1971 to 5.24 and 1.12 in 1993 in men and women respectively. The rate of increase was greater in older age-groups. The increase was seen in all sub-sites of the oesophagus. The same figures for SCC were 2.64, 2.08, 2.74 and 2.42. Gastric cardia AC also increased from 2.42 to 5.98 in men and 0.65 to 1.63 in women during the same time period.

111 PATHOLOGY OF EARLY ADENOCARCINOMA OF THE OESOPHAGO-GASTRIC JUNCTION: THERAPEUTIC IMPLICATIONS

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Background: Endoscopic treatment modalities are increasingly being utilised for early oesophago-gastric tumours as an alternative to surgery. The aim of this study was to evaluate local growth patterns and regional dissemination of early adenocarcinoma (ACA) of the oesophago-gastric junction (OGJ) in surgically resected specimens in order to clarify the optimal therapeutic strategy to manage such tumours.

Methods: The clinico-pathological data of 64 consecutive patients with ACA of the OGJ confined to the mucosa or submucosa who underwent surgery from 1/4/90 to 1/10/00 were studied. Patients with lower oesophageal ACA (n=49) underwent radical transthoracic subtotal oesophagectomy whereas a transhiatal radical total gastro-oesophagectomy was employed for tumours of the cardia (n=15).

Results: The median age was 66 (31–79) with a male to female ratio of 4:1. The incidence of adjacent intestinal metaplasia for oesophageal tumours was 96% (47/49) compared to only 47% (7/15).
EFFECT OF HELICOBACTER GASTRITIS ON GASTRIC

Background/Aims: H. pylori infection is associated with delayed healing of peptic ulcers. Ulcer healing is dependent upon angiogenesis or new blood vessel formation. Proliferation of endothelial cells (ECs) is a crucial process in angiogenesis. This study aimed to determine whether genotypically different strains of H. pylori inhibited the proliferation of ECs in vitro.

Methods: Three H. pylori strains were tested on human dermal microvascular ECs (HuDMECs): a cagA+ vacA s1/m1 (toxigenic) strain, its VacA- (non-toxigenic) isogenic mutant and a cagA- vacA s2/m2 (non-toxigenic) strain. Campylobacter jejuni and Escherichia coli were also tested. An MTT assay quantified overall HuDMEC viability. Dual staining using Hoechst and Propidium Iodide distinguished between apoptosis/necrosis and allowed total viable cell counts to be determined. HuDMECs were seeded into 96 well plates and exposed to 50μL aqueous extracts of bacteria or PBS. The two assays were performed after 24, 48, 72 and 96 hours.

Results: Cell viability and total cell number increased significantly (p<0.01) at all time points up to 96 hrs in both PBS and E. coli treated cells. However, no increases in viability or total cell number were observed at any time point with H. pylori or C. jejuni treated cells. This anti-proliferative effect observed with H. pylori and C. jejuni was not accompanied by apoptosis or necrosis.

Conclusion: All H. pylori strains decreased the proliferation of HuDMECs due to a cytostatic but not cytotoxic effect. This effect also appears to be associated with the Campylobacter family. Inhibiting the proliferation of ECs would prevent angiogenesis at the ulcer site. This may explain the delay in ulcer healing associated with H. pylori infection.

Stomach/Duodenum Posters: 112–142

112 EFFECT OF HELICOBACTER GASTRITIS ON GASTRIC ANTIBIOTIC SECRETION IN MAN

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Introduction: Subgroup analysis of Helicobacter eradication trials suggests that patients with more severe gastritis have a higher rate of treatment success.

Aim: To test the hypothesis that H. pylori gastritis increases gastric secretion rates of metronidazole, amoxicillin and clarithromycin by studying patients before and after treatment.

Methods: 22 patients and 9 healthy volunteers underwent gastroscopy to diagnose gastritis and H. pylori status. Subjects received a intra-gastric phenol red infusion and an intravenous antibiotic infusion, after a five day pretreatment with omeprazole and an intra-gastric phenol red infusion and an intravenous antibiotic infusion. Pyloric losses were corrected for infusion, after a five day pretreatment with omeprazole and an intra-gastric phenol red infusion and an intravenous antibiotic infusion. Pyloric losses were corrected for infusion, after a five day pretreatment with omeprazole and an intra-gastric phenol red infusion and an intravenous antibiotic infusion.

Results: Gastric clearance of antibiotics (ml/min) (table 1).

Abstract 112, Table 1

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Amoxicillin</th>
<th>Clarithromycin</th>
<th>Metronidazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. pylori -ve volunteers</td>
<td>0.270 ± 0.205</td>
<td>6.61 ± 2.82</td>
<td>1.85 ± 1.03</td>
</tr>
<tr>
<td>H. pylori +ve patients</td>
<td>0.434 ± 0.418</td>
<td>5.66 ± 6.14</td>
<td>1.76 ± 0.76</td>
</tr>
<tr>
<td>post-treatment</td>
<td>0.362 ± 0.361</td>
<td>10.18 ± 7.70</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusions: Contrary to expectations, Helicobacter gastritis did not significantly increase gastric antibiotic transfer. This may be due to the large inter-subject variability in gastric antibiotic secretion rates, which limits the usefulness of human experiments for examining gastric antibiotic secretion mechanisms. PV Sherwood was supported by an Astra Research Fellowship.

113 EFFECTS OF GENOTYPECALLY DIFFERENT STRAINS OF HELICOBACTER PYLORI ON HUMAN MICROVASCULAR ENDOTHELIAL CELL PROLIFERATION IN VITRO

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Mutations in the 23S rRNA gene were examined in the nine macroside-resistant H. pylori strains. Seven of the nine isolates had mutation at position 2143 (A to G). Two of the seven isolates had an additional T to C mutation at either position 2182 or 1934. Mutation at position 2182 (T to C) has previously been found not to be associated with macrolide resistance. However, the mutation at position 1934 has not previously been reported. Of the nine isolates, one carried only a T to C mutation at position 2182 and one had no mutation in the 23S RNA, implying that other mechanisms are responsible for the resistance in these strains. The results show that macroside resistance, occurring by different mechanisms, is currently found in 13% of our H. pylori isolates.
COST EFFECTIVENESS OF HELICOBACTER PYLORI ERADICATION IN PATIENTS ON LONG-TERM H2 RECEPTOR ANTAGONISTS. A LARGE PROSPECTIVE STUDY IN GENERAL PRACTICE

S. Verma, M.H. Gaffar. Dept of Gastroenterology, Hull Royal Infirmary, Anlaby Road, Hull HU13 OEL, UK

Objectives: To assess the economic and symptomatic benefits of Helicobacter pylori (HP) eradication in primary care in patients maintained on long-term H2 receptor antagonists (H2,RA).

Design: Prospective study.

Setting: Six practices in the Humberside area.

Subjects: 1100 patients identified to be on long-term H2RA in the six practices.

Interventions: Identifying HP status using serology. HP positive patients were then offered standard seven-day proton pump based triple therapy, followed by a urea breath test (UBT) to confirm HP eradication.

Main outcome measures: Improvement in dyspepsia symptom scores, impact on amount of H2RA being consumed, and economic benefits.

Results: Sixty-three (297) percent of the patients tested had a positive serology for HP, the majority of whom (58%, 172) had prior evidence of peptic ulcer disease. The mean duration of therapy and mean time since endoscopy/barium studies was significantly longer in patients with peptic ulcer disease compared to their counterparts with non-ulcer dyspepsias and gastro-oesophageal reflux disease. After successful HP eradication, on an intention to treat basis 62% of the patients could either stop or significantly reduce dosage of their H2RA. There was also significant reduction (p<0.00001) in the mean dose of H2RA being used and severity of symptoms at the end of the study period.

Conclusion: Almost two thirds of patients on long-term H2RA will have a positive serology for HP, the majority of whom will have peptic ulcer disease. In 60% of cases HP eradication led to significant improvement in symptom scores and reduction in dosage of H2RA being consumed. Cessation or reduction in long-term H2RA prescribing is cost effective.

DOES HELICOBACTER PYLORI ERADICATION LEAD TO GASTRO-OESOPHAGEAL REFLUX 7A LARGE PROSPECTIVE STUDY IN PRIMARY CARE

S. Verma, M.H. Gaffar. Dept of Gastroenterology, Hull Royal Infirmary, Anlaby Road, Hull HU13 OEL, UK

Background: Helicobacter pylori (HP) eradication is widely recommended in patients with peptic ulcer and treatment may also be useful in some patients with non-ulcer dyspepsia (NUD). It has been suggested recently that gastro-oesophageal reflux may follow HP eradication.

Aim: To assess patients with dyspepsia in HP positive patients on long-term H2 receptor antagonists (H2,RA) in primary care, with special emphasis on the prevalence of gastro-oesophageal reflux after HP eradication.

Patients and methods: A population of patients receiving long-term H2,RA were identified from the computerised records of 6 practices. Dyspeptic symptoms (abdominal pain, indigestion, heartburn, nausea/vomiting, and bloating) were noted and their severity graded as none (0), mild (1), moderate (2) and severe (3) to give a minimum symptom score of 0 and maximum score of 15. The dyspeptic symptoms were further classified into one of the four categories: ulcer-like, reflux-like, dysmotility-like and unspecified. HP status was determined by using standard serological method and those with a positive test were offered a standard one-week HP eradication therapy followed by a urea breath test to confirm HP eradication. Patients were followed up at 0 weeks, 6 weeks, 6 months and 12 months. At each visit the severity of symptoms, nature of dyspepsia and symptom score were recorded.

Results: 297 patients on long-term H2RA with a positive serology for HP were studied. 58% had documented peptic ulcer disease, 19% had non-ulcer dyspepsia and 5% had gastro-oesophageal reflux disease. Successful HP eradication was achieved in 250 patients (84%). 247 patients completed the one-year post HP eradication follow-up. At entry 75% of the patients had unspecified dyspepsia and only 1% were dyspepsia free. At the end of one year 43% were symptom free (p<0.00001). HP eradication also resulted in significant improvement in mean symptom scores (0.5 ± 0.4 vs. 2.1 ± 0.1, p<0.00001). 129 patients (57%) had some degree of reflux prior to HP eradication that persisted in only 31 patients at 12 months (p<0.00001). Only two (0.6%) patients both of whom had duodenal ulcer developed new onset reflux symptoms after HP eradication, which were mild in both the patients and required no treatment.

Conclusion: Unspecified dyspepsia is the commonest type of dyspepsia in HP positive patients on long-term H2,RA. Irrespective of endoscopic diagnosis. Most reflux symptoms noted after HP eradication were also present prior to HP eradication. Denovo gastro-oesophageal reflux symptoms are uncommon after HP eradication.

AN AUDIT OF 13C-UREA BREATH TEST SELF TESTING

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Background: The 13C-urea breath test (13C-UBT) is a reliable, safe, non-invasive and accurate test for the diagnosis of Helicobacter pylori. It is the most accurate test for evaluating H. pylori status following eradication therapy. Since 1998 the Pylobactell kit has been available as a 13C-UBT for use in routine clinical practice. The kit is licensed as a medicinal product and is available as a Prescription Only Medicine. The Pylobactell kit contains all the components for carrying out the test, apart from the test meal. A suitable test meal is 200ml pure orange juice. Usually the 13C-UBT is performed in the hospital under the supervision of a nurse.

Aim: To assess the ability of patients to successfully perform the 13C-UBT in their own home using the Pylobactell kit. To assess the reliability of the results of 13C-UBT performed at home. To test patient’s satisfaction with home testing.

Audit design: Patients referred to the hospital were audited. Each patient performed two 13C-UBT: the first at home and the second at the hospital. The samples were sent blinded for analysis to BSIA analysis centre. Patients were required to complete two questionnaires, one at the time of the home test and one at the hospital.

Results: 50 patients were sent Pylobactell kits. 31 patients provided results to the audit.

Data was analysed using a paired t-Test to examine the results between breath testing at home and in the hospital. There was no significant difference between the results collected at home or in the hospital (p=0.82). Out of 31 patients audited, only 1 patient’s result did not correspond (+ve at home, -ve at the hospital).

Conclusions: Home 13C-UBT is a practical possibility. 100% of patients audited found the Pylobactell test kit easy to use. 81% found the instructions easy to follow. 91% were able to perform the test without any help.

TESTING FOR AND ERADICATION OF H. PYLORI INFECTION IN PATIENTS WITH BLEEDING PEPTIC ULCERS

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Background: H. Pylori (HP) infection should be sought and treated in patients with peptic ulcer bleeding. Successful HP eradication should be confirmed to prevent further bleeding episodes.

Methods: Patients presenting with gastrointestinal haemorrhage and endoscopic evidence of peptic ulcer from January 1998 to January 2000 had their casenotes reviewed. NSAID use, assessment of HP status at initial endoscopy, treatment of HP infection and confirmation of HP status after eradication were studied.

Results: 110 patients (mean age 64 years, range 20–92 years, m:f 71:39) with bleeding peptic ulcers (GU 42, DU 60, GU+DU 8, NSAID related 50) were identified. NSAIDs were continued in 6 cases. HP status was established in 74% (79 / 110). 91% (72 / 79, 48 HP positive, 24 HP negative) were managed appropriately according to their HP status. 12 of the 31 (39%) patients whose HP status was unknown received empirical HP eradication therapy. 7 patients were not available for follow-up. HP testing and treatment is summarised: Overall 26% (27 / 103) were confirmed to be HP negative over the follow-up period (median (range), 14 (1–25) months). Successful HP eradication was documented in only 24% (12 / 51) of patients HP positive at initial endoscopy.

Conclusion: Assessment of HP status in patients with bleeding peptic ulcers is inadequately performed by endoscopists. Although
WHEN IS INITIAL ENDOSCOPY FOR DYSPEPSIA IN PATIENTS OF 50 YEARS OF AGE AND OVER? EXTRAPOLATION BASED ON RESULTS OF A PRIMARY CARE–BASED RCT

Dept of Primary Care and General Practice, The University of Birmingham, UK

Introduction: Dyspepsia may be managed initially either by endoscopic investigation and treatment based on the findings, or by empirical prescribing. An RCT has shown that at one year initial endoscopy is probably cost effective at £1728 per patient ‘cured’. As the initial cost of endoscopy was partly recouped by reductions in prescribing of proton pump inhibitors, we aimed to estimate the time point when the cumulative cost of initial endoscopy was equivalent to usual management. At this point initial endoscopy would be ‘cost-saving’ even if the benefit in symptoms was not maintained.

Methods: Patients with dyspepsia over the age of 50 years were randomised to initial ‘open access’ endoscopy or usual management. Monthly cumulative costs per patient were calculated for the first 2 years following entry to the trial. Costs included dyspepsia medication, courses of H pylori eradication therapy, GP consultations, outpatient attendances and investigative procedures. The cost difference declined from £181 at 3 months to £112 at 24 months. This decrease in cost difference over time was modelled using regression analysis. A projection of cost difference at 5 years, discounted at 3% per annum, was estimated from the best fitting model. A sensitivity analysis to the annual discount rate for costs from 0% and 6% was performed.

Results: The trend in cost differences was best explained by a linear model (R²=0.89). Model: Cost difference= 173.74–3.1 x Month. By 4 years 6 months (95% CI - 4 years 2 months - 4 years 11 months) the initial cost of investigation had been recouped. Discounting costs at 0% and 6% per annum changed this threshold to 4 years 8 months and 4 years 6 months respectively.

Conclusions: Initial endoscopy in dyspeptic patients over the age of 50 may be a cost-saving intervention at 5 years.

DYSPEPSIA PATIENTS ON THERAPY REMAIN SYMPTOMATIC WITH IMPAIRED QUALITY OF LIFE

C. Craig, R.C. Stuart, C. Morrán, H. Burns, K. Harden, A. Power, D. Walsh, A.J. Morris. ACID1 Study Group, Digestive Diseases Centre, Glasgow Royal Infirmary, UK

Despite the scale of prescribing for dyspepsia, little is known about the symptom profile or quality of life of patients receiving maintenance therapy in the community.

Aim: to measure symptoms and quality of life in dyspeptic patients receiving regular acid suppression therapy in the preceding 12 months.

Methods/Results: 4003 such patients were invited to attend a nurse led community dyspepsia clinic and 2353 attended. Exclusions were patients receiving < 3 prescriptions/12 months, patients on therapy in whom cessation of therapy would be inappropriate, and those previously receiving proven successful H pylori eradication. Symptons were assessed using the Glasgow Dyspepsia Severity Score (GDSS) and a digestive disease specific quality of life tool (DDQol). c 12 Urea Breath Testing was performed and 50.8% were positive.

Conclusion: Despite PPI or H. pylori therapy dyspeptic patients remain surprisingly symptomatic and have poor quality of life. Young patients, females, and those on PPI therapy with non-ulcer dyspepsia have highest symptom scores. Age, drug and diagnostic categories had no adverse effect on quality of life. There is considerable room for improvement of dyspepsia symptoms in the community.

SYMPTOMS AND QUALITY OF LIFE IN DYSPEPSIA: A COMPARISON OF CONTINUOUS AND INTERMITTENT THERAPY

C. Craig, A.J. Morris, C. Morrán, H. Burns, K. Harden, A. Power, D. Walsh, R.C. Stuart. ACID1 Study Group, Digestive Diseases Centre, Glasgow Royal Infirmary, UK

Over 2.6 million prescriptions for acid suppression therapy were dispensed in 1999 in Scotland. Patients may receive either continuous or intermittent therapy.

Aim: to assess the factors determining continuous versus intermittent therapy and correlate these with symptoms.

Patients/Methods: 2353 patients receiving ≥ 3 prescription/year attended a community based nurse led dyspepsia clinic. Symptom scores and disease specific quality of life measures were performed using the Glasgow Dyspepsia Severity Score (GDSS) and the Digestive Disease Quality of Life (DDQol) respectively. Carstairs Deprivation Index was used to assign social class.

Results: 58.2% were on continuous therapy and 41.8% were on intermittent therapy. The average number of prescription/year was 7.45.

In this multivariate logistic regression analysis pattern of prescribing did not differ in relation to diagnosis, age or sex. In a separate multivariate linear regression analysis continuous therapy was associated with low GDSS, P<0.05. There was no correlation between prescribing pattern and DDQol scores.

Conclusions: 41.8% of patients receiving regular (≥3 prescriptions/year) acid suppression therapy are on intermittent treatment. Patients from social class 1 & 2 and those receiving PPI therapy are more likely to be on continuous treatment. Continuous treatment was associated with lower symptom severity scores.

THE APPROPRIATENESS OF MEASURING THE BENEFIT OF DYSPEPSIA MANAGEMENT IN TERMS OF QUALITY ADJUSTED LIFE YEARS


Introduction: Cost-effectiveness analyses are often used to assess the health economics of dyspepsia management. This type of analysis is helpful in establishing the most efficient strategy (technical efficiency) and the amount of money spent on managing dyspepsia is appropriate (allocative efficiency). Determining the cost/quality adjusted life year (QALY) gained from dyspepsia management and comparing it with other health care strategies would inform health care decision makers on whether the amount being spent on dyspepsia is appropriate.

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**Methods:** Patients attending an open access endoscopy service were interviewed with the Leeds Dyspepsia Questionnaire and the EuroQol (a validated tool for measuring QALYs). These questionnaires were completed again six months after the endoscopy.

**Results:** 200 patients were recruited to the study (mean age 50 years, range 18–79 years, 48% male) and 165 (83%) were followed up at 6 months. The mean QALY score at baseline was 0.78 (95% CI = 0.75 to 0.81). There was no gender difference in QALYs and there was a trend for QALYs to be negatively correlated with age (<0.002 /year 95% CI = -0.02 to -0.004). Patients with peptic ulcer disease (9%) or oesophagitis (35%) had significantly lower QALY compared to those with a normal endoscopy (0.70 versus 0.79; mean difference 0.1 (95% CI = 0.01 to 0.19)). There was an increase in QALY score of 0.012 6 months after endoscopy but this was not statistically significant (95% CI = -0.02 to 0.05 QALY). 45 patients (27%) were lost during follow-up at 6 months. The mean QALY score at baseline was 0.78 (95% CI = 0.75 to 0.80). Patients with peptic ulcer or oesophagitis (9%) was a trend for QALYs to be negatively correlated with age (-0.002/year 95% CI = -0.004). Patients with peptic ulcer or oesophagitis (9%) had significantly lower QALY compared to those with a normal endoscopy (0.70 versus 0.79; mean difference 0.1 (95% CI = 0.01 to 0.19)). There was also no statistical difference in the change in QALY score between those with peptic ulcer or oesophagitis and those with a normal endoscopy.

**Conclusion:** QALYs as measured by the EuroQol are too insensitive to be used as a tool to investigate dyspepsia.

**123 RABEPRAZOLE VS OMEPRAZOLE IN 7-DAY, TRIPLE-THERAPY H. PYLORI ERADICATION REGIMENS FOR PEPTIC ULCER**

C.J. Hawkey1, J.C. Atherton1, H.C. Treichel1, M. Ravic1, B. Thodleifsson1. 1University Hospital, Nottingham, UK, 1Johanniter Krankenhaus, Genthin, Germany; 1Eisai Ltd, London, UK; 1Landsdópólninn, Reykjavík, Iceland

**Introduction:** Triple-therapy with a proton pump inhibitor (PPI), clarithromycin and amoxycillin or metronidazole is the treatment of choice for H. pylori eradication. Because PPIs vary in their time to and extent of maximum acid inhibition whilst optimal intragastric pH may vary, it is important to measure the efficacy of regimens. We studied the equivalence of two 7-day rabeprazole based regimens (rabeprazole 20mg bd and clarithromycin 500mg bd with amoxycillin 1g bd (RCA) or with metronidazole 400mg tds (RCM) as the supplementary antibiotic with equivalent regimens using omeprazole 20mg bd (OCA or OCM) in 345 patients with peptic ulcer disease and a positive H. pylori urease test. Eradication was defined as a persistently negative 13C urea breath test 4 and 12 weeks after completion of treatment. Factorial analysis was used to determine the overall efficacy of rabeprazole compared to omeprazole and the comparative efficiencies of metronidazole and amoxycillin.

**Results:** The overall H. pylori eradication rate was 87% for patients receiving rabeprazole (per protocol) versus 85% for omeprazole (difference 2%, 95% CI -2.2% to 9.7%, not significant). On intention to treat, the overall eradication rate was 77% for rabeprazole versus 75% for omeprazole. In the amoxycillin subset rabeprazole had a higher eradication rate than omeprazole (per protocol) (95% CI -0.7%, +20.4%). Analysis revealed a significant statistical interaction between the individual PPIs and the supplementary antibiotic used (p=0.017, intention to treat). Eradication rates are shown in the table.

**Abstract 123, Table 1**

<table>
<thead>
<tr>
<th></th>
<th>RCA</th>
<th>OCA</th>
<th>RCM</th>
<th>OCM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eradication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>84</td>
<td>80</td>
<td>80</td>
<td>83</td>
</tr>
<tr>
<td>PPC</td>
<td>94%</td>
<td>84%</td>
<td>79%</td>
<td>86%</td>
</tr>
<tr>
<td>IPP</td>
<td>96%</td>
<td>96%</td>
<td>96%</td>
<td>96%</td>
</tr>
</tbody>
</table>

**Conclusions:** This pivotal phase III study shows that rabeprazole based regimens are highly effective in H. pylori eradication. In particular, eradication rates were especially high with RCA, consistent with previous phase II findings. The differential effect of rabeprazole on the efficacy of amoxycillin and metronidazole has not been shown for a PPI previously and should be treated with caution because it appears statistically implausible and could be a chance finding, but warrants further pragmatic and mechanistic study.

**124 REBOUND ACID HYPERSECRETION AFTER RANITIDINE IS NOT DUE TO IMPAIRED INHIBITORY CONTROL**

D. Gillen, A.A. Wirz, K.E.L. McColl. Dept of Medicine & Therapeutics, Western Infirmary, Glasgow, Scotland, UK

**Introduction:** We have previously reported that there is significant rebound basal and GRP-stimulated acid hypersecretion after 7 days of ranitidine treatment. GRP stimulates secretagogues and inhibitory acid secretory hormones. The GRP-stimulated rebound acid hypersecretion after treatment therefore raises the possibility that the phenomenon may be due to impairment of oxyntic inhibitory control.

**Aim:** To determine whether rebound acid hypersecretion after ranitidine is due to impaired oxyntic inhibitory control of acid secretion.

**Methods/Results:** 14 H. pylori-negative healthy subjects were studied both before and after treatment with ranitidine 300mg/day for 8 weeks. Each subject was studied with basal, Gastrin-17 and CCK-8 stimulated MAO and GRP-stimulated acid secretion studies.

**Abstract 124, Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Before ranitidine</th>
<th>After ranitidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAO (mmol h⁻¹)</td>
<td>2.8 (0.0–13.7)</td>
<td>5.0 (0.6–17.3)</td>
</tr>
<tr>
<td>AO to GRP 40μmol Kg⁻¹ (mmol h⁻¹)</td>
<td>5.0 (1.2–11.6)</td>
<td>10.2 (3.2–25.7)</td>
</tr>
<tr>
<td>% CCK-8 MAO/G-17 MAO</td>
<td>28.9% (5.8–60.1)</td>
<td>26.9% (8.3–48.2)</td>
</tr>
</tbody>
</table>

All values are medians (range); *indicates significantly greater than pre-ranitidine at p<0.006

**Discussion:** We have confirmed that there is significant basal and GRP-stimulated rebound acid hypersecretion after ranitidine. CCK-8 acts equipotently with gastrin at the CCKA/gastrin receptor on the ECL cell to stimulate acid secretion and also on the CCK receptor on oxyntic D cells to inhibit acid secretion. Impairment of inhibitory control would therefore manifest itself as an increased ratio of CCK MAO to G-17 MAO. No such change is found from before to after treatment. This is consistent with there being no impairment of inhibitory control of acid secretion.

**Conclusion:** Rebound acid hypersecretion after ranitidine is not due to impairment of oxyntic inhibitory control. The exact mechanism remains unclear, although it is most likely to be due to increased responsiveness of the H2 receptor to histamine.

**125 ULCER CURED, SYMPTOMS RELIEVED?**


**Introduction/Aim:** We compared omeprazole-based and ranitidine bismuth citrate (RBC)-based H. pylori triple therapy, of which relatively little is known, assessed long-term (1y) outcome, and the impact of eradication (erad) on subsequent symptoms.

**Methods:** Patients with endoscopy-proven healed DU or GU and positive rapid urease & 13C-urea breath tests (UBT) were randomly allocated to receive twice daily for 7 days RBC 400mg/metronidazole (MET) 400mg and either clarithromycin 500mg (RMC), tetracycline 400mg (RMT) or amoxycillin 20mg+amoxycillin 1g + MET 400mg (OAM). Antibiotic susceptibility was assessed by disc diffusion.

**Abstract 125, Table 1**

<table>
<thead>
<tr>
<th></th>
<th>RMC n %</th>
<th>RMT</th>
<th>RMA</th>
<th>OAM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 0</td>
<td>84</td>
<td>80</td>
<td>80</td>
<td>83</td>
<td>327</td>
</tr>
<tr>
<td>Wdrn AE</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8w erad</td>
<td>67/84(80)</td>
<td>48/80(60)</td>
<td>55/80(69)</td>
<td>61/83(73)</td>
<td>71%</td>
</tr>
<tr>
<td>MET-suscept</td>
<td>65/80(81)</td>
<td>38/58(66)</td>
<td>48/67(72)</td>
<td>50/64(78)</td>
<td>78%</td>
</tr>
<tr>
<td>MET res</td>
<td>2/4 (50)</td>
<td>10/22(45)</td>
<td>7/13 (54)</td>
<td>11/19(58)</td>
<td>52%</td>
</tr>
<tr>
<td>Recrudesc</td>
<td>12/67(18)</td>
<td>6/48 (13)</td>
<td>11/55(20)</td>
<td>12/61(20)</td>
<td>18%</td>
</tr>
<tr>
<td>1y erad</td>
<td>55/94(65)</td>
<td>42/80(53)</td>
<td>44/80(53)</td>
<td>49/83(59)</td>
<td>58%</td>
</tr>
<tr>
<td>Erad = negative UBT at 8w.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Mean dyspepsia scores:** Wk 0 6.4, erad (8w,1y) 2.1, 1.9; failed erad 2.4, 1.6. During 1y follow-up after erad (n=190) 34% required H2RA or PPI (2/3 for pre-existing reflux). Endoscopy at 1y in 109/129 followed off treatment showed lesions in 30% (15 with newly developed esophagitis, only 1 with DU) but with little or no symptoms.

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Role of Nurse Led Clinics in the Community: Potential to Improve Care and Reduce Acid Supressant Drug Costs

D.C. Chan 1*, C.U. Onyekwere1, J. Bowey2, P. Patel1. *Gastroenterology Unit, Southampton University Hospital; 1Alma Road Surgery, Southampton; 2Central Southampton Primary Care Group, UK

Background: Costs of acid suppressant drugs (ASD) account for 12% of GPs' budgets. The largest portion of this is for maintenance therapy. However, there is no consistent policy for reviewing the need for long-term therapy.

Aim: To evaluate the impact of nurse led review clinics (RC) in patients receiving long-term acid suppression.

Method: Criterion of long-term acid suppression was defined as those receiving more than 8 weeks of treatment in previous 12 months. Initial tawal of patients was from computer records followed by notes search to establish investigations performed and findings. Patients were invited by post to attend clinic to have drug review according to local guidelines and appropriate life style advice. Prescribing data was obtained from Prescription and Pricing Authority.

Results: Total practice population was 10,725 and 256 (prevalence 2.4%) long-term ASD users were identified. Ninety-three (36.32%) patients attended the clinic. The change in treatment was audited one year later. The following table shows change in treatment in the clinic and one year afterwards:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Review in clinic</th>
<th>One year later</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>Stop</td>
<td>29.31.18</td>
<td>28.30.11</td>
</tr>
<tr>
<td>Step up</td>
<td>2.2.15</td>
<td>3.3.23</td>
</tr>
<tr>
<td>Step down</td>
<td>38.40.86</td>
<td>29.31.18</td>
</tr>
<tr>
<td>No change</td>
<td>24.25.81</td>
<td>33.35.48</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td>93</td>
</tr>
</tbody>
</table>

Only half (6) of the patients with peptic ulcer disease accepted eradication treatment. The practice's pre-intervention (May 98–April 99) ASD costs were £97,940 and were the top drugs prescribed. One year (May 99–April 00) post intervention costs were reduced by £13,660 (-13.94%) to £84,280 and ranked number four.

Conclusion: Structured nurse led lifestyle advice and drug review clinics, based on clear guidelines, produced a sustained reduction in costs and was acceptable to patients.

Proton Pump Inhibitors: Understanding the Prescribing Behaviour of General Practitioners

A.S. Raghunath, A.P.S. Hungin.

Introduction: The introduction of a new class of powerful and effective drugs is recognised as a denominator of upward pressure on drug budgets. PPIs, introduced in 1987, account for £300 million annually, mainly in primary care. We aimed to get a better understanding of the prescribing behaviour of GPs using qualitative methodology.

Method: Focus groups comprising of 20 randomly selected GPs, and a non-random group (purposive sample) of 10 GPs, 15 GP registrars and 5 academic general practitioners were used. Following transcription, content analysis and interpretation was performed using standard qualitative methods (constant comparative; comprehensive data set analysis; deviant case analysis).

Results: Specific categories identified from the analysis included: knowledge and understanding of PPIs as a class of drugs; factors influencing the decision to prescribe them; conditions for which are considered appropriate; long-term prescribing; concerns regarding cost, safety, benefits and risks; views on PPIs being lifestyle drugs; patients' ideas, concerns and expectations; difficulties around practice prescribing and review processes; the role of Helicobacter pylori; step-up vs step-down therapy; gastroscopy referral and non-pharmacological measures.

Discussion: Most GPs had a good working knowledge and understanding of PPIs. However, there was a variation in their levels of knowledge regarding indications for PPIs and justifications for using them. Extreme opinions were held by some GPs and attitudes were influenced by the type of practice (training, inner city) personal experiences, and medicolegal concerns. The study revealed the pluralistic prescribing pattern of GPs with PPIs. This variability is likely to have been influenced by a multiplicity of factors. It follows that guidelines alone are unlikely to be the major influence in altering prescribing behaviour.

Proton Pump Inhibitors in Hospital Practice: Nice or Not


Introduction: Anti-secretory drugs (ASDs) are one of the most widely prescribed group of drugs in hospital practice. In 1996 a hospital audit of ASD use was carried out to accompany the introduction of a locally agreed prescribing protocol (Gut 1997; 40(S1): A39). This audit showed the increasing use of PPIs (45% of ASDs prescribed at that time) and that, despite introduction of an ASD protocol, 51% of patients did not have a licensed indication for their prescribed medication. In July 2000 the National Institute for Clinical Excellence (NICE) published ‘Guidance on the Use of PPIs in the Treatment of Dyspepsia’. An audit was performed in September 2000 to determine the current use of PPIs and the proportion of treatments adhering to this new guidance.

Methods: On three consecutive Tuesdays in September 2000, all acute medical patients prescribed ASDs were identified. Their case-notes were reviewed to identify whether those drugs were being appropriately prescribed according to the NICE guidance document. Appropriate indications include: peptic ulcer disease, H pylori eradication, co-prescription with non-steroidal anti-inflammatory drugs, severe gastro-oesophageal reflux disease, and Barrett's oesophagus.

Results: 329 acute medical patients were identified. 80 patients (24%) were taking ASDs and 50 of these had been prescribed a PPI. PPI use has significantly increased (p<0.05) from 45% to 63% of ASDs since the previous audit in 1996. Only 16 patients (28%) had a recognised indication for the use of a PPI in accordance with the NICE guidelines.

Conclusions: This audit has confirmed the widespread use of ASDs in hospital and the continued increase in PPI use. Despite the earlier introduction of a local protocol and the recent NICE guidance for a majority (72%) of patients are prescribed PPIs outside the current guidelines. The implications of this audit are that closer adherence to the NICE guidelines and continued audit could potentially offer a substantial reduction in the usage of PPIs and their associated drug costs.

Rheological Studies of Breakdown and Reformation of Gastic Mucus Gel Demonstrates Its Unique Flow Properties Which Are Essential to the Maintenance of an Intact Protective Barrier

C. Taylor, A. Allen, P.W. Dettmar, J.P. Pearson. Dept of Physiological Sciences, The Medical School, University of Newcastle upon Tyne, NE2 4HH; ‘RedbrickHealthcare, Davenham Lane, Hall HUB 7DS, VR

Introduction: We have previously demonstrated the presence of two distinct gastric mucus gels, termed shear resistant and shear compliant, which have the putative functions of protective barrier maintenance and lubrication respectively. Here we have investigated rheologically the shear resistant mucus gel barrier and its ability to recover gel properties following stress induced breakdown.

Methods: All measurements were carried out using a Bohlin CVO50 rheometer fitted with 25mm diameter serrated, parallel plates operating in oscillatory mode. Shear resistant pig gastric mucus gels were subjected to repeated up down stress sweeps in the range 0.15–500 Pa.
**Results:** Fresh shear resistant mucus gels (n=12) with phase angle values (a measure of gel strength) in the range 5–10^° were tested. Typically samples showed breakdown and recovery occurring in the range 75–150 Pa. With each gel there was remarkable consistency during repeat breakdown cycles, e.g. over 5 repeat cycles mean breakdown stress 126 Pa (range 125–127), mean recovery stress 121 Pa (range 119–122). Repeated breakdown did not lead to any loss of the elastic modulus (G'\) in the reformed gel.

**Discussion:** The adherent mucus gel barrier has been shown to possess great resilience to shear induced damage, being able to recover its gel properties after repeated stress induced breakdown. This ability is necessary for the maintenance of an intact and continual mucus gel barrier particularly when subjected to the mechanical stresses resulting from the digestive process.

**Background:** Liquid Gaviscon (LG) and Gaviscon Advance (GA) are established alginate formulations used in the treatment of GERD.

**Aims:** To evaluate the use of ultra-fast echo-planar magnetic resonance imaging (EPI) in assessing non-invasively the formation, location and retention of intragastric alginate rafts of LG and GA in healthy subjects. Secondly, to evaluate the feasibility of using transverse relaxation time T2 measurements to monitor changes in the rheological properties of the raft and meal.

**Methods:** In vitro studies were carried out to optimise the test meal and the imaging sequences. 20min after a small fat preload, 6 healthy subjects ingested 500ml of a liquid meal containing 150ml lemon juice. They then received a dose of either 20ml LG or 10ml GA in 2 separate sessions. They were imaged at 15min intervals using single-shot EPI on a 0.5 T dedicated scanner. T2 measurements were obtained using a 130 echo-planar magnetic resonance imaging sequence with the following parameters: echo time 150ms, repetition time 1500ms, field of view 40cm, matrix 128x128, 2 averages, slice thickness 3mm. The EPI investigation was well tolerated and could potentially be used as a tool to monitor the formation and stability of intragastric rafts.

**Results:** The rafts were clearly visible in the EPI images. It was possible to observe raft formation in all experiments for both LG and GA. They were seen reentering with the stomach contents at the bottom of the stomach body (which is the lowest region of the stomach in the supine position) and progressively floating. 45min after dosing the raft volumes were 61(8)ml for LG and 66(2)ml for GA. After the meal emptied a raft was still seen in the stomach in 60% of cases for LG and in 100% of cases for GA, suggesting a longer raft retention for GA. 3D volume reconstructions of raft and meal were produced and showed the raft spatial distribution within the gastric lumen in detail. T2 measurements were able to assess dynamic changes in the raft properties in vivo.

**Conclusion:** EPI shows great potential in monitoring Gaviscon raft formation and flotation in vivo, non-invasively and with high spatial resolution. The EPI investigation was well tolerated and could allow serial studies and comparisons of different product formulations. This work was supported by Reckitt Benckiser Healthcare.

**Introduction:** Gastrin is an endocrine and autocrine growth factor for gastric carcinoma. G17DT is an anti-gastrin immunogen.

**Aims:** To determine (i) antibody response, (ii) tolerability and (iii) efficacy of G17DT at raising functional G17 antibodies.

**Method:** G17DT was administered to 52 patients with gastric adenocarcinoma. In 47 patients this was given at weeks 0, 2 and 6 by intramuscular injection to the thigh in the following doses, 12 at 10 µg, 12 at 100µg and 23 at 250µg. An immunoassay was performed to determine the ability of G17DT-immunised patients’ sera to inhibit binding to gastrin/CCKB receptors on the rat pancreatic tumour cell line AR42J. Displacement was then compared to a positive control rabbit anti-human IgG serum.

**Results:** By week 12 of the study (i) 6/11 (54.6%) evaluable patients achieved an antibody response in the 10 µg group, 9/13 (69.2%) in the 100µg group, and 19/22 (86.4%) in the 250µg group. Antibody response was not affected by age (p=0.3), odds ratio (OR) 0.68) or disease stage (p=0.98, OR 1.02). The antibodies were mainly of the IgG isotype. (ii) G17DT was well tolerated in 50/52 patients. However, one patient developed swinging pyrexia which settled after 3 days, and a second developed a sterile abscess which resolved following aspiration, (iii) The immunoassay confirmed the ability of G17DT antibodies raised in patients to displace iodinated gastrin from CCKB receptors and that the level of displacement was related to antibody titre.

**Conclusion:** G17DT is a simple and well tolerated method of raising functional antibodies to G17 in patients with gastric carcinoma.

**Introduction:** There has been a renewed interest in gastric cancer incidence rates in Africa due to the reported discrepancy between high prevalence rates of Helicobacter pylori infection and low cancer incidence rates. Yet reliable estimations of cancer incidence rates in Africa are extremely difficult to obtain, with very few established cancer registries. This study documented the available information concerning incident cases of gastric cancer in part of Kenya's Eastern Province between 1991 and 1993.

**Method:** The records of all major health facilities in four administrative districts of Kenya's Eastern Province for the years 1991 to 1993 were reviewed for cases of gastric cancer. Population data was calculated from the 1989 national census. Incidence rates from the same area of Kenya were available from earlier studies to establish a comparison with the current study.

**Results:** Over the 3 year period, 200 cases of gastric carcinoma were identified. The mid 1992 population in the four districts was calculated to be 1,256,567. The annual average crude incidence rate was

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found to be 7.0 (95% CI 5.8–8.2) per 100,000 for males and 3.7 (CI 2.8–4.5) per 100,000 for females. From these figures, the World Age Standardised Rates were calculated to be 14.3 (CI 11.8–16.8) per 100,000 for males and 7.1 (CI 5.4–8.8) per 100,000 for females. A tenfold increase in the indirectly standardised incidence rate between the periods 1965–70 and 1991–3 was noted.

Recent incidence rates for gastric carcinoma in this part of Kenya are comparable to Western European figures and similar to those recorded in other highland regions of Africa. There is likely to be underascertainment of cases especially among the population aged over 65 years.

134 ASSOCIATION OF GASTRIC POLYPS WITH PROTON PUMP INHIBITOR THERAPY

A.L. Moore, C.H. Poh, R.J. McFarland, T.C.K. Tham. Division of Gastroenterology, Ulster Hospital, Belfast, Northern Ireland, UK

Introduction: Since 1992 there have been a few reports of the association of gastric polyps with the use of proton pump inhibitors (PPI). We describe our series of patients with gastric polyps which is one of the largest reported in the literature.

Method: This was a retrospective study. The hospital coding database provided a list of patients with a diagnosis of gastric polyps made between January 1996 and December 1999. The following was obtained from review of the patients’ hospital notes: demographics and drug history, reason for gastroscopy and the findings, dates of previous gastroscopies with their findings (particularly the presence or absence of gastric polyps).

Results: In total 1958 patients had gastroscopies in the 2 year period. Of the total patients, 341 had been using PPI therapy for various durations and 33 were found to have polyps. In 7 (3 male, 4 female, aged between 43 and 77) of these 33 patients there were documented previous gastroscopies which identified no gastric polyps at a time when the patients had not been using PPI therapy. In these cases it was assumed that the growth of the polyps was associated with the PPI. The incidence of PPI-related polyps was 7/341 x100 = 2%. The mean duration of treatment with a PPI was 48 months (range 2–188). Six patients developed fundic gland polyps: one patient had a single, 4 mm pedunculated polyp on the lesser curve/upper body of the stomach, two had multiple, 2–4 mm sessile polyps in the fundus, 2 others had multiple 3–5 mm pedunculated polyps along the greater curve/upper body and one had multiple 2–6 mm sessile and pedunculated polyps along the lesser curve/upper body. One patient developed a single 6 mm pedunculated metaplastic polyp at the cardia. Six patients had reflux disease of varying severity. One patient was investigated because of recurrent abdominal pain. All 7 patients were Helicobacter pylori negative and non-smokers.

Conclusion: The PPI-associated incidence of gastric polyps is approximately 2% and most of these polyps are of the fundic gland/cystic type. The clinical significance of such polyps is uncertain and requires further follow up.

135 PROSPECTIVE ANALYSIS OF THE TWO WEEK RULE FOR URGENT REFERRAL OF SUSPECTED UPPER GI CANCER

A. Mahmood, J. Millar-Smith, J.Y. Kang, J.D. Maxwell. St George’s Hospital and Medical School, London SW17 0QT, UK

Aims: To assess the effectiveness and compliance with the Two Week Rule (TWR), a new government initiative which requires patients with suspected upper gastrointestinal (GI) malignancy to be seen by a specialist within 2 weeks of referral by the General Practitioner (GP).

Method: All patients referred by GPs for first three months of the TWR initiative were analysed. In addition a clinical nurse specialist (CNS) examined all other GP referrals and upgraded some to TWR. Comparison between the GP and specialist assessment of TWR patients was made. Data was collected from referral letters, case notes and South West London cancer network referral forms. Data from 45 patient referrals was analysed.

Results: 80% of referrals were received within 24 hours. 11% were referred using the standard TWR referral proforma and 69% were upgraded by CNS. 89% were seen by the specialist within two week period. Following consultation median period to diagnosis was 9 days. There were discrepancies between GP and specialist in assessment of symptoms but not in identifying risk factors.

136 HYPERCOAGULABILITY IN ACUTE PEPTIC ULCER HAEMORRHAGE


Background: Patients with acute peptic ulcer haemorrhage (APUH) seem to have a hypercoaguable state, although this has not been well documented in the literature. It is unclear whether this response is partially reversed by blood transfusion.

Aims: To compare coagulation in patients with APUH with those undergoing venesection and to assess the effects of blood transfusion on these coagulation factors.

Methods: Fifty-two patients presenting with a significant upper GI bleed and found at endoscopy to have a peptic ulcer with active bleeding or a non-bleeding visible vessel were entered into the study. All patients received combined endoscopic therapy with heater probe and injection. Patients received blood transfusion according to local protocols. Blood samples were taken prior to endoscopy for analysis of Thrombin-antithrombin III (TAT), Fragment 1&2 (F1&2) and D-Dimers (DD). TAT is an indirect and F1&2 a direct means of monitoring the generation of thrombin; D-dimer can be used indirectly to assess the generation of fibrin. Blood samples were also taken post-treatment from 20 patients attending for routine venesection. TAT, Fragment 1&2 and D-dimer concentrations were determined by enzyme immunoassay using kits purchased from Dade Behring (Marburg, Germany).

Results: Patients with an acute GI bleed had significantly raised levels of TAT (p<0.002), F1&2(p<0.001) and fibrinogen(p=0.002) as compared to the venesection group. Blood transfusion had no effect on the coagulation parameters.

Conclusion: Patients with an acute GI bleed have a hypercoaguable state which is not seen in patients undergoing venesection. This hypercoaguable state is not affected by blood transfusion.

137 INTENSITY OF MANAGEMENT IN ACUTE UPPER GI HAEMORRHAGE


Despite advances in medical care, the mortality of elderly patients following acute upper GI haemorrhage remains high. We investigated the relationship between age-related mortality and intensity of management taking central venous pressure monitoring as a surrogate marker of treatment intensity.

Methods: We prospectively collected data on all consecutive cases of upper GI haemorrhage admitted to our institution over a 3-year period. Cases were subdivided into 3 age groups (0–59, 60–74 and 75+). and analysed with regards to outcome and intervention.

Results: Of the 1349 episodes 562 (41.7%) occurred in those aged 75+. This group received CVP monitoring less frequently than the 60–74 (p=0.016) or 0–59 (p=0.003) age groups and had a higher
2-week mortality (p=0.006 and p=0.001 respectively). The percentage of patients dying who received CVP monitoring fell with increasing age (44%, 21% and 13% respectively) despite the increase in mortality. Rebleeding rate was not significantly different between the groups. The 75+ age group underwent surgery less frequently than the 60–74 age group (p=0.033) but not the younger age group.

Conclusions: The mortality associated with upper GI haemorrhage increases with age. This cannot be explained by more frequent rebleeding but could be partly explained by less aggressive monitoring of elderly patients who might be more vulnerable to the adverse effects of hypovolaemia and/or fluid overload.

Abstract 137, Table 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Episodes</th>
<th>2-week mortality</th>
<th>Rebleeding</th>
<th>Surgery</th>
<th>CVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-59</td>
<td>469 (34.8%)</td>
<td>16 (3.4%)</td>
<td>98 (20.9%)</td>
<td>12 (2.6%)</td>
<td>70 (14.9%)</td>
</tr>
<tr>
<td>60-74</td>
<td>318 (23.6%)</td>
<td>14 (4.4%)</td>
<td>65 (20.4%)</td>
<td>15 (4.7%)</td>
<td>45 (14.2%)</td>
</tr>
<tr>
<td>75+</td>
<td>562 (41.7%)</td>
<td>54 (9.6%)</td>
<td>103 (18.3%)</td>
<td>12 (2.1%)</td>
<td>50 (8.9%)</td>
</tr>
</tbody>
</table>

Subjects and Methods: All patients referred for surgical intervention from July 1996-9 (N=98, mean age=69.5 years, 58.5% male) with non-variceal UGH (predominantly peptic ulcer disease) in a single hospital. Classification was according to their surgical assessment: accepted or declined. SAPSII were retrospectively assessed at the time of referral for surgical intervention. This was converted into a mortality probability using multiple regression analysis. The clinical outcome was defined as either survival to discharge or death whilst an in-patient.

Results: Mean SAPSII for death=35.7 (R28–46, median=37). Mean SAPSII for survivors=30.1 (R15–53, median=31). No patient with a SAPSII <28 died. The 2 groups did not differ with respect to their SAPSII (t=0.8, p=0.44). Patients who were declined for surgery had a greater increase in death compared to those who were accepted (p=0.08; Odds ratio 2.3 [95% CI 0.8–6.2]). The observed mortality was consistent with mortality predicted in the operative group but for those declined their actual mortality was twice that predicted.

Abstract 139, Table 1

<table>
<thead>
<tr>
<th>Number</th>
<th>Accepted</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean SAPS II score (range 15–53)</td>
<td>31.7</td>
<td>30.2</td>
</tr>
<tr>
<td>Mortality probability</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Pre-discharge mortality (%)</td>
<td>10 (13%)</td>
<td>10 (30%)</td>
</tr>
</tbody>
</table>

Conclusion: This is the 1st study to assess SAPSII in UGH. Subjective clinical assessment may deprive some patients of a potentially life saving operation. Mortality predictions using SAPSII suggests that clinical selection criteria for patients undergoing surgery may be inconsistent.

140 AN AUDIT OF DUODENAL ULCER TREATMENT AFTER A BLEEDING EPISODE

J. Gröning, H. Griffiths, M.J. Hall. Dept of Gastroenterology, County Hospital, Hereford HR1 1SQ, UK

We have audited the practice of Helicobacter testing, treatment and follow up in patients who presented with bleeding duodenal ulcers in a District General Hospital over a five year period.

Methods: Using Endoscopy Department records all cases of acute gastrointestinal haemorrhage due to duodenal ulceration between January 1995 and December 1999 were identified. Information on Helicobacter pylori testing at the time of endoscopy (biopsy urease test, histology or serology) and subsequent treatment was obtained. Follow up of outcome of H. pylori eradication treatment was documented.

Results: 98 episodes of bleeding duodenal ulceration in 97 patients were identified of which 44 were treated with an eradication regimen. 59 patients of the 64 survived for more than three months. 19 of the 44 patients were followed up by subsequent H.pylori testing and all were found to be negative. No attempt in the remaining 40 patients was made to establish the success or otherwise of H.pylori eradication treatment. Assuming a failure rate of 10% for standard eradication treatment at least four patients are likely to have remained infected with Helicobacter pylori. 34 patients out of 98 did not receive eradication treatment of which 25 survived for more than three months. Five patients received long-term acid suppression but 20 received only short-term acid suppression or no treatment at all. Therefore at least 24 patients out of 84 survivors (29%) were left at risk of recurrent peptic ulceration and possible haemorrhage.

Conclusion: In this hospital where patients with gastrointestinal haemorrhage are managed by a wide variety of teams, a significant number of survivors from bleeding duodenal ulcers are inadequately treated. A gastroenterology led service for GI bleeding is likely to improve on this position.

141 SURGERY FOR PEPTIC ULCER—ARE TRENDS STILL CHANGING?

N.I. Church, S.J. Nixon, K.R. Palmer. Western General Hospital, Edinburgh, UK

Background: Elective surgery rates for peptic ulcer have fallen significantly but a number of published series report that rates of emergency surgery for ulcer complications are increasing, and that mortality rates may be rising. This is thought to be due to increasing...
THE MANAGEMENT OF GASTRIC VOLVULUS—A NUTRITION TEAM

I.R. Daniels, D.J. Ferguson, E.M. Chisholm.

Introduction: A gastric volvulus is defined as an abnormal rotation of the stomach and an acute gastric volvulus is a rare surgical emergency that carries a high mortality and morbidity, while elective surgery after fundoplication for acute peptic ulcer bleeding in the years 1995–1999.

Methods: A retrospective analysis was performed using computerized data from the Lothian Surgical Audit database. Comparison was made with previously published historical controls.

Results: Between 1983 and 1998 377 operations for ulcer were carried out. For all ulcer operations the annual operation rate fell by 65% over the period. Vagotomy rates fell by 100%, whereas under-running rose by 85%, 84 patients underwent surgery for recurrent bleeding after endoscopic therapy between 1995 and 1999. The mean age was 68 years (range 21–93) and this remained constant. 76% of bleeds were from duodenal ulcers with 24% from gastric ulcers. Operation rate rose from 10 in 1995 to 21 in 1999. 82% of procedures were to under-run the bleeding point with 13% involving partial gastrectomy. This ratio remained constant. Rebleeding following surgery occurred on average in 12% and this was unrelated to type of operation or to time. Average mortality was 24% and was variable, showing no significant trend with time. Mortality rose in relation to age and post-operative rebleeding.

Conclusion: In Lothian patterns of ulcer surgery between 1983 and 1999 had followed those in other centres, with a change from predominantly elective vagotomy to predominantly emergency under-running. Significant increases in the age of the population requiring surgery for bleeding have not been demonstrated. In the last 5 years rates of emergency surgery for rebleeding after endoscopic therapy have increased slightly, but post surgical mortality has not shown a consistent increase and is comparable with other centres. Under-running has been the favoured emergency operation and this has not resulted in adverse outcomes.

NUTRITION TEAMS FUNCTIONING AS GATE-KEEPERs FOR INTRAVENous FEEDING: IMPROVE THE COST AND QUALITY OF SERVICE

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Background: Intravenous feeding or parenteral nutrition (PN) is expensive and associated with a greater risk of complications than enteral feeding. The multidisciplinary nutrition support teams (NSTs) can advise on patient care and have been shown to improve cost and quality of care. However, NSTs act only in an advisory capacity in most hospitals in UK, with no documented evidence that such a function significantly influences prescribing practice by clinicians.

Aim: To assess whether a NST with prescribing authorisation on the use of PN can further improve cost and quality of nutrition support services.

Methods: A prospective audit was carried out on all PN requested +/- provided in non ITU patients over two 8-month periods: Sep 97 to Apr 98 and Sep 98 to Apr 99—the former when the NST was “advisor” and the latter when it had its prescribing mandate. Data recorded include indications for PN, duration of PN, and line sepsis. The PN provided was categorised into “appropriate”, “inappropriate” or “avoidable” according to previously published guidelines (7 Parenteral Enteral Nutr 1986:10:441–5). The costing data based on raw materials only was estimated to be £45 for a bag of PN over 24 hours.

Results: 110 referrals were made in the 1997/8 period and 72 in 1998/9. Of these 108 (98%) and 45 (62.5%) patients were fed intravenously, with 2 (1.8%) and 27 (37.5%) inappropriate requests refused respectively (p<0.0001). The proportion of “inappropriate” or “avoidable” PN were 47% and 24% for the two time periods (p<0.05). The total number of feeding days was 1082 and 544, at a cost of £48,690 and £24,480 respectively, leading to a saving of £24,210 over 8 months. Of those refused PN, there was a total of 291 days of alternative (enteral or oral) nutrition support at an estimated cost of £1309. Proven feeding line sepsis were 7 (6.5%) and 2 (4.5%) respectively.

Conclusion: NSTs controlling access to the use of intravenous feeding improve the cost and quality of nutrition support service.
A TWO YEAR AUDIT ON PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: IS THE NUTRITION SUPPORT TEAM GENERATING MORE WORK?

D.H.L. Ng, L. Timmis, T.E. Bowling. Dept of Gastroenterology, North Staffordshire Hospitals NHS Trust, Stoke-on-Trent ST4 6QG, UK

Percutaneous endoscopic gastrostomy (PEG) is increasingly being used as a means of providing nutritional support. One of the many roles of a nutrition support team (NST) is to assess patient suitability for PEG placement. We examined the patient outcomes following PEG, comparing the results before and after formation of the hospital NST. We also examined the outcomes of those patients who were rejected for PEG. All patients referred for PEG over a 12 month period after the formation of the NST were included in this audit prospectively. Their suitability for PEG was assessed by the NST. A retrospective study was also conducted examining the patient outcomes of all the PEG placed in the 12 month period immediately prior to the formation of the NST when all PEG requests were accepted without prior assessment. 37. 74 out of 204 requests (36%) for PEG were rejected. 40% of patients in this group died within 7 days of being assessed and 26% were able to eat.

Abstract 145, Table 1

<table>
<thead>
<tr>
<th>Metric</th>
<th>Pre-NST</th>
<th>Post-NST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age and range</td>
<td>66.2 (17-93)</td>
<td>65.3 (17-92)</td>
</tr>
<tr>
<td>No. of PEG request</td>
<td>104</td>
<td>204</td>
</tr>
<tr>
<td>No. of PEG placed</td>
<td>104</td>
<td>130 (64%)</td>
</tr>
<tr>
<td>Mortality at 30 days</td>
<td>18/104 (17.3%)</td>
<td>26/130 (20%)</td>
</tr>
<tr>
<td>6 months</td>
<td>11/104 (10.6%)</td>
<td>26/130 (20%)</td>
</tr>
<tr>
<td>Alive at 6 months: PEG removed</td>
<td>32/104 (30.8%)</td>
<td>30/130 (23.1%)</td>
</tr>
<tr>
<td>Using PEG</td>
<td>43/104 (41.3%)</td>
<td>48/130 (36.9%)</td>
</tr>
</tbody>
</table>

Our results confirmed that the demand for PEG has increased. However, the formation of NST did not improve patient outcomes following PEG placement, but there was a large number of inappropriate referrals. This could be due to a combination of an increase in awareness of clinical nutrition and an increase in pressure on acute hospital beds leading to more patients being referred even though they were more ill. Despite this, the NST is an important gatekeeper to inappropriate referrals. All doctors placing PEGs should be involved in assessing patient suitability rather than simply assuming the role of a technician.

HUNGRY IN HOSPITAL? A CROSS SECTIONAL STUDY

J. Tharakan. Addenbrooke’s Hospital, Hills Road, Cambridge CB2 2QQ, UK

Concern has been expressed by the Association of Community Health Councils for England and Wales regarding patients going hungry in hospitals. We attempted to ascertain whether the problem existed in our hospital. On a single day, all elderly (over 75) patients on our 2 care of elderly wards, were given a questionnaire on hunger. This comprised of how hungry they had been during their stay, graded as mild, moderate or severe, and whether they were distressed by hunger, and how their hunger in hospital compared with their hunger when at home. A body mass index (BMI) was also performed on all patients. We attempted to ascertain whether the problem existed in all hospitals. We attempted to ascertain whether the problem existed in all hospitals.

Methods: Our nutrition support team conducted a cross sectional study on a single day has shown that the majority of patients on our wards are not going hungry. This is reassuring. One of the reasons could be the close collaboration between catering staff and the nutrition team. In addition, nursing staff are available at all times during the serving of meals, to provide assistance and encouragement.

MID UPPER ARM CIRCUMFERENCE IS PREFERABLE TO BODY MASS INDEX AS AN INDEX OF HOSPITAL UNDERNUTRITION

S. Vlaming’, A. Biehler’, E.M. Hennessy, C. Archer’, K. Durman’, J. Powell-Tuck’. 1Dept of Human Nutrition, and 2Wifton Institute of Preventative Medicine, St Bartholomew and the Royal London Hospital School of Medicine and Dentistry; Dept of Dietetics and Nutrition, Royal London Hospital, Whitechapel, London E1 1BB, UK

A nutritional supplementation trial gave us the opportunity to assess the nutrition of 1561 patients on emergency admission to medical (1097), surgical (335) and orthopaedic (129) services of the Royal London Hospital. Because no significant benefit occurred and the confidence intervals for difference in mean length of stay for supplements vs placebo were narrow (<2 to 1.2 days) we have used the data to compare anthropometric measures as predictors for length of stay and mortality. Patients acutely admitted to the 15 relevant wards were identified. They were weighed and their height and mid non-dominant upper arm circumference (MUAC) measured, and their weight three months prior to admission estimated. MUAC measurements were obtained in 95% (848m, 635p) patients, but, because weight and/or height could often not be measured for clinical reasons, BMI could be assessed in only 44% (408m, 285 f). Weight loss data were obtained in 509 patients. These measurements combine to demonstrate that 18.1% of patients were undernourished (At least one of: BMI < 20kg/m’ or MUAC < 25cm or loss of weight > 10%). The relationship between BMI & MUAC was different in men and women (p=0.006 for sex) and was affected by age. The BMI regression equations were for men: BMI = 1.02 x MUAC + 0.03 x age - 6.7, (R² = 0.77), and for women: BMI = 1.10 x MUAC + 0.023 x age - 8.0, (R² = 0.76). We examined statistically how hospital length of stay and death during the admission was predicted by MUAC, and by BMI and MUAC analysed separately in those patients for whom both were available. Those in whom it was possible to measure BMI had a mean (sd) MUAC of 29.4 ± 4.6 whereas those in whom BMI could not be obtained had a mean (sd) MUAC 29.9 ± 4.8 so the inability to measure BMI did not bias MUAC results. In all cases MUAC produced a more statistically significant prediction of mortality and length of stay than BMI.

PATIENT SURVIVAL AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

A. Sinha, B.L. Litchfield, J.M.D. Nightingale. University Hospitals, Leicester, UK

Background/Aims: Percutaneous endoscopic gastrostomies (PEG) are commonly used to feed patients with a functioning gut and an inadequate oral intake. This study reviews the indications, outcomes and documented complications of PEG inserted over 9 years (1991–1999).

Methods: A standard pull technique was used for PEG insertion. Prophylactic antibiotics were not used. Data were collected from computerised endoscopy records and patient case records.

Results: 419 patients had PEG insertion, the number increasing from 2 in 1991 to 82 in 1999. The proportion of patients with cerebrovascular accidents (CVA) remained constant. Ear, nose and throat (ENT) patients constituted an increasing proportion. 4 patients developed leakage around the PEG site and 3 had entry site infections in the first 2 months. 8 patients developed aspiration pneumonitis in the 2 months following PEG insertion. 30-day mortality following PEG insertion was 21.3% with wide variability (CVA 26.3%, Multiple Sclerosis (MS) 4.3%, HIV 0%). Patients with a CVA had a 1-year survival of 49% (median survival 6 months, range 0–102) following the procedure. Patients with trauma had 1-year survival of 96% (median survival 46 months, range 4–77) and median PEG duration 2 months (range 0–14). HIV patients had a 1-year survival of 22% (median survival 5.5 months, range 1.5–18). Patient survival was better in the trauma (p<0.001) and MS (p<0.05) groups than other groups.

Conclusions: The majority of PEG tubes are placed in patients with a CVA who have a poor survival. Patients with a CVA need to be carefully selected prior to PEG placement.
Malnutrition in Patients with Neurological Osteoporosis and Inflammatory Bowel Not All Dietary Fibres Are Equal: Selection underweight and close to 50% acute admissions have biochemical percentile) and 1 (4%) was mildly malnourished (BMI<20, MAMC seleniun, copper, zinc, vitamin A, D, & E, and PTH. haematinics, U&E, LFT, Ca, PO4, cholesterol, prothrombin time, muscle circumference (MAMC). Samples were obtained for FBC, circumference (MAC), triceps skin fold thickness (TSF), mid arm mid arm was followed by nutritional assessment and anthropometric measure- ments including height, weight, body mass index (BMI), mid arm cir- cumference (MAC), triceps skin fold thickness (TSF), mid arm circum- ference (MAMC). Samples were obtained for FBC, haematinics, U&E, LFT, Ca, PO4, cholesterol, prothrombin time, selenium, copper, zinc, vitamin A, D, & E, and PTH.

Results: The mean age was 69 years (range: 33–91). Mean duration of feeding was 15 months (range: 6–42). Of the 24 patients, 16 (67%) were found to have anthropometric and/or biochemical evidence of malnutrition of whom 6 (25%) had evidence of both. 8 patients (33%) had anthropometric evidence of malnutrition, 5 (12%) had severe malnutrition (BMI<16, MAMC or TSF<5th percentile), 4 (17%) were moderately malnourished (BMI=18, MAMC or TSF<5th percentile) and 1 (4%) was mildly malnourished (BMI<20, MAMC or TSF<15th percentile). 8 patients (33%) were anemic but with nor- mal haematocrits, 15 (62.5%) had elevated urea, 15 (62.5%) had low albumin and zinc was low in 12 patients (50%). The rest of the measured biochemical parameters were normal.

Conclusions: A significant proportion of these patients are malnourished highlighting the need for regular biochemical and dietary assessment of nutritional status.

Osteoporosis and Inflammatory Bowel Disease—are Guidelines for Dietary Calcium Being Met?

Background: In January 2000 Guidelines for Treating and Preventing Osteoporosis in Cocid Disease and Inflammatory Bowel Disease (IBD) were published in the international journal Gut. These guidelines recommend that all patients with IBD should achieve a calcium intake of 1500 mg/day. This figure is more than double the Reference Nutrient Intake (RNI) for calcium set for the adult population in the U.K. (DoH, 1991&1998) and may be di- erence Nutrient Intake (RNI) for calcium set for the adult population. Our aim was to establish the intake of dietary calcium in patients with IBD and compare with the RNI for adults of 700 mg/day and the recent Osteoporosis guidelines.

Methods: 52 patients with IBD; 32 patients with ulcerative colitis and 20 patients with Crohn’s disease, age range 26 yrs—69 yrs, 21 males, and 31 females were recruited from Gastroenterology outpatient clinics. Dietary calcium was determined using a 10-day weighed food intake and subsequent analysis using McCance and Widdowson dietary data.

Results: Median calcium intakes for patients with ulcerative colitis and Crohn’s disease was 735 mg/day (range = 350 mg/day—1500 mg/day) and 810 mg/day (range = 530 mg/day—1270 mg/day) respectively. There was no significant difference between median intakes for males and females. Although the median exceeded the RNI of 700 mg/day, 20 % of patients with Crohn’s disease, 34 % of patients with ulcerative colitis and all following a milk-free diet (4/32 ulcerative colitis patients) failed to achieve this lower figure. Only those consuming up to a pint a day of milk plus other dairy products achieved an intake > 1000 mg/day (9/52) and only one of these patients achieved an intake of 1500 mg/day. In total, 98% (31/32) failed to achieve the 1500 mg/day target. These preliminary results therefore suggest that patients with IBD are unlikely to achieve a calcium intake of 1500 mg/day from diet alone.

Conclusions: Further education and advice to improve intake of dietary calcium is required for patients with IBD if the new guidelines are to be achieved. Many patients may require calcium supplements.
Background: It is becoming clear that there is no simple relationship between total fibre intake and colon cancer risk. We have previously shown that intake of galactose-containing dietary fibre is protective against colorectal cancer (Gut 1997;41(suppl 3):A124) and suggested that this effect is mediated via inhibition of proliferative dietary and microbial lectins which bind the galactose that shows increased mucosal expression on oncotelal carbohydrate antigens in colon cancer pre-cancer (Gastroenterology 1998;114:44). We have now compared dietary fibres for their ability to inhibit the galactose-binding peanut lectin (PNA) in vitro in order to select those which might prove most protective in vivo.

Methods and results: Various concentrations of dietary fibres were incubated with 0.5 ml 4 μg/ml PNA in PBS for 1 h on a roller shaker. After centrifugation the supernatant was tested for the ability of PNA to agglutinate sialidase treated (galactose-exposed) human red blood cells. 1 mg each of plantain, polygalacturonic acid and apple fibre showed 93.8%, 87.5 and 50% inhibition of lectin activity respectively. The supernatants from the fibre incubations were freeze dried and run on SDS-PAGE with appropriate lectin controls to assess the concentration of unbound lectin. Of a wide variety of dietary fibres tested, plantain fibre had the highest inhibitory potency for PNA, followed by polygalacturonic acid, apple and grapefruit fibre. Fibres from wheat bran, soya, green beans, carrots, broccoli and red cabbage were found to be non inhibitory. Plantain fibre also bound to and inhibited other galactose-binding lectins: *Abraeranthus cusadatus* agglutinin, Jacalin and *Aegires bicolor* agglutinin as assessed by haemagglutination inhibition assays and SDS-PAGE.

Conclusions: Dietary fibres from plantain, apple and grapefruit can bind to and inhibit galactose-binding lectins including PNA. These fibres should now be tested in vivo for their ability to prevent colon neoplasia.

154 ASSESSMENT OF CALCIUM INTAKE OF PATIENTS WITH COELIAC DISEASE

F. Moor, G.K.T. Holmes. Depts of Medicine and Dietetics, Derbyshire Royal Infirmary, London Road, Derby DE1 2QY, UK

Introduction: A reduced intake of calcium is a major factor in the genesis of osteoporosis which commonly occurs in patients with coeliac disease (CD), is a risk factor for fractures and is potentially treatable. Within a non-coeliac population 25% of calcium is derived from bread and cereals but many coeliacs have a reduced intake of both these foods and also ingest less milk. We studied calcium intake in patients with CD who were established on a strict gluten free diet (GFD).

Methods: 20 patients with CD attending a coeliac clinic for an annual review were chosen at random. Their ages ranged from 25–77 years and 16 were women. The time on GFD ranged from 2–15 years. Calcium intake was assessed by a diettian who used a ready “ready reckoner” form.

Results: Intake of calcium varied from 360–2623 mg/day. 70% of patients ingested less than 1054 mg/day while in 45% the intake was below 860 mg/day. The main reasons for the low calcium intakes were a reduced intake of bread and milk and a reduced consumption of cheese containing dishes such as pizza and pasta.

Conclusions: This study has highlighted the high proportion of patients with CD who, although on a strict GFD, are at increased risk of developing osteopenia and osteoporosis because of low intakes of calcium. Such patients, especially those ingesting less than 860 mg of calcium per day, are potentially at increased risk of fracture, particularly of the neck of the femur which can be life-threatening. This emphasises the need for an annual review of patients so that dietary advice can be given to those with inadequate intakes. Calcium supplements are a valuable source of calcium for those who cannot tolerate an increase in calcium containing foods. If calcium intake can be increased to 1500 mg/day, the recommended amount for coeliacs, the bone density of patients with CD may improve with a reduction in the fracture risk.
used, however it is expensive, has a number of potentially serious complications, and enteral nutrition (EN) has been suggested as an alternative. EN when given by nasogastric tube in HEG exacerbates the nausea and vomiting and risks aspiration. Although post-pyloric placement of feeding tubes has been suggested to avoid some of these hazards, generally this has necessitated radiation exposure; recently naso-enteral tubes have been placed endoscopically and some have used percutaneous endoscopic gastrojejunostomy.

**Method:** We have successfully used blind-placed nasojugal (NJ) tubes in two patients with hyperemesis, avoiding the risks of both endoscopy and radiation. Both were self-propelling ‘Bengmark’ tubes, which have a coil at the end to aid transpyloric passage. Both patients were dehydrated, had electrolyte imbalance, ketonuria and weight loss and both had been hospitalised for weeks. Both returned to normal weight while being enterally fed, one patient returned to oral feeding but the second required tube feeding until after her delivery. Both had normal deliveries and healthy, normal babies at term. The average time the tubes remained in place was 19 days, although we believe that as experience accumulates tubes will be kept in longer and there is still improved cost-effectiveness over PN. Both patients were discharged despite dependence on EN with improved psychological benefits in addition to the obvious resource advantages.

**Comment:** PN has more serious and more frequent side-effects that EN, although there are no studies comparing PN to EN in pregnancy or HEG. PN is expensive; the mean cost of nutritional support is empirically estimated at 4–10 times greater in PN than in EN. EN in HEG has traditionally been dependent on intensive nursing back-up; however, as a result of our success with the tubes our nutrition support team has adopted NJ feeding by Bengmark tube as the preferred method of nutrition in hyperemesis gravidarum.

### Neurogastroenterology Posters: 157–173

#### PREVALENCE OF PERCEIVED FOOD AND DRUG ALLERGIES IN FUNCTIONAL AND ORGANIC GASTROINTESTINAL DISORDERS

K. Bhat, A. Harper, D.A. Gorard. Wycombe Hospital, High Wycombe, Bucks HP11 2TT, UK

Many individuals presenting with abdominal symptoms believe they are allergic or intolerant to various foods. This study assessed whether self-reported allergy is linked to a subsequent functional or organic diagnosis. 1,000 new patients (42% male), attending a gastroenterology clinic completed a brief questionnaire immediately prior to being diagnosed. 1000 new patients (42% male), attending a gastroenterology clinic completed a brief questionnaire immediately prior to being diagnosed.

**Abstract 157, Table 1**

<table>
<thead>
<tr>
<th>Allergy Type</th>
<th>Organic (n=565)</th>
<th>Functional (n=467)</th>
<th>Odds Ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug allergy</td>
<td>74</td>
<td>116</td>
<td>1.9 (1.4–2.7)</td>
</tr>
<tr>
<td>Food allergy</td>
<td>33</td>
<td>105</td>
<td>4.1 (2.7–6.3)</td>
</tr>
<tr>
<td>Food worsens symptoms</td>
<td>98</td>
<td>199</td>
<td>3.1 (2.3–4.1)</td>
</tr>
<tr>
<td>Food and Drug allergy</td>
<td>61/13.2</td>
<td>42/8</td>
<td>2.8</td>
</tr>
<tr>
<td>Food and Drug allergy and worsens food</td>
<td>1</td>
<td>24</td>
<td>27 (3.6–198)</td>
</tr>
</tbody>
</table>

None of the 5 newly-diagnosed coeliac patients had recognised dietary gluten/wheat causing their symptoms. All 6 patients who were convinced they had coeliac disease had normal duodenal biopsies. Patients claiming drug or food allergies or worsening of symptoms with various foods are more likely to have a functional than an organic illness.

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It has been shown that the 5-HT₄ receptor agonist, sumatriptan (S) induces premature jejunal phase III activity and shortens the cycle length of the MMC at the expense of phase II (Tack et al, Gut 1998;42:36; Houghton et al, Gastroenterology 1988;94:1276). The effect of S on interdigestive antro-pyloro-duodenal motor activity however, has been less well characterised. In 9 healthy volunteers (5 male, 4–13 kg, 3 cm apart), pressure in the antrum (5 sites 1.5 cm apart), pylorus (sleeve sensor, positioned by measurement of transmucosal PD.) and duodenum (4 sites, 3 cm apart) were therefore measured for two phase III’s of the MMC and then following subcutaneous injection of either S (6 mg) or saline control for a further 2 phase III’s. Treatment order was randomised and double blind.

**Results:** S significantly prolonged the cycle length of the MMC (median increase from pre-injection S 125 min, placebo –5 min, difference 130 min, range –197, 417 min, p<0.03) and this was associated with an increase in duration of phase II (S 82 min, placebo –10 min, difference 92 min, range 175, 350 min, p<0.03) but not phase I (S 30 min, placebo 9 min, difference 21 min, -125, 58 min) or phase III (S 2 min, placebo –1 min, difference 3 min, -5, 1 min). Furthermore, similar proportions of phase III’s started in the antrum for both S (57%) and placebo (54%). Examination of the patterns of activity during phase II showed a tendency for a greater amount of coordinated activity to involve the duodenum following S compared with control (median in number occurring pre to post injection S 22, placebo –5, difference 17, range 3, 143, p = 0.086) but no difference in that involving the antrum (S 0, placebo 0, difference 0, -27,105).

**Conclusion:** In contrast to previous observations in the jejunum, the cycle length of the MMC in the stomach and duodenum is prolonged by the 5-HT₄ receptor agonist, sumatriptan. This is associated with an increase in the duration of phase II, which appears to have a greater proportion of it’s coordinated activity involving the duodenum rather then the antrum. These results provide further evidence for the involvement of 5-HT₄ receptors in the regulation of the gastrointestinal MMC activity in man. Glaxo Wellcome kindly supplied the sumatriptan for this study.

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**Background:** 5-HT₄ receptors are found on enteroendocrine cells, vagal and spinal afferent neurones and myenteric neurones. 5-HT₄ antagonists inhibit human fasting antral phase III motor activity and block the associated motility rise. This suggests that 5HT₄ agonists stimulate fasting antral motility, however their effect on fed antral motility is not known.

**Aim:** To assess the effects of MKC-733 (a selective 5-HT₄ agonist) on fasting and fed antral manometry in humans.

**Study Design:** Double blind, randomised, placebo-controlled, 4 period, cross-over study.

**Subjects:** 12 healthy male volunteers aged 18–45 years.

**Methods:** A 6 channel, solid state, transducer catheter was inserted on the day before the study and allowed to migrate into the small bowel overnight. The proximal 4 transducers were placed in the antrum (20, 22.5, 25, 27.5cm from the tip). Fasting subjects received a single oral dose of MKC-733 (0.2, 1.0 or 4.0mg) or placebo. Fed manometry was recorded for 8 hours before a second dose of drug was given followed, 30 minutes later, by a mixed nutrient meal (2796kJ). Fed manometry was recorded for 3 hours following the meal.

**Results:** (Expressed as mean ± SE; p = linear trend) Fasting: The number of MMC’s arising from the gastric antrum per hour was significantly increased (placebo = 0.360 ± 0.026, hour, 0.2mg = 0.390 ± 0.027 /hour, 0.4mg = 0.429 ± 0.025 /hour, 4mg = 0.549 ± 0.027 /hour, p < 0.001). There was significant increase in the number of antral contractions during phase II of the MMC (placebo = 111.5 ± 28.14, 0.2mg 175.2 ± 28.34, 1.0mg = 161.8 ± 26.42, 4mg = 216.1 ± 28.34, p = 0.036) but not the motility index. The duration of phase II of the MMC was significantly reduced (placebo = 526.8 ± 19.73min,
0.2mg ± 1.987min, 1.0mg = 314.7 ± 18.52, 4mg = 268.9 ± 19.87min, p = 0.031). Fed: There was no significant effect on the motility index, number and amplitude of antral contractions or the time to onset of fed antral activity.

Conclusions: Stimulation of 5-HT3 receptors during fasting in man increases the frequency of antral MMCs and the number of phase II antral contractions but has no significant effect on fed antral motility. This work was supported by Mitsubishi-Tokyo Pharmaceuticals Inc.

160 MKC-733, A 5-HT3 RECEPTOR AGONIST, STIMULATES SMALL BOWEL TRANSIT AND RELAXES THE GASTRIC FUNDS IN MAN

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Background: 5-HT3 receptors are abundant on enteroendocrine cells and nerves of the GI tract. 5-HT3 antagonists are potent anti-emetics and also increase jejunal absorption and slow colonic transit. However the role of selective 5-HT3, agonists has not yet been determined.

Aims: To assess the effect of MKC-733 (a highly selective 5-HT3 agonist) on small bowel transit (scintigraphy) and gastric fundal relaxation and antral motility (MRI).

Study design: 2 double-blind, randomised, placebo-controlled, 4 period, cross-over studies.

Subjects: Healthy males aged 18–45 years. All subjects received a single oral dose of MKC-733 (0.2mg, 1.0mg or 4mg) or placebo. 30 minutes later they consumed a pancake and milkshake (scintigraphy) or a viscous drink (MRI).

Results: Onset of action was dose dependently decreased (placebo = 276.4 ± 19.87min, 0.2mg = 265.3 ± 17.6min; p value for linear trend = 0.035). After a 4mg dose the small bowel transit time of the liquid meal was dose dependently decreased (placebo = 276.4 ± 17.6min, 0.2mg = 265.3 ± 17.6min, 1mg = 246.5 ± 17.6min, 4mg = 222.9 ± 17.6min; p value for linear trend = 0.035). After a 4mg dose the rate of gastric emptying increased significantly compared to placebo (placebo = 499 ± 36cm², 0.2mg = 486 ± 46cm², 1mg = 558 ± 39cm², 4mg = 635 ± 18cm², p = 0.02). There was no change in antral contraction speed or frequency in comparison with placebo.

Conclusions: MKC-733 agonists significantly relax the gastric fundus without inhibiting antral motility and may be useful in the treatment of functional dyspepsia with impaired gastric accommodation. Faster small intestinal transit may be due to a stimulatory effect on small bowel secretion and motility and suggests that these drugs may also be useful in the treatment of constipated IBS. This work was supported by Mitsubishi-Tokyo Pharmaceuticals Inc.

161 5-HYDROXYTRYPTAMINE (5-HT) TRANSPORTERS AND 5-HT RECEPTORS IN THE COLONIC MUCOSA: AN IMMUNOHISTOCHEMICAL ASSESSMENT IN IRRITABLE BOWEL SYNDROME (IBS) AND ULCERATIVE COLITIS (UC)

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Introduction: 5-HT is present in large quantities in the gastrointestinal tract and is implicated in the normal physiology of peristalsis, secretion and sensation. The distribution and transport of 5-HT has been studied in the brain in depression using immunohistochemical methods. In view of the developing role of the Brain-Gut axis in the pathophysiology of functional gastrointestinal conditions including the IBS we wished to examine the intestinal mucosal distribution of 5-HT, the serotonin transporter (SERT) and of 5-HT2A, 2B and 5HT3 receptors which are involved in colonic physiology.

Methods: Paraffin sections from patients with diarrhoea predominant IBS, constipation, ulcerative colitis and control (carcinoma resection margin) were examined. Immunohistochemistry was performed using the avidin biotin method ( Vectastain elite kit or Strept ABC kit). Antibody dilutions were determined by optimisation experiments with primary antibodies from DAKO, Chemicon and Oncogene Research. S100 antibody was used to stain for the presence of neuronal tissue. DAB chromogen was used in all cases except for SERT localisation where we used immunofluorescence with FITC.

Results: Immunohistochemistry studies showed that 5-HT and Chromogranin A staining enterochromaffin cells congregated mainly in the base of the crypts in all conditions. SERT and the 5-HT receptors were evenly distributed throughout the crypt epithelium in all conditions and neuronal tissue was comparable in all samples examined.

Conclusions: These studies indicate that the receptors and transporters of 5-HT in the colonic mucosa appear to be qualitatively similarly distributed in IBS and other gastrointestinal conditions.

162 ENTERO-ENDOCRINE CELLS ARE ELEVATED IN DIARRHOEA-PREDOMINANT IBS

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Introduction: Entero-endocrine (EC) cells are neuro-endocrine cells found throughout the GI tract, which store and secrete serotonin and other peptides, which may affect GI motility. Raised numbers of EC cells have been reported in patients with irritable bowel syndrome (IBS). We have investigated whether EC cell counts differ in clinical subtypes of IBS.

Methods: Thirty-four patients with IBS attending a gastroenterology outpatient clinic and 10 normal controls were asked detailed questions concerning their bowel habit. All rectal biopsies, which were normal by conventional criteria, were further immunostained for enterochromaffin cells using antibodies against neutral-1 and serotonin.

Results: Nineteen patients had diarrhoea predominant IBS (D-IBS), with loose stool passed every day. Fifteen patients had symptoms which were not exclusive for diarrhoea or constipation predominant IBS (alternating IBS, alt-IBS). The mean EC count in the d-IBS was 3.7 per 100 cells, in the alt-IBS group 2.5 and in the controls 1.5 (p<0.001).

Conclusions: Patients with diarrhoea predominant IBS have higher levels of entero-endocrine cells than those with alternating IBS. It has been suggested that patients with urge (U) and no-urge (NU) constipation predominant IBS (CP-IBS) have increased sensitivity of the rectum to distension. Furthermore, within both these groups, 2/3 are hypersensitive, which is similar to that seen in patients with diarrhoea predominant IBS (DP-IBS). As we have shown that patients with DP-IBS have increased sensitivity throughout the whole gut, it was the aim of this study to assess the whole gut in a similar way in CP-IBS.

Methods: Sensory responses to distension of the oesophagus (O), duodenum (D), jejunum (J), ileum (I), colon (C) and rectum (R) were measured in 10 patients with U-CP-IBS (aged 32–65yrs, 1 male) and 21 patients with NU-CP-IBS (aged 19–62yrs, 3 males) and compared with 31 healthy controls (aged 20–61yrs, 6 males).

Results: Patients with U-CP-IBS exhibited significantly lower discomfort thresholds to distension of the R (p<0.05), O (40(15,50)mm Hg, geometric mean (range) vs controls, 173(80, 400)mm Hg), i.e. greater pain sensitivity. In contrast, patients with NU-CP-IBS exhibited significantly increased discomfort thresholds to distension of the C (p<0.05) and J (p<0.05) compared with controls. Patients with U-CP-IBS were also more rectally sensitive than the NU-CP-IBS patients (p<0.05). Comparison of individual patient sensory thresholds with the 90% control comparison of individual patient sensory thresholds with the 90% control range, showed hypersensitivity in 50% of U-CP-IBS patients in R, 56% in C, 13% in J, 33% in I, 33% in D and 30% in O, whilst in the NU-CP-IBS patients, hypersensitivity was observed in 33% in R, 25%
IRRITABLE BOWEL SYNDROME DIAGNOSED IN PRIMARY CARE: HOW MANY PATIENTS FULFIL ROME 11 CRITERIA?

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Introduction: Many patients with functional gastrointestinal disease are excluded from clinical trials because they do not fulfil the diagnostic entry criteria. In September 1999, the Rome II consensus document was published including criteria for the diagnosis of irritable bowel syndrome (IBS). The aim of this study was to determine the number of patients with a GP diagnosis of irritable bowel syndrome who also fulfilled the diagnostic criteria described by the Rome II committee.

Methods: 37 GPs participated in the study and provided details of patients who had been seen at least twice in the previous year with abdominal pain or change in bowel habit in whom they were confident of a diagnosis of irritable bowel syndrome. No diagnostic instructions were given and Rome criteria were not provided. Patients were then asked to complete a questionnaire providing details of symptoms and duration, according to Rome II criteria.

Results: 98 of the 101 patients identified agreed to complete the questionnaire. 39 of these (40%) fulfilled Rome 11 criteria for irritable bowel syndrome. Of the 59 patients who did not fulfil the criteria, 36 had symptoms for less than 12 weeks in the preceding year. 52 patients fulfilled two of the three diagnostic criteria and seven patients met just one of the criteria.

Conclusions: Most patients with a GP diagnosis of irritable bowel syndrome do not fulfil the diagnostic criteria of Rome II. These patients are therefore unlikely to participate in clinical trials of new treatments but represent the largest number of potential beneficiaries. These results support the use of more pragmatic trials in irritable bowel syndrome even if greater representativeness results in a reduction in patient homogeneity.

DEMOGRAPHICS AND SYMPTOM PRESENTATION OF IRRITABLE BOWEL SYNDROME IN COMMUNITY BASED VOLUNTEERS

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Despite the high prevalence of irritable bowel syndrome (IBS) and the significant morbidity that is experienced by many sufferers it’s natural history remains poorly understood. Data from hospital specialist centres underestimates and may not be representative of the scale of the problem in the community. Relatively little is known about the natural history of IBS including disease presentation, consultation patterns, symptom frequency and pattern and treatment efficacy in the community. Most studies have been retrospective or short-term. Our aim is to gather prospective data about the natural history of IBS in community based ‘healthy volunteers’. Five hundred and three volunteers with IBS were recruited via a national newspaper advertising campaign (419 females (83%) median age 42.1) by a call centre. Volunteers with IBS were recruited via a national newspaper advertising campaign (419 females (83%) median age 42.1) by a call centre. The volunteers were given and Rome criteria were not provided. Patients were then asked to complete a questionnaire providing details of symptoms and duration, according to Rome II criteria.

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ABDOMINAL MIGRAINE IN ADULTS: AN UNDER-RECOGNISED VARIANT OF IBS?

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Background: Abdominal migraine is generally accepted as a distinct clinical entity in paediatric gastroenterology, characterised by recurrent abdominal pain with nausea and vomiting and a personal or family history of classical migraine. The community prevalence of abdominal migraine in children is between 1–4%. However abdominal migraine is rarely diagnosed in adults and its existence is controversial due to the lack of a precise definition and the high incidence of recurrent non-migrainous headaches reported in patients with irritable bowel syndrome.

Aims: To assess the clinical and biochemical features of five adult patients with suspected adult abdominal migraine.

Methods: The 5 patients had recurrent attacks of upper abdominal pain with normal biochemistry and haematology, normal upper GI endoscopy, small bowel radiology or CT scan of abdomen and lower GI imaging. Two patients had skin biopsies to exclude mastocytosis and one had a negative laparotomy. Median age was 40 years (range 24–42), 3 were female and the median duration of symptoms was 3 years (range 2–10). Migraine was defined by the International Headache Society (IHS) criteria and abdominal migraine was defined as previously described by Russell (Arch Dis Child 1995;72:413).

Results: All 5 patients fulfilled the criteria for abdominal migraine. Four of the five patients completed questionnaires on headache and 50% fulfilled IHS criteria for migraineous headache. Two of the five patients had urinary histamine measured during attacks and both of these were raised (229 and 21.9ng/ml (NR <20ng/ml)). All 5 patients reported impressive to prophylactic treatment with β blockers and general advice on avoidance of triggering factors.

Discussion: These cases suggest that abdominal migraine does exist in adults and is characterised by discrete stereotypic episodes of upper abdominal pain lasting more than an hour and resolving spontaneously which respond well to conventional treatment for migraine. Further studies are required to assess the relationship between classical and abdominal migraine and the utility of urinary histamine in diagnosing abdominal migraine.

EPIDEMIOLOGY OF THE FUNCTIONAL GASTROINTESTINAL DISORDERS DIAGNOSED ACCORDING TO ROME II CRITERIA: AN AUSTRALIAN POPULATION-BASED STUDY

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Background: The Rome II criteria for functional gastrointestinal disorders (FGIDs) have recently been defined. Population based studies are required to determine the prevalence and validity of the Rome criteria.

Aims: 1) To determine the prevalence of FGIDs defined according to the Rome II criteria; 2) To examine the relationship between FGIDs, psychological characteristics and mental functioning.

Materials and methods: Subjects included individuals aged 18 years and older (n=1225) from the Penrith population who were initially surveyed with The Penrith District Health Survey in 1997. Subjects were sent a self-report questionnaire that contained items on gastrointestinal symptoms applying the Rome II criteria. Subjects were also assessed on psychological factors and physical and mental functioning.

Results: The overall response rate for this study was 60.2%. 36.1% (n=436) of respondents were diagnosed with an FGID according to Rome II criteria. There were no differences in the number of males...
and females who were diagnosed with an FGID. The five most prevalent FGIDs were: functional heartburn (10.4%), IBS (8.5%), functional incontinence (7.6%), proctalgia fugax (6.5%) and functional chest pain (5.1%). Individuals with an FGID scored significantly higher on the Scale of Emotional Arousalability (t=3.38, p<0.001) and the Vulnerability Personality Style Questionnaire (t=4.38, p<0.001), than individuals who did not have an FGID, according to Rome II criteria. Furthermore, those with FGIDs (17.4%) were significantly more likely to be a GHQ-12 'case' than those with no FGID (5.8%) (χ²(17.76, p<0.001).

Conclusion: Individuals diagnosed with an FGID according to Rome II criteria show a higher level of impairment of physical and mental functioning than individuals without an FGID diagnosis. This project was supported by the Multinational Working Team for Diagnosis of Functional Gastrointestinal Disorders (Rome Committees).

169 ABDOMINAL DISTENSION IN FEMALES WITH IRRITABLE BOWEL SYNDROME (IBS): THE EFFECT OF THE MENOPAUSE AND HORMONE REPLACEMENT THERAPY


There is evidence to suggest that sex hormonal status of female patients with irritable bowel syndrome (IBS) may affect the severity of their symptoms. This study examines the effects of the menopause and hormone replacement therapy (HRT) on abdominal distension in female patients with IBS.

Method: A self-administered questionnaire on abdominal distension and hormonal status was completed by 27 pre-menopausal female IBS patients not taking the oral contraceptive pill (aged 29–43yrs), 23 post-menopausal patients not taking HRT (aged 61–72yrs) and 17 post-menopausal patients who were taking HRT (49–63yrs). All patients satisfied the Rome I criteria for IBS.

Results: Post-menopausal IBS patients not taking HRT experienced significantly more episodes of distension than pre-menopausal patients not taking the oral contraceptive pill (post-menopausal median (range): 7days/week (5–7)days/week v pre-menopausal: 3days/week (2–7)days/ week; p<0.005). The use of HRT by the post-menopausal patients however, significantly reduced the episodes of distension to pre-menstrual levels (3 days/week (2–5)days/week; p<0.005).

Conclusion: The results of this study suggest that sex hormonal status has a substantial effect on abdominal distension in female patients with IBS. Cognizance of these data may also be useful in the management of this condition as HRT appears to improve the symptom of distension.

169 IRritable bowel syndrome: can somatisation risk Factors affect symptom severity or response to hypnotherapy?

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Background: Somatisation may play a role in producing symptoms in at least some IBS patients. Individuals at risk for somatisation may display high levels of one or more of the following: neuroticism (N), catastrophising (C), social desirability (SD) and hypnotic ability, which interact to transduce psychological threat into physical symptoms or amplify symptoms in excess of pathophysiology. We have recently shown IBS patients to have higher levels of N, C and mental absorption (one component of hypnotic ability) compared with healthy controls (HC) (Gastroenterology 2000;118:A332). The aims of this study were to determine whether these risk factors influence severity of symptoms or their response to hypnotherapy (HT).

Method: 66 female IBS patients completed the Tellegen Absorption Scale, NEO-FFI, Zocco Scale and Marlowe-Crowne Scale, to measure absorption, N, C and SD, respectively, and an IBS scoring questionnaire. 45 patients who also received HT completed the IBS questionnaire again after treatment.

Results: Mean levels of N and C, but not SD, were higher in patients with IBS than HC (N (mean, 95% CI): 38.1(36.1–40.1) v 25.1(23.4– 26.8); C: 42.2(38.1–46.3) v 31.6(28.6–34.7), both p<0.001), and more patients had high mental absorption (IBS v HC: 44% v 25%, p<0.001). None of these measures correlated with symptom scores, except for N with reported degree of life interference (r=0.316, p<0.001). There were no significant correlations with symptom severity or their response to hypnotherapy (HT).

Conclusion: Sex hormonal status of female patients with IBS may affect the severity of their symptoms. This study examines the effects of the menopause and hormone replacement therapy (HRT) on abdominal distension in female patients with IBS.

170 COGNITIVE BEHAVIOURAL THERAPY AND RELAXATION THERAPY ARE NO BETTER THAN GOOD ROUTINE MEDICAL CARE FOR MANAGING IRRITABLE BOWEL SYNDROME

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Aim: To compare cognitive behavioural therapy (CBT), relaxation therapy (RT) and routine medical care (RMC) for managing Irritable Bowel Syndrome (IBS).

Methods: Subjects with clinically confirmed IBS (81% females, mean age 42 yrs, median duration of IBS 15 yrs) were randomly assigned to CBT (n=35), RT (n=36) or RMC (n=24). 78 subjects (74%) completed at least one half of the treatment sessions. Females were more likely to be non-completers as were subjects undergoing RT. Outcomes measures were the Bowel Symptom Severity Scale (BSSS), Hospital Anxiety and Depression Scales (HAD-A & HAD-D) and the SF-36 Physical and Mental Component Scores

171 ALVERINE CITRATE (SPASMONAL) FAILS TO RELIEVE THE SYMPTOMS OF IRRITABLE BOWEL SYNDROME: RESULTS OF A DOUBLE BLIND, RANDOMISED PLACEBO CONTROLLED TRIAL

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Background/Aims: Alverine citrate (Spasmonal) has smooth muscle relaxant properties and has been used in the treatment of IBS for many years at a dose of 120 mg three times daily. It has never been the subject of a randomised placebo controlled trial to demonstrate its efficacy. This study was designed to evaluate a new formulation of Alverine citrate, a 120 mg capsule, which is intended to improve patient compliance by reducing the number of capsules required each day.

Methods: 107 patients with the diagnosis of irritable bowel syndrome (satisfying the Rome criteria) were randomised to take 120 mg Alverine citrate (single capsule) three times daily or placebo for 12 weeks. Baseline observations were recorded in a 2 week run-in period. The main efficacy variables, analysed on an intention-to-treat basis, were the abdominal pain scores recorded at each clinic visit and on three 2 week patient diary cards. Secondary efficacy variables included scores for severity and frequency of abdominal bloating, nausea, early satiety and general well being.

Results: The treatment and placebo groups were well matched with regard to all demographic variables. The severity and frequency of abdominal pain improved in 66% and 68% of the patients treated with Alverine citrate respectively compared with 58% and 69% of the placebo group with no significant difference between the groups (n=0.50 and 0.65 respectively). The mean percentage reduction in patients’ diary scores for abdominal pain from baseline to the final 2 weeks, although greater in the Alverine citrate group (43.7%) compared with the placebo group (33.3%), was also not statistically significant (P=0.28). Other symptoms (bloating, nausea, early satiety and general well-being) improved steadily during the 12 week study but no significant difference between the treatment and placebo groups was evident. No serious adverse events were reported.

Conclusion: Alverine citrate is no better than placebo at relieving the symptoms of irritable bowel syndrome. This study was supported by Norgine (UK) Ltd.
PUDENDAL LATENCY: AN IMPORTANT PROGNOSTIC NON-INVASIVE TESTING FOR AUDIT OF THE “TWO WEEK CANCER RULE” FOR GASTROINTESTINAL MALIGNANCY

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It has been suggested that pudendal nerve terminal motor latency (PNTML) has little part to play in the prognosis after anterior sphincter repair. By using an artificial neural network we have been able to show that both PNTML and the results of biofeedback are an important part of the prognosis. 30 patients who underwent anterior sphincter repair had 32 preoperative investigations including anorectal physiology, endoanal ultrasound and PNTML measurements. 15 of them also underwent biofeedback therapy. The results of the repair were graded as 1 no change, 2 mildly improved, 3 socially continent, 4 excellent result. The variables were then processed through a neural network and a Spearman correlation between the predicted and actual results was performed. The neural networks were then altered by removing parts of the data (table 1).

Abstract 173, Table 1

<table>
<thead>
<tr>
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<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
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<tr>
<td></td>
<td>Correlation</td>
<td>P value</td>
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<tr>
<td>Full net</td>
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<td></td>
<td></td>
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<td>No biofeedback</td>
<td>90%</td>
<td>0.0001</td>
<td>74%</td>
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<td>No PNTML</td>
<td>58%</td>
<td>0.025</td>
<td>90%</td>
</tr>
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<td>PNTML only*</td>
<td>71%</td>
<td>0.003</td>
<td>56%</td>
</tr>
<tr>
<td>Biofeedback &amp; PNTML only*</td>
<td>48%</td>
<td>0.08</td>
<td>69%</td>
</tr>
<tr>
<td></td>
<td>38%</td>
<td>0.036</td>
<td>37%</td>
</tr>
</tbody>
</table>

Also age, functional length, high-pressure zone; Bold=significant.

The results show that the full use of preoperative data is necessary to get the best correlation and that if only PNTML and biofeedback are used then the correlation is poor. It also shows that by removing either has a dramatic effect on the correlation. However if PNTML only is used then the correlation at 12 months is 78%. From these results we can deduce that PNTML is an important factor in the pre operative investigation in patients who may receive an anterior sphincter repair.

Audits: The audit included 105/146 upper and 264/398 lower GI referrals. GI malignancy was found in 25% of upper and 14% and lower GI referrals. For upper GI compared to lower GI the median time (days) to initial assessment was 16 (range 0–53) vs 12 (1–181); diagnosis 20 (4–77) vs 30 (1–181) and treatment 29 (7–117) vs 34 (2–226). 85% of referrals fulfilled upper GI guidelines whilst 72% fulfilled lower GI guidelines. Cancers were only found in patients who satisfied the guidelines. The number of patients on the waiting list for endoscopy increased by 25% by the end of the study.

Conclusions: The detection rate of GI malignancy was good, with the majority of patients receiving their initial assessment within 2 weeks. The guidelines appear robust, as patients who did not fulfil the referral criteria did not have cancer. Although it is possible to provide a “two week cancer” service within existing resources, patients referred by the more traditional route have to wait longer.

Non-Invasive Testing for Helicobacter pylori may be associated with Delay in Diagnosis of Upper GI Malignancy


Background: Non-invasive testing for H. pylori (serology or radiolabelled ¹³C urea breath testing) is increasingly used without upper gastrointestinal endoscopy in selected patients with new onset of dyspepsia (the ‘test and treat’ strategy).

Aims: To determine whether non-invasive testing was associated with delay in referral and diagnosis in patients with upper GI malignancy.

Patients and methods: Patients diagnosed with gastric or oesophageal malignancy from 1st January 1997–31st December 1999 were identified from histopathology records. Non-invasive testing for H. pylori within 2 years of diagnosis of malignancy was identified from case notes, general practitioners’ records and microbiology records.

Results: 152 cases were identified, with mean age 70 years (range 34–91y, 4 patients younger than 45 years). 86 were male. 59 malignancies were oesophageal, 8 junctional, 77 gastric and one duodenal adenocarcinoma; in 7 the precise anatomical origin was undetermined. 22 patients (14.5%) had been tested for H. pylori prior to diagnosis (tested group), all by serology (9 oesophageal, 2 junctional and 11 gastric carcinomas); 20/22 were older than 45 years. The median interval between H. pylori serology testing and referral for endoscopy was 21 days (range 1–615 days, mean 109 days). There was a delay of more than 12 weeks between serology and referral in 6 patients; 17/22 patients had locally advanced or metastatic disease at diagnosis. Of all patients, median delay between referral and diagnosis to the endoscopy service and diagnosis of malignancy was 9.1 days (range 1–181 days, mean 24.0 days; medians 12 or 9.1 days in tested and untested groups respectively, p=NS). Of the patients aged 45 or older, 20/148 (13.3%) had H. pylori serology.

Conclusions: Serological testing for H. pylori was used in a significant minority of patients aged 45 years or older who were subsequently diagnosed with upper GI malignancy, and in some it was associated with considerable delay in referral and treatment. Non-invasive testing for H. pylori in patients with new onset of dyspepsia should be reserved for patients less than 45 years.

Neoplasia Posters: 174–190

Audit of the “Two Week Cancer Rule” for Gastrointestinal Malignancy

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Background: In order to assess resource issues necessary to support a successful “two week cancer” service, the Cornwall Gastrointestinal Unit introduced this service in January 2000.

Aims: To audit the “two week cancer” service for upper and lower GI malignancy.

Methods: A prospective audit of all GP referrals received over a 9 month period. The main outcome measure was the number of patients who were found to have cancer. The data were also analysed for: (i) time from GP referral to initial assessment, diagnosis and treatment and (ii) the number of referrals that fulfilled the “two week cancer rule” guidelines. Any patient who was referred under the “two week cancer rule” was seen irrespective of whether or not they met the guidelines. The number of patients on the waiting list for endoscopy was measured before and after implementation of the “two week cancer” service.

Results: The audit included 105/146 upper and 264/398 lower GI referrals. GI malignancy was found in 25% of upper and 14% and lower GI referrals. For upper GI compared to lower GI the median time (days) to initial assessment was 16 (range 0–53) vs 12 (1–181); diagnosis 20 (4–77) vs 30 (1–181) and treatment 29 (7–117) vs 34 (2–226). 85% of referrals fulfilled upper GI guidelines whilst 72% fulfilled lower GI guidelines. Cancers were only found in patients who satisfied the guidelines. The number of patients on the waiting list for endoscopy increased by 25% by the end of the study.

Conclusions: The detection rate of GI malignancy was good, with the majority of patients receiving their initial assessment within 2 weeks. The guidelines appear robust, as patients who did not fulfil the referral criteria did not have cancer. Although it is possible to provide a “two week cancer” service within existing resources, patients referred by the more traditional route have to wait longer.
176 IMPROVEMENT IN SURVIVAL IN PATIENTS WITH CANCERS DETECTED BY SCREENING HIGH RISK GROUPS

J.L. Whitling, A. Sigurdsson, D.C. Rowlands, M.T. Hallissey, J.W.L. Fielding. Dept of Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, UK

Of 1753 patients who attended open access endoscopy between 1984 and 1988, 22 (1.3%) had gastric cancer. 107 (6.1%) had ulcers and 212 (12%) were found to have atrophic gastritis or intestinal metaplasia. Patients with ulcers were re-examined every 2 months until ulcer healing and then offered annual surveillance. 48 accepted. Of the 212 with atrophic gastritis or intestinal metaplasia 34 accepted annual surveillance endoscopy. 14 new cancers were found over ten years, 4 of these in patients undergoing repeat endoscopy for ulcers. These 14 were of an earlier stage than the 22 diagnosed at open access (stage I & II 67% vs 23% p=0.05). Treatment was by D1 or D2 gastrectomy and 5 year survival was significantly better (50% vs 10% p=0.006). The 4 tumours detected on re-endoscoping ulcers that failed to heal may represent missed initial diagnosis rather than true screen detected cancers. Exclusion of these 4 cancers from the analysis improved survival to 60% in true screen detected cancers. For the 10 screen detected cancers both disease stage and survival were influenced by adherence to the original protocol. 2 cases did not attend for more than 4 years and presented with stage IVb and III disease and both have died. 2 cases who did not attend for 2 1/2 years had stage III and II disease. Both are still alive although the patient with stage III disease has liver metastasis. The remaining 6 cases had stage I (n=3), II (n=2) or III (Early gastric cancer with lymph node involvement n=1). 4 are still alive 10 years post diagnosis, one died post operatively and one had a non cancer related death. In patients with atrophic gastritis or intestinal metaplasia 10% of patients will develop gastric cancer over 10 years. Although the numbers involved in this study are small it suggests that in this group annual surveillance can detect tumours at an early and curable stage. The potential benefits of such a surveillance program are large and warrant further investigation in a multi-centre randomised controlled trial.

177 EXCHANGE OF DIGITAL IMAGES VIA E-MAIL IS NO SUBSTITUTE FOR SLIDE REVIEW IN DOUBLE REPORTING OF UPPER GASTROINTESTINAL DYSPLASIA

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Introduction: It is current practice to seek a second opinion in the biopsy diagnosis of upper gastrointestinal neoplasia before definitive treatment is planned as it is accepted that there will be disagreement in a proportion of cases. This audit was undertaken to assess the level of agreement between two pathologists on light microscopy (LM) and also to evaluate the potential usefulness of e-mailed digital images (static telepathology) as a possible method for rapid exchange of diagnostic opinion.

Methods: 52 biopsies from 32 patients were assessed by each pathologist and classified according to the Vienna classification of dysplasia: Negative, indefinite, low grade dysplasia, high grade dysplasia or carcinoma. In 23 cases digital images were taken by one pathologist and sent via e-mail to the other who graded them independently from the LM.

Results: In 43 of the 52 cases there was complete agreement between the two pathologists on LM assessment. In the 9 cases with disagreement this was by only 1 grade on the Vienna scale. The pathologist assessing digital images (23 cases) showed concordance between LM and digital diagnoses in only 7 cases. Where there was disagreement this was by 1 grade in 13 cases and by 2 grades in 3 cases. There was a marked tendency to under grade on the digital image assessment. Where there was disagreement by LM in this group the second pathologist tended to agree with the first on the digital image implying the introduction of bias by field selection.

Conclusions: There was good agreement between the two pathologists by LM, 82%. However, analysis of digital images showed only 30% agreement with the LM diagnosis. The exchange of digital images cannot therefore be recommended for obtaining a second opinion in upper gastrointestinal neoplasia.

178 HIGH TUMOUR TELOMERASE ACTIVITY CORRELATES WITH SHORTENED PATIENT SURVIVAL AND MORE ADVANCED TUMOUR STAGE IN GASTRIC BUT NOT IN OESOPHAGEAL ADENOCARCINOMA

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Background: The ribonucleoprotein telomerase extends telomeres in cancer cells and has been proposed as a prognostic marker for cancer. We measured telomerase expression in gastric adenocarcinomas and those arising in the lower oesophagus/gastro-oesophageal junction (GOJ) and atrophied oesophageal telomerase with pathological stage and post-operative survival.

Methods: Samples of cancer tissue were obtained at time of surgical resection. Telomerase activity of protein extracts derived from cancer specimens was determined using the Telomeric Repeat Amplification Protocol. A single pathologist blinded to the results of the telomerase assays reviewed all slides of cancers to assign T and N stages.

Results: Cancers exhibited a wide range of telomerase expression. There was no significant difference between telomerase activity (median in arbitrary units, 95% CI) of oesophageal/GOJ (551, 154–2394, n=26) and gastric (703, 139–1618, n=20) adenocarcinomas. In gastric adenocarcinomas however, high telomerase activity (median levels) was associated with poor patient survival (median 3.0 months) compared to low telomerase activity (median survival 22.4 months, p=0.01, log rank test). Cancers expressing high telomerase activity were significantly more advanced with regard to T stage than cancers expressing low telomerase levels (p=0.03, Mann Whitney U test). No such differences were observed for adenocarcinomas of the oesophagus/GOJ.

Conclusions: There is a difference between gastric and oesophageal/GOJ adenocarcinomas in terms of the relationship of telomerase expression and clinicopathological variables. Among patients with gastric adenocarcinoma, telomerase activity correlates with markers of advanced disease, whereas this relationship does not hold true in oesophageal adenocarcinomas. Telomerase activation may occur at different stages of the formation of the malignant phenotype in these two cancers and may reflect differences in their pathogenesis. Telomerase could be a prognostic marker in gastric but not in oesophageal adenocarcinoma.

179 THE ROLE OF THALIDOMIDE IN REVERSING CACHEXIA IN PATIENTS WITH INOPERABLE OESOPHAGEAL CANCER

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Background: More than 80% of cancer patients will develop cachexia before death. Thalidomide, which is an anti-TNF agent, has shown weight gain and lean tissue anabolism in patients with HIV disease even when caloric intake was kept constant.

Aim: To evaluate the role of thalidomide in reversing cancer induced cachexia in patients with oesophageal cancer.

Design: Preliminary report on five patients in a before and after design where patients were used as their own controls.

Methods: Five inoperable oesophageal cancer patients were included in the study. Patients were established on an isocaloric diet over a 10-day period after which baseline Body weight, Body Composition, REE (resting energy expenditure) and 24 hour urinary nitrogen/urea values were estimated. At the end of 2 weeks on diet alone both metabolic and body composition studies were repeated and patients were started on 200mg/day of thalidomide for a fortnight 3- Similar measurements were repeated after being on diet and thalidomide for 2 weeks.

Results: 1 female and 4 male patients with mean age 69 years (61–77yrs) lost weight on diet alone from a mean baseline weight of 73.9kg to 72.6kg in 2 weeks. After therapy with thalidomide for 14 days all patients experienced weight gain from a mean weight of 72.6kg to 74.3kg. Similar trend was shown in lean body mass in all these patients. There was an increase in REE in kcal/kg/day in 4 out of 5 patients on thalidomide therapy.

Conclusions: Thalidomide treatment is effective in causing weight gain mainly in the lean body mass in patients with inoperable oesophageal cancer. Its promising role as an anticachectic treatment in cancer needs further evaluation.
ASCORBIC ACID IS PRO-PROLIFERATIVE BUT REDUCES PROSTAGLANDIN PRODUCTION IN GASTRIC CARCINOMA CELLS IN CULTURE IN RESPONSE TO HELICOBACTER PYLORI

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Introduction: Ascorbic acid (vitamin C) is an antioxidant vitamin that is actively secreted into the gastric lumen. The presence of Helicobacter pylori infection reduces intraluminal ascorbic acid. A diet low in vitamin C is said to defer an increased risk of gastric adenocarcinoma.

Methods: Gastric cancer cell lines AGS, MKN-7 and MKN-45 were grown to confluence in RPMI / 10% serum, serum starved, then co-incubated with ascorbic acid in the presence or absence of Helicobacter pylori NCTC 11637 for 8 hours. PGE2 was measured using ELISA (R&D systems) and proliferation by measurement of conversion of MTT to a blue formazane dye, a reaction catalysed by mitochondrial succinate dehydrogenase. COX-1 and COX-2 expression were assessed by western blotting using monoclonal antibodies (Cayman Chemicals, USA).

Results: Ascorbic acid alone resulted in a dose dependent proliferation of all three cell lines and down regulation of PGE2 production. There was no down regulation of COX-1 or COX-2 production assessed by western blotting. Helicobacter pylori induced an increase in PGE2 production, accompanied by an increase in COX-2 expression. Ascorbic acid co-incubation resulted in a reversal of the increased PGE2 expression, but there was no change in the COX-2 expression. The table shows PGE2 production (pg/ml) with Hp and increasing concentrations of ascorbic acid (µM), n=5 in each group.

Abstract 180, Table 1

<table>
<thead>
<tr>
<th></th>
<th>Con</th>
<th>Hp+ 0.01</th>
<th>0.1</th>
<th>1</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGS</td>
<td>56</td>
<td>321</td>
<td>11</td>
<td>12</td>
<td>54</td>
</tr>
<tr>
<td>MKN-7</td>
<td>836</td>
<td>83</td>
<td>94</td>
<td>32</td>
<td>56</td>
</tr>
<tr>
<td>MKN-45</td>
<td>838</td>
<td>1595</td>
<td>948</td>
<td>746</td>
<td>661</td>
</tr>
</tbody>
</table>

Conclusions: Ascorbic acid induces a dose dependent proliferation of gastric cancer cells in vitro, but down regulates PGE2 production in both unstimulated and Hp stimulated cells. However there was no down-regulation of COX-1 or COX-2 production.

THE CARDIA IS EXPOSED TO HIGH CONCENTRATIONS OF NITRIC OXIDE GENERATED FROM SALIVARY NITRITE

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Introduction: 30% of ingested nitrate is resecreted in saliva and 25% of this converted to nitrite by oral bacteria. The swallowed nitrite reacts with gastric acid containing ascorbic acid forming nitric oxide (NO). The swallowed nitrite may be resecreted back into the stomach after swallowing.

Methods: To investigate luminal concentrations of NO in different regions of the stomach.

Results: Mean salivary nitrite concentration was 48 µmol/l and this decreased to 388 µmol/L after the nitrate meal. Under fasting conditions, 2mmol nitrate, equivalent to that in a salad meal. Plasma nitrate and gastric NO concentration ranged from 1–10µmol/l and following the nitrate meal increased to 2.5–48µmol/L (p<0.05). The highest concentrations of NO were observed in the cardia region where the swallowed nitrite first encountered acidic gastric juice (figure).

Conclusion: Nitrite in swallowed saliva generates high concentrations of NO in the most proximal cardia region of the stomach. High levels of NO are mutagenic and carcinogenic and its localised production may be an important factor in the development of intestinal metaplasia and cancer of the gastric cardia.

ALOE VERA GEL INHIBITS GASTRIC CARCINOMA CELL PROLIFERATION IN VITRO

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Background: Aloe vera gel (AV) is the mucilaginous aqueous extract of the leaf of Aloe barbadensis miller. It is a widely used herbal remedy for inflammatory and digestive disorders and is also claimed to have anti-cancer effects. Helicobacter pylori (Hp) causes an inflammatory gastritis and is implicated in gastric carcinogenesis.

Aims: To determine if aloe vera inhibits gastric adenocarcinoma cell proliferation in vitro.

Methods: AGS, MKN 7 and MKN 45 gastric epithelial carcinoma cell lines were cultured in RPMI medium/10% serum. Cells were then serum starved and co-incubated with varying concentrations of AV. Cell proliferation was assessed by measuring the conversion of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) to an insoluble blue formazan dye. This reaction is catalysed by mitochondrial succinate dehydrogenase and correlates with the number of viable cells present. Proliferation is expressed as the OD at 550nm as a percentage of control. Experiments were repeated with a co-incubation of Hp 100 cfu per cell. Finally, paper disks soaked in AV were placed on blood agar plates inoculated with Hp.

Results: AV showed a dose-dependent significant inhibition of proliferation at AV dilutions 1 in 10 to 1 in 10^4. Results are expressed as the median (interquartile range) percentage of control activity. p<0.05 for each concentration compared to control (table 1).

Abstract 182, Table 1

<table>
<thead>
<tr>
<th></th>
<th>AV dilution</th>
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<tbody>
<tr>
<td></td>
<td>1:10^5</td>
</tr>
<tr>
<td>AGS</td>
<td>52 (37–56)</td>
</tr>
<tr>
<td>MKN 7</td>
<td>53 (49–58)</td>
</tr>
<tr>
<td>MKN 45</td>
<td>61 (61–69)</td>
</tr>
</tbody>
</table>

There was no change in proliferation from control in cells co-incubated with AV and Hp. Hp growth on blood agar was not inhibited by AV.

Conclusion: Aloe vera gel inhibits cell proliferation in uninfected gastric carcinoma cells but has no effect in the presence of Hp infection. If AV has an anti-cancer action on gastric carcinoma cells, this appears to be negated by H pylori.

DOES THE DURATION OF SYMPTOMS AFFECT RESECTABILITY OF GASTRO-OESOPHAGEAL MALIGNANCIES?

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Aim: Since the new government initiative requires urgent (2-week rule –TWR) assessment of suspected GI cancer, we analysed the relationship between duration of symptoms prior to presentation to hospital and resectability of gastro-oesophageal malignancies.

Methods: Patients diagnosed to have gastro-oesophageal malignancy at St George’s Hospital over a two year period (May 1998–May 2000) were identified using a combination of coding and endoscopy records. Information about duration of symptoms, time from referral...
Effects of Epidermal Growth Factor on Symptomatic Neuroendocrine Tumours: Palliative Treatment for Many Months or Years

A.J. FitzGerald, R.A. Goodlad.

Background/Aims: Gastrointestinal growth can occur through two mechanisms, namely increased crypt cell production and increased crypt fission. Multiple intestinal neoplasia (Min) mice have a mutation in the murine adenomatous polyposis coli (Apc) gene and develop multiple intestinal adenomas, as in the familial adenomatous polyposis syndrome of humans. We have examined the effects of EGF on polyp development and proliferation in the Min mouse.

Methods: 25 Min mice (C57BK/6-ApcMin) and 25 wild type littermates, 4 weeks old, were divided into 2 groups, half received saline while half received EGF by means of a mini-osmotic pump implanted subcutaneously in the back of the animal. After 4 weeks of treatment, the number of polyps in the small and large intestines were scored, as well as the number of metaphase arrested cells and the percentage of branching crypts.

Results: There was no difference in the number of polyps between treatment groups. The saline group had a mean of 78.8±12.1 & 3.9±0.6 polyps for the small intestine and colon respectively while the EGF treated group had 68.5±8.8 & 27.1±5.1 polyps for the small intestine and colon respectively. The number of polyps in the small intestine and colon of the Min mice (p<0.01). There was also no significant difference in the diameters of any of the polyps found in the colon from either the EGF or saline treated groups, however proliferation was significantly increased in the diameters of any of the polyps found in the colon from either the EGF or saline treated groups, however proliferation was significantly increased in the small intestine and colon of the Min mice (p<0.01).

Conclusion: EGF had little effect upon the number of polyps in the small intestine and colon, despite increasing proliferation, suggesting that this is not a marker of neoplastic change in this model.

Use of Low Activity I-131 mIBG in the Treatment of Neuroendocrine Tumours


Patients with disseminated neuroendocrine tumours (NETs) are not normally suitable for surgery and often do not respond to chemotherapy: These patients may be polysymptomatic and require palliative treatment for many months or years. It has been reported that Iodine-131 meta iodosobenzyguanidine (I-131 mIBG) can have significant anti-tumour activity in NETs. The normal dosing regimen is expensive and difficult to administer.

Aim: The aim of this study was to determine the safety and efficacy of a low activity regimen in patients with disseminated NETs.

Methods: A total of 14 patients with histologically confirmed NET (13 carcinoid and one gastrinoma) with disseminated disease were treated. All had good uptake on I-123 mIBG scintigraphic imaging. Patients were selected if tumour related symptoms were not controlled or there was radiological evidence of progressive disease. Patients were treated with 1--6 cycles, 3 monthly 2.7--3.7GBq, I-131 mIBG. Assessment of response was determined by change of measurable tumour size by CT imaging.

Results: Immediate side effects of the treatment included mild nausea and occasional tumour pain. There was no other significant toxicity from the treatment. Continued progression of disease was seen in 4 patients. In 7 patients there was stability of previously progressive diseases with stability continuing for a minimum 6 months after treatment. In 3 patients there was disease regression (25--50%). Tumour regression was often delayed and could lag behind the patient's tumours will be found to clinic assessment, histological diagnosis, time to treatment and outcome were recorded. Stage of tumour at diagnosis was categorised as resectable or unresectable based on clinical and imaging information.

Conclusions: Treatment with low activity I-131 mIBG resulted in tumour stability or reduction in tumour size in 10/14 (70%) of NET patients. Treatment with low activity I-131 mIBG may be useful in patients with NETs.

Somatostatin Receptor Scintigraphy in Neuroendocrine Tumours—Is Single Photon Emission Tomography (SPECT) Required?


Introduction: Somatostain receptor scintigraphy (SRS) with Indium-111 (In-111) octreotide has become an accepted standard in imaging patients with known or suspected neuroendocrine tumours (NETs). However many of these tumours may be small and hidden by radioactivity in overlying tissues. This is particularly true in the upper abdomen where there is physiological activity of In-111 octreotide in the liver, spleen and kidneys. In this situation single photon emission tomography (SPECT) may be useful in identifying small volume NETs.

Aim: The aim of this study was to determine (i) the number of additional patients and (ii) additional tumours in patients with NETs who can be identified as somatostatin receptor positive using SPECT imaging.

Methods: The SRS imaging was reviewed in 66 patients imaged over 2 years with proven NET. All patients had whole body and SPECT In-111 octreotide imaging performed up to 24 hours after injection of up to 200 MBq of tracer using a twin headed Gamma camera fitted with medium energy collimators. The identification of known lesions using both methods was compared with the results of both planar and SPECT imaging.

Results: A total of 52 (78%) patients had a positive SRS on planar imaging alone. SPECT was able to identify tumour in 59 (89%) patients. Also many more additional lesions were found on SPECT. Most of the sites of tumour seen on SPECT but not planar imaging were in the liver or upper abdomen.

Conclusions: SPECT (especially of the liver and upper abdomen) should become an integral part of SRS, so that an additional 11% of patient’s tumours will be found.
1998 to June 2000 were notified on the monthly report card distributed to all consultant gastroenterologists and gastrointestinal surgeons. The reporting doctor then completed a questionnaire detailing the age and clinical presentation of the patients, tumour site, hormone assay level, and method of treatment. Survival data were obtained at the end of the study period. 244 cases were reported, including 32 prevalent cases and 2 inappropriate tumours. 57% of these cases had questionnaires completed, producing 106 cases for analysis. 64 had symptoms attributable to the hormonal effects of the tumours, such as peptic ulceration or diarrhoea, and 42 had non-hormonal symptoms such as bowel obstruction, or extra- gastrointestinal symptoms such as rash or confusion. The commonest tumours producing hormonal GI symptoms were carcinoids (n=44, 69%), presenting with diarrhoea as the main symptom in 83%. Other symptoms included flushing, weight loss or abdominal pain. 80% had liver metastases demonstrated at presentation. Gastrinomas accounted for 20% (n=13) of the tumours, presenting with peptic ulceration in 77%, and diarrhoea in 62%. Other tumours identified were VIPomas, phaeochromocytomas, thyroid medullary tumours, insulinomas, glucagonomas, somatostatinomas, hyperparathyroid tumours, and spindel cell tumours. 78% of all patients were alive at the end of the study period. Carcinoid syndrome was the commonest neuroendocrine condition causing gastrointestinal symptoms. Diarrhoea appears to be a more common presenting symptom of gastroin- testinal tumours than has previously been appreciated. With a series of tumours as large as in any previous UK survey, the BSG monthly surveillance system shows promising potential.

Abstract 188, Table 1

<table>
<thead>
<tr>
<th>Dukes' stage</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>CD3 3878 2794 3541</td>
<td>Zeta 3829 2712 3486</td>
<td>Tumour 2825 1581 2593</td>
</tr>
<tr>
<td>Tumour</td>
<td>Zeta 2771 1524 2523</td>
<td>0.34 0.09 0.04</td>
<td>0.34 0.09 0.04</td>
</tr>
</tbody>
</table>

Conclusion: Loss of ϶ chain expression is uncommon in TILs from patients with colorectal cancer and is unlikely to be a mechanism for immune escape in all CRC patients.

189 BUTYRATE: FOOD FOR COLONIC CANCER CELLS?

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Background: In vivo, colonocytes have a local energy source in the form of butyrate (a short chain fatty acid produced by bacterial fermentation in the colonic lumen) and receive glucose and glutamine from the vasculature. The preferred fuel source for these colonocytes is butyrate. In vitro, colonic tumor cells preferentially use energy sources such as glucose and glutamine. The metabolism of butyrate, glucose and glutamine in 5 different colon cell lines and of cells derived from primary colorectal cancer patients was investigated. The preferred fuel source for these colonocytes is butyrate. In vitro, colonic tumor cells preferentially use energy sources such as glucose and glutamine.

Method/Results: Cell lines were maintained in serum-free media and incubated with either [14C]-glutamine, [14C]-glucose or [1-14C] butyrate. Oxidation was measured by trapping 14 CO2 released on sodium hydroxide-saturated filter paper and counted. Results of butyrate metabolism are shown in the table.

Abstract 189, Table 1

<table>
<thead>
<tr>
<th>Cell line</th>
<th>μmol CO2/mg protein ± S.E.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT29 colon</td>
<td>40.2 ± 1.2</td>
</tr>
<tr>
<td>CaCo-2 colon</td>
<td>37 ± 6.8</td>
</tr>
<tr>
<td>COLO-20 colon</td>
<td>8.7 ± 0.2</td>
</tr>
<tr>
<td>LoVo colon</td>
<td>7.7 ± 0.9</td>
</tr>
<tr>
<td>SW620 colon</td>
<td>4.5 ± 0.5</td>
</tr>
<tr>
<td>Oe33 oesop</td>
<td>0</td>
</tr>
<tr>
<td>Hep-G2 liver</td>
<td>399 ± 52</td>
</tr>
</tbody>
</table>

Conclusion: Colonic cell lines from a primary tumor origin showed a greater ability to metabolize butyrate when compared to those from a secondary source. All colonic cell lines preferred butyrate as an energy source rather than glucose or glutamine.

190 PLASMA BIG ET-1 - A TUMOUR MARKER FOR UPPER GASTRO-INTESTINAL TRACT CANCERS


Introduction: Endothelin-1 (ET-1), the most potent vasoactive peptide has been associated with the development of various cancers. This study was performed to assess whether plasma big endothelin levels (big ET-1), a stable precursor of ET-1 could be used as a tumour marker in upper gastro-intestinal tract cancers.

Patients and methods: Plasma concentration of big ET-1 was measured in 26 patients with proven upper gastro-intestinal cancers prior to any treatment from February 2000 to August 2000 and in 20 age/sex matched controls. Plasma samples were analysed within 2 months of collection using sandwich enzyme linked immuno-assay (Biomedica, Austria).

Results: Median plasma levels of big ET-1 in patients with gastro-oesophageal cancer 3.6 pg/ml [range 1.3–30.2 pg/ml] (p=0.005 Mann-Whitney). However, median plasma levels of big ET-1 in patients with pancreatic cancer (n=12) 3.1 pg/ml [range 1.5–8.1] were not significantly elevated compared to controls (table 1).

Abstract 190, Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Median plasma big ET-1 levels (pg/ml)</th>
<th>Range (pg/ml)</th>
<th>Mann-Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>2.1</td>
<td>1.2–13.4</td>
<td>p=0.005</td>
</tr>
<tr>
<td>2</td>
<td>Gastro-oesophageal cancer</td>
<td>3.6</td>
<td>1.3–30.2</td>
</tr>
<tr>
<td>3</td>
<td>Pancreas</td>
<td>3.1</td>
<td>1.5–8.1</td>
</tr>
</tbody>
</table>

Conclusion: Plasma big ET-1 levels were significantly elevated in gastro-oesophageal cancer patients but not in pancreatic cancer patients. Plasma big ET-1 levels could be used as a tumour marker to detect the presence of gastro-oesophageal cancers.
**Colorectal/Anoректal Posters: 191–220**

**191 NON-STARCH POLYSACCHARIDE INTAKE AND THE PREVALENCE OF CONSTIPATION IN FREE-LIVING AND INSTITUTIONALISED OLDER PEOPLE**

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**Background:** Diagnosis of functional constipation using Rome II criteria includes an assessment of stool frequency, straining and sensation of incomplete evacuation. Few studies have compared the prevalence of these bowel function measurements in free-living (FL) and institutionalised (INS) elderly people.

**Aim:** To compare non-starch polysaccharide (NSP) intake and the prevalence of functional constipation according to three of the Rome II diagnostic criteria between FL and INS elderly people.

**Methods/Results:** 23 FL volunteers (48% male, mean age 75 years) and 13 INS volunteers (20% male, mean age 88 years) were recruited. NSP intake was measured using the 4-day weighed inventory method. Bowel habit was recorded by volunteers in a 7-day bowel habit diary. Results are shown in the table.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FL</th>
<th>INS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSP (g/d) mean (sd)</td>
<td>15.9 (5.7)</td>
<td>6.6 (1.9)***</td>
</tr>
<tr>
<td>Stool frequency</td>
<td>4</td>
<td>15**</td>
</tr>
<tr>
<td>(&lt;3/week)</td>
<td>No. 1</td>
<td>2</td>
</tr>
<tr>
<td>Straining to start</td>
<td>% 32</td>
<td>69*</td>
</tr>
<tr>
<td>(&gt;25% occasions)</td>
<td>No. 7</td>
<td>9</td>
</tr>
<tr>
<td>Straining to finish</td>
<td>% 20</td>
<td>61*</td>
</tr>
<tr>
<td>(&gt;25% occasions)</td>
<td>No. 5</td>
<td>8</td>
</tr>
<tr>
<td>Incomplete Evacuation</td>
<td>% 8</td>
<td>46**</td>
</tr>
<tr>
<td>(&gt;25% occasions)</td>
<td>No. 2</td>
<td>6</td>
</tr>
</tbody>
</table>

Significantly different between FL and INS: *p<0.05, **p<0.01, ***p<0.001.

**Conclusions:** This study suggests that the prevalence of functional constipation is higher in INS than in FL subjects. The higher prevalence of constipation in the INS may be due to the low intake of NSP. This research was fully sponsored by Reckitt Benckiser Healthcare.

**192 THE ANTEGRADE CONTINENCE ENEMA (ACE) PROCEDURE IMPROVES QUALITY OF LIFE IN CHRONIC CONSTIPATION AND Fecal LEAKAGE**

R.P. Baker, P. Neary, M.A. Ismail, A. Gardiner, G.S. Duthie. Castle Hill Hospital, Hull, UK

**Introduction:** The Malone reversed appendicococcygeostomy was first introduced in 1993 for the treatment of faecal leakage in children and is well established in paediatric surgery. We describe our experience of 10 adults who have undergone an appendicococcygeostomy to facilitate ACE for chronic constipation and faecal leakage.

**Methods:** 10 adults underwent appendicococcygectomy. They were retrospectively reviewed from case notes and stoma nurse records.

**Results:** 10 patients (8 female) mean age 29 have undergone the procedure. 7 laparoscopically, 6 had a history of lifelong chronic constipation, 3 faecal leakage and 1 a mixed picture. Post operatively all recovered well from the initial procedure. All feel their presenting symptoms have improved but minor technical difficulties with the enema procedure are commonplace and good stoma therapist support is needed. 2 had minor revision surgery of the stoma, 4 strictuoplastys and 1 became constipated again because of enema difficulties. QOL comparisons in the two groups has shown a significant improvement in the mean mental component score (MCS) on the SF-36 from 36.28 to 48.8 (p=0.038) and an improvement albeit not statistically significant in the physical component scores (PCS) from 36.28 to 43.8 (p=0.099).

**Discussion:** Adult ACE procedure is technically simple and effective in the treatment of constipation and faecal leakage. Significant improvement in the mean mental component score measured by the SF-36 is achieved.

**193 THE ROLE OF AN INTRA-ANAL TAMPON FOR Fecal INCONTINENCE: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY**

E. Mylonakis, S. Radley, N. Payton, M.R.B. Keighley. University Dept of Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK

The surgical treatment of faecal incontinence is not always successful. Some patients continue to complain of incontinence after operation and others wish to explore non-operative means to improve their quality of life. We have assessed the efficacy and acceptability of an intra-anal tampon (IAT) in 50 patients studied prospectively with anal incontinence before and one month after the IAT using the Cleveland Clinic Incontinence Score (CIS) and the Minneapolis Quality of Life Score (MQOL). One patient could not tolerate the tampon and all except 6 patients reported some discomfort whilst 16 complained of perineal pain during its use. Nevertheless, CIS was significantly improved from 13.7 (7–18) to 11.4 (4–17) (p=0.007). Furthermore, MQOL also significantly improved for lifestyle from 18 (11–38) to 21.4 (15–39) (p=0.002) and for behaviour 13.5 (10–31) to 17.5 (11–32) (p=0.001) and for embarrassment 5.8 (3–11) to 7.1 (5–11) (p=0.02) but not for depression. Twenty six (%52) stated that they wished to continue to use the IAT because it improved their quality of life. Thirty patients reported that they would recommend the device to other people. This study has indicated that the IAT is safe but causes some discomfort but for those who continue to use the device quality of life is improved.

**194 CAUSES AND TREATMENT OF MALE Fecal INCONTINENCE**

C. Bailey, F. Adedoji, J.S. Varma, S.M. Pluss. Dept of Surgery, Royal Victoria Hospital, Newcastle upon Tyne, UK

**Introduction:** Faecal incontinence in women has been extensively studied however there are few data on causes and outcome in men with this condition.

**Aims:** To analyse the causes, treatment and effectiveness of treatment for faecal incontinence in men.

**Methods:** We retrospectively reviewed the casenotes of men investigated for faecal incontinence between 1995 and 1999. The aetiology of incontinence and the outcome of treatment was examined.

**Results:** Records of 42 men (mean age 57 years, range 14–79) were reviewed. 19 (45%) had a history of anal surgery (haemorroidectomy 9, fistula surgery 5, abscess drainage 2, stretch 1, sphincterotomy 1). Eight (19%) had neurological problems, 3 related to spinal surgery and 1 to trauma. Two patients had a rectal prolapse, 1 a megarectum and the cause was not clearly defined in the remaining 12 (29%). Follow-up data was available in 35 cases. Thirty (83%) were treated conservatively, of whom 27 (90%) achieved a satisfactory improvement or complete resolution. Only 5 patients had surgical intervention (prolapse repair 2, graciloplasty 1, sphincter repair 1, colostomy 1).

**Conclusions:** Anal sphincter damage after anorectal surgery was the commonest cause of faecal incontinence in this group. Overt neurological disease was common and the aetiology was unclear in a significant number. Simple conservative measures lead to a satisfactory outcome in the majority of patients.

**195 CLOSED LATERAL SUBCUTANEOUS SPHINCTEROTOMY UNDER DIRECT ENDOSONOGRAPHIC CONTROL**

E. Mylonakis, D.G. Morton, S. Radley, M.R.B. Keighley. University Dept of Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK

Closed lateral subcutaneous sphincterotomy (CLSS) is the procedure of choice for chronic anal fissure because healing rates are high but there is a small risk of transient or permanent impaired continence.
This study was undertaken to determine if CLSS under direct endosonographic control (CLSSSEC) is more effective and safer than standard CLSS. Thirty two patients had CLSSSEC and 20 had CLSS. The groups were comparable for age, duration of follow up, all patients underwent clinical and anorectal physiological evaluation before and three months after the operation. Endoanal ultrasonography was used before and after CLSS and after CLSSSEC compared with 4 (20%) after CLSSSEC. Only 1 a, a CLSSSEC patient, had persistent impaired continence at three months. Ultrasound revealed a complete internal sphincter defect in all CLSSSEC patients but in only 4 of 10 in the CLSS group. The fall in resting pressure was greater after CLSSSEC; 98.4 ± 3.1 to 63.1 ± 19.4 (p<0.001) after CLSS; 94.9 ± 27.3 to 76.5 ± 20.1 NS. These data indicate that CLSSSEC is a more precise method of sphincterotomy but does not eliminate the risk of transient or even permanent impaired continence.

196 INCIDENCE AND SIGNIFICANCE OF A PREVIOUS HYSSTERECTOMY IN WOMEN ATTENDING FOR ENDOSCOPIC INVESTIGATION OF LOWER GI SYMPTOMS

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Background: The incidence of hysterectomy (HY) in women with lower GI symptoms attending for flexible sigmoidoscopy (FS) and its effect on the success rate of the procedure has not been formally studied.

Aims: To prospectively estimate HY incidence in women attending an endoscopy clinic with lower GI symptoms. Secondly determine if HY affected FS success rate or caused detectable differences in pelvic loop size/configuration as a result of pelvic adhesions.

Methods/Results: Over a 12 month period a single experienced endoscopist carried out 2 “fast track” surgical endoscopy lists per week. Non-sedated FS was carried out in 200 women using either a full-length adult or 130 cm paediatric colonoscope. The FS failure rate (defined as inability to reach the sigmoid/descending colon junction or beyond) was significantly higher (p=0.0112) in HY patients (16/50 or 32%) compared with 19/146 (13%) in the women with no HY history. Using magnetic endoscope imaging (MEI) combined with a biopsy probe (Gut 2000;46(suppl II A30) we showed that HY patients tended to form smaller/ tighter (and hence more painful) pelvic loops than other women. Furthermore when using an adult colonoscope (but not a flatter paediatric instrument) to perform FS, the median insertion depth before pain was first felt was significantly less (p=0.0002) in the HY patients.

Conclusion: Over 25% of female patients attending for lower GI investigations will have had a previous hysterectomy. A thinner/less stiff paediatric colonoscope is recommended for such patients.

197 A PROSPECTIVE STUDY TO ASSESS THE IMPLEMENTATION OF A FAST-TRACK SYSTEM TO MEET THE TWO-WEEK TARGET FOR COLORECTAL CANCER

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Aims: This prospective study assesses the introduction of a fast-track referral system for patients with suspected colorectal cancer.

Methods: The referral system was initiated in Yeovil District Hospital and Taunton and Somerset Hospital using six screening criteria to select high-risk patients. Data on all high-risk patients from 1 November 1999 to 30 April 2000 was recorded prospectively. Patients with proven colorectal cancer diagnosed between 1 November 1998 and 30 April 1999 have been identified for comparison.

Results: 453 fast-track referrals were received in the six month period, with 303 patients (70%) seen within two weeks. There were 158 new cases of colorectal cancer in total (111 elective, 47 emergency). 59 patients were diagnosed from fast-track referrals (53% of total elective cases). Median time to diagnosis in the fast-track group was 11 days versus 32.5 days for non-fast-track elective cases (p<0.001). Median time to diagnosis for all elective cases was 17 days versus 38.5 days for patients presenting one year earlier (p<0.001). 75% of fast-track patients were diagnosed within two weeks of non-fast-track elective patients (p<0.001). 48% of all elective patients were seen within two weeks versus 17% of patients presenting one year earlier (p<0.001). The proportion of emergency admissions was reduced from 40% to 30% (p=0.07) following introduction of this system.

Conclusions: A fast-track system for suspected colorectal cancer has led to a significant reduction in the time to diagnosis, with the majority of cases diagnosed within two weeks.

198 IMPACT OF THE “2 WEEK RULE” ON THE TREATMENT OF COLORECTAL CANCER

F.Y. Soo, R. Winterton, S.M. Plaus Dept of Surgery, Royal Victoria Hospital, Newcastle upon Tyne, UK

The government has pledged that all patients with suspected colorectal cancer will be seen within 2 weeks and they have published guidelines to identify high risk patients. This study analysed patients with colorectal cancer admitted to a single surgeon with no referral guidelines. The number who would have met the guidelines and the potential effect on overall time to treatment was determined by assuming the time to first out-patient appointment for this group would have been a maximum of 14 days and adjusting time to diagnosis and treatment accordingly. The case notes of 78 patients (32 (40%) female, mean age 68 years (range 24–96)) were studied. 81% of 32 patients with rectal cancer and 67% of 46 with colon cancer met the guidelines. Adherence to the guidelines in patients with rectal cancer would have had a small but significant effect on the time to first appointment (median 8 days, interquartile range 3–35 days, reduced to 8 (3–14) days. Wilcoxon matched pairs p=0.016). Time to diagnosis would also be reduced (26 (6–61) vs 17 (6–40), p=0.016) but there would have been no effect on time to surgery (117 (86–149) vs 96 (62–145), p=0.06) because of prolonged waiting times for staging and pre-operative radiotherapy. Time to first appointment with colon cancer would have fallen (28 (9–49) days vs 14 (9–14), p<0.0001). Time to diagnosis would also be reduced (26 (6–61) vs 17 (6–40), p<0.0001) and treatment (120 (56–143) vs 56 (40–117), p<0.0001) would also have been significantly reduced. Implementation of government guidelines and the 2 week rule would have had significant benefits in terms of treatment times for patients with colorectal but not rectal cancer. Their introduction is publishd to be combined with increased resources for staging and radiotherapy due to achieve significant improvements for patients with rectal cancer.

199 AN AUDIT OF Faecal OCCULT BLOOD TESTS IN A DISTRICT GENERAL HOSPITAL

J. Singh, D.A. Burke. Cumberland Infirmary, Carlisle CA2 7HY, UK

Introduction: Faecal occult blood tests (FOBTs) have been validated in colorectal cancer screening. Their value in other indications is less clear. Despite this use of FOBTs remains commonplace.

Aims: (1) To audit FOBT use with reference to their source, indications and results. (2) To determine if FOBTs altered in-patient management.

Methods: Computerised records of FOBT requests received by the biochemistry department in 1997 were retrospectively reviewed. For in-patient requests hospital notes were reviewed to determine outcome and what influence the FOBTs had on management.

Results: 1497 FOBTs from 630 patients (516 from primary care), 58.5% of hospital patients (HP) v 28.8% of primary care patients (PC) were positive (p<0.001). Median age 63 (1 month to 100 years). Complete collections of 3 faecal samples were greater in PC than in HP (61.8% v 36.0%; p<0.001). Indications from PC were anaemia 32.8%; frank GI bleeding 9.9%; altered bowel habit 20.7%; abdominal pain 13.8%; others 10.3%. An indication was not supplied in 12.4%. 15 of 121 GP s were responsible for 37% of primary care requests. Indications for HP were anaemia 43.9%; frank GI bleeding 18.4%; altered bowel habit 12.0%; abdominal pain 7.0%; others 14.9%. Elderly care wards 42 (36.8%); general surgery 25 (21.9%); nephrology 16 (14%); others 31 (27.2%). Decisions to
IMPACT OF THE NURSE LED RECTAL BLEEDING CLINIC

M.E. Vance, S.G. Shah, A.C. Windsor, B.P. Saunders. Whinf Unit for Endoscopy, St Mark’s Hospital, Watford Road, Harrow, Middlesex, UK

Background/Aims: Rectal bleeding is a common symptom referral often necessitating multiple hospital visits for initial assessment, investigation and subsequent management. Recently there has been a heightened awareness of colorectal cancer leading to an increased service demand. To meet this demand a nurse led open access rectal bleeding clinic was set up to provide a fast-track service to examine, treat and discharge patients with benign ano-rectal conditions and screen for neoplastic disease in a single session.

Methods: A rectal bleeding clinic was established in August 1999. Patients over the age of 45 with symptoms of bright red rectal bleeding only were referred directly by their GP to the Endoscopy unit. Referral letters were screened by a Consultant surgeon (ACW) and appointments arranged within a 4 week period. A full history and physical examination was performed with flexible sigmoidoscopy and video proctoscopy in all patients. Those with benign ano-rectal disease were treated and discharged on the same day. Patients with normal findings were referred for barium enema and in those with adenomatous polyps colonoscopy was performed. Patients were followed up at 1 and 3 year intervals.

Results: 220 patients were referred (118 male, 102 female, mean age 55.9yr (sd=14.8)). Indications: rectal bleeding (90%), 9% of referrals included bleeding/anal pain and bleeding/change in bowel habit (1%). Findings: benign ano-rectal disease (45%) (injection of haemorrhoids in 10%), diverticular disease/IBD (17%), polyps (adenomas>1cm) (10%) (median age 54yr (45–68); mean no. of polyps 1), cancer (2%) (median age 75.5yr (70–88)), and normal examination (26%). Of the cancers/polyps (4%) were within reach of a rigid sigmoidoscope (at 20cm). The remaining (96%) cancers/polyps were found in the distal/proximal sigmoid and descending colon. 45% of these patients also had co-existent haemorrhoids. 20 patients have been followed up at their one-year interval; only two have been re-referred for treatment of their haemorrhoids and discharged. Routine outpatient waiting times have been reduced from 16 to 8 weeks.

Conclusion: All patients with symptoms of rectal bleeding require at least a flexible sigmoidoscopy to exclude neoplastic disease. A nurse led clinic provides an effective ‘one-session’ service reducing outpatient clinic waiting times.

TOPICAL L-ARGININE LOWERS RESTING ANAL PRESSURE

N. Griffin, M. Jonas, K. Neal, J.H. Scholfield. Division of Gastro-intestinal Surgery, University Hospital, Queen’s Medical Centre, Nottingham, UK

Introduction: Chronic anal fissure is associated with raised resting anal pressure (RAP). The discovery of nitric oxide as a neurotransmitter mediating relaxation of the internal anal sphincter, led to investigation of exogenous nitric oxide donors, such as glyceryl tri-nitrate (GTN) as possible treatments for anal fissure. Endogenous nitric oxide (NO) is produced from cellular metabolism of L-arginine by NO synthase. This study investigated whether topical L-arginine may lead to increased NO production and reduced pressures in healthy volunteers.

Methods: Local ethics committee approval was obtained. Anal manometry was performed using a solid state catheter for 2 hours following application of 400 mg of L-arginine ointment to the anal verge in 15 volunteers. After a washout period of 2–4 weeks, 11 of the 15 volunteers repeated the study using a placebo gel (Aquagel) for a period of one hour.

Results: The pressure drop from the initial RAP is shown in the table below. Topical L-arginine caused a greater maximum fall in mean RAP than placebo (p<0.002, Mann-Whitney U, table 1).

<table>
<thead>
<tr>
<th>Time (mins)</th>
<th>Mean fall from initial resting anal pressure (cm H2O)</th>
<th>P value</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>15.7±2.8</td>
<td>0.001</td>
<td>7±2.8</td>
<td>0.06</td>
</tr>
<tr>
<td>30</td>
<td>20.3±3.4</td>
<td>0.001</td>
<td>4.6±1.7</td>
<td>0.03</td>
</tr>
<tr>
<td>45</td>
<td>15.3±4.8</td>
<td>0.011</td>
<td>6.9±3.1</td>
<td>0.12</td>
</tr>
<tr>
<td>60</td>
<td>14.5±5.0</td>
<td>0.015</td>
<td>4.1±3.8</td>
<td>0.37</td>
</tr>
<tr>
<td>120</td>
<td>17±5.0</td>
<td>0.006</td>
<td>16.1±2.5</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± S.E.M. The P value for the fall in RAP at each time point was calculated using Wilcoxon Rank Sign test.

Conclusion: Arginine effectively lowers RAP; its onset of action is rapid and duration at least 2 hours. Arginine shows promise as a possible alternative treatment for chronic anal fissure.
ILEAL POLyps in familial adenomatous polyposis

C.J. Groves1, I.G. Beveridge1, I.C. Talbot, A.B. Price, R.K. Phillips1. Dept of Histopathology and ICRF Colorectal Unit, St Mark’s Hospital, Harrow,

Background: Restorative proctocolectomy with ileal pouch-anal anastomosis has become more common as a prophylactic procedure in familial adenomatous polyposis (FAP) because of the advantage of removal of all cancer-prone mucosa. The recent finding (Gastroenterology 2000;118(suppl 2):A427), however, of adenomatous polyps of ileal origin arising in up to 66% of FAP pouches has prompted a closer inspection of FAP ileal mucosa which is not incorporated into a pouch.

Aim: To demonstrate ileal adenoma at the time of colectomy for FAP.

Subjects and Methods: 12 patients with FAP were examined intra-operatively by passing a video-colonoscope into the ileum immediately after colectomy and before the anastomosis was made. The surgeon then manually fed the tip of the endoscope 60cm proximally. The site, number and size of ileal polyps were recorded. Four biopsies were taken from normal looking ileum and four from polyp or other suspicious mucosa, therefore following the same protocol for pouchoscopy. In addition, the resected ileal cuff adjacent to the caecum was examined histologically for adenoma.

Results: The median age at colectomy was 25.5 yrs (14 to 56) and number of macroscopically visible colonic polyps in the histological specimen 68 (13–1180). Six of the 12 patients had visible ileal polyps up to 1cm in size but in all cases the lesions consisted of lymphoid hyperplasia, not adenoma. One of the biopsies from normal looking mucosa in one patient, and one of the resected ileal cuff specimens in another contained single-crypt and oligocryptic adenomas respectively.

Conclusion: The terminal ileum in these confirmed cases of FAP does not contain adenomatous polyps and has detectable microscopic adenoma only. This is in contrast to FAP pouch ileal mucosa in which visible and histologically confirmed adenomatous polyps are seen in two thirds of cases. Environmental changes (faecal stasis) associated with pouch formation may lead to growth of ileal adenomas. Incidence and nature of pouch adenomas in patients with familial adenomatous polyposis.

OUTCOME OF ANAL FISTULA SURGERY IN CROHN’S DISEASE

E. Mylonakis, M.R.B. Keighley. University Dept of Surgery, Queen Elizabeth Hospital, Edgbaston, Birmingham, UK

We have prospectively studied the results of operations for symptomatic anorectal fistulas (AF) in Crohn’s disease (CD). Thirty patients with 37 AF and CD were studied clinically and using a continence score and anorectal physiological studies before and three months after operation; 18 women, mean age 37.8 (range 25–53 years). Three of 37 AF were superficial, 13 of 37 were intersphincteric, 20 of 37 were trans-sphincteric and 1 of 37 supra-sphincteric. Thirteen AF were laid open and 24 were treated by a seton. Furthermore, surgical treatment achieves healing in only three quarters of all patients.

Conclusion: Thirteen AF were superficial, 13 of 37 were intersphincteric, 20 of 37 were trans-sphincteric and 1 of 37 supra-sphincteric. Thirteen AF were laid open and 24 were treated by a seton. Furthermore, surgical treatment achieves healing in only three quarters of all patients.

SERUM B12 falls after pouch surgery but bacterial overgrowth is not the cause


The long-term effect of totally stapled restorative proctocolectomy (TRSP) on vitamin B12 levels is unknown. We routinely measure vitamin B12 levels in our 164 patients, at follow-up after TRSP. Since bacterial overgrowth is suspected as a cause of B12 deficiency in these patients, hydrogen breath tests were performed on those with low serum B12. Three patients were B12 deficient prior to pouch formation. At follow-up thirty nine (23.8%) had low B12 (<188pg/ml), at a median of 2.4 years (0–7) of pouch function. In addition forty seven (73.4%) patients with multiple B12 measurements showed steadily decreasing levels. 34/35 (97.1%) patients with B12 deficiency who subsequently had a hydrogen breath test were negative for bacterial overgrowth (table 1).

Abstract 205, Table 1

<table>
<thead>
<tr>
<th>Elapsed Time After TRSP</th>
<th>Patients With B12 Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10.0%</td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>17.0%</td>
</tr>
<tr>
<td>&lt;3 years</td>
<td>21.2%</td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>22.9%</td>
</tr>
<tr>
<td>&gt;7 years</td>
<td>23.4%</td>
</tr>
</tbody>
</table>

These data show that almost one in four patients after TRSP will have low serum B12 within 7 years. We recommend lifelong follow-up of vitamin B12 levels. In this study, bacterial overgrowth does not appear to be the cause of this B12 deficiency.

PATIENT VERSUS PHYSICIAN DELAY IN COLORECTAL CANCER: CAN WE DO BETTER?

P.A.H.A. Gunawardhana, S.R.E. Wijesuriya, K.I. Deen. Dept of Surgery, University of Kelaniya, Sri Lanka

Background: Altered bowel habit and rectal bleeding are considered ominous symptoms. Negligence may cause considerable delay in diagnosis of colorectal cancers. We have prospectively analysed presenting symptoms, patient’s delay, and physician’s delay in colorectal cancer patients who were admitted to our unit.

Method: Questionnaire survey of time interval between onset of symptoms and first visit to physician and time interval from first visit to diagnosis of colorectal cancer.

Results: 63 patients (24 male; median age 60 years, range 23 to 78 years) were evaluated, 34 (53.9%) had rectal cancer, 12 (19%) had right colon cancer, 11 (17.4%) had left colon cancer and 6 (9.5%) transverse colon cancer. Presenting symptoms in rectal cancer were (n=34): bleeding (n=27; 79.4%), altered bowel habit (n=23; 67.6%), and abdominal pain (n=9; 26.4%). Some patients had more than one symptom. Presenting symptoms in colon cancer (n=29) were: altered bowel habit (n=24; 82.7%), and abdominal pain (n=16; 55.1%). Some patients had multiple symptoms. Patient’s delay (median) in seeing a physician was 08 weeks (range 1–32 weeks) for rectal cancer versus (median) 06 weeks (range 01–364 weeks) for colon cancers. Time to definitive diagnosis following the first visit to a physician was: rectal cancer (median) 18 weeks (range 01–192 weeks) versus colon cancer (median) 12 weeks (range 01–32 weeks).

Conclusion: There was an unacceptable delay in time to diagnosis of colorectal cancers from the time of patient first visit to the physician.

COMPUTED TOMOGRAPHIC COLOGRAPHY (CTC) FOR COLON CANCER AND POLYP DETECTION

D.A. Nicholson1, C. Summerton, H. Burnett1. Dept of Gastroenterology, Trafford General Hospital, Trafford, Manchester; 1Dept of Radiology, Hope Hospital, Salford, UK

CTC is a new technique allowing minimally invasive imaging of the colon. We are conducting a clinical trial, which has been funded by the North West R&D NHS scheme to determine the accuracy of CTC compared to fibreoptic colonoscopy (FC) in detecting colonic polyps and cancer.

Methods: Patients undergo CTC prior to/on the same day as FC. CTC / FC is performed after standard bowel cleansing/preparation. Two CT acquisitions are performed with the patient supine and then prone using a single spiral CT following administration of intravenous Buscopan and colonic air insufflation. The findings of CTC are correlated with the findings of FC in each patient.

Results: To date 112 patients have been recruited. The FC patient diagnoses were as shown in the table.

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37 right hemicolectomy specimens were studied. During routine specimen dissection, at least one additional tissue block was taken to include the tumour and the RSM. The distance of the tumour from the RSM was measured using a microscope and vernier scale. The Dukes’ stage, TNM stage and presence or absence of anterior peritoneal surface (APS) TI was also recorded in each case. RSM and APS TI were defined as the presence of tumour (or an involved lymph node) within 1mm of the RSM and APS respectively.

**Results:** RSM and APS TI were present in 4 cases (11%) and 26 cases (70%) respectively. Direct (ie non-nodal) RSM TI (2 cases) only occurred in posterior or circumferential tumours.

**Conclusion:** RSM TI, although less common than APS TI, occurs within a significant number of caecal carcinomas. The rate of RSM TI identified in this study compares favourably with a previously published local recurrence rate of 10% in caecal carcinoma (Ann Surg 2000; 232:181–6), suggesting that RSM TI is an important predictor of recurrence in caecal carcinoma. It is possible that patients with RSM TI may benefit from postoperative radiotherapy.

**208 DISTRIBUTION OF COLORECTAL ADENOMAS: CAN FLEXIBLE SIGMOIDOSCOPY BE EFFECTIVE FOR SCREENING?**

H. Ferguson, R.J. Moorehead, T.C.K. Tham. *Divisions of Gastroenterology and Surgery, Ulster Hospital, Dundonald, Belfast, Northern Ireland, UK*

Screening flexible sigmoidoscopy has the potential to reduce colorectal mortality by detecting polyps followed by colonoscopy and polypectomy. However the effectiveness of flexible sigmoidoscopy depends on the frequency of proximal polyps in the left colon within reach of the flexible sigmoidoscope. We have therefore determined this frequency in our population.

**Methods:** Consecutive patients were included if at least one colorectal polyp was detected during index colonoscopy. These patients were searched from endoscopy databases and hospital diagnostic codes.

**Results:** 234 patients had at least one polyp at index colonoscopy. Colonoscopy was performed for investigations of lower gastrointestinal symptoms and anaemia. The caecum was intubated in 209 (89%). The mean age was 62 years (range 33–89 years). 199 patients (85%) had at least one adenoma (the rest had hyperplastic polyps or carcinoma). 119 (60%) were male and 80 (40%) were female. 21 (11%) subjects had more than two adenomas. There were a total of 269 adenomas of which 195 (72%) were in the rectosigmoid colon. There were 199 “high risk adenomas” (adenomas larger than 10 mm in diameter, adenomas containing villous components, or adenomas with severe dysplasia). 146 (73%) of these were in the rectosigmoid colon. 32 (16%) subjects had adenomas only proximal to the sigmoid colon, including 18 (9%) subjects with “high risk adenomas”.

**Conclusion:** 72% of adenomas were within the rectosigmoid colon and could have been detected by flexible sigmoidoscopy. 16% of patients with proximal polyps would have been missed by flexible sigmoidoscopy. These figures support the recommendation of flexible sigmoidoscopy for colorectal cancer screening.

**209 RETROPERITONEAL MARGIN TUMOUR INVOLVEMENT IN CAECAL CARCINOMA**

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**Background:** Mesorectal plane tumour involvement is a well established predictor of local recurrence in rectal carcinoma. However, the relationship between retroperitoneal surgical margin (RSM) tumour involvement (TI) and local recurrence in caecal carcinoma is poorly characterised.

**Aim:** To assess the rate of RSM TI in caecal carcinoma and to compare this with the previously published rate of local tumour recurrence.

**Methods:**

**Abstract 207, Table 1**

<table>
<thead>
<tr>
<th>Distribution of Adenomas</th>
<th>= 57 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal/Incomplete</td>
<td>= 15 patients</td>
</tr>
<tr>
<td>Diverticular Disease</td>
<td>= 3 patients</td>
</tr>
<tr>
<td>Colitis (UC + Crohn’s)</td>
<td>= 11 patients</td>
</tr>
<tr>
<td>Polyps &lt; 1cm</td>
<td>= 11 patients</td>
</tr>
<tr>
<td>Polyps &gt; 1cm</td>
<td>= 3 patients</td>
</tr>
<tr>
<td>Cancers</td>
<td>= 7 patients</td>
</tr>
<tr>
<td>Cancer + polyps</td>
<td>= 2 patients</td>
</tr>
</tbody>
</table>

**Results:**

FC was completed to the caecum in only 79% of patients whereas CTC was completed in all. A total of 65 polyps were detected by FC. CTC detected 20 of 22 polyps greater than 1cm but only 22 of the 43 polyps less than 1cm in diameter. In addition 5 false positives on CT were identified. 9 cancers seen at FC were all detected by CTC. Additionally CTC detected two further cancers in the right side of the colon not reached at FC and a renal cell carcinoma in a patient presenting with pain and change in bowel habit.

**Discussion:** Initial results show that CTC is a sensitive method of detecting colonic cancers and the majority of polyps > 1cm. All cancers and 91% of 1cm polyps have been identified by CTC. Up to date figures from this study will be presented.

**210 LOW INCIDENCE OF COLORECTAL CANCER IN SOUTH ASIANS RESIDENT IN THE UK**

S. Samuels1, K.W. Scott1, E.T. Swarbrick1, A.M. Veitch1. Depts of ‘Gastroenterology and Histopathology’, New Cross Hospital, Wolverhampton, UK

**Background and aims:** Colorectal cancer is relatively uncommon in India. Data from the 1970’s showed reduced mortality from colorectal cancer in South Asians in the UK (BMJ 1984;289:1185–7). There had, however, been no large studies of racial differences in colorectal cancer incidence in the UK. Many South Asians have been resident in the West Midlands for several decades. We aimed to determine whether there was a reduced incidence of colorectal cancer in South Asians in Wolverhampton, and whether there were trends in incidence over the past decade.

**Methods:** Cases of colon and rectal cancer from 1990–99 were identified from the Histopathology Dept database. South Asian patients were identified by surname/forename analysis, and African and Oriental subjects excluded. Age-sex standardised incidences were calculated using Census data.

**Results:** From 1990–99 the median age-sex standardised incidence of colorectal cancer was 14.69/100,000/year in South Asians compared to 37.20/100,000/year in non-Asians (96% white, 4% black Caribbean) (p=0.0002). For rectal cancer the median age-sex standardised incidence in South Asians was 4.26/100,000/year compared to 22.57/100,000/year in non-Asians (p=0.0002). There was a trend towards increasing incidence of colorectal cancer from 1990–99 in non-Asians (p=0.03), but no significant trend in Asians. Rectal cancer incidence is increasing in Asians (p=0.049), but not in non-Asians. Standardised Morbidity Ratios for cancer in South Asians is shown in the table.

**Abstract 210, Table 1**

<table>
<thead>
<tr>
<th>Year</th>
<th>90</th>
<th>91</th>
<th>92</th>
<th>93</th>
<th>94</th>
<th>95</th>
<th>96</th>
<th>97</th>
<th>98</th>
<th>99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>0.30</td>
<td>0.52</td>
<td>0.52</td>
<td>0.62</td>
<td>0.42</td>
<td>0.27</td>
<td>0</td>
<td>0.61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal</td>
<td>0.00</td>
<td>0.38</td>
<td>0</td>
<td>0.32</td>
<td>0.52</td>
<td>0.51</td>
<td>0</td>
<td>1.35</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** There is a markedly reduced incidence of colorectal and rectal cancers in South Asian immigrants compared to whites and black Caribbeans. The rates of colorectal cancer in South Asians have not increased over the last 10 years as might be expected with prolonged exposure possible western environmental factors predisposing to colorectal neoplasia. Rectal cancer is increasing in this group, however.

**211 SIGNIFICANCE OF PROXIMAL COLONIC TUMORS IN PATIENTS WITH DISTAL COLONIC POLYPS**

V. Godi, A. Campbell, M.H. Giatffer. Gastroenterology Unit, Hull Royal Infirmary, Anlaby Road, Hull HU3 2JF, UK

Colonic polyps are mainly distal in distribution and proximal polyps are infrequent and associated with low recurrence rate. This audit was designed to assess the distribution of colonic polyps discovered at colonoscopy in symptomatic patients with emphasis on the characteristics of proximal lesions (Proximal to the Splenic flexure) in patients
with distal polyps. Two hundred and four polyps were resected endoscopically from 99 patients who presented with altered bowel habits and/or rectal bleeding. There were 58 males and 41 females with a mean age of 65 ±14 (SEM). They had been symptomatic for a mean of 6 ±17 months before undergoing colonoscopy. One hundred and fifty (74%) polyps were resected at the index colonoscopy of which only 13 (9%) polyps were proximal and 137 (91%) were distal. 34 other polyps were resected at subsequent surveillance colonoscopy of which only 9 (17%) were proximal and 45 distal. 83 polyps (41%) showed evidence of high grade dysplasia, 22 (11%) showed low grade dysplasia, in the remaining 99 polyps there was no dysplastic changes. The 22 proximal polyps, 12 (55%) showed high grade dysplasia and 2 (10%) low grade dysplasia as compared to 39% and 11% respectively for distal polyps. There were four colonic cancers diagnosed either at the index colonoscopy (2) or at surveillance colonoscopy (12 and 60 months). All four cancers were Duke A/B and successfully resected. The index colonoscopy (2) or at surveillance colonoscopy (12 and 60 months) of 63 patients completed a total of 181 colonoscopies. Distal cancers were found in 63% of all cancers identified. Significantly, the majority of cancers are found in the distal colon. Proximal lesions constituted less than 10% of all tumours resected but a significant proportion of proximal polyps had high grade dysplasia. This contrasts with distal lesion when high grade dysplasia was evident in just over a third of all specimens.

**Results:** Tumour regression was seen in all patients; 3 (25%) had grade 1 regression, 2 (17%) had grade 2 regression, 2 (17%) had grade 3 and 5 (42%) grade 4 regression. Median nodal harvest was 3 (range 0–11) after NAT compared with 9 (range 1–19) in those without NAT (p<0.05). Tumour deposits were identified in 6 of 44 nodes (14%) after NAT (p<0.01, t-test). Median size of the harvested nodes after NAT was 0.48 vs 2.21±0.53 mm (SEM) (p=0.03).

**Conclusion:** These studies show a lower total colonic mucosal 5-HT level in IBS than controls. In contrast higher numbers of 5-HT staining EC cells were seen in IBS than controls. This apparent discordance might be explained by the increased release and consequent depletion of 5-HT from the colonic mucosa in IBS with a compensatory chronic increase in the number of EC cells which would appear not to reflect the total 5-HT concentration since the immunostaining does not quantitate intracellular levels of 5-HT.

**Background:** Neo-adjuvant therapy is known to cause tumour downstaging in rectal cancer. This study evaluated the impact of NAT on tumour regression and lymph node harvest.

**Patients and Methods:** Twelve patients (6 males; median age 58 years, range 26–72) with rectal cancer were subjected to high dose neo-adjuvant therapy (4500cGY in 25 fractions). Tumour regression (TRG) was graded 1–5. TRG1- no residual tumour cells; TRG2- rare residual tumour cells with marked fibrosis; TRG3-marked fibrosis with scattered tumour cells or groups; TRG4-abundant cancer cells with little fibrosis; TRG5- no tumour regression. Lymph nodes were harvested by dissecting along blood vessels. Data was compared with 10 randomly selected non irradiated controls. (3males, median age 54 years, range 22–65 years).

**Results:** Tumour regression was seen in all patients; 3 (25%) had grade 1 regression, 2 (17%) had grade 2 regression, 2 (17%) had grade 3 and 5 (42%) grade 4 regression. Median nodal harvest was 3 (range 0–11) after NAT compared with 9 (range 1–19) in those without NAT (p<0.01, t-test). Median size of the harvested nodes after NAT was 0.48 vs 2.21±0.53 mm (SEM) (p=0.03).

**Conclusion:** Although NAT down stages rectal cancer, it results in a significantly lower lymph node yield which are also significantly smaller in size compared with non irradiated controls. Histopathologists must be aware of this to ensure adequate sampling, and hence accurate reporting of lymph node status in irradiated rectal cancer.

**References:**

1. S.R.E. Wijesuriya1, K.I. Deen1, J. Hewavisenthi2, J. Balawardana3, M.Peerers may have food intolerances, an abnormal colonic flora and malabsorption. The probiotic Lactobacillus plantarum 299V (Probi AB, Lund, Sweden) has been shown to promote colonic fermentation in healthy volunteers and to improve symptoms in a group of IBS subjects.

**Methods:** Twelve patients with IBS fulfilling the Rome criteria were randomised to a double-blind intervention trial of 12 months. Each patient received either L. plantarum 299V (5x10^7 cfu/ml) daily against a placebo drink of similar colour and taste. Unbeknown to patients and investigators all received placebo or probiotic for the first 6 months. After this period all received probiotic for the second 6 months. This study was performed to assess any difference in symptoms between IBS patients treated with probiotic or placebo.

**Results:** Breath hydrogen excretion after lactulose was reduced by the probiotic (median at 120 mins 6ppm; placebo, 17ppm p=0.019).

**Conclusion:** L. plantarum 299V had a beneficial effect on colonic fermentation reflected in reduced breath hydrogen after lactulose, but not sufficient to reduce total hydrogen production, or to affect patients’ symptoms.

**Introduction:** IBS may be associated with food intolerances, and malabsorption of food residues in the colon leading to excess hydrogen production (Lancet 1998;352:1187–9). Malabsorption might provide the basis for a diagnostic test to identify IBS patients suitable for dietary treatment.

**Abstract 214, Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Active</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median symptom score</td>
<td>8.5 (6.25–11.25 IQR)</td>
<td>8 (6.75–13.5 IQR)</td>
</tr>
<tr>
<td>Maximum rate of gas production (ml/min)</td>
<td>0.55 (0.4–1.1 IQR)</td>
<td>0.42 (0.45–1.5 IQR)</td>
</tr>
<tr>
<td>Median hydrogen 24hrs (mls)</td>
<td>189.7 (118.3–291.1 IQR)</td>
<td>208.2 (146.2–350.9 IQR)</td>
</tr>
</tbody>
</table>
Methods: Colonic fermentation, measured by continuous measurement of gaseous exchange over 24hrs in a 1.4 m tent calorimeter, was compared in 18 unselected subjects fulfilling the Rome criteria for IBS, 10 normal volunteers and 12 patients with IBS who had previously failed to respond to an exclusion diet. Immediately after calorimetry, each subject, fasting, received 20gms of lactulose and end expiratory breath samples were collected every 30 minutes for three hours. Hydrogen concentrations in tent gases and breath samples were determined by an electrochemical cell (GMI, Renfrew, UK).

Results: Total 24hr excretion of hydrogen, as in earlier studies, was significantly greater in the IBS group (median 333.7nmol/24hrs, IQR 234.7–445.67) compared to the normal volunteers [median 203.1nmol/24hrs, IQR 131.4–256, p = 0.002] or the failed-diet group [median 204.5nmol/24hrs, IQR 111.35–289.13, p = 0.015]. However, no difference was detected in breath excretion of hydrogen following lactulose in any group. Small bowel transit was similar in IBS subjects and controls.

Conclusion: This confirms, in a larger number of patients, our earlier report that total hydrogen production over 24hrs is increased in IBS associated with food intolerance. The lactulose hydrogen breath test, however, does not reflect total 24hr hydrogen production and has no diagnostic value in identifying this subgroup of IBS.

216 COMPARISON OF THE CAECAL AND FAECAL MICROFLORA OF HEALTHY SUBJECTS AND PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

J.A.J. Madden, S. Plumtree, S. Son, K. Dear, S. Terry, J.O. Hunter. Dept of Gastroenterology, Addenbrooke’s NHS Trust, Cambridge CB2 2QQ; 1Cultech Ltd., York Chambers, York St., Swanslea SA1 3NJ, UK

Introduction: Colonic malfermentation has been suggested to be a factor producing IBS and IBS patients have been shown to have lower numbers of lactic acid bacteria in their stools with increased aerobic counts. The caecum is the most important colonic region for bacterial fermentation, but it is not known if the faecal flora is representative of that of the caecum.

Methods: 7 subjects referred for investigation of rectal bleeding whose bowel function and colonoscopy were normal, were considered healthy controls. These and 8 IBS patients were prepared for colonoscopy by a single 100ml enema to empty the sigmoid, leaving the proximal colon undisturbed. The colonoscopy was then passed to the caecum using CO2 for insu

**Results:** Differences in the caecal and faecal flora of may be a factor contributing to colonic malfermentation and the development of IBS.

217 IRRITABLE RECTUM: THE MOST COMMON CAUSE OF FAECAL INCONTINENCE IN A SPECIALIST COLORECTAL PRACTICE


Faecal incontinence (FI) is a common symptom in patients referred to coloproctology and may be due to many causes. We investigate all patients of patients undergoing surgery. A profile of the consecutive series of these patients is presented. 100 consecutive patients with FI were investigated by ano-rectal physiology, endosonography (USG) and where indicated video proctography. The median age of the patients was 55 years (22–84); 79 were female of whom 44 had an adverse event during childbirth. On investigation the anal basal canal pressure was <60mmHg in 82 patients and <30mmHg in 36. The corresponding maximum squeeze pressure was <100mmHg in 83 patients and <50mmHg in 26. The pudendal terminal latency was prolonged in only 20 patients. Rectal sensitivity was assessed using an intra-rectal balloon: 56 patients were unable to tolerate inflation beyond 50 ml. Sphincter defects were identified on USG in 10 patients (3 of IAS, 1 EAS and 7 both internal and external sphincters). On the basis of both clinical history and investigation the aetiology of the FI was considered to be multi-factorial in 47 patients. The predominant diagnoses were: diffuse pelvic floor weakness 16 patients, sphincter dysfunction 11: hypersensitive rectum 53 patients. 29 patients had no demonstrable abnormality of the pelvic floor or sphincters. These data suggest that the cause of FI is often multi-factorial. In this series hypersensitivity of the rectum was an important and previously unrecognized cause of faecal incontinence. This has important implications for treatment especially if surgery is considered.

218 SMOKING AND ANASTOMOTIC LEAK FOLLOWING ANTERIOR RESECTION OF THE RECTUM

P. Baragwanath1, C.D. Sutton1, L. Toogood1, W.M. Thomas1, 1Depts of Surgery and 1Anesthesia, University Hospitals of Leicester NHS Trust, Leicester, UK

Introduction: Anastomotic leak is a major cause of morbidity and mortality following colonic resection and occurs in 2% to 17% of cases. The level of anastomosis, integrity of blood supply and obesity have previously been considered risk factors for leak.

Methods: Clinical details of all patients undergoing anterior resection of the rectum over a two year period were reviewed.

Results: Two hundred and eight patients (116 male) underwent anterior resection of the rectum. There were 25 surgical and radiological leaks (12%). Anastomotic breakdown was significantly associated with a history of smoking (χ²=5.85, 1.d.f., p=0.016) or the failed-diet group [median 203.1ml/24hrs, IQR 131.35–289.13, p = 0.015]. However, no difference was detected in breath excretion of hydrogen following lactulose in any group. Small bowel transit was similar in IBS subjects and controls.

Conclusions: Smokers are 3 times as likely to suffer an anastomotic leak following anterior resection of the rectum than non-smokers. Smoking was the strongest independent risk factor studied in this series. The increased risk of leak from smoking is not reduced in patients who have given up for greater than ten years prior to surgery. A history of smoking, past or present, should influence the decision to perform a concurrent defunctioning stoma in patients undergoing an anterior resection of the rectum.

219 EPIDURAL INCREASES INFECTION RATE FOLLOWING LEFT-SIDED COLONIC RESECTION

K.L.R. Grace1, P. Durdey1, T. Gould1, M.G. Thomas1, 1Depts of Surgery and 1Anesthesia, Bristol Royal Infirmary, Bristol BS2 8HW, UK

Background: There is an increasing use of epidural anaesthesia during left-sided colonic resections, it is however unknown if the anaesthetic technique and post operative provision of analgesia influ

Methods: A retrospective analysis of 148 patients’ consecutive left-sided colonic resections over a 25 month period was undertaken. Analysis of observed complication rate was compared to POSSUM expected morbidity. POSSUM morbidity was calculated using the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity and Portsmouth correction (P-POSSUM) are accepted as physiological audit tools to predict morbidity and mortality in GI surgery, allowing cross group analysis. In comparing observed to expected morbidity, observed complications are equally weighted between mild and severe.

Methods: A retrospective analysis of 148 patients’ consecutive left-sided resections over a 25 month period was undertaken. Analysis of observed complication rate was compared to POSSUM expected morbidity with FI. A prod mortality; Portsmouth corrected morbidity and correlation between type of anaesthesia/analgesia was also assessed.

Results: Observed:Expected mortality was 0.359 (P-POSSUM 1.062, O:E morbidity 1.74. Of these 148 patients, only 15 received PCA. 46.3% of observed morbidity were injective, 82.8% were mild

(pyrexia of unknown origin, urinary, chest or line), and 17.2% severe (deep infection or sepsis). Expected Mortality and Morbidity of patients receiving PCA and Epidural were similar (p=0.343 and p=0.348). A greater infection rate is seen with Epidural (45.1%, 18.4% severe) compared to 20% patients receiving PCA, of which none were severe (p<0.02). 12.5% patients receiving Epidurals experienced hypotension ( systolic<90mmHg for >2hrs), and of these 58.9% had septic episodes (p=0.053).

Conclusions: In patients undergoing left-sided colonic resection, patients receiving epidural analgesia were more than twice as likely to experience an infective adverse event as those receiving PCA. This may in part be due to hypotensive episodes associated with epidural.

USE OF WHOLE CRYPT MOUNTS TO QUANTIFY APOPTOSIS IN HUMAN COLONIC CYTOKS EXPOSED TO IONISING RADIATION OR DIETARY INTERVENTION WITH FISH OIL

J.M. Gee1, A.C.J Polley1, M. Watson1, M. Rhodes2, C.J.M. Speakman1, W.S.L. Stebbings2, I.T. Johnson1. 1Institute of Food Research, Norwich Research Park, Norwich NR4 7UA; 2Norfolk & Norwich Hospital, Brunswick Road, Norwich, NR1 3SR, UK

In healthy colonic mucosa a balance is maintained between cell production and loss via apoptosis or exfoliation. Crypt cell apoptosis is a relatively rare event, but is essential for deletion of DNA-damaged cells from the crypts. Having previously shown that dietary intervention with fish oil can increase crypt cell apoptosis in rat intestine (Car- cocaine 20:645–50), we have quantified apoptosis in the distal colons of cancer patients who received either a placebo or fish oil immediately before surgery, and compared the results with the effects of preoperative radiotherapy.

Methods: Samples of colonic mucosa (5, 10, 15, 20 and 25cm from the tumour) were taken from the resected tissue of patients (n=7) diagnosed with left-sided colon carcinoma, who had received X-ray therapy (25Gy in 5 fractions over 5 days) before surgery. Patients with a similar diagnosis, not requiring pre-operative radiotherapy, were randomly assigned to receive fish oil capsules (1500mcg) or a placebo, (n=24) for 7-21 days pre-operatively. All tissue samples were immediately transferred to fixative for storage. Following rehydration and staining with Feulgen's reagent, whole crypt mounts were prepared to assess mitosis and crypt cell apoptosis using morphological criteria.

Results: Samples of colonic mucosa (5, 10, 15, 20 and 25cm from the tumour) were taken from the resected tissue of patients (n=7) diagnosed with left-sided colon carcinoma, who had received X-ray therapy (25Gy in 5 fractions over 5 days) before surgery. Patients with a similar diagnosis, not requiring preoperative radiotherapy, were randomly assigned to receive fish oil capsules (1500mcg) or a placebo (n=24) for 7-21 days pre-operatively. All tissue samples were immediately transferred to fixative for storage. Following rehydration and staining with Feulgen’s reagent, whole crypt mounts were prepared to assess mitosis and apoptosis, using morphological criteria.

Conclusions: The whole crypt mount technique can be used to visualise and quantify apoptosis in human intestinal mucosa, and to assess the effects of dietary or other interventions.

Pancreas Posters: 221–223

ASSESSMENT OF IMMUNE RESPONSE IN PATIENTS WITH Pancreatic CANCER VACCINATED WITH GAS- TROINTESTINAL TOXOID (G17DT)

S.C. Smith1, C.V. Bouvier1, D. Michael1, R.E. Pounder1, M.E. Caplin1. 1Dept of Gastroenterology, Royal Free and University Medical School, London, UK; 2Aption Corporation, California, USA

G17DT is a conjugate of an epitope derived from gastrin 17 linked to Diptheria toxoid (D'T). Gastrin is an autocrine growth factor in pancreatic and other GI tract cancers. In a phase II study of G17DT for advanced pancreatic cancer only 6/13 (45%) formed antibody to 1 mcg of G17DT however 15/18 (83%) formed antibody to the higher dose of 250mcg. The median survival of the whole group was 7 months. Side effects were limited to mild local pain and erythema with 3 patients forming an abscess. Patients with pancreatic cancer are thought to have a suppressed immune response compared to other GI cancers.

Aim: To assess anti-DT antibody level pre and post vaccination to determine its correlation with Gastrin antibodies and relationship with immunogen side effects.

Methods: 26 of the 31 vaccinated patients had serum available. 18 had developed antibody to gastrin (G+) and 8 had not (G-). Anti-DT antibody level was determined by in-vitro tissue culture neutralisation of purified DT.

Results: 16 (88%) of the G+ group had non-protective levels of anti-DT antibody before vaccination compared with 7 (87%) of the G- group. In cases given 100mcg of G17DT and remaining G-, 3/6 (50%) produced protective levels of antibody to DT; the median rise in DT antibody was 1 fold. Both of the 2 cases given 250mcg and remaining G- failed to become DT protected. In those who became G+ after 100mcg of G17DT, 16/18 (89%) were DT immune. The rise in the DT titre was 64 fold in the 100mcg group and 256 fold in the 250 mcg group. In the 3 who formed an abscess, all achieved high anti-gastrin antibody levels and had non-protective anti-DT baseline titre, with a median increase of 256 fold in anti-DT antibody.

Conclusions: 250mcg of G17DT produces higher titres of anti-DT as well as a higher proportion of G+ patients. Response to G17DT is not dependent on pre-vaccine DT antibody. An anti-DT response was seen in some G- patients therefore suggesting that this group is not uniformly immunosuppressed.

ONE-YEAR AUDIT OF THE MANAGEMENT OF Pancreatic CANCER AT A DISTRICT GENERAL HOSPITAL

S.J. McAree1, A.P. Catterall1, S.M. Greenfield1,2, P.B. McIntyre. 1QE 2 Hospital, Wiltshire Garden City; 2Lester Hospital, Stevenage, UK

Introduction: The treatment of Pancreatic cancer remains a challenge to a good endoscopic service. Three Gastroenterologists provide the ERCP service for the 500 000 population of East and North Hertfordshire NHS Trusts. Over 300 ERCP’s are performed annually. In common with other units, we are finding that an increasing number of ERCP’s are therapeutic. We wished to review the efficacy of our diagnosis and endoscopic treatment of pancreatic cancer.

Methods: Patients were identified between 31.03.1999 and 31.03.2000 from the endoscopic database and from diagnostic coding. 51 patients were identified, all with complete ERCP data. 10 patients notes were incomplete with regard to non ERCP data and have been excluded.

Results: 92% presented with recent onset jaundice and a background of weight loss. 72% presented as medical emergencies to the on call medical team. Of the technically feasible procedures ERCP alone provided palliation of jaundice in 77% of patients within 10 days. Of those referred to PTC, 67% of Pancreatic fluid samples were adequate. PTC provided a tissue diagnosis in one patient with 66% adequate samples. In 12 ERCP’s and 2 at PTC’s there was no attempt at tissue diagnosis. 25% of stents needed to be replaced with a mean survival of 89 days.

Conclusion: Pancreatic cancer tends to present as a medical emergency with icterus. The success of palliation with ERCP and PTC is comparable with other studies (J R Coll Surg Engl 1992;74:338–42). The adequacy of samples taken at ERCP and PTC is also comparable as was stent survival (Gut 1997;40:671–8). Our referrals to the surgeons seemed appropriate, however only 6 were referred to an oncologist. After discussion it was felt that we should: a) Endeavour to collect brushings and small bowel biopsies at ERCP to improve our tissue diagnosis rate. b) That we were under referring patients to our oncology service.

FAECAL CALPROTECTIN IS ELEVATED IN Pancreatic INSUFFICIENCY

D. Watts, N. Anderson, S. Campbell, G. Brydon, S. Ghosh. Gastrointestinal Unit, University of Edinburgh, Western General Hospital, UK

Background: Calprotectin is a stable 36kDa neutrophil derived bactericidal protein. Elevated faecal calprotectin has been reported by us and others, in inflammatory and neoplastic diseases of the intestinal tract. In pancreatic insufficiency (PI) faecal calprotectin levels may be elevated due to bacterial proliferation or local inflammatory processes. We aimed to determine the association of faecal calprotectin with PI.

Aim: To determine whether faecal calprotectin is elevated in PI.

Methods: Previous studies have defined PI as a reduction of exocrine pancreatic function to less than 60% or a rise in faecal elastase 1 (FE1) above 200 mcg/g. The study included patients with established PI, confirmed by FE1 and/or endoscopic retrograde cholangiopancreatography (ERCP) and normal or elevated faecal calprotectin levels.

Results: 20 patients were recruited with established PI (n=15) or elevated faecal calprotectin levels (n=5). Faecal calprotectin levels were significantly higher in patients with established PI (mean 129 mcg/g, range 73-833) compared to normal controls (mean 4 mcg/g, range 0-16). There was a significant correlation between faecal calprotectin levels and FE1 (r=0.57, p=0.03).

Conclusions: Faecal calprotectin is elevated in PI, possibly reflecting bacterial overgrowth or local inflammatory processes. Further studies are required to determine the role of faecal calprotectin in the diagnosis and management of PI.
tract. It has been suggested that faecal calprotectin might be a useful screening tool in distinguishing organic from functional bowel disease, especially in children. We report, for the first time, elevated faecal calprotectin in patients with diarrhoea due to pancreatic insufficiency.

**Method:** A total of 115 patients (77 women: 38 men; age 19–85) with chronic non bloody diarrhoea were screened in this study. Both pancreatic elastase and calprotectin were assayed by ELISA in faecal samples (normal: calprotectin < 30 µg/g, elastase >150 µg/g). Pancreatic imaging in those with low faecal elastase was carried out by a combination of CT scanning, endoscopic pancreatograms and endoscopic ultrasonography.

**Results:** Twenty six (21%) patients had low faecal elastase. Of these, 5 were confirmed radiologically to have chronic pancreatitis. All 5 patients were shown to have abnormally high faecal calprotectin levels (90–534 µg/g). 14 patients had suspected pancreatic insufficiency in the absence of other causative pathology. 13 (93%) of these patients had elevated faecal calprotectin (73–799 µg/g). 7 patients with low faecal elastase and ‘watery’ faecal samples were subsequently shown to have probably normal pancreatic function and an alternative explanation for symptoms (adenoma, Clostridial colitis, small bowel bacterial overgrowth, diverticular disease). Of these patients, 2 (29%) had abnormally high faecal calprotectin (176 µg/g/adenoma, 2670 µg/g/C.diff colitis) (table 1).

**Conclusion:** Pancreatic insufficiency may be associated with high faecal calprotectin in the absence of neoplastic or inflammatory intestinal disease. Low faecal elastase may also be associated with watery diarrhoea secondary to inflammatory intestinal disease, itself associated with an elevated faecal calprotectin concentration.

**Symposium: Guts, Liver and Bones: 224–225**

**224 GUIDELINES FOR OSTEOPOROSIS PREVENTION: HOW FAR HAVE WE YET TO GO?**

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**Background:** The British Society of Gastroenterology has published guidelines for the prevention and treatment of osteoporosis in patients with coeliac disease and inflammatory bowel disease (IBD) (Gut 2000;46(suppl 1):118). This has important implications for the planning of clinical services, especially with the limited availability of DEXA scanning. We have undertaken a assessment of the need for DEXA scans in our gastroenterology out-patient population.

**Methods:** In a district general hospital, population 460,000, we identified all patients with coeliac disease and IBD attending all gastroenterology out-patient clinics (3.5 consultant gastroenterologists, total 6 clinics per week) over a one month period. We assessed the number of these patients who required DEXA scanning and further investigation according to the BSG guidelines.

**Results:** Over a four week period 124 of a total 204 patients with either coeliac disease or IBD were found to require a DEXA scan according to the guidelines. The mean age of those requiring a scan was greater than those who did not (54.1 (18.6) vs 38.6 (12.3) age (sd)). All 21 patients with coeliac disease required a scan. Of those with Crohn’s disease 43/72 required a scan as did 60/111 patients with ulcerative colitis. Reasons for scans in patients with IBD are given in the table. DEXA scans had already been requested in 12 patients and 5 patients were on treatment (table 1).

**Conclusions:** Currently we are achieving BSG guidelines in less than 10% of our patient population. Introducing guidelines will mean that almost 2/3 of patients with Crohn’s disease and more than half of our ulcerative colitis patients will require a DEXA scan. Subsequently scanning will be required for patients with a new diagnosis of IBD, those requiring long courses of steroids and those reaching the age thresholds, as well as those on bone protection treatment. Patients with coeliac disease who require a scan at diagnosis place less pressure on resources.

**Abstract 224, Table 1**

<table>
<thead>
<tr>
<th>Total patients</th>
<th>Low elastase</th>
<th>High calprotectin</th>
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<tbody>
<tr>
<td>Confirmed pancreatic disease</td>
<td>5</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Possible pancreatic disease</td>
<td>14</td>
<td>14 (100%)</td>
</tr>
<tr>
<td>No pancreatic disease</td>
<td>96</td>
<td>7 (7%)</td>
</tr>
</tbody>
</table>

**225 PREVALENCE OF FRACTURE IN COELIAC DISEASE AND INFLAMMATORY BOWEL DISEASE**

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**Background:** Osteoporosis is a common complication of both inflammatory bowel disease and coeliac disease, but there is little information on the prevalence of fragility fracture in these patients.

**Methods:** Ambulant patients with coeliac disease (102), Crohn’s disease (88) and ulcerative colitis (130) completed a questionnaire detailing their fracture history. Fractures involving major trauma e.g. Road Traffic Accidents, falls from greater than three feet and sports injuries were excluded from analysis.

**Results:** 42% of patients with coeliac disease had experienced a previous fracture. Commonest fractures involved the distal radius (32%) and ankle (16%). Prevalence was higher in females than males (46% vs 33%). Females were younger than males (52.3yrs vs. 59.1yrs) and were diagnosed at an earlier age (45.9yrs vs 52.3 yrs). In neither sex was age at diagnosis related to history of fracture. 99 patients were diagnosed after the age of 25, when peak bone mass is achieved. 130 patients with ulcerative colitis (47 male, 83 female, mean age 45.7yrs) and 88 patients with Crohn’s disease (31 male, 57 female, mean age 38.7yrs) completed the questionnaire. 29% of patients with ulcerative colitis and 30% of patients with Crohn’s disease had suffered a fracture. Patients incurring fractures after diagnosis of ulcerative colitis had earlier onset of disease (mean 28.6yrs vs 37.9yrs) and longer duration (14.0yrs vs 7.7yrs) than patients without fractures. Fracture risk was unrelated to disease extent, use of systemic corticosteroids, smoking and family history of fragility fracture.

**Conclusions:** Fractures are very common in patients with coeliac disease and inflammatory bowel disease. To prevent, detect and treat low bone mineral density may reduce this prevalence.

**226 IMMUNE RESPONSES IN BARRETT’S METAPLASIA**

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**Introduction:** Barrett’s metaplasia (BM) is a chronic inflammatory disorder of the oesophagus in response to persistent gastro-oesophageal reflux and is associated with two distinct complications: benign oesophageal strictures and a 125-fold increased risk of developing an oesophageal adenocarcinoma. Benign strictures usually form in proximal areas of BM whereas adenocarcinomas arise distally. The characteristics of the inflammation and its role in the development of these complications have however been unclear.

**Hypothesis:** We propose that different immune responses are involved in the pathogenesis of these complications and that inflammation in BM is not a homogenous condition.

**Methods:** Endoscopic biopsies were obtained from normal oesophageal mucosa (n=10), oesophagitis (n=10) and paired biopsies from proximal and distal BM (n=20). The samples were assessed using immunohistochemistry, immunofluorescence, western blotting, and PCR amplification of DNA isolated from paraffin-embedded biopsies with consensus primers TCRβ, TCRγ and IgH.

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Results: We have shown that two distinct areas exist within BM based on cytokine production and inflammatory cell phenotype. Proximal segments of BM were associated with more intense inflammation and a polyclonal population of CD4 lymphocytes, CD8 lymphocytes and macrophages (CD68). Distal segments of BM were however significantly less inflamed and were characterised by a predominant monoclonal CD4+CD8- lymphocyte population. Proximal segments were associated with increased production of interferon-γ, interleukin 1β, interleukin 2 and interleukin 12 suggesting a TH1-type immune response whereas distal segments were associated with production of interleukin 4, interleukin 5 and interleukin 10 suggesting a TH2-type immune response. In both areas the majority of inflammatory cells were located around the bases of the crypts and deep glands with significantly fewer cells at the luminal surface.

Conclusions: Our data suggest that BM is not a homogenous condition but that benign stricture and adenocarcinoma formation are associated with distinct immune responses and different pathogeneses.

Background: The gastric epithelium is characteristically invaginated to form tubular glands, and tubule-like structures are a feature of some gastric tumours. Other epithelial cells e.g. mammary and kidney, form tubules when cultured on basement membrane.

Aims: To determine the factors regulating formation of tubular structures by gastric epithelial cells.

Methods: Gastric cancer cell lines (AGS, MKN-45, HGT-1), non-transformed cells (RGM-1), and AGS cells stably transfected with the gastrin-CCK receptor (AGS-G1), were cultured on plastic or artificial basement membrane (Matrigel).

Results: None of the cell lines formed tubule-like structures when cultured on plastic. However, AGS and RGM-1 cells (but not HGT-1 or MKN-45 cells) assembled within 3–6 hours into linear, branching, tubule-like arrays when cultured on Matrigel in medium containing 5–10% fetal calf serum. Gastrin (30 to 300pM), a known gastric morphogen, stimulated the formation of tubule-like arrays in AGS-G1 cells cultured on Matrigel in serum-free conditions. The response to gastrin was blocked by the gastrin-CCK antagonist, L-740,093 (100nM), and partially inhibited by the protein kinase C inhibitor, Ro-32-0432. Similar cellular assemblies were also formed in serum-free media in response to 

1. etoposide (PMA, 100nM), which stimulates PKC, had a similar effect to gastrin. The effect of PMA was fully reversed by Ro-32-0432. Similar cellular assemblies were also formed in serum-free media in response to etoposide. Moreover, etoposide induced apoptosis in the murine small intestine.

Conclusions: The assembly of gastric epithelial cells into tubule-like structures is regulated by PKC and stimulated by gastrin. Similar signalling systems may control gastric epithelial organisation in vivo.

Conclusions: The assembly of gastric epithelial cells into tubule-like structures is regulated by PKC and stimulated by gastrin. Similar signalling systems may control gastric epithelial organisation in vivo.

Current Affairs: Etoposide induces apoptosis via a mechanism dependent on the tumour suppressor p53, the cyclin dependent kinase inhibitor p21 and the pro-apoptotic protein Bax.

Methods: BDF (wildtype mice, p53, p21 and Bax knockout mice) were injected with etoposide intraperitoneally at n=4 for each. The small intestines were isolated over a series of time points and scored for apoptotic and mitotic bodies relative to position along the crypt/villus axis by histological examination. Clonect Atlas Mouse 1.2 Gene array analysis was performed three times on mRNA extracted from small intestinal epithelial cells isolated 4.5 hours after etoposide treatment. p53 knockout mice and wildtype littermates.

Results: At 4.5 hours after administration, etoposide induced apoptosis is p53 dependent and occurs maximally between positions 3 and 9 along the crypt/villus axis. Furthermore, etoposide induced adenocarcinoma. The age range at resection was 39–83 years (mean age 63 years). Resection staging was 17.5% T1, 14.1% T2, 68.4% T3, 58.8% N1 and 6.1% M1. Sections taken from the microarrays were then stained using 10 immunohistochemistry antibodies representing markers of cell cycle, proliferation and some known tumour suppressor genes.

Results: Successful implantation of the tissue core was achieved in 96.7% of cores taken (1145 of 1184) and the intended histology was sampled in 82.2%. The histology has remained the same with depth in 89.5% of the cores sectioned. The immunohistochemistry experiments for all 114 patients took 3 days to perform. Tumour cores were positioned in 43.1% p53 (44 of 102), 88.9% cyclin D1 (88 of 99), 91.9% Rb (91 of 99), 22.8% p16 (23 of 101), 59.4% p21 (60 of 101), 28.3% K67 (28 of 99), 40.6% PCNA (41 of 101), 43.9% c-myc (43 of 98), 61.6% MLH1 (61 of 99) and 41.0% MSH2 (41 of 100).

Conclusions: The accuracy of microarray construction in our study is largely consistent with published results. Tissue microarrays do appear to be a realistic and practical way of screening for expression of proteins, which may be important in looking for markers of malignant potential.
apoptosis is independent of p21 and Bax, both thought to lie downstream of p53 in the DNA damage induced pro-apoptotic pathway. Gene array analysis of wildtype and p53 knockout mice dosed with etoposide shows 42 genes exhibiting a p53 dependent increase in expression, including MAP kinase kinase 3 (4 fold increase ±0.8), and 13 genes exhibiting a p53 dependent decrease in expression, of particular note is the c-abl protooncogene (2 fold change ±0.4).

**Conclusions:** Etoposide induces apoptosis via a p53 dependent p21/Bax independent pathway, possibly involving a range of genes identified by the gene array analysis.

### 231 INHIBITION OF TUMOUR FORMATION IN A MODEL OF HUMAN DIETARY COLORECTAL TUMOURIGENESIS BY THERAPEUTIC TARGETING OF NF KAPPA B DEPENDENT APOPTOSIS

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Curcumin is a potent inhibitor of NF kappa B which may influence apoptosis. This study investigates Curcumin effects on (i) regulatory pathways of apoptosis in human intestinal epithelium in vitro and (ii) apoptosis and tumourigenesis in a model for human diet related colon cancer, comprising APC<sup>min</sup> mice treated by the human dietary carcinogen, 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP).

Curcumin inhibited TNFα induced NFκB activation and promoted p53 expression in HCT116 and INT407 cells. PhIP induced small intestinal epithelial apoptosis in vivo and though levels were lower in APC<sup>min</sup> than in wild type C57Bl6 APC<sup>−/−</sup> mice (1.9% APC<sup>−/−</sup> vs 3.7% APC<sup>+/+</sup> at p<0.001). PhIP promoted tumour formation in APC<sup>−/−</sup> proximal small intestine (4.6 PhIP alone vs 2.1 untreated; p<0.05). Curcumin enhanced PhIP induced apoptosis (4.0% PhIP + Curcumin vs 2.1% PhIP alone; p<0.01) and inhibited PhIP tumourigenesis in the proximal small intestine of APC<sup>−/−</sup> mice (4.6 PhIP alone vs 2.2 Curcumin + PhIP; p<0.05).

**Conclusion:** Curcumin is a potent inhibitor of NFκB which may influence apoptosis.

### 232 EFFECT OF PPARα ACTIVATION ON CELLULAR PROLIFERATION AND APOPTOSIS IN HCA7 COLON CANCER CELL LINE

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**Introduction:** PPARs have been proposed to act as a critical link in the multistep process of carcinogenesis. Moreover, the prominence of different subtypes of crypt fission appears to differ in various models of intestinal adaptation and pathology. **Aims:** To quantify crypt branching and subtypes of branched crypts in animal and human models of altered mucosal proliferation and of carcinogenesis.

**Methods:** Carnoy’s fixed rat and human tissue was stained with the Feulgen reaction and carefully microdissected to reveal individual crypts. The percentage of crypts in fibrosis and the different subtypes of crypts seen (symmetrical or asymmetrical) were scored under the microscope.

**Results:** Reduced fission and a higher proportion of symmetrical crypts were seen in rats after infusion of KGF or EGF. Approximately 50% of the branched crypts were symmetrical, 25% asymmetrical, 13% of the budding subtype and approximately 5% were multiple. Branching also increased in hyperplastic human tissue and to a greater extent in adenomatous polyps. All of these neoplastic tissues had significantly increased tumour formation. Curcumin reverses this apoptosis resistant phenotype through the NFκB pathway and inhibits PhIP tumourigenesis in proximal APC<sup>−/−</sup> mouse small intestine.

**Conclusion:** Crypt fission is significantly increased in carcinogeneduced fibrosis in both animals and in man. The different forms of crypt branching may reflect different fission dynamics and contribute to the development and amplification of carcinogenesis. Symmetrical subtypes are higher in growth factor treatments and asymmetrical subtypes are dominant in carcinogenic processes.

### 233 CRYPTO FISsION AND ITS SUBTYPES IN COLONIC ADAPTATION AND CARCINOGENESIS

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**Background:** Crypt fission involves the longitudinal splitting of branched intestinal crypts to produce two new crypts. Fission is essential for intestinal development and increased fission is seen after damage, following dietary changes and after administration of growth factors. Crypt fission is significantly increased in carcinogenesis (in the Min mouse, in FAP and in hyperplastic and adenomatous polyps in man). Crypt fission is thus likely to be intimately involved in the multistep process of carcinogenesis. Moreover, the prominence of different subtypes of crypt fission appears to differ in various models of intestinal adaptation and pathology.

**Aims:** To quantify crypt branching and subtypes of branched crypts in animal and human models of altered mucosal proliferation and of carcinogenesis.

**Methods:** Carnoy’s fixed rat and human tissue was stained with the Feulgen reaction and carefully microdissected to reveal individual crypts. The percentage of crypts in fibrosis and the different subtypes of crypts seen (symmetrical or asymmetrical) were scored under the microscope.

**Results:** Reduced fission and a higher proportion of symmetrical crypts were seen in rats after infusion of KGF or EGF. Approximately 50% of the branched crypts were symmetrical, 25% asymmetrical, 13% of the budding subtype and approximately 5% were multiple. Branching also increased in hyperplastic human tissue and to a greater extent in adenomatous polyps. All of these neoplastic tissues had significantly increased tumour formation. Curcumin reverses this apoptosis resistant phenotype through the NFκB pathway and inhibits PhIP tumourigenesis in proximal APC<sup>−/−</sup> mouse small intestine.

**Conclusion:** Crypt fission is significantly increased in carcinogeneduced fibrosis in both animals and in man. The different forms of crypt branching may reflect different fission dynamics and contribute to the development and amplification of carcinogenesis. Symmetrical subtypes are higher in growth factor treatments and asymmetrical subtypes are dominant in carcinogenic processes.

### 234 RELATIONSHIP BETWEEN CYCOXOGENASE-2 TUMOUR EXPRESSION AND SURVIVAL IN COLORECTAL CANCER PATIENTS TREATED WITH CHEMOTHERAPY

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**Background:** Expression of cyclooxygenase COX-2 is a poor prognostic marker in colorectal cancer and is linked with both lymph node and haematogenous metastases. Recent evidence suggests a potential action of aspirin and NSAIDs in chemoprophylaxis of colorectal cancer. The use of these drugs as adjuvant chemotherapy has been suggested. The aim of this study was to determine if COX-2 expression in colorectal cancer influenced survival in patients receiving standard 5-FU chemotherapy regimes.

**Methods:** 60 unselected patients with previous tumour resection and who had received chemotherapy over the period 1999–2000 with 5-FU based regimens were evaluated retrospectively. Paraffin embedded sections of primary tumour were cut and stained by immunohistochemistry for COX-2 protein using the avidin biotin technique. Extent of staining was graded by the percentage staining of epithelial cells positive for COX-2 by two blinded independent pathologists. Patient data were retrieved by chart review and communication with patients’ primary care physicians if necessary.

**Results:** Of the 60 patients, mean age was 60.8 years at diagnosis (M:F 2:1). All tumours were regraded for Dukes, TNM and Jass staging. Twenty-four were Dukes B, 25 Dukes C and 11 Dukes D. All patients received 5-FU and folinic acid except two who received 5-FU

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A-GLIADIN 51–70 TOXICITY ASSESSED IN AN ORGAN CULTURE SYSTEM

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Background: Three related DQ2-restricted immunodominant epitopes, which reside within the region of A-gliadin 57–75 have been recently identified. Their immunological activity has been indirectly assessed using peripheral blood mononuclear cell secretion of IFN-γ, while small intestinal T-cell clones from coeliac patients have been shown to be selectively stimulated, Tγ deamination at Q65 being crucial for T-cell recognition and DQ2 binding.

Aims: To investigate using an organ culture system in vitro toxicity of region 51–70 of A-gliadin, a similar N-terminal peptide, overlapping the above mentioned sequences.

Methods: Jejunal biopsies obtained from each of 9 treated coeliac patients were cultured in vitro for 18 hours in presence of A-gliadin 51–70 (200 µg/ml), organ culture medium only, peptic-tryptic digested gliadin (1mg/ml) or ovalbumin (1mg/ml), the last two acting as positive and negative controls respectively. Morphometric analysis involved measuring the cell height of 30 enterocytes, randomly selected from the middle third of different villi for each section. Mean enterocyte cell heights (ECH) were compared with values for specimens cultured in medium alone.

Results: In 7/9 patients (78%) A-gliadin 51–70 was significantly toxic, p<0.0001 (Kruskal-Wallis analysis of variance) causing a 25% decrease in ECH compared to medium alone. In 2/9 subjects (22%) the peptide did not show any toxic effect. In all cases we found that both positive and negative controls worked as expected.

Conclusions: We showed that sequence 51–70 is characterized by in vitro toxicity to the coeliac jejunal mucosa, correlating with recent findings of an immunological role of similar peptides within A-gliadin.

IGA-ANTITISSUE TRANSGLUTAMINASE: SENSITIVITY AND SPECIFICITY FOR DIAGNOSING COELIAC DISEASE

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Introduction: Tissue transglutaminase (tTG) is probably the main endosomal antigen in coeliac disease (CD). Our aims were to define a reference range for IgA antibodies to tTG (tTGA), to compare sensitivity and specificity for the diagnosis of CD with IgA antigliadin (AGA) and endomysial (EMA) antibodies and to confirm that the assay can detect subjects with selective IgA deficiency.

Methods: AGA: quantitative in-house ELISA; EMA: immunofluorescence (monkey oesophagus, Binding Site, Birmingham, UK); tTGA: quantitative ELISA (Bindazyme MK038, Binding Site, Birmingham, UK); samples were diluted 1 in 25 to improve precision.

Results: The 97.5th percentile for tTGA in the 409 control subjects was 0.2 U/mL. The assay identified 17 of 18 subjects with selective IgA deficiency.

Conclusions: This study has defined the normal range for tTGA for this assay and confirmed the high sensitivity and specificity of this marker for the diagnosis of CD. However tTGA is not as sensitive and specific as EMA for diagnosing CD. These data support the use of tTGA instead of AGA as the first line screening test for CD.

PREVALENCE OF UNDIAGNOSED COELIAC DISEASE IN THE GENERAL POPULATION OF ENGLAND

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Introduction: Recent estimates from several European countries suggest that the prevalence of Coeliac disease (CD) is between 0.5 and 1%. No data have previously been reported from mainland UK. We aimed to estimate the prevalence of CD in the general population based on subjects aged 45–74 recruited from General Practice age-sex registers in Cambridge for a UK health survey.

Methods: Stored serum collected during the Cambridge General Practice Bone Health Study 1990–94 were tested for total IgA and anti-endomysial antibody (EMA: immuno-fluorescence—monkey oesophagus, Binding Site, Birmingham, UK). The specificity of EMA is at least as high as 99.9%. 3354 of approximately 8000 samples have been tested to date. IgA antitissue transglutaminase assays are currently being conducted (Bindazyme MK038, Binding Site, Birmingham, UK).

Results: The distribution of age, sex and proportion of positive EMA results are shown in the table.

Conclusions: This study found the estimated prevalence of undiagnosed CD in this general population sample is 1.3% (95% CI 0.9–1.6%). Prevalence is similar in men and women. This is the largest general population sample studied and the prevalence of CD is higher than that of any previous study in the UK or elsewhere. CD may therefore affect up to 1 in 80 people aged 45–74 years in England.

MANAGEMENT OF ADULT COELIAC DISEASE: IMPLEMENTATION OF CURRENT BSG GUIDELINES THROUGH A SPECIALIST CLINIC

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Introduction: An audit of the management of patients with coeliac disease (CD), attending our Gastroenterology clinic, was undertaken to compare management with current British Society of Gastroenterology Guidelines. Subsequently a CD review clinic has been established to continue patient care.

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Results: 232 patients were identified and 192 sets of case notes reviewed. Age and mode of presentation, sex distribution and co-morbidity did not differ significantly from other published series. Small bowel biopsy (SBB) had been performed on 181 patients (95.6%), however SBB had only been repeated in 91 (48%) of cases to assess response to gluten free diet (GFD). 32 patients were responsive, 42 showed no histological response, and 7 had serious complications. Compliance with GFD was considered to be good in 118 (61.5%) of patients, and poor in the remainder. IgA antireticular antibodies (ARA) had never been checked in the majority (57.8%) of cases. DEXA scans had been performed in 341 patients (77%), although of those performed 27 (79.4%) show osteoporosis (BMD >2.5SD below mean for young adults). The CD review had been established to allow review of all patients by a clinician and dietician. To date 125 patients have been reviewed (43 men, 82 women). Compliance with GFD was considered to be good in 82 cases (65.6%), of which 59 (72%) were ARA negative, 10 (12.2%) were ARA positive and equivocal in 13 (15.9%). Only 51.2% of patients were members of the Coeliac Society. Nutritional deficiencies were detected in 28.2% (19 patients folate deficient, 12 iron deficient, 3 B12 deficient, 2 vitamin D deficient). DEXA scans were requested on 91 patients, 65 have been examined to date, of which 25 (38.5%) show osteoporosis and 10 (15.4%) show osteopenia.

Conclusions: Management of CD in our unit did not meet the standards suggested in current guidelines. As a consequence complications, particularly osteoporosis and ongoing nutritional deficiencies, were not being detected at routine follow up. The establishment of a specialist clinic has enabled a co-ordinated approach between clinician and dietician, and enabled compliance with current guidelines.

Objective: Primary small bowel malignancy is rare and little is known about its prevalence in the UK. This prospective survey aimed to obtain information regarding its presentation and prevalence and, in particular, its association with coeliac disease.

Study design: Cases were collected nationally over 24 months (June 98—May 2000) using the BSG monthly reporting system followed up by a preliminary form for confirmation. Further details of confirmed cases were obtained via a detailed questionnaire.

Results: A mean of 1400 cards was sent out each month, the mean response rate of returned cards was 44.5%. A total of 552 cases were requested on 91 patients, 65 have been examined to date, of which 25 (38.5%) show osteoporosis and 10 (15.4%) show osteopenia.

Conclusions: Strong BCl-2 expression by acinar cells and of Bax by acinar and endocrine cells. Increased Bcl-2 protein expression by acinar cells in CP may differentially promote apoptosis within these cell populations. Increased Bcl-2 protein expression by acinar cells in CP may differentially promote apoptosis within these cells. These data confirm that these malignancies are a rare tumour type.
PaO₂ levels [91.43 (2.2) mmHg, P<0.0001] and the rise in serum creatinine [78.9 (4) μmol/L, P=0.028]. There was reduction in morphometric measurement of areas of acinar necrosis as a percentage of total acinar tissue in histological sections in the treated group compared to pancreatitis [29.61 (0.79) versus 39.66 (1.47) %, P<0.0001].

**Conclusion:** In this experimental model of severe acute pancreatitis treated with L-NIL two hours after induction of pancreatitis, corrected circulatory failure, ameliorated renal and respiratory functions, and limited the progression of pancreatic necrosis. L-NIL may prove to have a useful role in the supportive treatment of a severe attack.

**INCREASED SYSTEMIC NITRIC OXIDE IN PATIENTS WITH SEVERE ACUTE PANCREATITIS IS ASSOCIATED WITH ALTERED GUT MACROMOLECULAR PERMEABILITY; AN ENDOTOXIN MEDIATED INFLAMMATORY RESPONSE?**


**Background:** There is considerable evidence implicating nitric oxide (NO) as a critical mediator of the systemic inflammatory response to bacterial endotoxaemia. Severe acute pancreatitis (AP) is associated with alterations in intestinal permeability, and bacterial translocation may in part contribute to the local and systemic manifestations of this disease. However, the mechanisms remain speculative and the role of NO in humans with AP has not been studied.

**Methods:** Patients with a clinical and biochemical diagnosis of AP were studied within 72 hours of onset of abdominal pain. The 24-hr urinary nitrite excretion, reflecting NO production, was measured using the Greiss reaction. The ratio of renal excretion of the enterally administered polyethylene glycol (PEG) 3350/400 was measured to determine intestinal macromolecular permeability. The IgM/IgG EndoCAb ratio was used as a marker of systemic endotoxin exposure. Attacks were classified as mild or severe according to Atlanta criteria.

**Results:** Sixty-five patients with AP (severe 20) and 20 healthy control subjects were studied. Urinary nitrite excretion was significantly increased in patients with severe attacks (median 20.6) compared to mild attacks (median 15.7, p = 0.003), and the latter was significantly greater in healthy controls (median 6.3, p = 0.004). PEG excretion ratios were significantly increased in patients with severe attacks compared to mild attacks (r = 0.8, p < 0.01). In patients with severe disease, urine nitrite excretion demonstrated a positive and significant correlation with intestinal macromolecular permeability and the IgM/IgG EndoCAb ratio (r = 0.7, p = 0.006, and r = 0.8, p = 0.001 respectively).

**Conclusion:** Systemic NO is increased in AP, and is greatest amongst patients who develop a severe attack. The strong correlation with altered gut permeability and endotoxin exposure suggests that the mechanism may be mediated through bacterial up-regulation of inducible nitric oxide synthase activity.

**EVALUATION OF ENDOSCOPIC ULTRASOUND VERSUS HELICAL COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF PANCREATIC MASSES: RESULTS FROM A UK CENTRE**

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**Introduction:** Endoscopic ultrasound (EUS) is an emerging diagnostic modality which has been shown to be more accurate in the diagnosis, and locoregional staging of pancreatic carcinoma than conventional computed tomography (CT). The aim of this study was to determine the local staging accuracy of EUS, compared with helical computed tomography (HCT) in a United Kingdom centre.

**Patients, materials and methods:** Between September 1999 and October 2000, 43 consecutive patients underwent radial EUS (GF-UM20) and HCT for assessment of pancreatic masses. Of these, 17 patients underwent percutaneous needle aspiration biopsy (NAB) of the pancreatic mass, followed by surgical exploration. Staging procedures included radical lymph node clearance in all cases, and portal vein resection where necessary. Tumour size, portal venous invasion, and nodal involvement were assessed and compared with histopathological examination of the resected specimens as the reference standard. The χ² test for paired data was used to compare groups.

**Results:** Of the 17 patients, who underwent surgery 15 had a pancreaticoduodenectomy (Whipples) procedure, one a distal pancreatectomy, and one a laparotomy without resection. The portal vein was infiltrated in three patients, and resected in two. 10 patients had adenocarcinoma, 2 neuroendocrine tumour, 4 focal pancreatitis, and 1 chronic pancreatitis. Beta3-integrin-deficient mice were used as they develop acinar tissue in histological sections in the treated group compared to pancreatitis (29.61 (0.79) versus 39.66 (1.47) %, P<0.0001), and was as accurate as HCT with respect to size (76% vs 47% within 0.5cm, p=0.07), and portal venous involvement (94% vs 82%, p=NS). All patients with portal vein invasion were detected by EUS.

**Conclusion:** EUS is accurate in the local, and nodal staging of pancreatic masses, and is sensitive in the assessment of portal vein invasion.

**HEPATOcyTES DERIVED FROM BONE MARROW STEM CELLS SHOW POLYPOLYDIZATION IN HUMANS AND MICE**

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**Background and aims:** Using a technique to detect Y-chromosomes within human liver we have previously demonstrated in patients that have received sex mis-matched bone marrow or liver transplants that human hepatocytes can be derived from bone marrow stem cells. These cells may provide an alternative source of hepatocytes following liver damage. Using the technique of Y-chromosome detection we have examined livers from patients undergoing surgery for polyploidization. This is of relevance as polyploidization is an integral feature of hepatocyte replication.

**Method:** Beta3-integrin-deficient mice were used as they develop cirrhosis following polyploidization. This is of relevance as polyploidization is an integral feature of hepatocyte replication.

**RESULTS:** Of the 17 patients, who underwent surgery 15 had a pancreaticoduodenectomy (Whipples) procedure, one a distal pancreatectomy, and one a laparotomy without resection. The portal vein was infiltrated in three patients, and resected in two. 10 patients had adenocarcinoma, 2 neuroendocrine tumour, 4 focal pancreatitis, and one anaplastic tumour on histological examination. EUS was more accurate than CT in the accuracy of lymph node staging (82% vs 47%, p=0.03), and was as accurate as HCT with respect to size (76% vs 47% within 0.5cm, p=0.07), and portal venous involvement (94% vs 82%, p=NS). All patients with portal vein invasion were detected by EUS.

**Conclusion:** EUS is accurate in the local, and nodal staging of pancreatic masses, and is sensitive in the assessment of portal vein invasion.

**DOES ENDOSCOPIC ULTRASOUND (EUS) IMAGING, IN THE ABSENCE OF BIOPSY, HAVE A ROLE IN STAGING CANCERS OF THE PANCREAS AND AMPULLA?**

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**Background:** The clinical value of Endoscopic Ultrasound (EUS) in staging tumours of the pancreas and ampulla, like all other imaging modalities individually, is uncertain. Although EUS does provide a method of sampling tissue without the potential for coelomic spread, such biopsy equipment is not widely available.

**Aim:** To determine the clinical value of radial diagnostic imaging in tumours of the pancreas and ampulla.

**Methods:** All patients (n=36; m:20, f:16; Age range 42yrs to 78yrs, median age 66yrs) with suspected tumours underwent EUS, dual-phase contrast helical CT and where appropriate EUS. EUS was performed under conscious sedation (midazolam/fentanyl) using Olympus GFUM20 and GFUM200 radial echoendoscopes. Follow-up data of at least six months was available on all patients and surgical data on 15 cases.

**Results:** The patient cohort included pancreatic head adenocarcinomas (n=20); resection, n=8); ampullary carcinoma (n=10; resection, n=4) and pancreatic neuro-endocrine tumours (n=4; resection, n=4;insulinoma, n=3 and morphologically unclear, n=1). Duodenal stricturing limited EUS in two cases of pancreatic head carcinoma. In three cases of adenocarcinoma, EUS identified an operable tumour not identified on CT, in one case EUS missed vascular invasion of the portal vein, although review of films identified this to be present. EUS identified vascular (SMA, SMV, PV) involvement seen on CT. All cases of ampullary carcinoma undergoing surgery were correctly staged by EUS. EUS identified 3 of 4 neuro-endocrine tumours, the fourth being identified by MRI. EUS identified enlarged nodes more readily than CT, but specificity and sensitivity were low (53% and 62% respectively).

**Conclusion:** Radial EUS provides additive information to that yielded by helical CT in the assessment of pancreatic/ampullary tumours. EUS is particularly helpful in identifying small adenocarcinomas undetectable by CT. Like other imaging modalities, EUS cannot differentiate between benign and inflammatory regional lymph nodes.
body gamma irradiation with 1000 rads to ablate their bone marrow and then received male wild type bone marrow transfer by tail vein injection. Animals were killed eight-weeks following bone marrow transplant and their livers were analysed using a murine Y chromosome probe for hepatocytes of male origin. In addition the livers of female patients who had received male bone marrow transplant and males who had received female liver transplants were also examined for evidence of Y-chromosome positive polyploid hepatocytes.

**Results:** We found evidence of Y-chromosome positive hepatocytes of both diploid and polyploid class in tail-sections of female mice that had received bone marrow transplants, female patients who had received male bone marrow transplants and male patients who had received female liver transplants.

**Conclusion:** The diverse ploidy status identified within hepatocytes derived from bone marrow stem cells suggests that they can undergo polyploidization and are capable of replicating within the liver. This indicates that these hepatocytes of bone marrow origin are able to contribute to hepatic regeneration following liver damage.

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**STEM CELL FACTOR LIMITS LIVER INJURY INDUCED BY PARACETAMOL POISONING**

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**Background and aims:** Paracetamol (acetaminophen) remains a common cause of acute liver failure and emergency liver transplantation in both the UK and USA. The cytokine networks involved in the pathogenesis of paracetamol induced acute liver injury are poorly understood. Stem cell factor (SCF) is a cytokine involved in cell growth and repair which was studied in a murine model of paracetamol poisoning.

**Methods:** CBA mice were injected IP with paracetamol solution following an 8 hour fast. SCF was quantified by ELISA, neutralised with anti-SCF antibodies and constituted with recombinant SCF (rSCF).

**Results:** Paracetamol injection lead to significant reduction in hepatic SCF concentration measured by ELISA (control 2100+300ng/gm liver, mean+sem, paracetamol 970+170, n=7, p<0.05) at 24 hours. Injection of 200mg/kg paracetamol was associated with 80% survival at 96 hours, but inhibition of SCF in this “sublethal” model was associated with survival of only 40% at 96 hours (p<0.05, n=20 in each group): this was associated with significantly increased areas of liver necrosis at 96 hours in the survivors (control 11.6+5.4 % total area of liver, mean+sem, anti-SCF treated 25.7+8.5, n=5, p<0.05). Conversely administration of rSCF (1ug) improved survival of mice injected with 300mg/kg paracetamol improved survival from 30% at 96 hours to 90% (p<0.05, n=20 in each group): this was associated with histopathologic liver histology at days 1, 2, 4 and 6 in the rSCF treated group. SCF treatment was correlated with significant reduction in cytochrome P4502E1 expression in both murine liver and culture murine cell lines.

**Conclusions:** Hepatic SCF plays an important role in modulating paracetamol induced liver injury in a murine model. A potential mechanism for this effect is the inhibition of paracetamol activation by cytochrome P4502E1. Other mechanisms such as an effect of SCF on hepatocyte proliferation are currently under investigation.

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**LIVER DISEASE MORTALITY IN THE BLACK COUNTRY 1993–1999**


**Background:** Treatment of advanced liver failure is a major burden on healthcare resources. To determine incidence of liver disease mortality and any underlying trends we analysed data in three boroughs of the West Midlands “Black Country” (Wolverhampton, Dudley and Sandwell, total population 845,000) from 1993–1999.

**Methods:** Public health mortality files were analysed for liver-related deaths using ICD reference codes and keyword searches. Case notes were analysed in cases of liver disease of unspecified cause. In-patient episode data for 1995–1999 were obtained from health authority records.

**Results:** There was a stepwise increase in liver-related mortality from 6.6 per 10^5 population in 1993 to 13.9 per 10^5 in 1999. This increase was exclusively due to alcoholic liver disease (ALD); incidence 3.1 per 10^5 in 1993 rising threefold to 9.3 per 10^5 in 1999, whilst mortality due to other defined liver diseases was stable at 0.5 per 10^5. In Wolverhampton and Sandwell (which have large Asian communities) ALD mortality rates in Asian and white populations were similar but Asian subjects died at an earlier age (median age at death 46 years vs. 55 yrs in whites, p<0.001). These data probably underestimate true ALD mortality since unspecified liver disease (around 20% of all liver mortality) was due to ALD in 62% of cases as judged by case note analysis; also ALD deaths increased by 8% when accounting for ALD “misclassified” as other diseases. Finally, in-patient liver disease episodes increased stepwise from 41 per 10^5 population in 1993 to 57 per 10^5 in 1999 which correlated significantly with mortality rates (r=0.74, p=0.01).

**Conclusions:** Liver disease mortality due to alcohol has increased dramatically in recent years, and if sustained this trend has important implications for gastroenterologists and public health specialists.

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**CORRELATION BETWEEN CEREBRAL PROTON MAGNETIC RESONANCE SPECTROSCOPY (1H MRS) AND NEUROPSYCHOMETRIC ABNORMALITIES IN PATIENTS WITH CHRONIC HEPATITIS C (HCV) INFECTION**

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Patients with chronic HCV score lower on quality of life scales compared to normal individuals and patients with chronic hepatitis B (HBV). We examine the hypothesis that a direct cerebral effect of HCV underlies this. Computerised and paper-based psychometric tests batteries were administered to 26 patients with histologically mild HCV hepatitis and 10 HCV antibody+ve, PCR-ve age, sex and intelligence-matched controls. 12/26 patients vs 8/24 controls (p=0.01) and 8/24 patients vs 0/10 controls (p=0.07) were impaired
on computer and on paper-based batteries respectively. There were no differences according to a history of intravenous drug abuse (IVDA). In vivo 1H MR spectra were acquired from voxels in the basal ganglia (BG), white matter (WM) and occipital grey matter (GM) with a 1.5T spectroscopy system in 3 patient groups: 1) 30 patients with biopsy-proven mild HCV infection (mean age 44 yr, 47% M, mean liver necroinflammatory score 2.4/18, mean fibrosis score 1.6/6). 67% had a history of IVDA; 2) 12 hepatitis B eAg+ve patients without cirrhosis, none IVDA+ve; 3) 29 healthy controls (mean age 42 yr, 52% M), none IVDA+ve.

Results: A significant elevation in BG and WM choline/creatine (Cho/Cr) was seen in the HCV group compared to the other groups (*p<0.005).

Abstract 249, Table 1

<table>
<thead>
<tr>
<th></th>
<th>HCV</th>
<th>HBV</th>
<th>Volunteers</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG Cho/Cr</td>
<td>1.17 (0.14)*</td>
<td>1.04 (0.14)</td>
<td>1.06 (0.13)</td>
</tr>
<tr>
<td>WM Cho/Cr</td>
<td>1.35 (0.22)*</td>
<td>1.16 (0.12)</td>
<td>1.18 (0.14)</td>
</tr>
</tbody>
</table>

No difference was seen in the HCV group according to IVDA+ve status. Fourteen HCV patients also had psychiatric testing, showing correlations between BG Cho/Cr and indices of sustained attention (r=0.699, p=0.005) and quality of working memory (r=-0.544, p=0.04).

Conclusion: Both cognitive impairment and cerebral metabolic abnormalities are seen in patients with mild HCV hepatitis. This may be due to a cerebral effect of systemic cytokines or direct infection of the CNS by HCV (as in HIV infection where similar 1H MRS abnormalities are seen).

250 CHARACTERISING THE EFFECTS OF THYROID HORMONE ON THE LIVER: A NOVEL APPROACH TO INCREASING LIVER MASS

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Background: Liver growth can occur as part of two distinct mechanisms: 1) Compensatory Regeneration: Following resection, viral/ drug injury; 2) Direct Hyperplasia: A primary mitogen increasing liver mass directly.

Aim: a) To assess if thyroid hormone acts as a primary mitogen. b) To characterise the effects of thyroid hormone when administered prior to a 70% partial hepatectomy (PH)—testing a primary mitogen with an established model of regeneration.

Method: a) Male Sprague-dawley rats (n=7 per group) were injected with a single dose of tri-iodothyronine (T3) and sacrificed at intervals of 1,2,4,7,10 and 14 days. A control group received vehicle only twenty four hours prior to PH. All animals were sacrificed 24 hrs after partial hepatectomy. Cell Proliferation - Assessed by bromodeoxyuridine (BRDU) incorporation into nuclei and immunohistochemical recognition.

Results: a) Liver mass was increased in animals treated with T3 as compared with controls. Maximum effect was seen on day 10 with a 20% increase in liver mass (p<0.05). A corresponding increase in total DNA (p<0.05) and liver protein (p<0.05) was seen at this time point. Proliferation - Peaked at day 1: 7% hepatocytes labelled compared to <1% in controls (p<0.01). b) In animals treated with T3 three and ten days prior to partial hepatectomy the liver weight at sacrifice was greater (p<0.05) than controls. There was a corresponding increase in liver protein (p<0.05) and total DNA (p<0.05) at these time points. Prophylaxis - Peaked when T3 was administered 24 hrs prior to PH 36% hepatocytes labelled compared to 26% in controls (p<0.01).

Conclusions: Thyroid hormone acts as a mitogen and synergistically with a 70% partial hepatectomy. This raises the possibility of preoperative T3 administration to perform larger liver resections.

251 HEPATIC CO-FACTORS IN END-STAGE, ALCOHOL RELATED, LIVER DISEASE

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Alcohol consumption is well recognised as an independent cause of cirrhosis and as an accentuating factor in the pathogenesis of advanced liver disease in hepatitis C carriers. However, a history of alcohol consumption may contribute to erroneous diagnoses or the failure to recognise significant co-factors. We undertook a retrospective analysis of these variables in 159 patients referred for liver transplantation with a primary diagnosis of alcoholic liver disease between 1996 and 2000.

Of the 159 patients, 31 (20%) had recognised chronic viral hepatitis (24 anti-HCV positive, 5 HBsAg positive, 2 anti-HCV & HBsAg positive). These 31 patients were younger than the remaining 128 patients without viral hepatitis (mean 49 vs 52 years, P = 0.03) and younger than a separate cohort of 79 non-alcoholic abusing hepatitis C carriers with end-stage liver disease (mean 49 vs 53 years, P = 0.01). In 12 out of the 128 non-viral alcohol abusers the primary diagnosis was not alcoholic liver disease: 2 Autoimmune hepatitis, 2 Caroll's disease, 2 Nodular Regenerative Hyperplasia, 2 PBC, 2 PSC, 1 Sarcoidosis, 1 Haemochromatosis (C282Y homozygous). In a further 16 patients co-factors were identified: 14 hepatic siderosis (grade 3/4), 2 alpha-1 antitrypsin deficiency (MZ phenotype). Of the siderotic patients only 2 had HFE gene mutations detected, 1 had aceruloplasminaemia. Hepatocellular cancer was identified in 23 patients, 7 were discovered incidentally in the explanted liver.

Mean serum IgA was significantly higher in the alcohol cohort than the separate hepatitis C cohort (5 vs 7 g/l, P = 0.002), but no other discriminatory laboratory variables were identified.

This study reveals a 10% erroneous diagnosis rate in patients referred with a diagnosis of alcoholic liver disease. It confirms the accelerated progression to cirrhosis in hepatitis C carriers abusing alcohol. Significant co-factors were present in a further 13%; this went unrecognised in most cases before transplantation. Despite advances in screening for hepatocellular carcinoma, 30% of the tumours were undiagnosed before transplantation. These data suggest a need for a more circumspective assessment of alcohol consuming patients with end-stage liver disease.

252 THALIDOMIDE BUT NOT PENTOXIFYLLINE LOWERS PORTAL PRESSURE IN HUMAN ALCOHOLIC CIRRHOSIS

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Introduction: Blockade of tumour necrosis factor alpha (TNFα) activity reduces portal pressure in portal vein-ligated rats. We investigated the ability of two inhibitors of TNFα production, thalidomide and pentoxifylline, to reduce portal pressure in humans.

Methods: Abstinent patients with stable alcoholic cirrhosis and oesophageal varices were treated for two weeks with open-label pentoxifylline 1800mg daily (n=9) or thalidomide 200mg daily (n=10). Portal and systemic haemodynamics were measured invasively. The hepatic venous pressure gradient (HVPG-mmHg) was calculated by subtracting free from wedged hepatic venous pressure gradients.

Results: Thalidomide (T) consistently reduced HVPG (Table 1) and increased hepatic blood flow 1164 (738–2260) ml/min to 1505 (1054–2943) ml/min. Hepatic vascular resistance fell from 1498 (460–2546) to 559 (269–1039) dynes/sec/cm5 (p=0.028). Pentoxifylline (P) had no effect. Side effects led to dose reduction/withdrawal in 4 (T) and 5 (P). Two patients (T) withdrew without reason. Data for patients completing two weeks treatment are expressed as median (range) and analysed using Wilcoxon signed ranks test (p=0.028).

Abstract 252, Table 1

<table>
<thead>
<tr>
<th>N</th>
<th>Age (yr)</th>
<th>Child A/B/C</th>
<th>HVPG before (mmHg)</th>
<th>HVPG after (mmHg)</th>
<th>Change in HVPG</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>6</td>
<td>51 (45–64)</td>
<td>3/2/1</td>
<td>19.2 (14.3–24.7)</td>
<td>20.9 (18–22.8)</td>
</tr>
<tr>
<td>T</td>
<td>6</td>
<td>59 (45–72)</td>
<td>3/3/0</td>
<td>19.7 (9.3–23.5)</td>
<td>12.2* (4.7–19.5)</td>
</tr>
</tbody>
</table>

(460–2546) to 559 (269–1039) dynes/sec/cm5 (p=0.028). Pentoxifylline (P) had no effect. Side effects led to dose reduction/withdrawal in 4 (T) and 5 (P). Two patients (T) withdrew without reason. Data for patients completing two weeks treatment are expressed as median (range) and analysed using Wilcoxon signed ranks test (p=0.028).
There was no significant change in systemic haemodynamics, bilirubin, albumin, INR or creatinine in either group. **Conclusion:** Anti-TNF therapy with thalidomide effectively reduces portal pressure and hepatic vascular resistance supporting a role for TNF in the pathogenesis of human portal hypertension.

**253 TIPS and BUDD–CHIARI SYNDROME**


**Background/aims:** Patients with Budd–Chiari who are not amenable to hepatic vein recanalisation are usually treated either medically, with surgical shunt formation or liver transplantation. We reviewed the outcome of 17 patients who were treated with TIPS.

**Methods:** A retrospective case note analysis was undertaken of all patients with Budd–Chiari Syndrome who had a TIPS attempted.

**Results:** TIPS was attempted in 17 patients with a median age of 43 years (range 20–59) and median length of history 9 weeks (range 2–364 weeks). An underlying aetiology was found in 16 patients. 15 patients had a technically successful TIPS performed, neither of the 2 patients developed adverse sequelae following failed TIPS attempts. Of the 15 patients, one died soon after TIPS and one died of a subdural haematoma 6 weeks later. The remaining 13 have been followed up for a median of 31 months and have had excellent symptom resolution and have required an average of 0.92 re-interventions per patient.

**Conclusion:** In appropriately selected patients with Budd–Chiari, TIPS can provide a definite treatment advantage at least in the medium term.

**254 RANDOMISED CONTROLLED TRIAL OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC STENT-HUNT (TIPSS) VERSUS TIPSS AND VARICEAL BANDING (VBL) IN THE PREVENTION OF VARICEAL REBLEEDING**


TIPSS is highly successful in treating variceal haemorrhage and preventing variceal rebleeding. We have previously shown TIPSS to be superior to VBL in the prevention of variceal rebleeding. However patients with a TIPSS require regular radiological surveillance in order to ensure patency. It is not known whether the combination of TIPSS and VBL can prevent the need for regular surveillance without compromising efficacy.

**Aims:** To compare the efficacy of TIPSS against that of TIPSS in combination with VBL in the prevention of variceal haemorrhage.

**Methods:** Between 1996–2000 eligible patients who required a TIPSS following an oesophageal variceal bleed were randomised to the TIPSS only arm (n=36, group 1) or TIPSS and banding arm (n=31, group 2). Average follow up was 24 and 26 months respectively. In group 1 patients underwent regular portography and stent dilatation or parallel shunt insertion if required. In group 2 TIPSS surveillance was performed for the first year only with VBL to achieve variceal eradication following the TIPSS.

**Results:** There was no difference in the average age, and aetiology of liver disease. Average Child-Pugh score was 9.25±0.34 and 8.47±0.40 in groups 1 and 2 respectively. Three patients in group 1 and 4 patients in group 2 rebled from oesophageal varices. However 1 patient bled from gastric varices and 3 from portal hypertensive gastropathy in group 2. In all cases of variceal bleeds the TIPSS was occluded or narrowed. 17 and 11 patients died in groups 1 and 2 respectively. There was no significant difference in the cumulative risk of rebleeding or mortality, and in the incidence of encephalopathy or ascites.

**Conclusions:** These interim results demonstrate that the combination of TIPSS and banding is as effective as TIPSS plus surveillance in preventing variceal rebleeding. Combining TIPSS and banding without long term angiographic surveillance is a treatment option. This may be especially relevant to patients with less advanced liver disease, since they are not committed to lifelong invasive TIPSS checks.

**255 THE IMPACT OF ALGINATE AND EPIDERMAL GROWTH FACTOR ON ENDOCYTOSIS—A STUDY IN FOUR OESOPHAGEAL CELL LINES**

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There is considerable evidence to suggest that epidermal growth factor (EGF) and its receptor (EGFR) play an important role in tissue repair, cell proliferation and migration. EGF also inhibits acid production and imparts a cytoprotective mechanism against refluxed gastric contents entering the oesophagus.

Alginate biopolymers are widely used in the treatment of Gastrooesophageal Reflux Disease (GORD). Like EGF they have cytoprotective biological effects although their mechanism(s) of action have not been specifically identified. Alginate biopolymers up-regulate endocytosis, although this activity is not strictly dependent on the interaction of EGF with its receptor. There is, however, evidence of a co-operative relationship.

The action of EGF is due to the ligand binding to its receptor, EGFr, resulting in its activation, generating membrane signalling and subsequent internalisation of EGF and the receptor. Glycolipids are involved in the transport of proteins in the endocytic pathway. We have evidence to suggest that glycolipids such as gangliosides Gm and Gm may participate in the regulation of EGF/EGF mediated endocytosis. It is known that Gm inhibits EGF.

In our study we have examined four cell lines derived from oesophageal carcinomas (2 squamous cell carcinomas and 2 adenocarcinomas). Direct immunofluorescence protocols with confocal microscopy and FACScan® techniques have been employed to observe the relationship between EGF, alginate, EGFR and gangliosides.

**Results:** Alginate up-regulates fluid phase endocytosis. EGF up-regulates fluid phase endocytosis. EGF and alginate up regulates fluid phase endocytosis. Alginate does not up-regulate receptor mediated endocytosis.

**256 CO-CULTURE OF HUMAN SQUAMOUS OESOPHAGEAL AND FIBROBLAST CELL LINES IN ACTIVATION OF PROMMP-2 RESULTING IN A DOWN REGULATION OF INTEGRIN αV3 EXPRESSION AND MMP-2, MT1-MMP EXPRESSION**

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**Background and aims:** Over expression of various matrix metalloproteins (MMPs) and decreased expression of tissue inhibitors of metalloproteases (TIMPs) have previously been speculated to correlate with tumour progression in a variety of cancers. The aim of this study was to investigate MT1-MMP and αVβ3 interactions in the activation of MMPs in human oesophageal cancer cell lines during co-culture with human fibroblasts.

**Methods:** Gelatin zymography, western blotting and real-time PCR were used to investigate the protein and gene expression of MMP-2, -9, MT1-MMP, TIMP1 and TIMP2 in cell lines: OE19, OE33 (adenocarcinomas) and OE21 (squamous carcinoma). Immunoprecipitation was used to investigate levels of integrin αVβ3 by western blotting. Contact and non-contact co-culture experiments were undertaken involving the tumour cells and the human fibroblast line, 46 Br.1G1.

**Results:** The squamous oesophageal carcinoma (OE21) produced significant 14 fold greater levels of MMP-2 and -9 mRNA (p<0.01) compared with that of the adenocarcinoma oesophageal cell lines (OE19, 33). This correlated with increase of levels of proMMP-2 (2.5 fold) and proMMP-9 (2 fold) at the protein level. Integrin αVβ3 protein expression was also exclusively expressed in OE21 cells. Contact co-culture of OE21 and fibroblasts produced a significant decrease of
EFFECT OF DIFFERENT STRAINS OF HELICOBACTER PYLORI ON CYCLOOXYGENASE-2 PROMOTER ACTIVITY—VAC A AND CAG A NOT INVOLVED

M.F. Byrne, P.A. Corcoran, J.C. Atherton, D.J. Fitzgerald, F.E. Murray.

Several studies have demonstrated that *H. pylori* induces COX-2 in gastric mucosa and suggested that this may explain the increased risk of gastric cancer with *H. pylori* infection. We have previously described regulation of the COX-2 gene by *H. pylori* at a transcriptional level. It has been suggested that certain strains of *H. pylori* are more virulent than others for induction of peptic ulcer disease or gastric cancer. We thus examined the effect of different strains of *H. pylori* on COX-2 induction at the promoter level.

COX-2 promoter activity was measured in a cancer cell line of gastric origin (AGS) using transient transfections with 5' deletion constructs of the COX-2 promoter driving luciferase reporter gene expression. Eight fragments were used ranging in size from ~500 to ~1800 base pairs upstream of the transcriptional start site. Transfected cells were incubated for 8 hours with four strains of *H. pylori*, two vacA and cagA positive (61901 and M99) and two vacA and cagA negative (TX30a and 87203) (2x10^5 CFU/mL). Results were corrected for transfection efficiency.

COX-2 promoter activity was induced by all *H. pylori* strains used. In uninfected and treated cells, there appeared to be a positive regulatory element between ~500 and ~800 bp upstream from the transcriptional start site, a region that contains a cAMP response element (CRE). With constructs larger than 161 base pairs, there was increased expression of the COX-2 promoter in cells treated with *H. pylori* compared to uninfected cells. The increased expression corresponded to the inclusion of an NF-kB binding site at ~222 base pairs.

The overall pattern of COX-2 promoter induction was similar with all the strains used, irrespective of Cag and Vac status of the organism.

These data confirm that *H. pylori* regulates COX-2 at a transcriptional level and that the NF-kB site on the COX-2 promoter at ~232 bp may be critical in this regulation. However, CagA and VacA do not play a significant part in COX-2 induction.

There was a 2–3 fold increase in PMN adhesion to IL-1β treated HUVEC and an even more pronounced 5–7 fold increase on the *H. pylori* treated cells.

*H. pylori* causes upregulation of adhesion molecules in endothelial cells with resultant increased neutrophil adhesion. Upregulation of P-selectin is also known to be important in *H. pylori* activation of platelets. Increased white cell adhesion may play a role in the pathogenesis of *H. pylori* induced ulcer disease.

Although COX-1 is often referred to as a constitutively expressed gene, we have previously described induction of COX-1 as well as COX-2 by *H. pylori* suggesting that COX-1 may contribute to inflammatory responses. We have also shown transcriptional regulation of the COX-2 gene by *H. pylori* using promoter constructs. The aim of this study was to determine if *H. pylori* exerts a regulatory effect on the COX-1 promoter.

COX-1 promoter activity was measured in a gastric cancer cell line (AGS) using transient transfections with a 5' deletion construct of the COX-1 promoter driving luciferase reporter gene expression. The COX-1 promoter differs from that of COX-2 in that it contains no TATA box but has several transcriptional start sites. We used a 2075-base pair fragment (~2095 to ~2115 relative to the translation start codon). Transfected cells were incubated for 8 hours with live *H. pylori* (strain 60190, torC++, cagA+) at a concentration of 2x10^5 bacteria per ml. *H. pylori* caused an increase of mean 31.3 % (+/− 6.9 %) in COX-1 promoter activity with this construct compared with uninfected cells. Of note, this region of the COX-1 promoter contains two Sp1 binding sites known to activate basal gene transcription.

This is the first report of regulation of the COX-1 gene by *H. pylori* at the promoter level. We speculate that previously described “housekeeping” promoter binding sites such as Sp1 may be important in this regulation. This work strongly supports the suggestion that *H. pylori* exerts its effects on the stomach via induction of COX-1 as well as COX-2.

HELICOBACTER PYLORI, OXIDATIVE DAMAGE AND GASTRIC CARCINOGENESIS

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Background: Mutation of the p53 tumour suppressor gene is the most common genetic alteration in human cancers and has been implicated as a key factor in early gastric carcinogenesis. In addition, Helicobacter pylori (HP), is a class 1 carcinogen whose presence is associated with cancer of the mid or distal stomach. We hypothesised that HP may bring about its carcinogenic effect by promoting reactive oxygen species.

Aim: To investigate this relationship in an *in vitro* system, using hydrogen peroxide as a generator of reactive oxygen species.

Method: A transformed human gastric cell line was dosed with 0µM, 100µM and 300µM of hydrogen peroxide to mimic oxidative damage. Following DNA extraction the restriction site mutation (RSM) assay was employed to analyse mutations occurring in 8 restriction enzyme sites of the human p53 gene, exons 5–8. Each restriction site was analysed in triplicate for each dose range.

Results: Mutations were only found in the MspI restriction site (hotspot 248) and were mainly GC to AT transitions (60%). This experimental data implicates the 5-hydroxy-cytosine adduct in these mutations and not the 8-hydroxy-guanosine adduct which is the most common cause of oxidative damage. This finding is not surprising as 8-hydroxy-guanosine is only weakly mutagenic and easily repaired whereas 5-hydroxy-cytosine is highly mutagenic.

Conclusion: This experiment shows that the RSM assay can be used as a detection method for oxidative damage in early gastric cancer. It will now be applied to patient biopsy samples (normal, gastritis and intestinal metaplasia), in order to elucidate what mutations occur in potentially pre-cancerous gastric tissue.
261 MECHANISMS OF H. PYLORI INDUCED PLATELET AGGREGATION—CO-SIGNALLING BETWEEN PLATELET GPIb AND Fc-RIIa BUT NO ROLE FOR PLATELET ACTIVATING FACTOR

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Human and animal data have demonstrated H. pylori induced platelet aggregation in gastric vasculature. Formation of platelet aggregates may contribute to the pathogenesis of H. pylori associated gastric injury and may also explain the link with cardiovascular events. Recent work has suggested that induction of platelet aggregation by H. pylori is due to secretion of platelet activating factor (PAF) or PAF like substances by H. pylori. We have previously described a mechanism for induction of platelet aggregation by H. pylori which is platelet glycoprotein (GP) Ib dependent. The aim of this study was to further define the signalling pathways of this mechanism and also to investigate the role of PAF.

50 µl of bacterial suspension (H. pylori 60190 4x10³ CFU/ml) were added to 450 µl of platelet rich plasma. Platelet aggregation was measured by changes in light transmission. In a separate experiment, CHO β-IX cells were transiently transfected with GPIbα (interaction site of GPib). FITC labelled mock and transfected CHO cells were then incubated with labelled H. pylori strain 60190.

H. pylori strain 60190 induced platelet aggregation (mean 62% ± 2%). Using confocal microscopy we found that CHO β-IX cells transfected with GPIbα bound H. pylori 60190 whereas no binding occurred in mock transfected cells confirming the role of GPIbα. Also, H. pylori- induced aggregation of platelets via GPIbα is dependent on signalling through the platelet bound FcγRIIa receptor as FcγRIIa blocking antibody (CD 16/32)(10µg/ml) inhibited H. pylori induced platelet aggregation by 69.3% (p=0.0001). However, PAF is not involved as PAF antagonist (1µM) had no effect on H. pylori induced platelet aggregation but completely inhibited PAF induced platelet aggregation.

These data confirm that H. pylori induces platelet aggregation by initial activation of the platelet via GPIbα involving co-signalling with the platelet FcγRIIa receptor. This mechanism is dependent of PAF. These data support the suggestion that H. pylori induced platelet microthrombi in gastric vasculature may be an important early event in gastric injury.

262 DIFFERENTIAL EXPRESSION OF RAS ISOSFORMS IN NORMAL HUMAN PANCREAS: AN IN VIVO IMMUNOHISTOCHEMICAL ANALYSIS

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Background: Ras monomeric GT-Pases play a vital role in cellular signalling pathways by linking cell surface receptors and integrins to intracellular machinery and thus influencing proliferative and apoptotic events. Ki-Ras in its mutated oncogenic form is known to occur commonly in various pancreatic pathologies but wild-type Ras isoforms (H-, K-, and N-) have not been studied in normal human pancreas.

Methods: Archival formalin-fixed, paraffin embedded specimens of normal pancreas were cut and consecutive 4µm sections were processed and incubated (overnight at 4°C) with pan-Ras and isoform-specific Ras monoclonal antibody (mAb) with appropriate positive and negative controls. Detection by immunohistochemistry involved using a modified polymer system. Two independent observers carried out semi-quantitative analysis.

Results: Pancreatic ductal cells expressed Ha-Ras in the cytoplasm and Ki-Ras in the apical region and N-Ras (50% of cases) in a supra-nuclear distribution. The acinar cell complex showed mild staining with pan-Ras, nuclear staining with Ki-Ras and supra-nuclear distribution of N-Ras (50% of cases). The cells of the Islets of Langerhans showed marked staining with pan-Ras, Ha- and Ki-Ras mAb but mild staining with N-Ras mAb. Fibroblasts showed staining with pan-Ras and Ki-Ras mAb, but no staining with Ha- or N-Ras mAb.

Conclusions: This work suggests that the Ras isoforms have distinct and separate cellular functions. Understanding these functions in detail is an essential step if Ras is to be targeted in the pancreatic or gene therapy.

263 TISSUE TRANSGLUTAMINASE INCREASES THE BINDING OF A-GLIADIN 31–49, A COELIAC TOXIC EPITEPO, AND A-GLIADIN 51–70, TO HLA-DQ8

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Introduction: Presentation of gliadin peptides in association with DQ2 or DQ8 to gluten specific small intestinal T-cells is thought to be one of the key pathogenetic mechanisms in coeliac disease (CD). Tissue transglutaminase (TG) enhances binding of certain gliadin peptides to DQ2 and DQ8 by deamidation of specific glutamine residues. A- gliadin 31–49 (31–49) has been shown by us to have in vitro and in vivo coeliac toxic activity, and to bind to DQ2 and DQ8. However there is recent evidence for one or two dominant DQ2 restricted epitopes within A-gliadin 56–75 with rTG deamidation of Q65 being important for T-cell recognition. Here we assess binding of 31–49 and A-gliadin 51–70 (51–70), containing the putative dominant epitopes, to DQ8 and with and without rTG.

Methods: Binding of biotinylated peptides was assessed with murine fibroblast transfectants expressing only human DQ8. Following incubation double staining with avidin-D-FITC was undertaken before FACS analysis of live cells. Mean FL-1 fluorescence, the measure of binding, was adjusted for class II surface expression using a monoclonal to DQ8. For rTG (guinea pig liver) assays, peptides were incubated with rTG at 37°C for 2 hours before addition to cells.

Results: The mean level of binding of 51–70 to DQ8 compared to 31–49 was 128.3%. rTG treatment enhanced the binding of both peptides, by a factor of approximately 3.5 for 51–70 and 1.5 for 31–49.

Discussion: It is not known whether DQ2 and DQ8, both strongly associated with CD, share a similar repertoire of gliadin T-cell epitopes. The binding motifs of these molecules are similar in that both have a propensity for accepting negatively charged residues, which can be generated by the action of rTG. Here a peptide similar to peptides thought to be dominant CD epitopes binds to DQ8 with lower affinity than a peptide with in vivo CD activity (whether this is true specifically in DQ8 patients is not known). rTG enhances this binding. It is suggested that 51–70 may be involved in disease pathogenesis in DQ8 and DQ2 CD. It is possible that these class II heterodimers share the same, possibly narrow, repertoire of gliadin epitopes.

264 DIFFERENTIAL EFFECTS OF TRANSFORMING GROWTH FACTOR (TGF) β ISOSFORMS ON THE EXPRESSION OF TISSUE INHIBITOR OF METALLOPROTEINASE-1 (TIMP-1) AND MATRIX METALLOPROTEINASE-3 (MMP-3) IN INTERTESTINAL MYOFIBROBLASTS (IMFs): IMPLICATIONS FOR STRICTION FORMATION IN CROHN’S DISEASE

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Background and aims: We have previously shown that, compared to normal and ulcerative colitis IMFs, Crohn’s disease IMFs constitutively release more TGFP-β2 and less TGFB-β3. TIMP-1 and MMP-3 are expressed in mucosal tissue with active inflammatory bowel disease. In this study, we have investigated the effect of recombinant isoforms of TGFP-β1, TGFB-β2 and TGFB-β3 on the expression of MMP-3 and its inhibitor TIMP-1, by primary human IMFs.

Methods: Monolayers of primary normal colonic IMFs (n=10) were cultured with rTGFP-β1, rTGFP-β2 or rTGFB-β3 (5ng/ml) or control medium for 24 h. Concentrations of MMP-3 and TIMP-1 in supernatant samples were determined by ELISA. Results are expressed as median (range) of TIMP-1: MMP-3 ratios.

Results: Compared to control medium [14.8 (9.4–18.4)], rTGFP-β1 [17.0 (14.7–22.9)] and rTGFP-β2 [16.4 (11.4–18.7)] treated IMFs, the TIMP-1: MMP-3 ratios were significantly lower in rTGFP-β1 [12.1 (6.9–15.2)] and rTGFP-β2 [p<0.046, p<0.005 & p<0.011, respectively]. TIMP-1: MMP-3 ratios between control and rTGFP-β1 treated cells did not reach statistical significance (p=0.059).

Conclusions: In contrast to rTGFP-β1 and rTGFP-β2, rTGFB-β3 significantly reduced the expression of TIMP-1 relative to MMP-3 in IMFs. Greater activity of MMP-3, in the presence of TGF-β3, may inhibit excessive deposition of fibrous tissue by breaking down components of the extra cellular matrix. Thus, reduced constitutive expression of TGFP-β3 by Crohn’s disease IMFs may lead to excessive deposition of fibrous tissue and stricture formation.
COX2 EXPRESSION AND ACTIVITY IS DEPENDENT ON P38 STRESS ACTIVATED PROTEIN KINASE IN COLONIC EPITHELIAL CELLS

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Introduction: COX2 is up-regulated in Inflammatory Bowel Disease (IBD) and in Colorectal Carcinoma (CRC). Indeed it has been proposed that the increased expression in IBD may be the reason that these patients are at increased risk of CRC. Therefore understanding the regulation of COX2 is essential in these conditions. The p38 stress activated protein kinase (SAPKinase) has been shown to play a role in the induction of COX2 in other systems although this has never been demonstrated in the colon.

Aim: To investigate the role of p38 in COX2 expression and activity in colonic epithelial cells.

Methods: COX2 expression and activity were assessed in the HT-29 colonic epithelial cell line. COX2 mRNA expression was assessed using northern analysis. Functional activity of COX2 was assessed by quantifying PGE2 production using an ELISA.

Results: TNFα (10ng/ml) and IL-1β (10ng/ml) were independently used to induce COX2 mRNA in HT-29 cells. For both cytokines this induction of COX2 was partially inhibited by pre-incubation with the specific p38 SAPKinase inhibitor SB203580 in a concentration dependent manner (0.3–30µM). To assess whether this effect was reflected on COX2 functional activity, TNFα induced PGE2 production was assessed at 72hours. In the presence of SB203580 (3 and 10µM) there was >90% inhibition of PGE2 production, a more marked effect than that seen on COX2 mRNA.

Conclusion: This work demonstrates for the first time that specific p38 SAPKinase inhibition inhibits cytokine induced COX2 expression and activity in colonic epithelial cells. It also implies that activation of p38 by TNFα and IL-1β plays an important role in the induction of COX2 in the colonic epithelium. Therefore p38 inhibition may provide a useful therapeutic target to inhibit COX2 in the future.

CYCLOOXYGENASE-2 AND ANGIogenesis IN HUMAN SPORADIC COLORECTAL ADENOMAS

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Background: We have previously reported that cyclooxygenase (COX)-2 is expressed predominantly by interstitial macrophages in human sporadic colorectal adenomas. In this study, superficial areas containing COX-2-positive macrophages were often noted to be very vascular. A putative role for COX-2 during intestinal tumorigenesis is via promotion of angiogenesis. Therefore, we investigated the association between microvessel density (MVD), COX-2 expression and several clinicopathological correlates in human sporadic colorectal adenomas.

Methods: CD31 immunohistochemistry (IHC) was performed on a series of human sporadic colorectal adenomas (n=37) for which we had previously determined COX-2 expression levels by IHC. The mean MVD from 3 high power field (x400) views of vascular “hotspots” in both superficial and deep interstitial areas was assessed by two independent observers blinded to adenoma origin and COX-2 expression level. MVD was correlated with adenoma characteristics, including COX-2 expression level (scored 0–3).

Results: Superficial MVD was increased in COX-2-positive adenomas (median [IQR] 35 [18–43]) compared with COX-2-negative adenomas (13 [7–30]; P=0.037, Mann-Whitney U test). There was a non-significant trend towards increasing superficial MVD with increasing COX-2 expression level (P=0.08, one way ANOVA). However, multiple linear regression analysis of clinicopathological data, including COX-2 level, demonstrated that adenoma size (P=0.007) was the only significant predictor of MVD. No relationship was evident between MVD and the COX-2 expression level in deep interstitial areas of adenomas.

Conclusion: COX-2 protein expression by superficial interstitial cells in human sporadic colorectal adenomas is associated with increased angiogenesis. However, in this series, adenoma size was a stronger predictor of increased MVD in superficial areas of adenomas. Promotion of angiogenesis may play an important role during early stages of intestinal tumorigenesis in humans.

HUMAN COLORECTAL CANCER IS ASSOCIATED WITH DOWN REGULATION OF THE Ca2+-ACTIVATED CHLORIDE CHANNELS CLCA1 AND CLCA2

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Background: The role of ion channels in carcinogenesis and tumour progression remains unclear. CLCA1 and 2 are members of a novel Ca2+-dependent chloride channel family that are expressed mainly in the digestive tract. Both share significant sequence identity with a dual-function cell adhesion/chloride channel molecule and CLCA2 is a tumour suppressor in breast cancer.

Methods: Suppression subtractive hybridisation, reverse northern dot blot analysis and in silico cloning resulted in the identification of mRNAs differentially expressed between paired normal colonic epithelium and carcinoma. One was CLCA1 and its transcription, as well as that of CLCA2, was quantitated by real-time RT-PCR analysis in a further 44 paired normal and carcinoma samples.

Results: CLCA1 and CLCA2 mRNA was detected in 44 and 38 paired samples, with no difference in mRNA copy numbers in nine and four paired samples, respectively. CLCA1 mRNA levels were significantly increased in one and decreased in 35 tumours, with median copy numbers reduced from 3.2x105 to 5.5x105 per µg RNA (P<0.0005, Mann Whitney U-test). CLCA2 was up regulated in two and down regulated in 32 tumours with its copy number reduced from 2.7x105 to 1.3x105 per µg RNA (P<0.001). Transcription of CLCA1, but not of CLCA2, was significantly associated with that of c-myc in normal tissue (R=0.82, p<0.0001, Spearman rank correlation), with deregulation observed in the tumour samples (R=0.36, p<0.015). Transcription of both mRNAs was virtually absent from three colorectal cancer cell lines, T84, HT29 and Caco2 (<1copy/cell).

Conclusion: Our results show that reduced CLCA1/2 transcription is associated with colorectal tumorigenesis and suggest that their gene products may function as tumour suppressors in colorectal cancer.
nuclear protein import. Further studies are needed to assess the functional importance of its glycosylation with sialyTF and to assess its potential as a target for cancer therapy.

**ENDOTHELIN-3 BLOCKADE PROMOTES PREMATURE NEURONAL DIFFERENTIATION IN AN ORGANO CULTURE MODEL OF HIRSCHSPRUNG DISEASE**


**Aims:** Pharmacological blockade of endothelin-3 (ET3) in an embryonic mouse gut culture system results in incomplete migration of enteric neural crest cells (NCC) along the gut and thus distal colonic aganglionosis. We aimed to determine the mechanisms controlling migration by analysing effects of endothelin blockade on NCC proliferation, differentiation, and apoptosis.

**Methods:** Gut was dissected from day 11.5 mouse embryos and transferred into culture with or without BQ788, a specific blocker for ET3’s receptor (the ET1 receptor). NCC proliferation and apoptosis were determined by BrdU incorporation and TUNEL reactions, respectively after 24h culture. NCC differentiation was determined using nitric oxide synthase (NOS) immunoreactivity after 24-72h culture.

**Results:** ET3 blockade had no effect on either proliferation or apoptosis of enteric NCC. After 72h, numerous NOS-positive neurons were identified in gut cultured with BQ788, but not in controls, and this was associated with distal colonic aganglionosis.

**Conclusions:** ET3 prevents enteric NCC differentiation rather than influencing proliferation or apoptosis. Thus, in the absence of ET3, migrating enteric NCC differentiate prematurely into non-migratory neurons and distal aganglionosis (Hirschsprung disease) results.

**EPIDERMAL GROWTH FACTOR, ITS RECEPTOR AND THE ROLE OF GANGLIOSIDES Gm3 and Gm1**

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Endocytosis is a process whereby eukaryotic cells take up extracellular material by a variety of different mechanisms. These endocytic functions are involved in the regulation of cell surface receptor expression, maintenance of cell polarity, cholesterol homeostasis and a host of other physiological processes. In this investigation we look for the internalisation of ligand/receptor complexes, in this case epidermal growth factor (EGF) and its receptor (EGFr). Gangliosides are necessary for the efficient functioning of this process and this study looks at the relationship between EGFr and gangliosides Gm3 and Gm1 in four oesophageal cell lines, and the impact of gangliosides on RME. We have also quantified the amounts of EGFr and gangliosides on the cell membrane. Their co-localisation suggests that a co-operative relationship exists between them. This evidence indicates that gangliosides are directly involved in the signalling mechanism that is induced when EGF binds to EGFr, a tenet supported by the inhibitory aspect of Gm1, on one effect of EGF.

**IMMUNOLOGY/INFECTION/INFAMMATION POSTERS: 271–287**

**INCORRECTED EXPRESSION OF HUMAN β-DEFENSINS (hBD) 1 AND 2 IN H. PYLORI-POSITIVE AND -NEGATIVE GASTRITIS**

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**Introduction:** H. pylori is the causative agent of most cases of chronic superficial gastritis in humans and a risk factor for the development of peptic ulcer disease and gastric cancer. Our understanding of the early host response to H. pylori infection is limited. We and others have previously shown increased expression of the anti-microbial peptide hBD2 by gastric epithelial cell lines in response to H. pylori infection. In the present study we investigated the mRNA and protein expression of hBD1 and hBD2 in H. pylori-positive and -negative gastric biopsy samples.

**Methods:** Gastric biopsies were obtained from patients with H. pylori-positive (n=11) and H. pylori-negative (n=5) gastritis and control subjects (n=8). hBD1 and hBD2 mRNA was quantified by quantitative and semi-quantitative RT-PCR. Immunohistochemistry was performed on archival gastric paraffin-blocked samples from patients with H. pylori- and non-H. pylori-related gastritis.

**Results:** A marked increase in hBD2 mRNA expression was observed in both groups of gastritis compared to control tissue (H. pylori-positive, p=0.006; H. pylori-negative, p=0.02). The constitutive hBD1 mRNA expression observed in control tissue was also upregulated (H. pylori-positive p=0.035, negative group p=0.01). A parallel increase was also observed in hBD1 and hBD2 peptides with the positive staining confined to the surface epithelium.

**Conclusion:** This is the first in vivo study showing increased expression of hBD1 and hBD2 in H. pylori-positive and -negative gastritis. These results suggest an important role for these peptides in the innate host defence during inflammatory episodes and infection.

**CD44 REGULATION AND FUNCTION IN ULCERATIVE COLITIS**

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We have shown that CD44v6 and CD44v3, variant isoforms of the cell surface glycoprotein CD44, are expressed on the baso-lateral surface of colonic epithelial cells in Ulcerative Colitis (UC) but not in other forms of colonic inflammation including colonic Crohn’s Disease (CCD). The regulation of enhanced CD44 expression and the function of CD44 in UC have not been explained. CD44 is known to act as an adhesion molecule, to play a role in lymphocyte activation and to aid lymphocyte homing by binding and sequestering cytokines. Using FACS we have investigated the role of cytokines in inducing the expression of CD44v6 and v3 on the colonic cancer epithelial cell line HT-29. Using a novel lymphocyte adhesion assay we have gone on to investigate the role of CD44v6 and v3 in activated peripheral blood (aPBL) and gut lamina propria lymphocytes (LPL).

**Results:** IL-4 and IL-13 induced CD44v6 and v3 on HT-29 but IFN-γ, TNF-α, IL-1, 2,6,7,8 and 10 did not. Time course experiments showed that expression was maximal at 12 hours. Co-incubation of HT-29 and IL-4 with hydrocortisone, TNF-α, IFN-γ, IL-2 and 10 resulted in down regulation of CD44v6 and v3. Using a novel adhesion assay we studied the adherence of aPBL and LPL to HT-29 monolayers pre-treated with IL-4 to induce CD44v6 and v3 expression. Monolayers of HT-29 cells were cultured in 96 well plates in the presence of medium alone or medium supplemented with IL-4 to induce CD44v6 expression in test wells. Fluorescently labelled PBL or LPL were added to the test and control wells, allowed
to adhere and then washed off. The effect of CD44 expression on PBL and LPL adhesion to HT-29 cells was determined by comparing the residual fluorescence in the presence or absence of CD44 induction. CD44 variant expression resulted in 2–3 fold increase in lymphocyte adhesion. This effect on adhesion could be blocked by pre-treating the HT-29 IL-4 wells with monoclonal antibodies known to block CD44 mediated adhesion.

Summary: Expression of CD44v6 and v3 on colonic epithelial cells is induced by IL-4. This effect can be competed out by TNF-α, IFN-γ, IL-2 and 10 and by hydrocortisone. CD44v6 and v3 mediate adhesion of PBL and LPL to colonic epithelial cells. This effect can be blocked by antibodies to CD44 that may have a therapeutic role in UC.

**273 FISH OIL SUBSTITUTED ELEMENTAL DIET IN ULCERATIVE COLITIS**

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**Introduction:** Elemental diet is an effective anti-inflammatory agent in Crohn’s disease but not in ulcerative colitis (UC). We have recently shown that elemental diet increases the IL1-receptor antagonist/IL1 ratio in Crohn’s disease, but not in ulcerative colitis in vitro. The lipid component of elemental diet is derived from coconut oil, canola oil and safflower oil in elemental diet (EAA) in ulcerative colitis in vitro.

**Methods:** Colonoscopic rectosigmoid biopsies in six patients with UC were incubated in an organ culture model for 24 hours, by diluting elemental diet-fish oil (EF) or EAA (E028, SHS, UK) with modified Waymouth’s complete medium (MB705/1) in dilutions of 1:20, 1:10, 1:5. Control was media alone without any added EF or EAA. The tissue viability was assessed by adding Bromodeoxyuridine (BrdU) to the culture fluid. The in-vitro uptake was confirmed by further immunohistochemical processing of the tissue and confirmation of BrdU labelled cells. The supernatant was collected after 24h and frozen at -70°C for immunoaassay. ELISA was performed for pro-inflammatory (IL-1β) and anti-inflammatory (IL-10) cytokines in the stored supernatants.

**Results:** Incubation of the organ culture specimens for 24 hours with EAA in 1:20,1:10 and 1:5 dilutions did not increase the IL1ra/IL1β ratio in Crohn’s disease, but in ulcerative colitis in vitro. The lipid component of elemental diet is derived from coconut oil, canola oil and safflower oil in elemental diet (EAA) in ulcerative colitis in vitro.

**Conclusion:** Fish oil substituted elemental diet increases the anti-inflammatory to pro-inflammatory cytokine balance in vitro, unlike standard elemental diet in ulcerative colitis. Clinical trials may be warranted if palatability problems can be overcome. This study corroborates a recent in vivo study showing reduction of disease activity in distal proctocolitis by n-3 PUFA administration.

**274 MORPHOMETRIC ANALYSIS OF MACROPHAGES CONTAINING INORGANIC PARTICLES IN INFLAMMATORY BOWEL DISEASE**

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**Introduction:** We have recently shown that microparticles can be transported across the intestinal epithelium. Such uptake of microparticles is more avid in inflamed epithelium compared to normal epithelium. We describe the presence and distribution of such particles within macrophages in IBD affected and normal intestine and nature of such particles.

**Methods:** Paraffin embedded sections from 12 surgically resected intestine (4 Crohn’s disease, 4 ulcerative colitis and 4 normal from unaffected segment of cancer) were stained with H & E and cells with particles were located. In confocal laser scanning microscope (LSM) non-biological nature of particles was determined. Electron spectroscopic imaging with X-ray microanalysis (EDX) with transmission electron microscopy (TEM) was done to determine the composition of the particles. Macrophages were detected in three step immunoperoxidase method using monoclonal antibody for CD68 antigen. Area of macrophages was measured under color detection system in image analysis (25 fields at x 400).

**Results:** Most macrophages in IBD, both Crohn’s and UC contained inorganic particles which are non-biological. In contrast control normal tissue, few particles were seen on one normal tissue. The particles were exclusively located in lysosomes within the cytoplasm of the macrophages. EDX analysis with TEM showed these particles to consist of titanium, silicon and aluminum. The area of tissue (µm²) occupied by CD68 stained macrophages was significantly higher in IBD affected tissues compared to normal tissues [mean ± SE; Crohn’s (585±77), UC (582±29) and normal (30±8), p<0.01]. Proportion of macrophages (mean ± SE) in the tissues was: Crohn’s (6.5±0.4), UC (4.5±0.2 and normal (2.3±0.15), p<0.01.

**Conclusion:** IBD affected tissues contained particles of titanium, silicon and aluminum. This study confirms previous reports on presence of similar particulate material in IBD tissue and clearly shows that particles are exclusively present within the cytoplasm of macrophages. This study for the first time shows that macrophage area was increased in IBD-affected tissues, especially in Crohn’s disease. Whether the presence of particles activates the macrophages to liberate pro-inflammatory cytokines and perpetuate inflammation requires further study.

**275 GUT BACTERIA AND ULCERATIVE COLITIS—THE ENEMY WITHIN**

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**Introduction:** Although ulcerative colitis (UC) appears to be the result of unrestrained inflammatory response, the antigen(s) which initiates and perpetuates this chronic, relapsing disorder remain uncertain. It has been suggested that ubiquitous luminal bacterial products are somehow involved in the pathogenesis of this disease. Furthermore, compelling evidence has been provided that the mere presence of bacteria per se that induces colitis, but certain bacteria are needed, such as Bacteroides spp. We tested this hypothesis by using human model of patients with ileal pouch-anal anastomosis (IPAA, these patients virtually have no colon) and with active UC with recently developed microbiologically representative method. We have also assessed the biological potentials of the bacterial products by using peripheral blood mononuclear cells (PBMC).

**Methods:** 19 patients with IPAA [10 with normally functioning pouch (NFP), median age 39 (28–73) and 9 patients with pouchitis, median age 36 (28–74) and 11 patients with active UC, median age 29 (19–66) as well as 12 age-matched healthy controls were investigated. All patients and controls underwent whole gut lavage (WGL) using polyethylene glycol-based solution drunk at a standard rate of 1 litre/h. The first clear effluent was collected and processed. IgA antibody against B. fragilis and a ‘cocktail’ antigen [Endotoxin core antigens were prepared from a range of Gram-negative bacteria (E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Salmonella typhi)] were measured by ELISA. TNF-α and IL-8 production were assessed by bioassay and radio-immunoassay respectively.

**Results:** The median value of IgA EndoCaB (antibody against endotoxin core antigens) in UC patients were significantly higher than that of controls and NFP (p<0.004 and p<0.003 respectively). Likewise, IgA EndoCaB concentration was significantly higher in pouchitis than that of NFP (p<0.008). The IgA antibody against B. fragilis in UC and pouchitis were significantly higher than that of NFP (p<0.04 and p<0.02). Both groups of bacterial antigens induces considerable amount of TNF-α and IL-8 in PBMC.

**Conclusion:** The study confirms that there is an unrestrained immune response against luminal bacterial antigens in the gut mucosa in patients with UC. The luminal antigens can induce inflammatory cytokines. Breakdown of tolerance towards mesorebro Gm-ve colonic bacteria may be a pathogenic mechanism of UC.
**Introduction:** Alpha-defensins are molecules produced by activated gastrointestinal mucosa, vascular endothelium and circulating leukocytes which regulate chemotaxis of leukocytes into areas of inflammation. This study examines the contribution of alpha chemokines and their receptors to chemotaxis in patients with ulcerative colitis (UC).

**Methods:** The cellular expression of alpha chemokine receptors CXCR1 and CXCR2 on circulating leukocytes was measured by flow cytometry using conjugated monoclonal antibodies. An in-vitro chemotaxis assay was used to quantify the effects of alpha chemokines produced by UC patients and healthy volunteers, together with the effects of CXCR1 and CXCR2 blockade by purified monoclonal antibodies.

**Results:** Polymorph expression of CXCR1 and CXCR2 in UC patients (n=32) was significantly lower than in controls (n=15) but similar to expression on leukocytes and monocytes. UC patients with inactive disease had no significant difference in receptor expression compared to those with active disease (p>0.01). Interleukin-8 was found to be the most potant chemokine for all groups, but was significantly less active in UC than in controls (p<0.02). Chemotaxis mediated by interleukin-8, GRO-alpha and ENA-78 was significantly reduced by blockade of CXCR1 and CXCR2 receptors respectively.

**Conclusions:** Patients with UC demonstrate reduced expression of alpha chemokine receptors on polymorphs and this does not appear to be a consequence of disease activity. Furthermore, the response to interleukin-8 is significantly lower in UC patients and healthy volunteers, together with the effects of CXCR1 and CXCR2 blockade by purified monoclonal antibodies.

277 **ALPHA-DEFENSIN EXPRESSION IN HUMAN JEJUNUM VARIES IN HIV INFECTION AND TROPICAL ENTEROPATHY**


**Introduction:** Paneth cells secrete α-defensins, endogenous antibacterial microbial peptides, but the extent to which expression varies in human populations or disease states is unknown. We set out to determine whether expression of human defensins (HD) 5 and 6 varies with HIV or parasitic infection or correlates with mucosal structure or function in jejunal biopsies from 84 adults participating in an ongoing study of tropical enteropathy in a poor urban community in Lusaka, Zambia. Approval for the studies was obtained from two ethics committees.

**Methods:** HD5 and HD6 mRNA expression was evaluated by quantitative RT-PCR, and peptide expression by immunohistochemistry using anti-HD5 kindly provided by Drs. Ganz and Porter (UC, Irvine, CA). Mucosal morphology was performed on well-oriented formalin-fixed sections.

**Results:** mRNA expression (log transcripts per μg total RNA) varied from undetectable to 7. HD5 (but not HD6) mRNA was lower in HIV seropositive adults (median 5.0, interquartile range 0-6.1) than in HIV seronegative adults (5.7, 4.9-6.9; p=0.01). HIV seropositive adults were also more likely to have undetectable HD5 mRNA than seronegative adults (OR 4.0, 95%CI 1.4-12.2; p=0.008). HD5 mRNA (but not HD6) was inversely correlated with both villous height and epithelial surface area by rank correlation (p=-0.41, p<0.003) but only in HIV seronegative adults. Correlation between HD5 and HD6 expression increased with increasing grade of enteropathy (p=0.04 in minimal but p=0.85 in severe enteropathy). Expression did not differ in the presence or absence of parasitic infection. By immunohistochemistry peptide levels varied less between samples and no correlation was found with mRNA expression.

**Discussion:** HD5 expression is altered in enteropathy and HIV infection, but the regulatory mechanism(s) remain to be identified.

278 **INTERLEUKIN-10 AND TGF-β1 REGULATE INFECTERON-γ-MEDIATED INHIBITION OF CRYPTOSPORIDIUM PARVUM DEVELOPMENT IN ENTEROCYTES**

V. McDonald, R.C.G. Pollok, M.J.G. Farthing. Dept of Adult & Paediatric Gastroenterology, St Bartholomew’s & The Royal London School of Medicine, London, UK

**Introduction:** Activation of macrophages by interferon (IFN)-γ to kill intracellular pathogens is down-regulated by interleukin (IL)-10, transforming growth factor (TGF)-β1 and IL-4. IFN-γ also activates enterocytes to inhibit development of intracellular pathogens, but the mechanisms regulating this are poorly understood. This investigation examined the effects of IL-4, IL-10 and TGF-β1 on IFN-γ-mediated inhibition of development of Cryptosporidium parvum.

**Methods:** The human enterocyte cell line, HT 29, was grown to confluence in 24-well plates at 37°C. Human recombinant IFN-γ with or without either IL-4, IL-10 or TGF-β1 was added to cell cultures starting 24h before infection (-24h) with C. parvum. Alternatively, IFN-γ was added at -48h and the modulatory cytokine introduced at -24h or vice versa. Twenty-four hours after infection with C. parvum, monolayers were fixed with methanol and stained with Giemsa so that numbers of intracellular parasites could be determined microscopically.

**Results:** Treatment of enterocytes with IFN-γ starting 24h or 48h before infection inhibited parasite replication by 70-90%. Addition of TGF-β1 or IL-10 to cell cultures at the same time as, but not 24h after, IFN-γ reduced the inhibitory activity of IFN-γ in a dose-dependent manner. In contrast, IL-4 had no significant effect on IFN-γ activity.

**Discussion:** These results suggest that IL-10 and TGF-β1, but not IL-4, may be important in down-regulation of Th1-mediated activation of gut epithelium infected by intracellular pathogens. Once activated by IFN-γ, however, enterocytes may be refractory to modulation by IL-10 or TGF-β1.

279 **MAP KINASE INHIBITION REVERSES CRYPTOSPORIDIUM PARVUM INDUCED IL-8 SECRETION BY ENTEROCYTES**

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**Introduction:** C. parvum is a major cause of diarrhoea world-wide. The parasite has previously been shown to induce the expression of the C-X-C chemokine IL-8 by infected enterocytes. Mitogenic and protein (MAP) kinase activation is important in signalling the regulation of inflammatory gene expression in response to a variety of external stimuli including pathogens. We determined the role of MAP kinases in mediating infection and in modulating the induction of IL-8 by enterocytes infected with C. parvum using selective inhibitors of our established in vitro model.

**Methods:** Cells of the intestinal cell line HCT 8 were grown to confluence in 24 well plates. Cells were treated with either non-selective MAP kinase inhibitor apigenin (Apig, 25μM), selective p38 kinase inhibitor SB203580 (20μM), selective inhibitor MEK PD98059 (50μM), the inactive related compound SB202474 (negative control, 20μM), or medium alone with or without DMSO. Treated cells were infected with C. parvum (0.25–2x10⁴ oocysts or purified sporozoites/well) and incubated 24–48h. Infected was quantified by immunofluorescence assay, using an anti-C. parvum polyclonal antibody 24h after parasite inoculation. ELISA was used to quantify IL-8 protein in supernatants collected 48h after parasite inoculation.

**Results:** C. parvum induced an inoculum-dependent increase in IL-8 in serum-starved HCT 8 cells, with a peak at 48h and 1x10⁴ sporozoites/ well (2629.5 pg/mL ± 90.1) compared with untreated controls (1334.1 pg/mL ± 21.6). MAP kinase inhibitors did not modify infection of HCT 8 cells. However MAP kinase inhibition was found to partially reverse C. parvum induced IL-8 induction (Apig 83.2 ± 6.4, p<0.01; SB203580 50.0 ± 4.2, p<0.05; PD98059 35.7 ± 4.9, p<0.05).

**Discussion:** Our findings indicate that MAP kinase inhibition may partially reverse the induction of IL-8 by C. parvum in vitro. In contrast MAP kinase inhibition had no action on parasite infection of enterocytes. We hypothesise that MAP kinase function as upstream mediators of NK-Fc receptor activation and resultant IL-8 gene induction following C. parvum enterocyte infection.

**Acknowledgements:** RCGF is a Wellcome Trust Training Fellow.
**Introduction:** We have previously shown IFN-γ may directly inhibit *C. parvum* infection of human intestinal cell lines. In this study we have examined the action of other pro-inflammatory cytokines, IL-1β, TNF-α, IFN-γ, IL-15, and the anti-inflammatory cytokine TGF-β1 on parasite infection of enterocytes in our established in vitro model. These cytokines may all be produced by enterocytes and are therefore potential mediators of the innate mucosal host immune response to infection.

**Methods:** HT29 intestinal cells grown on coverslips were infected with *C. parvum* oocysts (2x10⁴ oocysts/well) as previously described. Cell were pre-treated with IFN-α (0.01–1 ng/mL); IL-1β (1–100ng/mL); IL-18 (0.1 ng/mL); TNF-α (1 ng/mL); or TGF-β1 (5 ng/mL) for 24h prior to parasite inoculation. Infection was quantified by immunofluorescence assay, using an anti-*C. parvum* polyclonal antibody and Giems staining. Inhibition or enhancement of infection in the treated wells was calculated as percentage of infection in untreated controls.

**Results:** All of the pro-inflammatory cytokines assessed had an inhibitory effect on parasite infection. IFNα maximal inhibition was 35.3% ± 10.7 (ANOVA p<0.001). IL-15 maximal inhibition was 40.1% ± 8.1 (ANOVA p<0.001). IL-18 maximal inhibition was 31.1% ± 7.1 (ANOVA p<0.001). IL-1β inhibition was 33.0% ± 8.1 (p<0.001). TNF-α inhibition was 61.0% ± 7.8 (p<0.01). In contrast, TGF-β1 enhanced infection by 36.6% ± 7.8 (p<0.05).

**Discussion:** We have demonstrated that a range of pro-inflammatory cytokines may inhibit in vitro infection of intestinal epithelial cell by the parasite *C. parvum*. Production of these cytokines by the enterocyte offers a potential innate mechanism of mucosal immunity to infection.

**Acknowledgements:** RCGP is a Wellcome Trust Research Fellow.

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**THE ROLE OF IL-12 AND IFN-γ IN IMMUNITY TO CITROBACTER RODENTIUM INFECTION**

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Infection of mice with the intestinal bacterial pathogen Citrobacter rodentium (murine EPEC) results in colonic mucosal hyperplasia and a local Th1 inflammatory response similar to that seen in mouse models of IBD. In these latter models, and in patients with Crohn’s disease, neutralisation of TNF-α is of therapeutic benefit. Since there is no information on the role of TNF-α in either immunity to non-invasive bacterial pathogens such as Citrobacter, nor in the role of TNF-α in infectious colitis, we have investigated Citrobacter infection in TNFα-deficient mice. Production of TNFα is required for protective anti-bacterial immunity. The most striking feature of infection in TNFα−/− mice is that the enhanced infection does not alter weight gain, despite the presence of a high bacterial burden in the colon. In contrast, in TNFα−/− mice, there are higher bacterial burdens, but weight loss only occurs late in infection. Bacteria are however cleared showing that TNFα−/− is not needed for protective anti-bacterial immunity. The most striking feature of infection in TNFα−/− mice however is the markedly enhanced pathology, with increased mucosal weight and thickness, increased T-lymphocyte infiltration and a markedly greater mucosal Th1 response. The enhanced bacterial burden is probably due to the increased mucosal surface area in the TNFα−/− mice. To help explain the enhanced Th1-associated immune response we examined IL-12 expression. IL-12 p40 transcripts were markedly elevated in Citrobacter infected TNFα−/− mice and this was associated with enhanced STAT4 phosphorylation. TNFα−/− may therefore play a protective role in the intestine in response to bacterial infection by down-regulating tissue damaging Th1 responses.
the gut lumen. While little is known of their composition or metabolic activities, they are likely to play an important role in mucosal breakdown.

**Aims:** To investigate the formation of mucin biofilm communities, and to study physiological and enzymological factors that enable mucin degrading species to compete for substrates in biofilms.

**Methods:** Colonisation of mucin by facultative bacteria was studied using a two-stage chemostat, simulating conditions of nutrient limitation and mucin availability. Bacterial communities were obtained from different areas of the gut lumen. While little is known of their composition or metabolic activities, they are likely to play an important role in mucosal breakdown.

**Results:** Colonisation of mucin by facultative bacteria was studied using a two-stage chemostat, simulating conditions of nutrient limitation and mucin availability. Bacterial communities were obtained from different areas of the gut lumen. While little is known of their composition or metabolic activities, they are likely to play an important role in mucosal breakdown.

**Conclusions:** Intestinal bacterial populations colonising mucin surface epithelial crypts were shown to be phylogenetically and metabolically distinct from their planktonic counterparts. In vitro modelling of the microbiota in this way has wider applicability, for example, in studying the effects of antibiotics and drugs on gut biofilms.

**MIGRATION OF PRECURSORS OF INTRAEPITHELIAL LYMPHOCYTES (IELS) FROM HUMAN COLONIC LAMINA PROPRIA (LP)**

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**Background:** Together with epithelial cells, IELs represent the first cells of intestinal defence. IELs express the integrins αβ7 and a restricted repertoire of αβ T-cell receptors (TCR), as shown by restricted variable (V) region usage of the TCR β-chain (Vβ). In addition to V region, TCR β genes also consist of diverse (D), joining (J), and constant (C) regions. The epithelial basement membrane contains many discrete pores through which IEL precursors migrate in vivo from the lamina propria (LP) into the epithelium. Using an in vitro model, we have investigated the migration of IEL precursors from the colonic lamina propria.

**Methods:** Human colonic mucosal samples (n=11) were denuded of the epithelium and placed in medium. T cells migrating out of the lamina propria (via basement membrane pores) were collected after 1 h and 16 h culture and studied by FACS and quantitative PCR (for lamina propria (LP) cells migrating over 1–16 h culture period [8.7±2.2%] vs 1.8±0.5% for T cells respectively (n=4). ATP-induced apoptosis could be induced by purinergic ligands, with a potency order typical for P2X7 receptor agonists (BzATP>ATP>2MeSATP). The concentration of ATP required for 50% induction of apoptosis was 240±84 μM for macrophages and 20 μM for T cells respectively (n=4). ATP-induced apoptosis could be specifically inhibited both by annexin V staining and IL-1β release (sandwich ELISA) were used as functional assays. Ultrastructural changes were studied by transmission electron microscopy.

**Results:** Expression of P2X receptor mRNA was studied by RT-PCR. Concentration-dependent changes in pore formation (ethidium bromide influx), apoptosis (annexin V staining) and IL-1β release (sandwich ELISA) were used as functional assays. Ultrastructural changes were studied by transmission electron microscopy.

**Conclusions:** Following loss of the surface epithelium, majority of the αβ-expressing T cells migrating out of the human colonic lamina propria are CD8+. Cells migrating out of the lamina propria during the 1st h of culture express higher levels of αβ TCR transcripts and show a restricted repertoire of TCR Vβ. These cells are likely to be IEL precursors.
that were apoptotic was significantly higher than for normal (32%, n=8), and not further increased by BeAIP. α-AIP reduced the spontaneous IL-1β release in IBD samples. **Conclusions:** Expression and functional data support the presence of P2X, receptor on colonic mucosal macrophages and T lymphocytes. This may play a role in the immunopathology of inflammatory bowel diseases.

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**Small Bowel Posters: 288–307**

**288** IGA ANTIBODY TO TISSUE TRANSGLUTAMINASE IS A HIGHLY SENSITIVE PREDICTOR OF ADULT ONSET COELIAC DISEASE IN CLINICAL PRACTICE

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**Introduction:** Anti-endomysial antibodies have high specificity (90%) for the presence of coeliac disease, but there are ethical and cost issues associated with using mouse oesophagus for clinical tests. Tissue transglutaminase (tTG) is the main autoantigen recognised by endomysial antibodies and commercial tests have recently become available to measure tTG in serum.

**Aim:** To establish the diagnostic sensitivity, specificity, positive and negative predictive value of IgA anti-tTG in adult clinical practice.

**Methods:** The study comprised 48 patients (mean age 52 years: range 20-86, 31 females) undergoing investigation for possible coeliac disease 1. Patients with known coeliac disease were excluded from study. Serum IgA anti-tTG antibody titres were measured quantitatively by an enzyme-linked immunosorbent assay (QuantitaLITE tTG, Inova Diagnostics, Ca, USA). Samples were classified as negative (<20 units), weakly positive (20-30) or moderate to strongly positive (>30 units).

**Results:** Duodenal biopsies were normal in 40 patients and untreated coeliac disease was diagnosed in the remaining 8 cases. All 8 patients with coeliac disease had moderate to strongly positive anti-tTG antibody titres. In addition, 9 of 40 patients without coeliac disease were anti-tTG antibody titre positive (5 weakly positive, 4 moderate to strongly positive). Overall, IgA antibody titres had a diagnostic sensitivity, specificity, positive and negative predictive value of 100%, 94%, 78% and 100% respectively.

**Conclusion:** IgA antibody to tissue transglutaminase appears to be a highly sensitive predictor of adult onset coeliac disease in clinical practice. The relatively high false positive rates for tTG in this material requires further study.

**289** IS A RAISED INTRAEPITHELIAL COUNT WITH NORMAL VILLOUS ARCHITECTURE CLINICALLY SIGNIFICANT?

S. Mahadeva, J.J. Wyatt, P.D. Howdle. Dept of Medicine & Pathology, St James’s University Hospital, Leeds, UK

The significance of an increase in intraepithelial lymphocytes (IEL) within an otherwise normal duodenal biopsy remains uncertain. Although it may represent latent coeliac disease, there is very little information available about cases that do not have gluten-sensitive enteropathy.

**Methods:** A consecutive series of routine endoscopic duodenal biopsies from August’98-July’99 reported by a single pathologist was collected to assess the incidence of such a finding. Clinical details and indications for biopsy were examined in all patients. Those biopsies initially reported to have subjectively increased IELs with normal villi, together with a control group reported as normal, were reassessed by the pathologist blinded to the original report. IEL counts in the study group were compared to controls.

**Results:** Of 625 patients biopsied in the 12 month period, 507 were reported as normal, 104 had a specific duodenal pathology and 14 (2.2%) had increased IEL with normal villi. The ages, sex ratio and clinical indications for biopsy were similar in the latter 14 when compared to the 507 patients with a normal biopsy. Enumeration of the IEL/100 epithelial cells confirmed an increase in all 14 patients (range 26–46/100). In the normal control group, the mean was 12.4, giving an upper limit of normal as 21.5 (mean + 2SD). Of these 14, 3 were positive for coeliac antibodies. The other diagnoses included chronic liver disease (3), colonic tumours (2; 1 benign, 1 malignant), irritable bowel syndrome (2), chronic pancreatitis (1) and unexplained iron deficiency anaemia (3).

**Conclusions:** A raised IEL count with normal villi is not uncommon (2.2%). There is still no clear explanation for its finding in many patients. As it may represent latent coeliac disease, long term follow up studies are required, especially in those with positive coeliac antibodies.

**290** COELIAC DISEASE: EVIDENCE OF ADDITIONAL SUSCEPTIBILITY WHEN THE SECOND HAPLOTYPE IS A DR7 DQ2.1 OR A DR3 DQ2.2 IN DR3 DQ2.2 POSITIVE SUBJECTS

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**Introduction:** 90% of UK coeliac patients carry at least one DR3 DQA1*0501 DQB1*0201 (DQ2.2) haplotype. Patients without this haplotype nearly always carry either a DR4 DQ8 or encode the DQA1*0501 DQB1*0201 heterodimer in trans on DR5 and DR7 haplotypes. There is some evidence that in patients with a DR3 DQ2.2 haplotype increased susceptibility is conferred by the second haplotype being either a DR7 DQA1*0201 DQB1*0202 (DQ2.1) or a DR3 DQ2.2.

**Aims:** To assess whether a DR7 DQ2.1 haplotype conveys additional coeliac disease susceptibility in subjects with one DR3 DQ2.2 haplotype, and to compare this susceptibility to DR3 DQ2.2 homozygotes.

**Methods:** HLA haplotypes were determined in 58 family pedigrees each containing at least 2 coeliac patients. A PCR-SSP method was used to type for DR7, DR3, DQA1*0201, DQA1*0501, DQB1*0201 in 37 families, with 21 families only having typing for DQA1 and DQB1. In these 21 families two microsatellites, and in 29 families 1 flanking microsatellite flanking the HLA region were assessed following PCR using ABI 373 and 377 sequencers.

**Results:** 42 coeliac patients were identified where, having inherited a DR3 DQ2.2 from one parent, the other parent was heterozygous for DR7 DQ2.1 (in some families more than one coeliac patient was used). In 28 of these 42 cases the DR7 DQ2.1 haplotype was transmitted to the patient (p<0.05, McNemars test, Yates correction) demonstrating an additive effect of this haplotype on coeliac disease risk in DR3 DQ2.2 positive patients. In 18 of these cases the other parent was heterozygous for DR7 DQ2.1 with DR3 DQ2.2. In 11 of these 18 cases the DR7 haplotype was transmitted to the patient (p=NS). Compared to DR3 DQ2.2 negative subjects, the haplotype relative risk for DR3/DR3 homozygotes, DR3/DR7 heterozygotes and DR3/DR3 heterozygotes were 36, 1.35, 10.7 respectively. (*where x is not DR3 or DR7).

**Conclusion:** A DR7 DQ2.1 haplotype conveys additional risk for coeliac disease in DR3 DQ2.2 positive patients. This additional risk was no greater than for DR3 DQ2.2 homozygotes consistent with the additional effect of a DR7 DQ2.1 haplotype being a dosage effect of DQA1*0202.

**291** FOLLOW-UP LINKAGE STUDY OF COELIAC DISEASE: FURTHER EVIDENCE FOR THE EXISTENCE OF A SUSCEPTIBILITY LOCUS ON CHROMOSOME 11p11

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The susceptibility to coeliac disease has a strong genetic component, as demonstrated by a 10% disease risk in first degree relatives, 30–50% concordance in HLA identical siblings, and a 70–100% concordance in monozygotic twins. The contribution of the HLA region to this genetic component has been well described but it is clear that loci outside this region must also contribute to susceptibility. Two previous genome wide linkage studies using the affected sib pair
method have produced conflicting results. Our own family based linkage study of 16 highly informative pedigrees identified 17 possibly linked regions, each of which produced a result significant at p<0.05 or less. We have now investigated these 17 regions in a larger set of pedigrees using more finely spaced markers. A total of 50 multiply affected families were studied, comprising the 16 pedigrees from the original genome screen plus 34 new highly informative pedigrees. A total of 128 microsatellite markers were genotyped with an average spacing between markers of 5cM. Two point and three point linkage analysis using classical and model free methods identified five potential susceptibility loci with heterogeneity lod scores >2.0, at 6p12, 11p11, 17q12, 18q23, and 22q13.3. The most significant was a heterogeneity lod of 2.65 at D11S914 on chromosome 11p11. This marker maps to a position implicated in one of the two previous genome scans and taken together these results provide strong support for the existence of a susceptibility locus in this region.

Introduction: Coeliac disease (CD) remains an underdiagnosed condition. It commonly presents with anaemia. The antiendomysial antibody (AEA) test is a highly sensitive and specific test for coeliac disease, but the method and cost often precludes its use to screen large populations. The discovery that tissue transglutaminase (tTG) is the antigen recognised by AEA and the development of a routine ELISA suggests that it may be used as a tool for screening for CD.

Aims: To evaluate the role of a two step protocol employing tTG ELISA and AEA to screen for CD in two high-risk patient groups. 1. Clients who had been refused at blood donation due to anaemia. 2. Patients attending all out-patients in whom serum ferritin was requested and found to be low.

Methods: Anonymous blood samples (EDTA) were collected by a Regional Blood Transfusion service (BTS) as a routine on individuals requested and found to be low.

Results: Of 484 samples tested from the BTS, 8 (1.6%) were tTG +ve and of these 4 (1.21%) were AEA +ve (1:3). Of the 166 patients with a low ferritin, 18 (1.9%) were tTG +ve (1:3, m:5 and 10 (1:17) of these were AEA +ve, whereas 2 of 136 normal ferritins were tTG +ve (1:17) but only one was AEA +ve (1:136).

Conclusions: A high number of patients with positive serology consistent with CD has been found in anonymous testing of patients with a low ferritin, and to a lesser extent anaemic blood donors, in a secondary care setting. The two stage tTG ELISA and AEA regimen is a practical screening tool for CD in high risk groups. The validity of testing on EDTA samples needs to be confirmed.
Methods: All adults with CD at the 2 District General Hospitals within Southern Derbyshire (population circa 500,000) have been identified at diagnosis and prospectively followed. Data collected includes date of diagnosis, symptoms and signs at presentation and reason for referral. We analysed the data over 5 quinquennia (1975–99). Routine use of antigliadin antibody and antireticulin antibody began in 1987 and 1997 respectively.

Results: Trends in demographics, symptoms at presentation and reason for referral in 567 adult patients with CD are shown in the table.

Abstract 295, Table 1

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<td>264 (47)</td>
<td>96 (17)</td>
<td>69 (12)</td>
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Conclusions: We found a rapidly increasing rate of diagnosis of CD, accelerated with the introduction of accurate serological tests. Severity of illness appears to have declined. These results are explicable in terms of greater awareness and improved diagnostic methods rather than a true increase in incidence, consistent with the concept of the CD “iceberg” being revealed.

DOES SERUM IGA ANTI-TTG ANTIBODY CONCENTRATIONS REFLECT SEVERITY OF MUCOSAL DAMAGE IN UNTREATED COELIAC DISEASE?

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Introduction: The contribution of IgA anti-tTG antibodies to the pathogenesis of mucosal damage in coeliac disease is controversial. It has been suggested that anti-tTG antibodies interfere with cellular differentiation and may result in mucosal flattening. TTG has been shown to be important in wound healing and anti-tTG antibodies might prevent restitution of mucosal integrity after injury. On the other hand coeliac disease is common in selective IgA deficiency, casting doubt on any pivotal pathogenetic role of IgA anti-tTG antibodies.

Patients and methods: Fifty three prospectively diagnosed, untreated coeliac disease patients were included in this study. IgA anti-tTG antibody ELISA was developed in-house using tTG from untreated coeliac disease patients were included in this study. IgA anti-tTG antibody was performed (n=48) using di erential lactulose/rhamnose sugar absorption. Intraepithelial (IEL) CD3+ and γ/δ TCR were counted by immunochemistry using anti-CD3 and anti-γ/δ antibodies on cryostat sections and using image analysis. Micro-dissection of duodenal biopsies placed in Clarke’s fixative followed by IMS90 was carried out to quantitate crypt depth (n=26), villous height (n=20) and the number of mitoses/crypt (n=24).

Results: 14/22 (64%) patients with Marsh grade 1 & 2 compared with 21/31 (68%) with Marsh grades 3 & 4 had serum IgA anti-tTG concentrations above 2950 units/ml (p=0.1). In 19/97 patients with coeliac disease and 14/60 non-celiac controls, there was no correlation with IgA anti-tTG antibody concentrations (r=0.002; p>0.05). In 27/42 patients with coeliac disease and 11/30 non-celiac controls, there was no correlation with IgA anti-tTG antibody concentrations (r=0.002; p>0.05). The results were also not different with respect to serum folate, vitamin B12, serum calcium, alanine aminotransferase (ALT) and small bowel histology.

Conclusion: There was no significant association between Marsh grade, IEL, CD3 or γ/δ TCR counts, micro-dissection parameters or serum IgA anti-tTG antibody concentrations. Serum IgA anti-tTG antibody is unlikely to be directly responsible for causing mucosal lesions in untreated coeliac disease.

IS REFRACTORY COELIAC DISEASE AN ADULT FORM OF AUTOIMMUNE ENTEROPATHY?

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Enterocyte antibody (ECA) is the marker for autoimmune enteropathy in children. To date such an enteropathy has not been described in adults but ECA has been reported in 3 adult patients with refractory coeliac disease (CD) worldwide. We tested sera of 8 patients with refractory CD (7 F; median age 60 yrs, range 44–77; 2 with ulcerative jejunitis) for the presence of ECA. 10 patients with CD responsive to a gluten free diet (7 F; 24 [18–69]), 9 patients with irritable bowel syndrome (IBS) (6 F; 3 [19–47] and 5 healthy young adults (1 F) were also studied as controls. In the refractory group IgA endomysial antibody was present in 3 of 6 patients tested, antigliadin antibody in 3 of 7 patients and antireticulin antibody in 4 of 8. Antinuclear antibody was detected in 5 out of 8 patients with refractory disease, smooth muscle antibody in 4, antimitochondrial antibody (AMA) in 1 and thyroid microsomal antibody in 1.

Sera were tested on 3 separate blood group O human duodenal cryostat sections using immunofluorescence. Serum from a child with autoimmune enteropathy was used as a positive control. Sera containing AMA and liver/kidney microsomal antibodies were also tested as they stain the enterocyte cytoplasm with a different pattern to that seen for ECA.

We concluded that ECA detected in any of the refractory coeliac patients. ECA was not detected in healthy controls, in IBS patients and was not present in 9 responsive coeliac patients. 1 patient in the latter group, who was untreated at the time the serum was collected, had patchy positive reactivity within the mature enterocyte cytoplasm. These results suggest that patients with refractory coeliac disease do not have an adult form of autoimmune enteropathy.

COELIAC DISEASE IN SOUTH ASIANS RESIDENT IN BRITAIN: COMPARISON WITH WHITE CAUCASIANS

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Background: The catchment population of our hospital is ethnically diverse and we have seen a number of patients of South Asian origin with coeliac disease. We have suspected that there are clinical differences compared to white European coeliacs especially with respect to anaemia and vitamin D deficiency at presentation.

Methods: We retrospectively and prospectively reviewed the notes of patients attending the adult coeliac clinic over the last 10 years. All patients were diagnosed after 16. There were 39 South Asians (16M:23F; aged 16–55 mean 27 years) and 90 white Caucasians (38M:52F; aged 16–76 mean 46 years). Symptoms, haematology, biochemical, endomysial antibody status and small bowel histology at presentation and follow up were compared between the two racial groups.

Results: There were significant differences between the racial groups. South Asians were younger at presentation (mean age 27 v 47 years, p<0.0001); they were less likely to have ‘irritable bowel’ syndrome (IBS) symptoms (P<0.01), but more likely to have vitamin D deficiency. Their Ca(2+), serum ferritin and mean corpuscular volume (MCV) (P<0.0004), serum iron (P<0.01), transferrin saturation (p<0.05), 1,25 dihydroxyvitamin D3 (P<0.002), and serum albumin (p<0.05) levels were lower, whilst serum alkaline phosphatase levels were higher (P<0.04) than in white European coeliac patients. There were no differences with respect to serum folate, vitamin B12, serum calcium, alanine aminotransferase (ALT) and small bowel histology. IgA class endomysial antibody positivity was the common in the two groups (88.5% for Asians vs 73.5% for Europeans (p=0.153)). South Asians were less likely to stick strictly to a gluten free diet.
SUCCESSFUL INFLIXIMAB TREATMENT FOR STEROID REFRACTORY COELIAC DISEASE

I.D.R. Arnot1, S. Campbell1, A. Dahele1, M. McIntyre1, S. Ghosh1. 1Gastrointestinal Unit and 2Department of Pathology, Western General Hospital, Edinburgh, UK

Introduction: Coeliac disease is a T-cell mediated enteropathy induced by gluten in genetically predisposed individuals. The majority of patients respond to gluten free diet, but a small number do not. After the exclusion of gluten in the diet, ulcerative jejunitis and an enteropathy associated T-cell lymphoma, other treatment modalities such as systemic steroids and immunosuppressives may be necessary. Recent evidence has suggested that anti-TNFα antibodies have a role in the amelioration of an animal model of villous atrophy.

Case report: We report the case of a 47-year-old caucasian female with immunoglobulin A deficiency. She was diagnosed as coeliac disease with subtotal villous atrophy on jejunal biopsy together with positive anti-endomysial and anti-gliadin immunoglobulin G antibodies. Despite close adherence to a gluten free diet her weight continued to drop, she had diarrhoea, and her distal duodenal histology showed no improvement. Some improvement in her symptoms was seen with cyclosporin and systemic steroids but this was not sustained and after careful consideration she was given Infliximab. There has been a dramatic improvement in her weight, symptoms and distal duodenal histology. The response has been maintained for 4 months.

Conclusions: We conclude that Infliximab is an effective treatment that may be considered in a small number of patients with severely resistant coeliac disease.

CHANGES IN BONE DENSITY IN TREATED COELIAC PATIENTS DETECTED CLINICALLY AND BY SCREENING

R.G.P. Watson, C. Rodgers, S. Johnston, S. McMillan, M. Crone. Dept of Medicine, The Queen's University Belfast, Belfast BT12 6BA, Northern Ireland

We have previously shown that bone density (BD) is significantly reduced (with a T score < -1) in 63% of clinically diagnosed coeliacs (typical CD) and in 61% of unrecognised and relatively asymptomatic cases diagnosed in a screening programme (screened CD). The aim of this study was to investigate the effect of a gluten free diet (GFD) on bone density in both types of coeliacs. Forty one typical CD patients (31 females, mean age 48) and 18 screened CD patients (14 females, mean age 54) had bone density measured by DEXA scanner at lumbar spine and hip. After 12–18 months BD was repeated. Adherence and response to a GFD was assessed by anti endomysial antibody (EMA). It was negative in 30 of the typical CDs and in 12 of the screened CDs.

Results: Overall there was no significant improvement in both groups for bone density at lumbar spine or hip. There was also no improvement in the 2 groups when only patients compliant with a GFD were considered. However for patients with a starting BD < 1 who were compliant with a GFD there was a significant improvement in hip BD in the typical CD group (n = 16; median -2.0 to -1.95 p = 0.043). There was also a trend to improvement in lumbar BD with normalisation to > -1 in 4 patients. For the equivalent 7 patients in the screened CD group there were no significant increases although lumbar spine BD normalised in 2.

Conclusion: Treatment of coeliac disease with a GFD for 12–18 months does not produce a clear cut improvement in BD. Beneficial seen in some patients with a significantly low starting BD (< -1) but normalisation of BD to > -1 occurs in only a small number of cases. This result does not provide evidence to support widespread screening for asymptomatic coeliac disease. A longer term study is required.

ENTEROCYTE DYNAMICS IN THE TISSUE-ENGINEERED INTESTINE


Introduction: Native intestine possesses a dynamic mucosa. The aim of this study was to characterise the topography of enterocyte proliferation and apoptosis in the neomucosa of the tissue-engineered intestine.

Methods: Biodegradable polymers seeded with neonatal rat intestinal organoid units were implanted in adult rats to form neointestinal cysts. Five weeks after implantation, five of the rats underwent a side-to-side cyst-jejunal anastomosis. All rats were sacrificed at 6 months. Morphology, epithelial cell proliferation (BrdU immunohistochemistry) and apoptotic rates (TUNEL assay) were assessed for native jejunal (Jej) and non-anastomosed (N-N) and anastomosed (A-N) neointestinal tissues. Groups were compared using ANOVA.

Results: A-N neomucosa consisted of folds resembling native jejunal crypts and villi, whereas N-N neomucosa was poorly developed. The anastomosis was patent in 80% of the rats at 6 months.

Abstract 301, Table 1

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<tr>
<td></td>
<td></td>
<td></td>
<td>Muscular thickness (μm)</td>
<td></td>
</tr>
<tr>
<td>Jej</td>
<td>551.4±12.5</td>
<td>117.0±53.3</td>
<td>47.3±2.7</td>
<td>0.87±0.23</td>
</tr>
<tr>
<td>N-N</td>
<td>102.5±53.7*</td>
<td>337.9±171.8*</td>
<td>32.1±16.2</td>
<td>0.46±0.46</td>
</tr>
<tr>
<td>A-N</td>
<td>338.0±95.7†</td>
<td>338.2±34.0*</td>
<td>60.5±4.7</td>
<td>0.77±0.18</td>
</tr>
</tbody>
</table>

*<0.05 compared to Jej, †p<0.05 compared to N-N.

Neomucosal epithelial proliferation was confined to the lower third of the folds. Apoptosis was evenly distributed throughout the epithelium.

Conclusions: These results suggest that the tissue-engineered neomucosa can regenerate structural and dynamic features of the normal jejunum. Anastomosis to the native intestine is an essential step for the development of the neomucosa. Tissue engineering represents a novel approach to the treatment of patients suffering from short bowel syndrome.

302 INTESTINAL CELL PROLIFERATION AND CRYPT BRANCHING IN PARENTERALLY AND ORALLY FED RATS, EFFECTS OF GASTRIN AND GLYCINE EXTENDED GASTRIN

A.J. Fitzgerald, M.A. Ghatei1, N. Mandir2, S.R. Bloom3, L. Iverson, R.A. Goodlad1. Dept of Histopathology, Dept of Molecular Medicine and Clinical Pharmacology, Imperial College School of Medicine, Hammersmith Hospital, London; Histopathology Units, Imperial Cancer Research Fund, 44 Lincoln’s Inn Fields, London, UK

Background and aims: The role of gastrin in the modulation of epithelial cell proliferation in normal tissues other than the stomach is still controversial. A possible explanation is that the active agent is a processing variant of gastrin, glycine extended gastrin (G17-Gly). We investigated the effects of G17-Gly on rats fed by total parenteral nutrition (TPN) and in orally fed rats.

Methods: Five sets of six TPN fed rats were infused with either 0, 4, 20, or 100 μg/rat/day of G17-Gly, with a further group on 100 μg/rat/day of human gastrin as a positive control. Twelve orally fed rats had subcutaneous implantation of mini-osmotic pumps containing either saline or G17-Gly. After seven days, rats were killed 2 hrs after injections of vinceristine sulphate to arrest cells in metaphase. Metaphase arrest and crypt branching were studied in microdissected crypts.

Results: Gastrin produced a profound fall in gastric pH and an increase in the weight of the stomach and small intestine, which diminished distally. No effect of gastrin was seen on proliferation in the colon. G17-Gly had little effect on gastric pH, nor on weight or proliferation of the stomach, small intestine or colon. Neither agent affected crypt branching in the small intestine or colon. Both cell proliferation and crypt branching were very significantly decreased in the TPN groups when compared to the orally fed rats.

Conclusion: Gastrin is trophic to the stomach and proximal small intestine but the effects on the distal small bowel were not pronounced. No effect of gastrin on proliferation in the colon could be detected. G17-Gly is not a major mitogen for the normal intestinal epithelium.
A NOVEL EPITHELIAL CALCIUM CHANNEL AND GLICENTIN, AN ACTIVE ENTEROGLUCAGON, HAS A DOSE DEPENDENT EFFECT ON THE SMALL INTESTINE BUT NOT ON THE Colon

N.F. Barley, D. O’Callaghan, A. Howard, S. Legon, J.R.F. Walters. Imperial College School of Medicine, Hammersmith Campus, London W12 0NN, UK

The absorption of dietary calcium by the intestine is necessary for mineralisation of the skeleton and maintenance of bone mineral density. The fraction of calcium absorbed can vary between 10 and 60% in different individuals and is a factor in the development of osteoporotic fractures. The reasons for this individual variation are unclear. Less than half is explained by established factors such as vitamin D metabolites, PTH or dietary fat and fibre—suggesting that other mechanisms remain to be discovered. To investigate this further, we have studied the expression of a new class of apical membrane calcium channel in human duodenum.

Based on sequence data from the rabbit ECAC and rat CAT1 apical membrane calcium channels described last year, we synthesised primers to amplify both of these and used a PCR titre experiment to determine the best primer combination. Using these primers, we were unable to detect the other sequence, but ECAC1 and ECAC2 could be amplified from human kidney but only ECAC2, and not ECAC1, was amplified with these from human duodenum. The two genes have about 91% nucleotide identity in the region studied.

Expression was studied by northern blotting in a series of duodenal biopsies from 20 subjects using an ECAC2 probe. RNA expression varied considerably, with a 10-fold range between the lowest and highest values after correction for differences in loading. There was no correlation with serum calcium, suggesting that there is regulated expression the genes for calcium entry and exit. An ECAC1 specific 3’-probe gave no signal in duodenum. These results demonstrate important differences in the level of duodenal expression of ECAC2 between individuals. This may be a major factor producing vitamin D-independent variations in human calcium absorption.

GLICENTIN, AN ACTIVE ENTEROGLUCAGON, HAS A POTENTIAL SIGNIFICANT TROPHIC ROLE ON THE SMALL INTESTINE BUT NOT ON THE Colon

M. Sasaki, A.J. FitzGerald, N. Mandir, K. Sasaki, N.A. Wright, R.A. Goodlad. Dept of Histopathology, Imperial College School of Medicine, Hammersmith Hospital, London; 1Histopathology Unit, Imperial Cancer Research Fund, London; 2Nissin Kyojin Pharmaceutical Co. Ltd, Saitama, Japan

Background and aims: Various experiments have indicated that entero glucagon is associated with the proliferation of small intestine. However, recent studies have failed to show trophic effects of entero glucagon on the small intestine, and glucagon like peptide 2 has been shown to be a potent intestinal growth factor. In this study, we examined the effects of an active entero glucagon, glicentin, on intestinal proliferation using the sensitive TPN maintained rat model.

Methods: Male Wistar rats, fed a semi-synthetic diet, received gavages of ATL-101 or saline control on days 0, 1 and 2 of the experiment. Animals (5 lectin; 5 control) were killed 1, 2, 3, 4, 5 and 7 days after the first gavage. The small intestines were removed and weighed, and samples of proximal jejunum taken to determine crypt length, mitosis and apoptosis in whole crypt mounts. Mucosal alkaline phosphatase and diacylglycerol (DAG) levels were also determined. In a second experiment, rats were gavaged with lectin or saline for 3 consecutive days prior to injection with 5-FU or saline (i.p.) on the 4th day. Three days after animals were killed, and crypt cytogenetics were assessed as described above.

Results: Tissue hyperplasia was maximal after three doses of ATL-101. Crypt length and crypt cell mitosis peaked after two gavages, but there was no change in apoptosis. Reduced levels of alkaline phosphatase and increased intracellular DAG were seen in hyper proliferating mucosa. All measured parameters returned to pre-gavage levels 4 days after cessation of treatment. 5-FU significantly disrupted crypt cytogenetics, reducing jejunal crypt length (p<0.05) and mitosis (p<0.001). Pre-treatment with ATL-101 reduced the damage due to 5-FU, by increasing crypt cell mitosis (p<0.05) within the normal proliferative compartment in the lower half of the crypt.

Conclusions: Treatment with the lectin normalises crypt cytogenetics following 5-FU administration, by provoking a trophic response in the tissue, possibly mediated by a DAG-related pathway. This effect may be of benefit in the management of gastrointestinal mucositis.

A PLANT LECTIN FROM ROBINIA PSEUDOCACAEA (ATL-101) NORMALISES INTESTINAL CRYPT CYTOGENETICS AND MORPHOMETRICS FOLLOWING TREATMENT WITH 5-FU IN A RAT MODEL*

J.M. Gee, A.C.J. Polley, E.K. Lund, R.M. Palmer, C. Dunk, I.T. Johnson. 1Institute of Food Research, Norwich Research Park, Norwich NR4 7UA; 2Alizyme Therapeutics Ltd, Granta Park, Great Abingon, Cambridge CB1 6GS, UK

Background and aims: Plant lectins interact with cell membrane glycoproteins and influence the proliferation and differentiation of intestinal epithelial cells. Using a rat model, we have investigated the effects of a lectin (ATL-101), isolated from the bark of Robinia pseudoacacia, to attenuate the toxic effects of 5-fluorouracil (5-FU) against the intestinal mucosa.

Methods: Male Wistar rats, fed a semi-synthetic diet, received gavages of ATL-101 or saline control on days 0, 1 and 2 of the experiment. Animals (5 lectin; 5 control) were killed 1, 2, 3, 4, 5 and 7 days after the first gavage. The small intestines were removed and weighed, and samples of proximal jejunum taken to determine crypt length, mitosis and apoptosis in whole crypt mounts. Mucosal alkaline phosphatase and diacylglycerol (DAG) levels were also determined. In a second experiment, rats were gavaged with lectin or saline for 3 consecutive days prior to injection with 5-FU or saline (i.p.) on the 4th day. Three days after animals were killed, and crypt cytogenetics were assessed as described above.

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Conclusions: Treatment with the lectin normalises crypt cytogenetics following 5-FU administration, by provoking a trophic response in the tissue, possibly mediated by a DAG-related pathway. This effect may be of benefit in the management of gastrointestinal mucositis.

AN AUDIT OF THE INVESTIGATION OF IN-PATIENT DiARRHOEA IN A TEACHING HOSPITAL—TOO DIFFICULT?

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Introduction: Diarrhoea in hospital in in-patients is common with significant morbidity, mortality and cost implications. Often the cause is not due to infection but the investigation of such patients is inconsistent and may not focus on the most likely pathogens.

Methods: A prospective audit of 250 consecutive stool samples sent for microbiological investigation was carried out. Demographic data on all the patients concerned was collected. Case notes, therapy charts and patients were reviewed.

Results: 250 samples were analysed (117 m, 137 f). Mean age of the patients was 65.3 years (range 14 - 94). All 250 samples were tested for salmonella, shigella and campylobacter. 190 were tested for Clostridium difficile (only if requested or patient stated to be on antibiotics). Positive microbiological results were obtained in 42 samples as detailed below:

Abstract 306, Table I

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of samples</th>
<th>% of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>6</td>
<td>2.4</td>
</tr>
<tr>
<td>Salmonella</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>Giardia</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>Viral (SRV, SRSV)</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>29 (+2)*</td>
<td>11.6 (12.4)*</td>
</tr>
</tbody>
</table>

*29 patients were positive for C. difficile toxin. In addition, 1 patient had the diagnosis made at sigmoidoscopy and 1 at post-mortem. 186 patients with a negative stool culture, had a non-infectious cause for their diarrhoea identified as detailed below:

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*29 patients were positive for C. difficile toxin. In addition, 1 patient had the diagnosis made at sigmoidoscopy and 1 at post-mortem. 186 patients with a negative stool culture, had a non-infectious cause for their diarrhoea identified as detailed below:
Conclusions: In-patients with diarrhea usually have a non-infectious cause for their condition. In the most of these, the cause is iatrogenic. When the cause is enteric infection, by far the commonest cause is C. difficile (not routinely tested for), with all other pathogens (routinely tested for) being very uncommon. All in-patients with hospital-acquired diarrhea should be tested for Clostridium difficile infection routinely.

Methods: 56 patients with IBD (29 Crohn’s disease, 27 ulcerative colitis) and 19 healthy controls had venous blood drawn into EDTA and CTAD (citrate, theophylline, dipryidamole and adenosine). Samples were immediately mixed and then analysed by flow cytometry for P-selectin (CD62P—for platelet activation), L-selectin (CD62L—for neutrophil activation) and CD45/CD42a (leucocyte-platelet aggregates). Platelet activation was also assessed by analysis of mean platelet mass, an inverse composite measure of platelet degranulation and volume, using an ADVIA Haematology System (Bayer).

Results: We confirmed that leucocyte-platelet aggregation was increased in IBD (median 4.3 (range 1.2–17.3) compared with controls (3.3 (1.5–7.4), p<0.05). The mean platelet mass was lower in IBD (1.9 (1.6–2.2)) than in controls (2.0 (1.7–2.3), p<0.05), but activation of platelets as measured by CD62P and of leucocytes (CD62L) were similar in the two groups. Platelet (CD62P), but not leucocyte (CD62L), activation correlated positively with leucocyte-platelet aggregates in IBD (R=+0.44, P<0.01).

Conclusions: Leucocyte-platelet aggregation is increased in patients with IBD, and the correlation with platelet activation measured by P-selectin, supports the hypothesis that platelets may contribute to the pathogenesis of the disease by aggregating with circulating neutrophils. The formation of aggregates does not appear to be related to the expression of CD62L on neutrophils.

Background: Reduced sulphur compounds, such as sulphide, have been implicated in ulcerative colitis (UC). Sulphide may be produced either from fermentation of sulphur amino acids or reduction of sulphate by sulphate reducing bacteria (SRB). In faecal slurries ASAs and sulphasalazine (SAS) have been shown to reduce sulphide production from sulphate\(^2\) and from methionine.\(^3\)

Aims: To look at the effects of SAS, ASA and sulphapyridine (SP) in pure cultures on sulphide production from SO\(_4\) by SRB and sulphur amino acids by an amino acid fermenter.

Methods: An amino acid fermenter producing sulphide was isolated from a human faecal sample and provisionally identified as a fusobacterium. Desulphovibrio desulphuricans was the SRB used. The SRB was grown in Postgate C in universals and the fusobacterium was grown in Wilkins Chalgren anaerobe broth with 0.5g/l cysteine and 0.5g/l methionine. Concentrations of SAS, ASA or SP from 0 to 40mM were added to the universals prior to autoclaving. 20mM ASA is considered physiological. After cooling 0.5ml fusobacterium or SRB stock was injected into each universal and the culture was incubated at 37°C for 18hr. 1ml of solution was used for sulphide determination by microdistillation and HPLC.

Results: SAS achieved a 90% inhibition of sulphide production from SRB and fusobacterium at 1mM and 5mM respectively. ASA 90% inhibited SRB at 20mM but only achieved about 50% inhibition from SRB and fusobacterium at 1mM and 5mM respectively. ASA had no significant effect on sulphide production from either bacterium.

Conclusion: In pure bacterial cultures SAS is more effective than ASA in inhibiting sulphide production from SO\(_4\) and sulphur amino acids.


Background: We have recently shown that the formation of leucocyte-platelet aggregates is increased in the peripheral blood of patients with IBD (Irving, UEGW 2000). Platelets are known to have proinflammatory as well as thrombotic effects and their activation is increased in IBD (Collins, Gastroenterology 1994;106:840–5).

Aims: To assess whether platelet and/or leucocyte activation are correlated with, and might therefore induce formation of leucocyte-platelet aggregates in IBD.

Methods: 5 patients with IBD (29 Crohn’s disease, 27 ulcerative colitis) and 19 healthy controls had venous blood drawn into EDTA and CTAD (citrate, theophylline, dipryidamole and adenosine). Samples were immediately mixed and then analysed by flow cytometry for P-selectin (CD62P—for platelet activation), L-selectin (CD62L—for neutrophil activation) and CD45/CD42a (leucocyte-platelet aggregates). Platelet activation was also assessed by analysis of mean platelet mass, an inverse composite measure of platelet degranulation and volume, using an ADVIA Haematology System (Bayer).

Results: We confirmed that leucocyte-platelet aggregation was increased in IBD (median 4.3 (range 1.2–17.3) compared with controls (3.3 (1.5–7.4), p<0.05). The mean platelet mass was lower in IBD (1.9 (1.6–2.2)) than in controls (2.0 (1.7–2.3), p<0.05), but activation of platelets as measured by CD62P and of leucocytes (CD62L) were similar in the two groups. Platelet (CD62P), but not leucocyte (CD62L), activation correlated positively with leucocyte-platelet aggregates in IBD (R=+0.44, P<0.01).

Conclusions: Leucocyte-platelet aggregation is increased in patients with IBD, and the correlation with platelet activation measured by P-selectin, supports the hypothesis that platelets may contribute to the pathogenesis of the disease by aggregating with circulating neutrophils. The formation of aggregates does not appear to be related to the expression of CD62L on neutrophils.
Aims: To determine the levels of soluble (s) selectin (sE, sP, sL) in the serum of patients during active and inactive phases of IBD and examine their correlation with disease activity and laboratory markers (ESR, CRP, platelet count).

Methods: The levels of selectin in the serum of 14 patients with active Crohn’s disease (CD), 30 with active ulcerative colitis (UC) and 22 healthy controls were studied. A second blood sample was taken from IBD patients one month after remission was achieved. Disease activity in CD was evaluated by the CDAI score and in UC by the activity index as described by Walmsley et al. Selectin levels were expressed as mean±SD ng/ml.

Results: Both sE-selectin and sP-selectin levels were significantly higher (p<0.001) during the active phase of CD ([65±19.9] and [227±78.1], respectively) and active phase of UC ([57±23.5] and [227±173.5]) compared to those of inactive phase of CD ([40±12] and [154±196.9], respectively) or healthy controls ([38±21.5] and [156±865], respectively). sL-selectin levels were significantly higher (p<0.01) during active phase of UC (1241.3±240.6) compared to inactive phase (1021.6±245.6) or controls (915.5±195.8). No significant differences were found for sL-selectin levels between active and inactive phases of CD and the controls. No significant correlation between selectin levels and disease activity or laboratory markers was found.

Conclusions: Our data show that serum levels of sP and sE selectin are significantly different between active and inactive phases of IBD in the same patients but they do not correlate with disease activity. This is also true for sL-selectin levels, but only for UC patients.

312 THICKNESS AND CONTINUITY OF THE HUMAN COLONIC MUCUS LAYER IS DECREASED IN ACTIVE UC BUT REMAINS NORMAL IN QUIESCENT UC

V. Struglia, P.J. Hamsworth1, M.K. Bennett1, M. Hudson1, P.W. Dettman1, A. Conti3, J.P. Clarkson1, 2. 1Dept of Physiological Sciences, University of Newcastle upon Tyne, UK; 2Fremen Hospital, Newcastle upon Tyne, UK; 3Rechts & Colman Healthcare (UK) Ltd, Hull, UK

Introduction: The colonic epithelium is protected from luminal aggressors such as bacterial enzymes, toxins and shear stress by the adherent mucus layer. It has previously been shown that the colonic mucus layer is reduced in thickness in ulcerative colitis (UC). Here we present a blinded investigation into the effect of UC, active and quiescent, on the thickness and continuity of the rectal mucus layer using an improved method of visualising the mucus gel.

Methods: Rectal biopsies were taken from patients with either histologically normal bowel or with UC. Patients gave written informed consent. Biopsies were immediately snap frozen and cryostat sections were stained with periodic acid-Schiff/Alcin Blue under conditions which preserve the mucus layer. Mucus thickness and continuity were measured by light microscopy by an observer blinded to patient diagnosis.

Results: There was no difference in the thickness of the rectal mucus layer in normals (n=11) and patients with quiescent UC (n=21) [median (IQR) thickness of 25 (10–50) µm, which was fully continuous. Median (IQR) mucus thickness in active UC (n=19) was 10 (5–35) µm, significantly thinner than the mucus layer in both the normal and quiescent UC groups (p<0.0001). The mucus layer became discontinuous in active UC with a median percentage discontinuity of 19%, 8% and 4% in mild, moderate and severe UC respectively. As disease severity increased (Powell-Tuck symptom score) there was a significant correlation (p=0.003) with decreased continuity of the mucus layer.

Conclusions: The colonic mucus layer is compromised, in terms of both thickness and continuity, in active UC. This will allow luminal aggressors to gain access to and damage the underlying epithelium and exacerbate the disease. The mucus layer appears to be restored to normal thickness and continuity when UC enters remission.

313 ALTERED EXPRESSION OF FUCOSYL-TRANSFERASES IN INFLAMMATORY BOWEL DISEASE

K. Leiper, S. Javed, Y. Krishna, J.M. Rhodes, B.J. Campbell. Gastroenterology Research Group, Dept of Medicine, University of Liverpool L69 3GA, UK

Background: We have previously hypothesised that alterations in glycosyltransferases may be a key event in the pathogenesis of IBD. As support for this concept, mice transfected with human H fucosyltransferase spontaneously develop colitis (Gastroenterology 2000;118:A3769). Fucosyltransferases attach fucose to oligosaccharides forming structures such as Lewis and H blood groups. We have examined the expression of four fucosyltransferase genes (FUTs) in IBD epithelium.

Methods: With informed consent colonoscopic biopsies were taken from patients with normal colon (NC) (n=9), ulcerative colitis (UC) (n=8) and Crohn’s disease (CD) (n=5) and epithelial cells isolated, to exclude contamination by fucosyltransferases from other cell populations. Semiquantitative RT PCR was then carried out for FUT 1, 2, 5 and 6. Products were electrophoresed and band intensity measured. The results were calculated as the ratio of each FUT to cytokeratin 20 (an epithelial cell marker gene) and expressed as a percentage of normal colon expression. Statistical analysis was by ANOVA.

Results: Mean (SEM) abundance of FUT 1, 2, 5 and 6 expressed as a percentage of normal colon expression. *p<0.05, **p<0.001. Sia/Lewis’ (SLe).

Abstract 313, Table 1

<table>
<thead>
<tr>
<th>Epipto formed</th>
<th>NC (n=9)</th>
<th>UC (n=8)</th>
<th>CD (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FUT 1</td>
<td>H antigen</td>
<td>100 (8.9)</td>
<td>77 (5.0)</td>
</tr>
<tr>
<td>FUT 2</td>
<td>Secretor (Se)</td>
<td>100 (14.8)</td>
<td>47 (1.4)**</td>
</tr>
<tr>
<td>FUT 3</td>
<td>Lewis, SLe</td>
<td>100 (16.4)</td>
<td>168 (10.8)**</td>
</tr>
<tr>
<td>FUT 6</td>
<td>Lewis, SLe</td>
<td>100 (18.9)</td>
<td>108 (6.7)</td>
</tr>
</tbody>
</table>

Discussion: There was a significant decrease in FUT 2 and significant increase in FUT 5 expression in both UC and CD. These enzymes are involved in the production of the secretor and Lewis antigens respectively. This data suggest that changes in the abundance of fucosyltransferases may be important in the alteration in glycosylation seen in inflammatory bowel disease.

314 TNFα GENE POLYMORPHISMS AND EXTRATESTINAL MANIFESTATIONS OF IBD: FURTHER EVIDENCE FOR PHENOTYPE DETERMINING GENES IN THE MHC REGION

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Background: Type 1 and 2 peripheral arthritis (PeA), erythema nodosum (EN) and uveitis are distinct, but overlapping extraintestinal manifestations (EIMs) of inflammatory bowel disease. We have previously described the clinical association of Type 1 PeA with both EN and uveitis, and Type 2 PeA with uveitis only. In addition we have described associations with distinct HLA-B and HLA-DR alleles, which suggest that EIMs may be determined by genes in this region, in linkage disequilibrium with each other. To investigate this study was undertaken to examine polymorphisms of the TNFα gene in these EIMs. TNFα is an important cytokine in mediating inflammation, and the gene lies on chromosome 6 between HLA-B and HLA-DR.

Methods: EDTA blood was collected from 28 patients with Type 1 PeA, 24 patients with Type 2 PeA, 29 patients with EN and 29 patients with uveitis. DNA was extracted and the presence of four polymorphisms in the TNFα gene, at positions -1031, -380, -308 and -238 was assessed by a PCR based technique using sequence specific primers. The results of the different groups were compared with each other and with 261 healthy controls, using 2x2 contingency tables and Fisher’s exact test.

Results: There was a significant association between EN and possession of the -1031C polymorphism - 20/29 (69%) patients vs 96/261 (37%) of controls (p=0.001, pc=0.016). There was no significant difference in the prevalence of this polymorphism between EN and Type 1 PeA patients (69% vs 46%), but there was a significant difference between EN and Type 2 PeA (69% vs 25% respectively, pc=0.024), and between EN and uveitis (69% vs 34% p=0.006), although the latter did not withstand correction for multiple comparisons (p=0.07). No associations were seen at positions, -380, -308 or -238 with any EIMs.

Conclusions: These data demonstrate a strong association between EN and polymorphism -1031C of the TNFα gene. In addition they support the hypothesis that the clinical phenotype of extraintestinal manifestations may be determined by genes in linkage disequilibrium within the MHC region. This may determine the distinct yet overlapping clinical syndromes of arthritis, EN and uveitis.

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Background: The non-classical MHC class I like genes MICA and MICB are located within IBD3, a replicated area of linkage on chromosome 6. These genes encode stress inducible membrane-anchored glycoproteins, expressed by epithelial cells of the gastrointestinal tract that interact with NK and γδ T-cells through the receptor NKKG2D. Exons 2–4 encode the extracellular domain and are highly polymorphic. A previous study examining a limited number of alleles of MICA only found an association with patients of ulcerative colitis (UC) found an association with MICA*007. This study examined all known MICA/B alleles in a larger cohort of UC patients to determine whether disease susceptibility and phenotype may be determined by MICA/B alleles.

Methods: A PCR-SSP system was developed to identify the 45 known MICA and 9 MICB alleles. This typing technique was applied to 287 UC patients divided into 3 phenotypic subgroups (116 total colitis + no surgery; 68 total colitis + proctocolectomy / ileo-anal pouch formation; 103 proctitis + no surgery) and 296 healthy Oxfordshire controls recruited from General practice health screening clinics.

Results: Of the 45 previously reported MICA alleles 19 and 18 were identified in the UC and control populations respectively. 5 of the previously reported MICB alleles were identified in both the control and UC groups. 10 new alleles (frequency less than 1%) were identified (4 controls, 6 UC). No significant difference was found in allele frequencies between controls and UC patients when analysed by phenotypic subgroup or as a combined group.

Conclusion: Polymorphisms in exons 2–4 of the MICA/B genes appear not determine susceptibility or phenotype in patients with UC. Further work is now being carried out to evaluate the role of polymorphisms in exon 5 that encodes the transmembrane portion of the MIC molecule.

**References**

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3. A. Moody, S. Fisher, M. Mirza, J. Hampe, S. Bridge, A. Macpherson, S. Schreiber, A. Forbes, A. Cuthbert, C. Mathew. "Division of Medical and Molecular Genetics, QUT School of Medicine, Grey’s Hospital, London, UK; First Dept Medicine, Christian-Albrechts-Universitat, Kiel, Germany; Dept of Medicine, King’s College Hospital, London, UK; St Mark’s Hospital, Northwick Park, Watford Road, Harrow, UK"

4. A. Moody, S. Fisher, M. Mirza, J. Hampe, S. Bridge, A. Macpherson, S. Schreiber, A. Forbes, A. Cuthbert, C. Mathew. "Division of Medical and Molecular Genetics, QUT School of Medicine, Grey’s Hospital, London, UK; First Dept Medicine, Christian-Albrechts-Universitat, Kiel, Germany; Dept of Medicine, King’s College Hospital, London, UK; St Mark’s Hospital, Northwick Park, Watford Road, Harrow, UK"

5. M.J. Carter, F. di Giovinne, A. Cox, J. Sorrell, G.W. Duff, A.J. Lobo. "The Gastroenterology and Liver Unit and Division of Molecular and Genetic Medicine, University of Sheffield; Royal Hallamshire Hospital, Sheffield, UK"

6. T. Ahmad, M. Bunce, J. Crawshaw, K. Mulcahy-Hawes, O. Large, M. Barnardo, J. Cook, T. Orchard, K. Welsh, D.P. Jewell. "Deps of Gastroenterology and Transplantation Immunology, University of Oxford, Oxford; Dept of Immunology, St Mary’s Hospital, London, UK"


8. A. Moody, S. Fisher, M. Mirza, J. Hampe, S. Bridge, A. Macpherson, S. Schreiber, A. Forbes, A. Cuthbert, C. Mathew. "Division of Medical and Molecular Genetics, QUT School of Medicine, Grey’s Hospital, London, UK; First Dept Medicine, Christian-Albrechts-Universitat, Kiel, Germany; Dept of Medicine, King’s College Hospital, London, UK; St Mark’s Hospital, Northwick Park, Watford Road, Harrow, UK"

9. M.J. Carter, F. di Giovinne, A. Cox, J. Sorrell, G.W. Duff, A.J. Lobo. "The Gastroenterology and Liver Unit and Division of Molecular and Genetic Medicine, University of Sheffield; Royal Hallamshire Hospital, Sheffield, UK"
Transmission Disequilibrium Testing Confirms the Association of the TNF-α –1031C Allele With Crohn’s Disease

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Introduction: Increased tumour necrosis factor (TNF) expression in the TNF-α mouse model results in a Crohn’s disease (CD) like phenotype, and anti-TNF therapy is effective in treating CD. Linkage studies from five groups worldwide have confirmed an inflammatory bowel disease (IBD) susceptibility locus on chromosome 6p. We have previously reported a significant association with the TNF-α promoter –1031 C/T polymorphism in an independent family based population. In order to overcome potential false positive results from a case control study, IBD families were genotyped and the transmission disequilibrium test (TDT) was used to assess association.

Aims: To confirm the association seen in the case-control studies in an independent family based population.

Methods: We obtained complete genotypes for the TNF-α –1031 C/T polymorphism using PCR-SSP in 515 parent-child trios from the chromosome 7q22 which has been identified as a candidate IBD susceptibility locus on chromosome 6p. We have previously reported a significant association with the TNF-α promoter –1031 C/T polymorphism (rs1800624) in 515 parent-child trios from 343 European Caucasian nuclear families (349 simplex, 85 multiply affected). A permutation based probability test was used to calculate association independent of linkage (Apex).

Results: We observed significantly increased transmission of the TNF-α –1031 C allele for the CD but not IBD or UC phenotypes.

<table>
<thead>
<tr>
<th>n genotyped trios</th>
<th>C allele transmission</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD 515</td>
<td>TR 197 : NT 179</td>
<td>n.s.</td>
</tr>
<tr>
<td>CD 273</td>
<td>TR 118 : NT 81</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>UC 233</td>
<td>TR 77 : NT 96</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Under a multiplicative model the genotype relative risk of the C allele is 1.5, and the population attributable risk approximately 20%.

Conclusion: We have confirmed the association of the tnf -1031 polymorphism with Crohn’s disease by the TDT. This common allele (22% frequency), or one in linkage disequilibrium with it, influences nearly a fifth of the cases of Crohn’s disease in a Caucasian population.

Two Novel Mucin Core Genes MUC 11 and MUC 12 are Normally Expressed in Ulcerative Colitis

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Background: Two novel mucin core genes have recently been described, MUC 11 and MUC 12, both of which are downregulated in colon cancer (Cancer Research 1999;59:4083). Both are located on chromosome 7q22 which has been identified as a candidate IBD locus. Mucins are abnormal in ulcerative colitis (UC) where the mucin layer is thinner, less glycosylated and less sulphated. MUC 11 or MUC 12 may therefore represent potential candidate genes for UC. The aim of this study was to assess mRNA abundance of MUC 11 and MUC 12 in UC using Northern analysis and semi-quantitative RT-PCR.

Methods: With informed consent, colonic biopsies were taken from patients with ulcerative colitis and patients with normal colon. Twenty micrograms of total RNA was electrophoresed and transferred onto nylon membranes. Membranes were then sequentially hybridised with 32P labelled PCR generated cDNA probes for MUC 11, MUC 12 and 28S ribosomal RNA. mRNA abundance of MUC 11 and MUC 12 was expressed as a ratio of 28S RNA expression by phosphorimage analysis. For semi-quantitative RT-PCR 5ug of total RNA was subjected to first strand cDNA synthesis and then PCR was performed using specific oligonucleotide primers for MUC 11, MUC 12 and cytokeratin 20 (a marker of epithelial abundance). PCR band intensity was quantified and expressed as a ratio of cytokeratin 20 abundance. All results were expressed as a percentage of control normal colon (100%).

Results: Northern analysis for MUC 11 and MUC 12 revealed a polydisperse signal typical of mucins. A wide variation in expression of both mucins was seen with no significant difference between groups: MUC 11 (mean(SE) normals (n=10) 100±33%, UC (n=18) 144±30, MUC 12 normals 100±20, UC 120±17. Semiquantitative PCR likewise showed no significant differences between groups: MUC 11 normals (n=6) 100±18%, UC (n=6) 90±38% and MUC 12 normals (n=6) 100±54%, UC (n=6) 76±23.

Discussion: MUC 11 and MUC 12 are normally expressed in ulcerative colitis. It is unlikely that these are the candidate genes for IBD on the chromosome 7 locus.

Genetic Association Studies in IBD: Negative Results from Three Candidate Genes


Introduction: Candidate genes for susceptibility to inflammatory bowel disease include the chemokine receptor 5 (CCR5) gene, the vitamin D receptor (VDR) gene. All three represent positional candidate genes. Our results make it unlikely that these candidate genes for IBD are the chemokine receptor 5 (CCR5) gene, the vitamin D receptor (VDR) gene.

Aim: To determine whether previously positive results with CCR5 and VDR gene can be reproduced, and whether initial novel positive results with TNFSF6 gene represents a genuine association.

Methods: A total of 351 IBD patients comprising 251 UC and 100 CD were genotyped for the 32bp deletion (CCR5), and the vitamin D receptor (VDR) gene. All three represent positional candidate genes. The TNFSF6 gene represents a genuine association.

Results: There were no significant differences for both genotype or gene frequency between patients with UC or CD, when compared with controls. Gene frequencies were:

<table>
<thead>
<tr>
<th>Populations (n = 351)</th>
<th>CCR5 (Dexa 32)</th>
<th>TNFSF6 (Mva1)</th>
<th>VDR (Tagd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC1 (n=107)</td>
<td>11%</td>
<td>64%</td>
<td>39%</td>
</tr>
<tr>
<td>UC2 (n=144)</td>
<td>11%</td>
<td>50%</td>
<td>N/A</td>
</tr>
<tr>
<td>CD (n=100)</td>
<td>10%</td>
<td>54%</td>
<td>40%</td>
</tr>
<tr>
<td>Controls (n=107)</td>
<td>11%</td>
<td>50%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Conclusion: These three candidate gene association studies are negative. These results are important because previous positive associations have been reported. Our results make it unlikely that these polymorphisms have any influence on IBD susceptibility.

Coeliac Serology in Patients with Inflammatory Bowel Disease (IBD)

C.L. Ch‘ng, S. Lewis, J.G.C. Kingham. Swansea NHS Trust, SA2 8QA, UK

Introduction: There is an association between IBD and coeliac disease (CD), though its frequency is not known. Endomysial (EmA) and antigliadin (AGA) antibodies are useful serological markers of CD.

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Is passive smoking in childhood associated with inflammatory bowel disease?

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Background: Cigarette smoking is recognised as a risk factor for Crohn's disease (CD) and appears protective against ulcerative colitis (UC). The relationship between passive exposure to smoke in childhood and inflammatory bowel disease (IBD) is controversial.

Aims: To investigate the association between passive smoking by age 16 years and IBD.

Methods: Subjects were from the 1970 British Cohort Study (BCS70), a national prospective birth cohort study. Prospectively collected data on smoking and potential confounding factors were collected at parental interviews at birth, 5, 10 and 16 years. Diagnostic criteria of IBD by age 26yrs was confirmed by physicians. Cross-tabulation, chi-squared test and logistic regression analysis were used.

Results: 9577 subjects responded at age 26yrs. Of these, 30 had CD (23 with smoking data), 22 had UC (15 with smoking data). 6869 of 9577 responding subjects had complete data available for all variables. 71% subjects with CD and 92% subjects with UC were exposed to smoking in the family home by age 16yrs, compared with 91% of the remaining cohort. (Unadjusted OR 0.23, 95% CI 0.08 to 0.65 p=0.01, and OR 1.20 95% CI 0.15 to 8.88, p=0.89 respectively). Adjusting for sex, father's social class at birth, household crowding, ethnic origin and child's smoking habit did not affect these findings.

Conclusion: The incidence of juvenile-onset IBD in Scottish children is not related to economic deprivation.

Is the increasing incidence of juvenile-onset IBD in Scotland related to socio-economic deprivation?

M.C. Aldhous, H.E. Drummond, E. Armitage, S. Ghosh. GI Laboratory, Western General Hospital, Edinburgh, Scotland, UK

Introduction: We have recently shown that the incidence of inflammatory bowel disease (IBD) in Scottish children of under 16 years of age, is increasing. Environmental factors, such as childhood hygiene and infections have been implicated in the aetopathogenesis. Therefore, using data already collected, we investigated whether economic deprivation was important in juvenile-onset IBD.

Methods: Scottish children, of under 16 years old, with onset of IBD between 1981 and 1995 were identified. The methodology has been previously reported and the data included postcodes of addresses at onset of symptoms. 383 children had Crohn's disease (CD), 197 had ulcerative colitis (UC). The Carstairs Deprivation Score is a classification which takes into account levels of unemployment, car ownership and socio-economic status in each postcode sector. From this, a calculation can be made which gives a measure of deprivation (1 being most affluent, 7 being most deprived). The postcodes of addresses at onset of symptoms were classed for deprivation. The patient data were plotted according to their deprivation score and adjusted for the population aged under 16yrs in each area (1991 Census).

Results: The frequency of new cases of CD and UC appeared to be normally distributed in children from all backgrounds, 1 - 7. However, the age (<16yrs)- adjusted population incidence indicated that children with either CD or UC tended to live in the more affluent, as opposed to the more deprived, areas.

Conclusion: The incidence of juvenile-onset IBD in Scottish children is associated with economic deprivation.

A case-control study of childhood environmental risk: factors for the development of inflammatory bowel disease

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Background: There is increasing suspicion that environmental factors encountered in childhood may have an important influence on the risk of IBD in later life.

Aim: To clarify the relationship between childhood environment and the risk of developing Crohn's disease (CD) or ulcerative colitis (UC).

Subjects: The study groups comprised patients with CD (n=139) and UC (n=137) aged between 16 and 45, each matched for gender and age with an outpatient control.

Method: A case-control study, assessing the risk of developing IBD in relation to a series of historical and serological markers of childhood circumstance, analysed using the maximum likelihood form of conditional logistic regression.

Results: Helicobacter seroprevalence was substantially reduced in CD compared to UC (OR 0.18 (0.06 to 0.53)) but not in UC (OR 0.84 (0.35 to 2.01)). In UC, a strong negative association with childhood appendectomy was confirmed (OR 0.06; 0.01 to 0.55). CD was associated with childhood eczema (OR 2.80; 1.23 to 6.40) and the frequent use of a public swimming pool (OR 2.82; 1.17 to 6.80). There was no significant association between hepatitis A seroprevalence and either disease.
**Conclusion:** The links identified for CD are consistent with the hypothesis that improved childhood living conditions are associated with increased risk of disease, and this may account for the markedly increased incidence of CD over the last century. The study confirms that the previously described negative association between appendectomy and UC relates primarily to events in childhood. Overall, the findings provide strong support for the assertion that childhood environmental factors are important determinants of the risk of IBD in later life.

**329 GENERAL PRACTITIONER (GP) EVALUATION OF NURSE LED PHONE CLINIC (NLPC) FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)**

L. Miller, D. Lynch. Dept of Gastroenterology, Blackburn Royal Infirmary, Bolton Road, Blackburn BB2 3LR, UK

A 12-month pilot study of an NLPC identified 99% patient satisfaction with the service and enabled those in relapse to be seen urgently in clinic.

**Aims:** To determine GP perceptions of an NLPC.

**Method:** Postal questionnaire distributed to all GPs whose patients had received a phone consultation.

**Results:** 72 questionnaires distributed. 37 (48%) returned. 97% expressed NLPC was an acceptable method of providing clinical supervision for patients with IBD in remission. Approximately one third (30%) very satisfied, over half (56%) satisfied, one tenth (13%) neither satisfied nor dissatisfied. 70% would not consider patient co-op card useful. GPs’ views sought as to where long-term care for patients with various disease extents should receive follow-up.

**Abstract 329, Table 1**

<table>
<thead>
<tr>
<th>CD Area</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal UC</td>
<td>7%</td>
<td>7%</td>
<td>38%</td>
<td>24%</td>
<td>24%</td>
</tr>
<tr>
<td>Extensive UC</td>
<td>41%</td>
<td>38%</td>
<td>7%</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>Large bowel CD</td>
<td>14%</td>
<td>51%</td>
<td>14%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>CD other areas</td>
<td>3%</td>
<td>38%</td>
<td>31%</td>
<td>7%</td>
<td>21%</td>
</tr>
</tbody>
</table>

1) GP, 2) Outpatient clinic, 3) Phone clinic, 4) Shared care, 5) Combination UC, CD, Crohn's disease.

Some comments made by GPs on the service: “Good idea, enables problems to be picked up and an appointment arranged urgently when needed”;

“All GPs know how many patients are followed up in the outpatient department too frequently”; “One of the ways forward”; “Shared care all very well, if it means dumping your workload on primary care ... NO!!”

**Conclusion:** Although the response rate was low, the GPs who completed the questionnaire felt that phone clinics are an acceptable way to provide follow-up for patients with IBD in remission, and suggested that this method would be suitable for other gastrointestinal conditions, namely, coeliac disease, irritable bowel syndrome and peptic ulcer disease.

**330 AUDIT OF THE MANAGEMENT OF SEVERE DISTAL ULCERATIVE COLITIS IN A DGH**

J.M.C. Stenner, P. White, S.R. Gould, A.G. Lim. Epsom General Hospital, Epsom and St Helier’s NHS Trust, Surrey, UK

The outcome of severe ulcerative colitis (UC) has been reported to have improved since the advent of corticosteroids and guidelines for the timing of colectomy. The outcome of patients with severe UC had not been previously audited in our hospital. Our aim was to assess the investigation, treatment and outcome of these patients.

All patients coded as having UC been Jan 1994-Jan 2000 were identified, the notes were reviewed and data collected on a proforma. Patients were considered to have severe UC as defined by Truelove and Witt’s criteria. 92% (107/117) of the identified notes were identified, the notes were reviewed and data collected on a proforma. Patients were considered to have severe UC as defined by Truelove and Witt’s criteria. 92% (107/117) of the identified notes were reviewed. There were 32 episodes of severe colitis in 25 patients (median 36 years, range 17–81). In these patient episodes, 75% had a history of the disease, and an abdominal x-ray on admission. All patients not previously known to have colitis were started on antibiotics. All patients received iv steroids within 72 hours, no patient received cyclosporin. 50% were put on s/c heparin.

At day 10 there were 10 complete responses, 12 partial responses and 10 treatment failures. At final outcome, 17 patients left hospital without surgery, 9 patients had colectomies and there were a total of 6 deaths. Of the deaths, 3 died post operatively, 1 due to coexisting advanced PSC and 2 had post operative leaks. Of the others, 1 had a toxic reaction to azathioprine and 2 were considered not medical suitable for surgery.
Results: 14 (45%) of the 31 patients had an identifiable coagulation defect predisposing to thrombosis. This comprised raised factor VIII levels (n=4), Factor V Leiden (n=2), Protein C deficiency (n=2), lupus anticoagulant (n=3), anti-thrombin III deficiency (n=2), and prothrombin gene mutation (n=1). One patient had multiple coagulation defects.

Conclusions: A significant proportion of patients with IBD and venous thrombosis have abnormal procoagulant profiles. A full thrombophilia screen should be measured in all patients with IBD complicated by venous thrombosis.

333 PREVALENCE OF USAGE AND TOLERANCE OF ORAL IRON THERAPY IN INFLAMMATORY BOWEL DISEASE: ARE WE USING IT APPROPRIATELY AND COULD WE DO BETTER?

A. de Silva, M. Mlyonakis, D. Rampton. Dept of Adults and Paediatric Gastroenterology, St Bartholomew’s and the Royal London School of Medicine and Dentistry, London, UK

Background: Anecdotal evidence suggests that oral iron preparations are poorly tolerated and may even increase disease activity in patients with IBD, but there appears to be no formal support for this in the literature. However other evidence suggests that untreated anaemia may affect the quality of IBD patients’ lives.

Aim: To assess the prevalence, indications, tolerance and outcome of oral iron therapy in IBD.

Methods: The case records of 156 consecutive patients with Crohn’s disease, ulcerative colitis and indeterminate colitis attending this hospital were reviewed retrospectively using a standard proforma. Those attending the clinic for the whole period 1996–1999 and found to have been treated with oral iron therapy during that time were identified.

Results: During the 4-year period reviewed, 29/156 (19%) patients were treated with an oral iron preparation (ferrous sulphate 72%, ferrous fumarate 7%, sodium iron edetate 7%, unspecified 14%). Iron deficiency had been formally established (ferritin <20) in 11/29 (38%) of treated patients. 9/29 (31%) discontinued therapy due to intolerance (nausea, dyspepsia, abdominal pain, diarrhoea and/or constipation), and in 2/29 (7%) disease activity was shown to be increased (as shown by measurements in ESR, CRP, albumin and platelet count) during treatment. In only 10/29 (34%) of patients treated was repletion of iron stores checked by laboratory testing within 6 months, and of these only 5 had an adequate response to therapy during this period.

Conclusions: Even in a specialist IBD clinic, oral iron therapy is often inappropriately prescribed and monitored, and is commonly ineffective. It is poorly tolerated in nearly 1/3 of IBD patients; in a minority of these, iron therapy is associated with an increase in disease activity. Prospective studies are needed to investigate further the mechanisms involved in iron intolerance, and the value of alternative preparations for the treatment of iron deficiency in IBD.

334 DO WHITE CELL COUNT (WCC) AND NEUTROPHIL COUNT AT 4 MONTHS PREDICT FUTURE COUNTS DURING AZATHIOPRINE THERAPY?

S. Campbell, S. Ghosh. GI Unit, Western General Hospital, Edinburgh, UK

Background: Severe neutropenia is potentially one of the most serious side effects of azathioprine. It is common practice to regularly monitor blood counts in patients taking azathioprine even when apparently stable. Time of maximal azathioprine effect is approximately 3 months, during which time the most frequent monitoring occurs. It is not known whether WCC and neutrophil counts after this period vary significantly from that at the initial treatment period.

Aim: To examine the nadir of WCC and neutrophil counts and correlate this with the respective WCC and neutrophil counts at 4 months into azathioprine therapy.

Methods: We constructed a database of IBD patients taking azathioprine for a minimum of 6 months and who had been brought into remission. Data that was included were the nadir WCC, nadir neutrophil count, azathioprine dose (mg/kg), WCC and neutrophil counts at 4 months into therapy. There were a total of 173 patients (95CD: 78UC) taking azathioprine for a median period of 3.9 years, range 0.7–21 years. Mean azathioprine dose was 1.8mg/kg (SD=0.45) and median duration of azathioprine therapy was 3.9 years, (range 0.7–21 years). A steady azathioprine dose had been reached by 4 months in all patients.
Results: In IBD patients, the nadir of WCC and neutrophil count correlated well with the respective blood count parameter at 4 months (r = 0.7, p < 0.0005). This was true for UC and CD groups when analysed separately (UC: r = 0.8, p < 0.0005; CD: r = 0.6, p < 0.0005). Neutrophil counts changed little after 4 months of azathioprine therapy.

Conclusion: These results suggest that WCC and neutrophil counts at 4 months may be a good predictor of the lowest WCC and neutrophil count that may occur during azathioprine therapy over a relatively long follow up period. Patients with normal neutrophil count at 4 months after initiation of azathioprine therapy are very unlikely to develop significant neutropenia at a later stage. Full blood count monitoring is essential during azathioprine therapy, as dangerous neutropenia may occur unexpectedly, but patients with normal neutrophil count 4 months into azathioprine therapy may be monitored less intensively, unless neutropenic symptoms occur.

335 RESPONSES TO LOW DOSE AZATHIOPRINE IN PATIENTS WITH HETEROZYGOUS THIOPURINE METHYL TRANSFERASE DEFICIENCY


Introduction: Approximately one in ten Caucasians have heterozygous thiopurine methyl transferase (TPMT) enzyme deficiency. These individuals are at high risk of side effects on treatment with azathioprine but should, in theory, tolerate a lower dose of azathioprine.

Aim: To examine the outcome of low-dose azathioprine treatment in a group of patients with heterozygous TPMT deficiency.

Methods: From a database of TPMT-deficient patients, 24 (15 female, median age 37.5 yrs) were identified who had received azathioprine as a steroid-sparing agent at a reduced dose of 1 mg/kg (initially 0.5 mg/kg) according to departmental guidelines. Case records were examined to identify adverse effects and clinical response defined by ability to withdraw steroids (complete, partial (prednisolone dose <5 mg daily) or non-response).

Results: 17 patients were treated for inflammatory bowel disease (12 Crohn’s disease, 5 ulcerative colitis), 2 autoimmune hepatitis and one intestinal vasculitis. 4 received azathioprine for chronic oral disease (2 lichen planus, 1 Behcet’s disease and 1 oral ulceration). 5 of 24 (21%) patients had side effects requiring azathioprine withdrawal (2 pancreatitis, 3 nausea and malaise). 4 additional patients developed side effects which resolved on dose reduction to 0.5 mg/kg. Of the 19 patients who tolerated azathioprine, 17 responded favorably to azathioprine (89%). 15 (79%) withdrew steroids completely. 2 patients had no response.

Conclusion: Measurement of TPMT enzyme activity defines a group of patients with heterozygous TPMT deficiency that can be successfully treated with low-dose azathioprine.

336 ANTIMYCOBACTERIAL TREATMENT FOR CROHN’S DISEASE. DOES IT PREVENT SURGERY AND HOW FAST DOES IT ACT?

A. Douglass, M.G. Bramble, J.G. Silcock, P.A. Cann, South Cleveland Hospital Endoscopy Centre, UK

Introduction: Despite a better understanding of the pathogenesis surrounding the inflammatory process in the Crohn’s Disease, an overall cure remains illusive. Newer immuno-modulatory agents can produce rapid healing, but require continued treatment for long term effectiveness and are not without side effects or considerable costs. Unfortunately, surgery is often still required.

Paratuberculosis (pTB) has been suggested as a potential causative agent and with the improvement tissue sampling techniques, the detection rates have recently increased in CD specimens. Successful eradication therefore may represent a method of achieving a long-term CD cure.

We assessed the impact rifabutin, clofazamine, clarithromycin had upon patient with difficult to manage CD, with particular reference to speed of onset of symptomatic improvement, and ‘surgery sparing effects’.

Results: 3 patients intolerant of treatment and (therefore excluded from analysis) a further 4 developed side effects after 4-6 months and needed their treatment modifying (1) or discontinuing (3). 28 patients entered the study, 12 had previous surgery, 11 were intolerant of Azathioprine, 2 refused steroids and 5 were steroid dependant. 20 Patients showed a good initial improvement with a rapid onset of action (1 week - 5 weeks) but there was subsequent relapsed in 10 patients (7 after the treatment was discontinued), 10 patients have maintained a longer response (mean 12 month follow up since commencing treatment). 5 patients were considered to require imminent surgery prior to therapy (3 extensive large bowel, 1 entero-vesical fistula, 1 small bowel) 2 have subsequently required surgery. This was for inactive disease (fistula patient) and a limited small bowel resection following healing of extensive colonic disease with limited small bowel recurrence. Irrespective of outcome, there is a perception that after Rx patients respond better to conventional treatment (3 patients).

Conclusions: When tolerated, this treatment produced a rapid initial improvement, with 50 % demonstrating longer remission. Surgical candidates responded and colectomy was avoided. Patients that needed resection had more limited and less active disease than at presentation.

337 THE SAFETY OF SULPHASALAZINE AND MESALAZINE REASSESSED ACCORDING TO DISEASE INDICATION AND NUMBER OF PRESCRIPTION ITEMS DISPENSED IN THE COMMUNITY FROM 1991 TO 1998

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Introduction: 5-ASA as mesalazine was developed to reduce adverse effects of sulphasalazine by removing sulphapyridine. The actual adverse effect profile of these medications has not been predictable and can be compared using voluntary reporting to the Committee of Safety of Medicines (CSM) but has not been published.

Aims: To evaluate the adverse effects of sulphasalazine and mesalazine between 1991 and 1998 with respect to number of prescription items dispensed and disease indication.

Methods: Total number and subcategories of adverse reactions reported using ‘the yellow card’ system of the CSM were obtained for 1991–1998. Number of prescriptions dispensed for 1991–1998 were published.

Results: 4,672,000 prescriptions were dispensed for sulphasalazine and 2,798,000 for mesalazine with adverse events per million prescriptions summarised below and subdivided for sulphasalazine by disease indication.

Abstract 337, Table 1

<table>
<thead>
<tr>
<th></th>
<th>Mesalazine</th>
<th>Sulphasalazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>BI D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BI D</td>
<td>17.1</td>
<td>5.4</td>
</tr>
<tr>
<td>RA</td>
<td>17.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Blood dyscrasias</td>
<td>17.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Serious skin reactions</td>
<td>4.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Hepatitis and hepatic failure</td>
<td>2.6</td>
<td>1.9</td>
</tr>
<tr>
<td>Intestinal nephritis</td>
<td>10.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>6.4</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Conclusions: Within the limitations of using spontaneous reporting interstitial nephritis appears particular to mesalazine and blood dyscrasias with sulphasalazine are largely limited to patients with rheumatoid arthritis.

338 AN OPEN TRIAL OF THALIDOMIDE IN REFRACTORY CROHN’S COLITIS

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Background: TNF α is a proinflammatory cytokine associated with the inflammatory response of Crohn’s disease. Treatment with TNFα antibodies is efficacious in active disease. Thalidomide has recognised TNFα inhibitory properties and has demonstrated therapeutic efficacy in treating small bowel and fistulating Crohn’s disease.

Aims: To assess efficacy, tolerability and safety of thalidomide in steroid resistant Crohn’s colitis.

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Methods: 6 patients, 3 female and 3 male, with a history of active Crohn’s colitis (CDAI>150), resistant to corticosteroids, were recruited. After a 4 week observation period, they received 200mg of thalidomide per day for a total of 8 weeks. CDAI, ESR and CRP were measured at 0,4 and 12 weeks. Endoscopic sigmoidoscopic assessment was performed at 4 and 12 weeks.

Results: One patient withdrew after developing a truncal rash, which resolved after discontinuation of treatment. The five remaining patients completed the full 8 week course without any significant side-effects. Median CDAI, CRP and ESR remained unchanged after the 4 week observational period, but demonstrated significant improvements after 8 weeks of treatment, see table 1.

Abstract 338, Table 1

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post 4 weeks observation</th>
<th>Post 8 weeks treatment</th>
<th>P value (baseline v. post treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDAI</td>
<td>175 (153–381)</td>
<td>170 (154–381)</td>
<td>54 (28–152)</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>CRP</td>
<td>33 (9–62)</td>
<td>33 (9–62)</td>
<td>8 (4–18)</td>
<td>(P&lt;0.05)</td>
</tr>
<tr>
<td>ESR</td>
<td>36 (8–46)</td>
<td>24 (10–110)</td>
<td>12 (7–23)</td>
<td>(P&lt;0.05)</td>
</tr>
</tbody>
</table>

Endoscopic appearances improved over the 8 week treatment period with complete healing of ulceration in two patients and improvements in three.

Conclusion: Thalidomide at a dose of 200mg per day may be an effective treatment in steroid resistant Crohn’s colitis, with improvements in symptom score, inflammatory markers and endoscopic appearances. Side-effects are few and transient.

339 IS THE DIAGNOSIS OF LOW-GRADE DYSPLASIA IN ULCERATIVE COLITIS CONSISTENT?

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Colonoscopic surveillance for long standing ulcerative colitis (UC) relies on the histological detection of dysplasia as a precursor lesion to cancer. Many gastroenterology centres would advocate prophylactic colectomy for any grade of dysplasia. AIM: To assess the agreement between 5 UK Gastrointestinal Pathologists on the diagnosis of low-grade dysplasia.

Method: 160 patients with long standing UC were recruited into a colonoscopic surveillance programme between 1978-1990. 40 patients were reported to have low-grade dysplasia (LGD) by both specialist and non-specialist pathologists at least once during this period. All the original histology slides diagnosed as LGD were retrieved. In total 87 LGD, 3 HGD and 50 control (non-dysplastic) slides from other UC patients on surveillance were re-stained (H&E) and randomly numbered. The 5 pathologists assessed the 140 slides independently and allocated them one of 3 categories: negative for dysplasia, LGD or HGD. We used a statistical program to calculate the chance-corrected inter-observer agreement (kappa coefficient). k < 0.5 is considered as poor agreement or reproducibility, k=0.5–0.75 representing moderate to good agreement and > 0.75 as excellent agreement. We also calculated the value between the majority or consensus score and the original diagnosis.

Results: The frequency of each diagnosis ranged from 65.7% to 80% for negative, 16.4% to 32.1% for LGD, and 0.01% to 5% for HGD. The kappa coefficient for overall agreement between 5 Pathologists, κ = 0.30. (95% CI=0.253 - 0.347). Kappa for individual diagnoses: negative; κ = 0.36, LGD; κ = 0.25, HGD; κ = 0.52. Kappa coefficient between the original and consensus diagnosis, κ = 0.23. Only 14 patients out of the original 40 LGD (35%) had a majority diagnosis (at least 3/5 pathologists) of LGD.

Conclusion: The agreement between gastrointestinal pathologists on a diagnosis of LGD is poor. Therefore it is inappropriate to base a recommendation for surgery on a histological diagnosis of LGD in UC.
ACHALASIA IN CHILDREN: AN INCREASING AND MORE SEVERE PROBLEM? A SINGLE CENTRE EXPERIENCE

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Background: Achalasia in children is a rare disorder of oesophageal motility characterised by abnormal relaxation of the Lower Oesophageal Sphincter (LOS) and peristalsis. Among all ages the incidence is estimated to be between 0.03 -1.1 per 100 000 population / year. In this review we report 6 children who presented within a period of 18 months.

Methods: Retrospective case review.

Results: 6 children presented with achalasia over an 18/12 period (5 over 1 year), comprising 3 males and 3 females with ages ranging from 7/12 to 14 years (median 10 years). Prior to diagnosis there was a median 2 month duration of symptoms (range 2—12/12) including dysphagia, vomiting, feeding problems, pain and weight loss. On presentation a diagnosis of achalasia was made on barium swallow, and oesophageal perfusion manometry performed on all cases. Mean LOS pressure ranged from 37.5 — 70 mmHg (mean 50) with typical loss of LOS relaxation and absent peristalsis. Nifedipine was used as the first line agent with symptomatic improvement in 2 of the 6 for 2—4 weeks. Botulinum Toxin (BTX) was used as second line (endoscopic injection into LOS, <2 years—20 units / quadrant, >2 years—40 units / quadrant). All 6 had good clinical response within one week, lasting up to 3 months (median 8 weeks). 4 had repeat BTX injection (2 awaiting) with similar response. Of these 3 had oesophageal manometry showing a mean reduction in LOS pressure of 40mmHg (35—50) from diagnosis but no improvement in peristalsis. One had has surgical treatment and the other the two referred.

Discussion: This yearly incidence of achalasia is considerably higher than the 1 - 2 expected from the centre’s referral population. This may be partly explained by underdiagnosis, and we suggest barium studies as a first line investigation for recurrent or acquired vomiting, dysphagia or feeding difficulties. If available, oesophageal manometry is a valuable tool for diagnosis and monitoring treatment response. Nifedipine has no benefit. To our knowledge this is the first report of the use of Botulinum Toxin in children with achalasia in the UK, and the biggest single centre use. The short lived effects warrant repeat dosage at shorter intervals or combination with other therapy e.g. balloon dilatation. Surgery remains the definitive treatment.

THE MISSING 13C LABEL IN THE MIXED TRIACYLGLYCEROL BREATH TEST IS NOT IN THE STOOL

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Background: The 13Cmixed triacylglycerol (13C-MTG) breath test is a measure of intraluminal fat digestion. In normal digestion 20—40% of the 13C label is recovered in breath. The fate of the remaining 60—80% is unknown. It may be excreted in stool, or remain in slow-turnover carbon pools within the body. In this study, we aimed to identify the proportions of the ingested label that were excreted in stool and breath following ingestion of 13C-MTG by children with cystic fibrosis (CF).

Methods: 8 children with CF and 2 healthy controls ingested 20 mg/kg (CF) or 10 mg/kg (control) 13C-MTG with a standard breakfast, and their normal enzyme replacement therapy. Breath samples were collected at baseline, then half-hourly for 6 hours and hourly for a further 4 hours. All stools were collected from baseline to day 3. 

Conclusion: Opinion was divided as to whether to take endoscopic biopsies or not in a patient on warfarin although evidence shows that the risk of bleeding in warfarinised patients is negligible provided the INR is within the therapeutic range. Likewise there is an equal division of opinion as to whether bioprosthetic valve is a high-risk condition or not. It is noteworthy that a significant proportion of respondents (41%) did not consider atrial fibrillation with underlying heart disease and recurrent thromboembolism as a high-risk condition. This survey further confirms previous evidence that there is a huge variation in practice among endoscopists in the UK. This is not surprising in the absence of a national guideline. Recently the American Society for Gastrointestinal Endoscopy (ASGE) has published guidelines on this subject.

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ENDOSCOPY IN ANTICOAGULATED PATIENTS: A POSTAL SURVEY OF CURRENT PRACTICE IN WALES

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Background: In the setting of endoscopy in an anticoagulated patient, the endoscopist must assess the risk of complications related to intercurrent bleeding or thrombosis and plan the endoscopic procedure accordingly. A recent survey across the Northern region of England revealed a huge variation in practice. This is not surprising in the absence of a national guideline. Recently the American Society for Gastrointestinal Endoscopy (ASGE) has published guidelines on this subject.

Aim: To survey the current practice of endoscopy in anticoagulated patients across Wales using the ASGE guidelines as a benchmark.

Methods: A postal questionnaire was sent to all endoscopists identified from each endoscopy department across Wales irrespective of qualification and experience. The questionnaire was constructed based on the ASGE guidelines as follows. (1) Procedure risk— bleeding related to an endoscopic intervention carried out in the setting of anticoagulation, and (2) Condition risk— a thromboembolism event related to interruption of anticoagulation for a particular condition. High-risk procedures were— polypectomy, dilatation, endoscopic sphincterotomy, PEG, laser ablation/coagulation and all the rest were low risk procedures. High-risk conditions were— mechanical prosthetic valve, atrial fibrillation with underlying heart disease, recurrent thromboembolism and the rest were low risk conditions.

Results: A total of 90 questionnaires were sent and we received, 58 (52%) replies. There were 33 consultants, 7 middle-grade doctors, 4 general practitioners, 13 trainees and 1 nurse endoscopist. Twenty-seven (47%) respondents considered endoscopic biopsy as a high-risk procedure. Twenty-nine (50%) considered bioprosthetic valve as a high-risk condition. Twenty-four (41%) did not consider atrial fibrillation with underlying heart disease and recurrent thromboembolism as a high-risk condition and 8 (14%) considered atrial fibrillation without underlying heart disease as a high-risk condition. Six (10%) would not use intravenous heparin after stopping warfarin in high-risk conditions. All except 2 (3%) considered PEG as a high-risk procedure. Two (3%) would stop NSAIDs one week before high-risk endoscopic procedures.

Conclusion: Opinion was divided as to whether to take endoscopic biopsies or not in a patient on warfarin although evidence shows that the risk of bleeding in warfarinised patients is negligible provided the INR is within the therapeutic range. Likewise there is an equal division of opinion as to whether bioprosthetic valve is a high-risk condition or not. It is noteworthy that a significant proportion of respondents (41%) did not consider atrial fibrillation with underlying heart disease and recurrent thromboembolism as a high-risk condition. This survey further confirms previous evidence that there is a huge variation in practice among endoscopists in the UK. There is need for a national guideline to streamline the endoscopy practice in anticoagulated patients.
Patients attending for endoscopy are often on aspirin and/or anticoagulant therapy for medical reasons. Recent guidelines by the American Society of Gastrointestinal Endoscopy offer advice regarding management of these patients in the peri-endoscopic period.

**Aim:** To identify current practice and knowledge of guidelines in members of the British Society of Gastroenterology (BSG).

**Methods:** 645 questionnaires were sent to BSG members.

**Results:** 483 (75%) questionnaires were returned, of these 327 (68%) members performed endoscopy and were included in the subsequent analysis. 237 (72%) of questionnaires were returned from physicians, 84 (26%) from surgeons and 6 (2%) other. 305 (93%) of questionnaires were returned from the consultant grade, 14 (4%) from SpRs and 8 (3%) from others. Total number of endoscopy years experience was 5865 years, mean 18 years. 97% of members performed OGD, 92% flexible sigmoidoscopy (FS), 90% colonoscopy and 55% ERCP.

Aspirin and warfarin were discontinued for elective endoscopy by 2% and 19% of members performing OGD respectively, 4% and 21% performing FS, 8% and 40% performing colonoscopy and 17% and 73% performing ERCP. The time scale varied for stopping (1–14 days) and recommencing (0–14 days) these agents following the procedures. Members were asked if they would biopsy a patient attending for endoscopy on aspirin or warfarin, 95% and 36% would at OGD respectively, 95% and 34% would at FS and 94% and 35% would at colonoscopy. 19 members would biopsy on warfarin without knowledge of INR. 21% of members were aware of complications arising from biopsy whilst on these agents. Members were asked if they were aware of any guidelines in this area, 87% replied no, 12% yes and 1% no reply. Members were asked if they thought guidelines would be helpful, 75% replied yes, 13% possibly, 9% no and 3% no reply.

**Conclusions:** There appears wide variation regarding management of these patients and a lack of awareness about recent published guidelines. We feel that it is timely for local guidelines to be produced so that endoscopists’ can practice evidence base medicine in this area.

**IRON DEFICIENCY ANAEMIA IN PRE-MENOPAUSAL WOMEN**

J. Sayer1, S. Cullen1, M. Rees1, R. Long2, R. Chapman1. ‘John Radcliffe Hospital, Headington, Oxford;2City Hospital, Nottingham, UK

Iron deficiency anaemia in pre-menopausal women is usually attributed to menorrhagia. However, patients with no history of menorrhagia are often referred for gastro-intestinal investigations to exclude blood loss from the gut. We looked at the usefulness of endoscopic investigations to identify aetiological factors in iron deficiency anaemia in pre-menopausal women.

All pre-menopausal women with iron deficiency anaemia referred to the gastrointestinal clinic were invited to participate. The study was approved by the local ethics committees and all patients gave written informed consent. All patients had upper gastrointestinal endoscopy, including duodenal biopsies and either colonoscopy or barium enema examination. Patients were asked to complete a seven-day, diet diary and to provide two complete menstrual blood loss collections. These were measured using the alkaline haematin method.

**Abstract 346, Table 1**

<table>
<thead>
<tr>
<th>Cause</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood donation</td>
<td>5</td>
</tr>
<tr>
<td>Dietary iron deficiency</td>
<td>12</td>
</tr>
<tr>
<td>Menorrhagia</td>
<td>7</td>
</tr>
<tr>
<td>Gastritis/peptic ulceration</td>
<td>2</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>4</td>
</tr>
<tr>
<td>Colonic angiodysplasia</td>
<td>1</td>
</tr>
<tr>
<td>Carcinoma of colon</td>
<td>1</td>
</tr>
<tr>
<td>Colonic adenoma</td>
<td>1</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>2</td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatory drug</td>
<td>1</td>
</tr>
<tr>
<td>Warfarin</td>
<td>1</td>
</tr>
</tbody>
</table>

Forty-five women took part in the study. Sixteen completed diet diaries and seventeen provided menstrual loss collections. Contributing aetiological factors are listed in the table.

Seven patients had more than one contributing aetiology and in 6 patients no aetiological cause could be identified.

We conclude that pre-menopausal women with no clear history of menorrhagia should undergo gastrointestinal investigations to rule out malignant and pre-malignant gastrointestinal disease. However, patients should also be questioned about diet and blood donation as these are also important contributing factors in the aetiology of iron deficiency in these patients.

**DO SINISTER SYMPTOMS PREDICT SERIOUS ENDOSCOPIC FINDINGS IN DYSPEPTIC PATIENTS?**


**Introduction:** Early endoscopy is recommended for investigating dyspeptic patients when sinister symptoms (i.e. weight loss, dysphagia, persistent vomiting, family history of gastric cancer or history of gastric surgery) are present. This is based upon the assumption that serious pathology will be more prevalent in patients with such symptoms.

**Aims:** To compare endoscopic findings in patients referred for investigation of dyspepsia with and without sinister symptoms.

**Methods:** As part of a large prospective trial, 923 patients aged 55 years referred for investigation of dyspepsia unrelated to NSAID usage, had their symptoms recorded by a standard questionnaire prior to investigation. 215 had one or more sinister symptoms and were endoscoped. Of the 708 without sinister symptoms, half were randomised to endoscopic examination as part of the trial protocol.

The endoscopic diagnosis in the 215 (mean age = 38y) with and 352 (mean age = 35y) without sinister symptoms was compared.

**Results:** Those with and without sinister symptoms had a similar prevalence of normal endoscopy (49% vs 56%), DU (6.9% vs 8.0%), GU (4.4% vs 3.9%) and oesophagitis G I (12.5% vs 13.3%) and G II (2.3% vs 2.0%) and gastric cancer (0% vs 0%). In routine biopsies, low grade MALToma was found in one patient without, and sub-total villous atrophy in one patient with sinister symptoms. Serious oesophageal disease was the only finding more prevalent in those with (6/216) versus without (0/352) sinister symptoms (p<0.05). This consisted of G III oesophagitis, Barrett’s oesophagus and oesophageal cancer in 2, 3 and 1 patient(s) respectively. Five of the 6 patients with severe oesophageal pathology had dysphagia as their sinister symptom. Dysphagia was reported by 39.5% of those with sinister symptoms. The prevalence of severe oesophageal pathology in those with dysphagia was 5/85 (6%).

**Conclusions:** (1) Sinister endoscopic findings are rare in the absence of sinister symptoms; (2) sinister symptoms indicate an increased prevalence of serious oesophageal pathology; (3) Dysphagia is the most important sinister symptom.

**“DRIVERS” AND “INHIBITORS” FOR REFERRAL OF UPPER AND LOWER DIGESTIVE SYMPTOMS FROM PRIMARY CARE**

P.A. Cann, C.S. Cornford1. South Cleveland Hospital, Middlesbrough; G.P. Newlands Medical Centre, Middlesbrough, UK

The ever increasing demand for gastroenterology (GI) services from primary care necessitates clearer understanding of primary > secondary referral dynamics. This need is made more urgent because current initiatives to fast-track higher risk groups e.g. “2 week rule”, to reduce overall waiting times and also to inform the efficient and consensual development of open access and direct booking services. Some “drivers” or triggers for referral are easy to understand and sensible—others are more obscure and may not be acknowledged to be of use in secondary care. It is at least as important to identify the “inhibitors” for referral, in order to reduce the risk of our patients suffering delayed diagnosis / management.

Secretaries in 2 primary care group practices identified patients, aged 40 years or more, who had consulted with appropriate symptoms. Consecutive patients with upper (U) and lower (L) GI symptoms were noted for each GP. This produced 113 valid consultations—55 U (mean age 59 yr—60% female) & 58 L (57 yr—67% L). 33% of U were referred (18% open access / 15% clinic) vs. 38% of L (19%/19%).

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Each GP was seen later by the GP author and asked to reconstruct decision processes, according to a structured interview with both closed and open questions. Transcripts were analysed using the software package “QSR NUD*IST”, with respect to themes and categories. Some obvious drivers e.g. dysphagia & rectal mass resulted in universal referral—others had varied power (% in consultation / % referral), e.g. weight loss (2.5% / 33%), NSAID/aspirin (13% / 14%), rectal bleeding (29% / 55%), diarrhoea (38% / 41%), patient reassurance (6% / 100%). Family history did not feature as a key driver. Use of time to defer decision was employed in 29% U / 19% L (> referral in 31% / 0% of those cases). Key inhibitors were (% in consultation): plausible explanation (25%), short duration (22%), long duration (11%), no weight loss (12%), no sinister features (8%), normal blood tests (6%).

Conclusion: Insights of this kind are invaluable for establishing local educational needs and framing primary / secondary consensus guidelines / structures. Particular concern arises from the lack of importance attached to family history and the degree of false security arising from the absence of worrying / alarm / late symptoms.

Iron deficiency anaemia is a common finding across all age groups. The diagnosis may be made in any adult specialty.

Aim: To establish current methods of practice in the investigation of this condition.

Method: 10–20 patients were identified retrospectively by identifying low serum ferritin values from haematology department work sheets over a period of 12 months between July 1996 and July 1997. Patient records were then retrieved and analysed. Investigations performed were recorded for each patient, and in the case of colonoscopy, whether a complete examination had been performed (caecal intubation). Patients under the gynaecology department and patients under 16 years were excluded.

Results: 100 patients were identified with low ferritins (age range 16–87 yrs). 83% of these were female. 20 patients were found to have a haematological or haematological cause for low ferritin. 52 of the remaining 80 patients underwent gastroscopy. 12 patients underwent colonoscopy, of which 7 examinations were declared as complete. 4 other patients underwent flexible sigmoidoscopy and double contrast barium enema, 2 had barium enema alone. Thus 11% of patients had documented evidence of complete colonic imaging. 3 colonic tumours were found, 5 upper GI neoplasms were found and of the 15 patients in whom duodenal biopsies were taken, 3 had histological evidence of coeliac disease.

Conclusions: A low proportion of patients appeared to be undergoing complete colonic investigations, however 2 of these patients were diagnosed with colonic cancer. Although only 15% of patients had duodenal biopsies performed, a high proportion, 20% were positive for coeliac disease. We therefore suggested a departmental protocol to be devised to standardise investigation and to encourage referral for colonoscopy where there was no haematological or gynaecological cause for iron deficiency, in the absence of an upper GI neoplasm.

VARIATION IN METHODS OF INVESTIGATION FOR IRON DEFICIENCY ANAEMIA WITHIN A DISTRICT GENERAL HOSPITAL

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Introduction: Studies suggest that iron-deficiency anaemia (IDA) is caused by gastrointestinal malignancy in 10–20% of cases. In 1998 an analysis of historical data from our institution revealed that 20 patients with gastrointestinal cancer who were initially referred with IDA had an average wait of 11 weeks (median 8 weeks) from referral to diagnosis. In December 1998 we therefore established a nurse led IDA clinic and herein report the results of the first 100 patients.

Methods: Local GPs were notified of the new clinic and were encouraged to refer patients directly. The patients were seen by a clinical nurse specialist who followed an established protocol to elicit a medical history and undertake a limited physical examination. Following discussion with a Consultant Gastroenterologist appropriate investigations were initiated.

Results: All 100 patients were seen within 2 weeks of referral. 15 patients had no further gastrointestinal investigations (5 refused investigation, 2 had prohibitive co-morbidity and 8 were referred directly to other specialists because of normocytic anaemia, menorrhagia and recurrent epistaxis). Of the 85 patients investigated 73 (86%) had an OGD and colonic investigation (67 had colonoscopy and 6 had barium enema). 8 patients with obvious symptoms or signs (e.g. dysphagia) had only the relevant area investigated and 4 patients with clinical features of small bowel disease had an OGD and barium follow-through study.

All patients had initial investigations within 6 weeks. At initial assessment 15 patients were thought to have worrying symptoms or signs and were investigated within 2 weeks. Overall nineteen patients were found to have gastrointestinal cancer (17 colonic, 2 oesophageal). In these 19 patients the mean time from GP referral to diagnosis was 4 weeks and 79% had a diagnosis within 3 weeks.

Conclusion: This nurse-led open access IDA clinic greatly improved our referral to diagnosis time for patients with gastrointestinal malignancy. As recent recommendations include IDA is an indication for urgent referral (i.e. within 2 weeks) we would suggest other institutions audit their IDA data and consider developing such a service.

WHAT IS THE OPTIMAL CLINICAL BACKGROUND FOR A NURSE ENDOSCOPIST?

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Introduction: There has been some debate regarding the most appropriate clinical background for nurses undertaking endoscopy, with some coming from an endoscopy-unit background and some who are colorectal nurses with no previous endoscopy experience. A six-month course was developed to facilitate the theoretical knowledge and practical skills relating to flexible sigmoidoscopy and
the management of colorectal diseases. The hypothesis was that the endoscopy nurses would produce better results in relation to the endoscopic skills but that the colorectal nurses would demonstrate a better understanding of colorectal disease management.

**Methods:** Retrospective analysis was undertaken to establish whether the nurses’ clinical background determined probable success in different aspects of the course. Results of three theoretical assessment methods were used to ascertain whether any difference existed between the two groups. Two of these methods assessed endoscopic skills theory, (an oral viva and written exam), and a short answer exam was used to test knowledge of colorectal disease. The mean scores for each assessment method were noted for the two groups. The course had a total of 23 students of which 12 were colorectal nurses and 11 endoscopy nurses. Three were male, of which two were endoscopy nurses, as were nine of the 20 females. The ages ranged from 25–49 with a mean of 36 years.

**Results:** No significant difference existed between the two groups in the endoscopy assessments. However there was statistical significance in the colorectal module results with p = 0.0284.

**Conclusion:** Whilst there was no significant difference between endoscopy and colorectal nurses in their ability to deal with theoretical issues related to endoscopy, there was a variation regarding colorectal disease management that can be linked to clinical background with the colorectal nurses demonstrating a greater depth of knowledge in this area. These findings would support the view that colorectal nurses with no previous experience of working in an endoscopy unit setting, can make capable nurse endoscopists whilst also possessing an in-depth knowledge of colorectal disease management.

**353 THE DEVELOPMENT OF A NURSE LED PRACTICAL TRAINING PROGRAMME FOR TRAINEE NURSE ENDOSCOPISTS**

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**Background:** Currently trainee nurse endoscopists must perform a minimum of 100 endoscopic procedures under Consultant supervision prior to providing an autonomous endoscopy service. There are currently recognised documented difficulties with facilitating adequate training for clinicians in endoscopic practice due to a shortage of protected training sessions. This shortage has meant that trainee nurse endoscopists are not having individual protected training sessions but are competing with registrars for training slots.

**Aims:** To assess the ability of a trained nurse endoscopist in flexible sigmoidoscopy and colonoscopy to replace the Consultant as principle trainer, providing a complete practical training programme for trainee nurse endoscopists.

**Methods:** 2 trainee nurse endoscopists, with no previous experience of endoscopy, received practical flexible sigmoidoscopy training from the nurse endoscopist for all procedures. At set intervals the trainee attended consultant lists for assessment of skills and endoscopic knowledge. All procedures were video recorded. On completion of the training programme an expert panel blindly assessed 10 of the complete procedures for assessment of accuracy and endoscopic technique on withdrawal using the published Rex scoring system.

**Results:** The nurse trainees have completed their training programme. All videos assessed by the expert panel were passed for scope knowledge. All procedures were video recorded. On completion of the trainee attended consultant lists for assessment of skills and endoscopic knowledge. All procedures were video recorded. On completion of the training programme an expert panel blindly assessed 10 of the complete procedures for assessment of accuracy and endoscopic technique on withdrawal using the published Rex scoring system.

**Conclusion:** Whilst there was no significant difference between endoscopy and colorectal nurses in their ability to deal with theoretical issues related to endoscopy, there was a variation regarding colorectal disease management that can be linked to clinical background with the colorectal nurses demonstrating a greater depth of knowledge in this area. These findings would support the view that colorectal nurses with no previous experience of working in an endoscopy unit setting, can make capable nurse endoscopists whilst also possessing an in-depth knowledge of colorectal disease management.

**355 AUDIT: TO DETERMINE THE DEGREE OF INFORMED CONSENT IN PATIENTS ATTENDING A DGH DAY UNIT FOR OGD, COLONOSCOPY OR FLEXIBLE SIGMOIDOSCOPY**

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Achieving informed consent is not an isolated event and should ideally be obtained by the endoscopist prior to the test date and include written material. Effective communication of sufficient information is necessary. This audit examines the degree of consent in competent adults attending a day unit.

109 patients were interviewed after giving written consent (67 day case, 42 open access endoscopy), 97% understood which investigation was being performed and the site to be examined, 86% acknowledged that they had received written information (75% by letter) but all were appropriately prepared for an investigation. 93% said they had spoken to a health care professional (78% to a nurse) but each had signed a consent form with a doctor. 88% had good understanding of what was to happen during the test and 90% following the test. 34% had poor understanding of the benefits of the test (40% of open access patients, 33% of day cases), 75% had little or no idea of any associated risks (80% of open access patients, 70% of day cases).

**Conclusion:** The audit demonstrated patients’ poor understanding of the benefits and risks of procedures, especially for the open access service. Improvements should include consent forms containing this information being sent to patients. Consent needs to be multidisciplinary, involving the referring clinician, endoscopic nurses as well as the endoscopist.

**356 A PROSPECTIVE COMPARISON OF THE BSG AND A STANDARD NHS MANAGEMENT EXECUTIVE CONSENT FORM FOR ENDOSCOPY**

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**Background:** There is a move toward providing more information to enable informed consent. An example consent form recently published by the BSG is more explicit in outlining risks of endoscopic procedures than previously used forms (Gut, 1996).

**Aims:** To compare patients’ attitudes to the BSG consent form with those to a standard NHS Management Executive (operation consent) form.

**Methods:** Consecutive patients were given written information quantifying complications and asked to study the two consent forms (a standard NHS consent) form.

**Results:** 140 gastroscopy and 57 colonoscopy patients were studied (52% male, median age 53 (range 19–93)). 61% of gastroscopy and 53% of colonoscopy patients felt that the right amount of information was given on the BSG compared to 36% (P<0.001) and 18% (P=0.001) respectively on the standard NHS form. 29% of gastroscopy and 53% of colonoscopy patients felt that insufficient information was given on the BSG form, compared to 56% (P<0.001) and 61% (NS) respectively on the standard NHS form. Only 1% of colonoscopy patients felt that the BSG form contained too much
SELF EXPANDABLE METAL STENTS (SEMS) FOR MALIGNANT AND BENIGN COLONIC OBSTRUCTION

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Background: SEMS have been described as a useful procedure for both palliation of malignancy and as a “bridge to surgery” in acute obstruction. Little data exists on their use in benign obstruction.

Methods: A retrospective case note review was performed of all patients who had undergone colonic stent insertion (CSI) over a 4-month period (Dec 1999-Sep 2000). The site/nature & degree of obstruction (partial or complete), type of stent used, rate of successful decompression (symptomatic resolution/radiological improvement), complications (early (<30 days), late), and long-term stent patency were recorded.

Results: CSI was performed in 21 patients using a combined endoscopic/radiological approach. The majority of patients had acute malign biliary obstruction secondary to a left-sided tumour (18) (4 complete; 14 partial) with a partially obstructing lesion in the transverse colon in one case. 2 patients had benign disease, one with a post-surgical stricture after sigmoid colectomy for diverticular disease and one with a descending colon Crohn’s stricture. Strictures were successfully negotiated in 18/21, in 3 cases the stricture was reached but a guide-wire could not be passed. In the 18 successful cases, initial guidewire passage across the stricture was achieved through-the-scop in 16 but only with the use of semi-steerable angiographic catheters in 2 cases. Types of stent used: Wallstent® (10), Ultraflex® (5) and Bard® membrane stent (3). Successful colon decompression was achieved in 100%. Early complications occurred in 6/18 patients (33%) (stent migration (3), perforation (requiring sigmoid colectomy) (1), minor self-limiting rectal bleeding (1) and focal ulceration (1)) with late complications in 2/18 (11%) cases due to re-obstruction (150 and 425 days post-procedure). In both cases repeat stent insertion was successful. Of the 19 patients in whom stent insertion was successful 6 remained alive (2 benign stricture; 4 malignant) with 2 patients having had radical surgery (median follow-up 6 months (1–12)). In the 12 patients who died (median survival 4.5 months (2–17)) the stent remained patent without further obstructive episodes.

Conclusions: In our experience stenting is a useful procedure both for treatment of colonic malignant obstruction and for selected cases of benign obstruction. A high technical success rate for stent deployment can be achieved with a combined radiological/endoscopic approach.

EXPANDABLE METALLIC STENTS—EFFECTIVE PALLIATION OF MALIGNANT PYLORIC AND DUODENAL OBSTRUCTION

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Introduction: Vomiting due to malignant obstruction of the pylorus or proximal small intestine is an extremely distressing symptom and almost impossible to palliate pharmacologically. Patients are often unfit for even minimally invasive bypass surgery. We present our initial experience of self-expanding metallic stents which offer a non-surgical alternative.

Patients: Between April 1999 and August 2000, 11 patients (6 male, mean age 67.5 yrs, range 55–87), presented terminally-ill with intractable vomiting due to malignant pyloric or duodenal obstruction. All patients were deemed unfit for surgical bypass procedure.

Methods: Outcome measures were time to discharge post-procedure, overall survival time, percentage of survival time spent out of hospital, and need for readmission or repeat procedures. Hospital records were examined for this information. This was augmented by telephone inquiry to patients GP and to the local Hospice. In all cases, a Wallstent enteral® stent (Boston Scientific) was inserted under sedation using a combined endoscopic and fluoroscopic approach.

Results: There were no complications of stent insertion. Mean time to discharge was 12.6 days (range 4–55). Mean survival 71.7 days (18–159) with a mean 69% (13–100) of that time spent outwith hospital. 6/11 patients required readmission to hospital or hospice, 3 due to vomiting. There were 3 stent failures, 2 requiring balloon dilatation, 1 re-stent with a covered Ultraflex®. 5/11 patients required no further inpatient care.

Discussion and conclusions: The combined endoscopic/fluoroscopic procedure was easy to perform and well tolerated. Our stent failures were due to an exuberant, hyperplastic mucosal reaction rather than tumour recurrence. The uncovered Wallsten® offered excellent results in these cases. Patients can be discharged promptly and cared for at home during their final illness. The precise role of palliative stenting is poorly defined and we suggest that there is a need for a randomised, multi-centre trial of enteral stenting versus minimally invasive surgical bypass.

AUDIT OF ERCP IN A SMALL UNIT

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Guernsey has a population of about 60,000, which would be expected to produce an approximate annual requirement of only 40 ERCPs. In order to assess whether such a small number of procedures is adequate to maintain acceptable standards, audit, with particular reference to success and complication rates, has been performed ever since ERCP was established as a core service in April 1996.

From 1st April 1996 to 10th October 2000, 156 patients underwent 213 procedures (47 per year). These comprised 156 prime indications, 30 clinically indicated repeat procedures, e.g. stent change, and 27 repeat attempts after initial failure. All but 5 procedures were performed by a single operator.
A ONE YEAR 30 DAY AUDIT OF DAY CASE ERCP

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Background: A recent North American ERCP study of same-day discharge endoscopic biliary sphincterotomy (ES) provides a helpful if rather complicated multivariate risk analysis for complications. Their readmission rate following ES was 12%, with 76% of complications occurring within 6 hours of the procedure (Gastrointest Endosc 1999;49:512-580). Day case ERCP is not common practice in the UK. No guidelines based on British experience exists as to the optimal post procedure period of observation.

Aims: To prospectively audit our Day case ERCPs in which we used a simple 6 hour post procedure discharge protocol.

Methods and results: From 1 May 1999 to 31 April 2000, our unit (DGH serving a population of 330,000) carried out 221 ERCPs. We carried out a 30 day post procedure audit of the 70 patients deemed suitable for the procedure to be performed as a day case. These 70 patients 1) had all been seen in outpatients, 2) lived within 30 min car drive of the hospital and 3) had a sensible adult to look after them. No. Night. The 70 patients had a total of 89 ERCPs of which 53 (59.6%) were elective. Our simple protocol ensures that a) most complications are detectable, b) readmissions are infrequent. They fed the patients 4 hours post procedure and 2 hours later, ask the gastroenterology team to confirm fitness for discharge. 9 patients required admission during the 6 hour observation period (pancreatitis 5, cholangitis 2, bleeding 1 and pain and vomiting 1). The readmission rate was only 1/89 (1.1%) and occurred in a patient who bled 3 days post ES.

Conclusion: Day case ERCP in selected cases is safe and cost effective. Our simple protocol ensures that a) most complications are detected in the 6 hours post procedure and b) readmissions are infrequent.

A SIMPLER GRADING SCALE TO ASSESS ERCP TECHNICAL DIFFICULTY: AN ATTEMPT TO PRODUCE QUALITATIVE OUTCOME DATA

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Background and objective: ERCP is a highly advanced endoscopic procedure that requires considerable training and experience to perform effectively and safely. It varies from a simple diagnostic to a highly specialised interventional procedure. Simple outcome measures such as success and complication do not reflect the actual competence of the department doing these procedures. A grading scale to assess the technical difficulty can improve the accuracy of outcome data.

Methods: A technical difficulty grading scale for ERCP procedures was constructed and applied prospectively to all ERCP procedures over a 12 month period. Grade I: simple diagnostic, Grade II: standard biliary sphincterotomy, balloon sphincteroplasty, removal of extra-hepatic stones >1cm using basket or balloon, Grade III: precut sphincterotomy, large stones >1cm, intrabiliary stone removal, mechanical lithotripsy, stricture dilatation, cytology, stent/ nasobiliary drain insertion, Grade IV: sphincter of oddi manometry, ERCP after Billroth II surgery, combined procedures (PTC & ERCP) other advanced bile duct therapeutic procedures and all pancreatic duct therapeutic procedures.

Results: There were 306 ERCPs in 243 patients from 1st Sept’99 to 30th Aug’00, male: 162, female: 144, age range 17-97, mean 70 years. Overall success of 241 (79%) with complications in 13 (4%): bleeding 5 (1.6%), cholangitis 1 (0.3%), pancreatitis 5 (1.6%), perforation 2 (0.7%). Success rate was highest for Grade I 48/55 (87%), followed by Grade II and III 186/240 (78%) compared to Grade IV procedures 7/11 (63%). Our findings indicate a statistically significant linear trend towards a lower success rate from Grade I to IV (p = 0.045). Complications were similarly low in Grade I, II and III procedures 12/295 (4%) compared to Grade IV procedures 1/11 (9%). However, the numbers were too small for test of statistical significance.

Conclusion: Success and complications in ERCP are influenced by technical difficulty of the procedure. Further validation work is needed for this grading scale. Outcome data incorporating a grading

PUSH ENTEROSCOPY IN COELIAC DISEASE, ENDOSCOPIC AND HISTOLOGICAL FINDINGS

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Introduction: Endoscopic small bowel biopsy is the investigation of choice in the investigation of coeliac disease (CD) and the endoscopic appearances of this condition are well documented. We report a retrospective review of appearances at push enteroscopy compared with the histological results of biopsies taken during those procedures.

Methods: 97 procedures were carried out on 78 patients (27 male, 51 female, mean age 50.7 years) with CD. The indication for enteroscopy was: investigation of malabsorption n=18, repeat small bowel biopsy n=57, and refractory sprue n=22.
scale such as the one used in this study gives more accurate information when auditing the qualitative outcomes of ERCPs performed. This can provide a platform for structured objective evaluation.

### 364 EMERGENCY (OUT OF HOURS) UPPER GI ENDOSCOPY SERVICE IN THE UK

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**Background:** There are few data on the availability of emergency endoscopy out of normal working hours in the UK. The aims of this study were to find out: (i) the number of endoscopy units providing out of hours endoscopy and (ii) the practical issues of running the service.

**Methods:** A postal questionnaire was sent to 470 consultant gastroenterologists working in 268 Hospital endoscopy units. Some questionnaires were also distributed at local and international gastroenterology meetings. The questionnaire specifically addressed the number of units providing emergency endoscopy (outside 9am-5pm Mon-Fri), staffing of on-call rota, written request guidelines, facilities for endoscopy, specialised nursing support and reasons for delay in establishing a formal service.

**Results:** 295 (63%) questionnaires were returned, of which 282/295 (96%) respondents from 188 (70%) units were suitable for analysis. In total 162/188 (86%) units perform emergency endoscopy; (i) informal on call rota (n=86) with a mean number of gastroenterologists per unit of 2 and (ii) formal on call rota (n=76) with 3 gastroenterologists per unit. In contrast, in the 26 Units with no emergency out of hours endoscopy service, the mean number of gastroenterologists was 2 per unit. Manpower for the on-call rota consists of consultant medical gastroenterologists (142/162 units) and/or gastrointestinal surgeons (106/162) with 8 (5%) units staffed by non-consultants alone. Written guidelines for emergency endoscopy request were present in 80/162 (49%) units. 18 units have fixed weekend lists, with 5 operating both Saturday and Sunday. Emergency endoscopy takes place in endoscopy units in 90 (56%) units and/or operating theatre 92 (57%). On-call endoscopy nursing support was available only in 72 (44%) units. The major reasons for deferring a formal on call service (n=63) were: (i) lack of medical manpower (37%), (ii) lack of nursing support (27%) (iii) lack of funding (30%).

**Conclusions:** Less than 50% of endoscopy units in the UK have a formal arrangement for emergency (out of hours) endoscopy. The factors negatively influencing development in this area include: (i) lack of funding (ii) medical and nursing manpower issues.

### 365 A REALISTIC PHANTOM OF THE OESOPHAGUS FOR 3D ENDOSCOPIC ULTRASONOGRAPHY

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**Introduction:** EUS is now an established modality for staging of upper GI malignancy. There is a need for a multi-purpose phantom for endoscopic ultrasound B-mode and 3D imaging.

**Methods:** An agar based tissue mimicking material was used to construct the phantom. Different combinations of the Al2O3 (3 and 0.5%), and SiC (400 grain) particles were used to produce the layers of the oesophagus. Two, 3 and 5 mm cylindrical channels were constructed to assess caliper accuracy. Cylindrical spirals, cones and ellipsoids were used mimic the tumours, cysts and lymph nodes. The Olympus EU-M30 / GF-UM20 scope was used to acquire images at 7.5 and 12 MHz. Image sensitivity and contrast measurements were performed on the B-mode images and were assessed visually. 3D volumes were reconstructed from the B-mode images of the structures within the phantom and a comparison was made between the actual and measured 3D volumes. The acoustical properties of the phantom components were assessed using a scanning acoustical macroscope and the pulse echo substitution technique for attenuation and speed of sound measurements.

**Results:** A realistic 3 layer model of the oesophagus was constructed, with acoustical properties of the phantom components between 0.1-0.5 dB/cm.MHz for the attenuation, relative backscatter power between –6 to 10 dB relative to the normal tissue mimic, with speed of sound of 1540 m/s. Caliper measurement by the endoscopist resulted in a maximum error of 5% from the true diameter. The sensitivity of the image was high enough for a 2mm diameter fluid filled channel to be clearly observed in the image obtained by scanning. 3D representations of the phantoms were volume rendered from the B-mode images and preliminary volume measurements of the objects resulted in a maximum error of 5%.

**Conclusions:** The phantom had appropriate acoustical properties and produced images similar to those obtained during actual patient scanning. Our phantom can provide a practical standard for quality assurance, teaching, and 3D research.

### 366 FLEXIBLE SIGMOIDOSCOPY IN SYMPTOMATIC PATIENTS — THERE ARE SIGNIFICANT BENEFITS TO USING A PAEDIATIC COLONOSCOPE IN FEMALE PATIENTS

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**Background:** Flexible sigmoidoscopy (FS) is used to investigate colorectal symptoms as well as for CRC screening. Women experience more pain and have a lower insertion depth than men.

**Aims:** To establish if using a ‘floppier’ paediatric endoscope conferred any benefit over an adult colonoscope in symptomatic patients.

**Methods:** Flexural rigidity measurements confirmed that the Olympus 11.2 mm diameter PCF240L colonoscope (P-C) was significantly ‘floppier’ (P<0.001) than either the Olympus CF240L or CF230L adult colonoscopes (A-C). We conducted a trial of ‘Fast’ and ‘Regular’ surgical FS in 310 patients allocated alternatively to P-C or A-C. Magnetic Endoscope Imaging plus ‘painometer’ was used to study depth of insertion, anatomical segment of the colon reached and number of episodes of discomfort/pain.

**Results:** There were 99 patients in the P-C group (52 female) and 100 in the A-C group (41 female) (11 exclusions). Female patients had more pain (P<0.0002) and a lower median insertion depth (P<0.0001) than males. In all females and b) those with a hysterectomy the P-C permitted a greater insertion depth (P<0.02 and P<0.001 respectively) than the A-C.

**Conclusion:** At FS, the use of floppier instruments such as the P-C merits more detailed evaluation especially in women with a past history of pelvic surgery.

### 367 EVALUATION AND VALIDATION OF A VIRTUAL REALITY BASED FLEXIBLE SIGMOIDOSCOPY TRAINER

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**Introduction:** Gastrointestinal endoscopy is currently taught by hands on training in the clinical setting. There are no adequate cadaveric or synthetic models to facilitate training. The Pre-Op (HT Medical) is a computer based virtual reality simulator for flexible sigmoidoscopy. It is able to record many different parameters of performance. There are six clinical modules.

**Methods:** Forty-five subjects participated in the study divided into three groups: novice (never performed lower GI endoscopy), intermediate (between 5-50, median 30), and trained (more than 200, median 747). Subjects received identical familiarisation and training on simulation modules 1 and 2, and were then assessed on module 3, which they attempted three times. Results are expressed as the geometric mean and 95% confidence intervals. Mann-Whitney U tests were used to compare each of the groups in turn.

**Results:** There was a significant difference between all three groups with respect to % mucosa visualised procedural time and the efficiency ratio (%mucosa/ time). In addition, the novice group had a lower instrument path length score compared to the other two groups.

**Conclusions:** The results show that the Pre-Op virtual reality simulator is a valid discriminator of flexible sigmoidoscopic experience. Its effect on training needs to be explored.
THE IDEAL FLEXIBLE SIGMOIDOSCOPE? A RANDOMISED PROSPECTIVE COMPARISON OF THREE INSTRUMENTS OF VARYING FLEXIBILITY

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Background: Most endoscopists perform flexible sigmoidoscopy using a 60cm instrument with the aim of reaching at least the descending colon, if not the splenic flexure. In reality, the descending colon is infrequently visualised (<40% of the time), with failure to examine the entire sigmoid colon, in up to 24% (Endoscopy 1996;31:227–31).

Aims: To compare anatomical depth of insertion and patient discomfort, using a conventional 60cm flexible sigmoidoscope (60FS), a standard 130cm paediatric colonoscope (PC), and a 100cm ‘ultra-flexible’ narrow calibre Olympus prototype endoscope (100FS), at routine non-sedated flexible sigmoidoscopy.

Methods: Consecutive non-sedated flexible sigmoidoscopy examinations were randomised to be performed using one of three instruments (60FS, PC, 100FS). All patients were prepared using two sachets of Citramag (35g magnesium citrate) & a low-residue diet for 24hr. Using MEI the anatomical depth of insertion after 60cm of instrument had been inserted, and the maximum insertion depth was determined. Patient discomfort was scored using a 100mm VAS.

Results: 52 consecutive patients were studied, 18 randomised to 60FS (7 male, mean age 53.3yr [sd 10.6]), 17 to PC (8 male, mean age 59.3yr [sd 13.1]), and 17 to 100FS (8 male, mean age 56.2yr [sd 13.1]). After 60cm of instrument had been inserted, the descending colon (DC)/splenic flexure (SF) was reached in 3/18 (17%) patients in the 60FS group, 9/17 (53%) patients in the PC group, and in 10/17 (59%) patients in the 100FS group (p=0.0231). Failure to examine the entire sigmoid colon (ie. to reach the sigmoid-descending junction) occurred in 8/18 (44%) patients in the 60FS group due to either pain (6) or atypical spiral looping (2) in association with previous hysterectomy/diverticular disease, in 3/17 (18%) patients in the PC group due to pain (1), atypical spiral looping (1) or looping within a long sigmoid colon (1), and in 3/17 (18%) patients in the 100FS group due to looping in a long sigmoid colon (2) and pain (1). (p=0.1464). Mean patient pain scores were similar in the 3 study groups.

Conclusions: Both the paediatric colonoscope and the 100cm narrow calibre, ‘ultra-flexible’ endoscope perform significantly better than standard 60cm instruments, enabling deeper intubation at 60cm.

4-YEAR OUTCOMES OF AN OPEN ACCESS COLONOSCOPY SERVICE

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Introduction: The Open Access Colonoscopy (OAC) Service offers a full (F) endoscopy to patients aged 45 years or over with a change in bowel habit, or a limited (L) procedure to the splenic flexure, to all patients with rectal bleeding only. Limited investigations are converted into a full examination if significant distal pathology is found.

Aim: To examine the outcomes and trends in the first 4 years of the service (May 1996—April 2000).

Results: (expressed for each calendar year / part year—96,97,98,99,00).

For each year, when limited examinations were converted to view the caecum after finding pathology below splenic flexure, the yield was 1%.

ENDOSCOPIC RESECTION BE FIRST-LINE THERAPY?

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Introduction: Complete endoscopic resection of large (>2cm), sessile colonic adenomas can be technically difficult and has led some endoscopists to refer patients straight for surgery. Complete endoscopic resection of large (>2cm) sessile and broad-based colorectal polyps by two specialist colonoscopists (BPS & CBW) at a single UK centre.

Methods: An endoscopy database search was performed to identify all sessile or broad-based polyps >3cm diameter diagnosed between 1/1995 and 7/2000. Polyps containing cancer were only included if endoscopic resection had been attempted.

Results: During the 67 month study period, 99 sessile or broad-based polyps (median size 30[20–80]mm) were seen in 95 patients (median age 66[25–85] years; 54 males). 38 polyps were located proximal to the splenic flexure. 86 were benign adenomas, with severe dysplasia present in 24. There were 6 cancers (4 Dukes ‘A’; 1 Dukes ‘B’; stage not available in one patient who declined surgery). There were 4 IBF-associated dysplastic lesions, one benign-appearing poly with no histology available and two were non-neoplastic. Of 93 benign lesions, endoscopic resection was technically successful in 78 (piecemeal resection in 73; saline assisted in 38). 53 had been followed up at least once with no evidence of recurrence (median number of colonoscopies to achieve resection: 1 [1–4]), follow-up is pending in 20 and 5 patients have been lost to follow up. In 9/93 cases endoscopic resection was unfeasible at the 1st colonoscopy and was not attempted, with subsequent referral for surgery. In 6/93, endoscopic resection was attempted but was unsuccessful after 2–3 attempts, with subsequent referral for surgery. Endoscopic resection was also attempted for 6 polyps which were later confirmed to be cancers. Of these, 4 were Dukes ‘A’ cancers and one was successfully managed by piecemeal resection, with clear follow-up. Surgery was performed in 3 of 4, and in one, no residual cancer was found. The Dukes ‘B’ cancer was diagnosed when surgical resection was performed after 3 attempts at endoscopic polypectomy (with benign histology) had failed. There were no serious complications. 6 patients had minor, self-limiting procedural bleeding and 2 experienced pain and were conservatively managed.

Conclusion: Colonoscopic polypectomy is effective and safe for excision of large benign colonic adenomas and should be considered first-line therapy.

PATIENTS RESPONSE TO VIRTUAL COLONOSCOPY COMPARED TO FIBRE OPTIC COLONOSCOPY

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Purpose: Virtual Colonoscopy (VC) is a new CT based method for detection of colorectal polyps and cancer. For VC to become established as a diagnostic test it must be well tolerated and accepted by patients.
Methods: Patients undergoing evaluation of colonic symptoms underwent VC prior to FC. All patients had standard colonic cleansing/preparation. The data for VC is acquired by performing a CT scan of the abdomen/pelvis after air insufflation and intravenous Buscopan. The CT examination generally takes less than 15 minutes. FC was performed using standard intravenous sedatives and muscle relaxants after the CT. Before and after both tests patients completed a Questionnaire concerning their symptoms of discomfort/pain, abdominal bloating, anxiety and overall preference of techniques. The patients were asked to score each variable on a 100 point scale. Two control groups also filled out the questionnaires: Patients undergoing only FC or barium enema.

Results: To date 84 patients have been evaluated. Regarding symptoms of discomfort and pain; 32% of patients experienced no difference with either technique. 50% found FC more comfortable than VC with only 18% tolerating VC better than FC. Regarding patient preference scores 16% patients had no preference, 24% preferred FC whereas 60% would prefer a VC in the future.

Conclusion: The on-going results from this study will be presented including comparison with the control groups. To date it appears patients experience more discomfort/pain with regard to VC compared to FC. However patients prefer VC when asked to choose between these two techniques of colonic imaging.

372 COLONOSCOPY: CAECUM OR BUST?
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Endoscopy of the colon is either a colonoscopy or a flexible sigmoidoscopy. Much has been made of the need for visualisation of the caecum if colonoscopy is the examination requested and endoscopy units and endoscopists are judged on their colonoscopy completion rates. Flexible sigmoidoscopy on the other hand reaches only the splenic flexure. Many units, including ours, use colonoscopes for an examinations and stop at the descending colon or splenic flexure if the examination requested is a flexible sigmoidoscopy. We propose a different way of looking at endoscopy of the large bowel that breaks from the sigmoidoscopy/colonoscopy dichotomy. The importance of reaching the caecum is assessed by the endoscopist prior to starting the procedure and expressed as a score of 1 (no attempt at caecal intubation) to 4 (full caecal intubation). A score of 1 indicates that visualisation of the caecum is not necessary and 4 that reaching the caecum is essential. Thus 1 would correlate with flexible sigmoidoscopy and 2–4 with colonoscopy. We applied this method to 267 endoscopic examinations of the large bowel and calculated crude and adjusted completion rates (in which cases of non-completion due to strictures, poor bowel prep and scope failure were excluded) for each score. In addition we recorded the incidence of pathology found beyond the splenic flexure for all complete examinations.

Results: 27.7% of cases were given a score of 1, 22.5% a score of 2, 32.2% a score of 3 and 17.6% a score of 4. In all patients in whom ‘colonoscopy’ was attempted (scores 2–4) the crude completion rate was 79.8% and the adjusted rate was 87.5%. In those in whom total colonoscopy was deemed to be essential (score 4) the crude completion rate was 95% and the adjusted rate was 100%. In all patients in whom the caecum was reached, no pathology beyond the splenic flexure was found in those given scores of 1 or 2. 5 of 56 (8.9%) of patients scored as 3 had right-sided pathology as did 5 of the 32 (15.6%) patients given a score of 4.

Conclusion: We have proposed a new way of looking at endoscopy of the colon based on the perceived importance of reaching the caecum and demonstrated high completion rates in those in whom visualisation of the caecum was deemed essential.

373 BENEFITS OF ILEOSCOPY IN PATIENTS UNDERGOING COLONOSCOPY—A DGH AUDIT
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Ileoscopy was attempted only in selected group of patients with chronic diarrhoea, strong suspicion or known IBD, abnormal small bowel Barium studies, or any other suspected small bowel pathology. We performed a retrospective clinical audit to assess whether ileoscopy was beneficial in the above group of patients presenting for colonoscopy in our unit.

All colonoscopies performed since Jan 1998 to Oct 2000 (period since SpR has been attached for training) were analysed. Total colonoscopies performed were 850. Caecal intubation was achieved in 92%.

374 IS TERMINAL ILEAL INTUBATION ESSENTIAL TO ENSURE COMPLETE COLONOSCOPY?
A.P. Malalasekera, K.I. Deen. Dept of Surgery, Faculty of Medicine, Kelaniya, Sri Lanka

Introduction: Traditionally, the standard for ensuring total colonoscopy has been terminal ileal intubation and histological confirmation of ileal mucosa. The additional step of terminal ileal intubation is time consuming and poses a diathesis to colonoscopy. We propose ileoscopy to confirm caecal intubation is an alternative but requires additional equipment and bears the risk of irradiation. Our hypothesis was that visualisation of the appendix orifice and ileocaecal valve, as a composite landmark, is sufficient to ensure complete colonoscopy.

Patients and methods: Fifty consecutive patients (female—20, male 30; median age—44 years; range—18 to 73 years) who required terminal ileoscopy as part of total colonoscopy were examined after standard bowel preparation and midazolam sedation. The caecum was intubated, the ileocaecal valve and appendix orifice visualised and expressed as a score of 1 to 4. A score of 1 indicates that visualisation of the caecum is not necessary and 4 that reaching the caecum is essential. Thus 1 would correlate with flexible sigmoidoscopy and 2–4 with colonoscopy. We applied this method to 267 endoscopic examinations of the large bowel and calculated crude and adjusted completion rates (in which cases of non-completion due to strictures, poor bowel prep and scope failure were excluded) for each score. In addition we recorded the incidence of pathology found beyond the splenic flexure for all complete examinations.

Results: The terminal ileum was intubated in all 50 patients. Indications for intubation were: right iliac fossa pain - 28%, altered bowel habits - 12%, bleeding per rectum - 6%, combination of above features - 38% and other - 16%. Endoscopy findings were: diverticulae - 10%, haemorrhoids - 4%, polyps 6%, colitis - 4% and normal 76%. There were no complications. Visual confirmation of total colonic intubation matched terminal histology in all patients. (Sensitivity and specificity of 100%).

Conclusion: We believe that visual landmarks in caecal intubation are sufficient in confirming terminal ileal intubation. Terminal ileal intubation, merely for confirming caecal intubation, will increase colonscopy time and is unnecessary.

375 PATIENTS WITH ACROMEGALY HAVE LONGER COLONS AND ARE MORE DIFFICULT TO COLONOSCOPY THAN NormalS
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Background: A previous barium enema study suggested that patients with acromegaly have longer colons than normal patients and therefore might be more difficult to colonoscope. We have previously used a combination of magnetic endoscope imaging (MEI) and specially developed software to accurately measure the lengths of different sections of the colon at the time of colonoscopy (Med. Biol. Eng. Comput., 1999;37:673).

Aims: To establish if acromegalic colons are significantly longer than normal and if so whether colonoscopy is any more difficult.

Methods and results: We used our MEI system in a series of 25 patients with acromegaly (AP) and 45 patients without acromegaly (NP) who were colonoscoped by a single experienced endoscopist.

Total colonoscopy was recorded in 21 (84%) AP and in 43 (95.6%) NP using MEI. The median distance to the caecum in AP was 104cm (IQ range, 93.7–130.5) as compared to 87cm (79–100) in NP (p=0.0009, Mann Whitney U). The median maximum length of colonoscopy inserted was 127.5cm (110–155.1) in AP compared to 110cm (105–120) in NP (p=0.0023). The greatest difference was in the length of colonoscopy inserted to reach the sigmoid-descending junction, 78.5cm (62.9–94.1) in AP compared to 51.3cm (42.4–61.5) in NP (p<0.0001). This was associated with greater complex looping in the sigmoid colon in AP (5/24) than in NP (4/44) (chi square). The median time to the caecum was 772sec (613.5–1063) in AP compared to 563.5sec (400.8–853.6) in NP (p=0.0267, Mann Whitney U).

Conclusion: Patients with acromegaly are more difficult to colonoscopy than normal patients because they have longer colons, which are more prone to loop formation.

PATIENT PAIN DURING COLONOSCOPY—AN ANALYSIS USING MAGNETIC ENDOSCOPE IMAGING (MEI)

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Background: Colonoscopy is generally perceived as being a painful procedure. Stretching of the peritoneal attachments from looping of the colonoscope shaft, overinflation of the degree of torque/force applied to the colonoscope shaft, and patient pain threshold are contributory factors.

Aims: To determine the frequency of pain episodes experienced and the corresponding colonoscope configuration during colonoscopy.

Methods: Consecutive out-patients undergoing colonoscopy were studied. Patients with previous colonic resections were excluded. Procedures were commenced with buscopan only and patient sedation/analgesia self-administered whenever significant discomfort was experienced, using a PCA syringe pump. All ‘demands’ were correlated with the MEI record, which was subsequently analysed.

Results: Pain with the instrument tip in the rectum accounted for 1% of the total demands (5/675). 77% (521/675) of all demands occurred with the colonoscope tip in the sigmoid colon, coinciding with looping (340), stretching of the apex of the sigmoid colon (77), pulling back/shortening colon (30), straightening of a loop (27), sigmoid fixation (2), and with no visible loop (45). 7% (47/675) of demands occurred with the colonoscope tip in the descending colon, coinciding with sigmoid looping (31), straightening of a loop (10) or with a straight scope (6). 6% (39/675) of demands coincided with either recurrent sigmoid looping (28) or sigmoid stretch (11) at the splenic flexure. In the Transverse colon 5% of the total demands (33/675) were secondary to either looping of the sigmoid anteriorly (12), deep transverse looping alone (7), both deep transverse & sigmoid looping (6), shortening of a loop (2), or no visible loop (10). Demands were least frequent in the proximal colon (4% of total 30/675) and coincided with either sigmoid looping (10) or deep transverse/sigmoid looping (13) in the majority. 7 demands were associated either with straightening of a reverse loop or with no visible loop, with the colonoscope tip in the caecal pole.

Conclusions: The majority of pain/discomfort episodes (85%) experienced were due to looping of the colonoscope shaft, most frequently in the sigmoid colon, with overinflation being an infrequent cause (9%). Use of MEI may improve pain control by enabling the endoscopist to ‘target’ patient analgesia, pre-empting any pain episodes.

INTRINSIC ANTI-ENDOTOXIN ANTIBODY MAY BE PROTECTIVE IN INFLAMMATORY BOWEL DISEASE PATIENTS UNDERGOING COLONOSCOPY

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Introduction: Bacteraemia and endotoxaemia may occur following lower gastrointestinal endoscopy. Endotoxaemia is a frequent feature of inflammatory bowel disease (IBD) but there is no apparent increase in morbidity following colonoscopy. This study investigates the hypothesis that anti-endotoxin antibody concentrations are elevated in IBD and may therefore protect patients undergoing colonoscopy.

Methodology: Forty-four patients requiring lower gastrointestinal endoscopy were investigated. Blood was taken before endoscopy to assess IBD severity, endotoxin and endotoxin-core antibody (EndoCAb) concentrations and bacteriological status. Further samples were collected at 1 hour and 1 week after endoscopy for bacteriology and measurement of endotoxin and EndoCAb concentrations.

Results: Seven patients with disease other than colitis were excluded from study. Comparing normal and IBD patients before endoscopy there was no significant difference in the incidence of bacteraemia or endotoxaemia. Endotoxin concentrations were increased in IBD patients 1 hour after endoscopy (p<0.02) but endotoxin concentrations were not significantly higher in colitics. The colitics however had a higher incidence of bacteraemia 1 hour after endoscopy (p=0.05), being most evident in those with severe disease (p=0.01). Compared with controls IBD patients had higher EndoCAb concentrations before 1 hour and 1 week after endoscopy (p<0.02). Patients with more severe disease also had higher EndoCAb concentrations than those with mild disease 1 hour after endoscopy (p=0.03).

Conclusion: Antibodies to endotoxin are higher in IBD patients and systemic concentrations correlate with disease activity. No significant change in endotoxin concentrations in these patients following endoscopy, despite an increased incidence of bacteraemia, would suggest that anti-endotoxin antibodies have a protective effect.

ENDOSCOPIC SURGERY FOR CHOLEDOCHOLITHIASIS WITHOUT SUBSEQUENT CHOLECYSTECTOMY—ANALYSIS OF LONG-TERM RESULTS

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Aims: To analyse the results of endoscopic treatment of bile duct (BD) stones without subsequent cholecystectomy in patients over 64 years old or those undergoing BD clearance.

Methods: All consecutive patients undergoing endoscopic bile duct clearance during six years to 31.12.98 were analysed from various prospectively collected data sources. Statistical analysis—chi-squared test with Yates’s correction.

Results: 174 patients were included (median age of 76 years) of whom 13 were <65 years but were unfit for surgery (age range 49–64). Successful endoscopic sphincterotomy (ES) was achieved in 93% of patients but 29 required surgery to clear the bile duct. Following endoscopic duct clearance, 143 patients were discharged with gallbladders in situ. Mean follow-up was 41.2 months. 15% required subsequent cholecystectomy (due to acute cholecystitis in 8 and recurrent biliary colic in 8 patients). 13% required further endoscopic BD surgery. There was no recurrence of biliary pancreatitis. 58% of patients in the age group 65–70 yrs at initial presentation required subsequent intervention (SI) as compared to 19.5% in patients over 70 (p value = 0.0003). Overall complication rate of ERCP/ES was 5%.

Conclusions: ERCP/ES along without subsequent cholecystectomy is safe and effective for treating high-risk patients with choledocholithiasis, effectively preventing recurrence of biliary pancreatitis and does not increase the risk of subsequent acute cholecystitis. Subsequent cholecystectomy rate of 15% is higher than <11% previously reported. More than 50% patients in 65–70 yrs age group will need further treatment after endoscopic BD clearance. Majority of SI take will place in first 2 years following endoscopic BD clearance. Rate of SI is not related to the length of follow-up. Comparison with laparoscopic bile duct surgery is needed.

GALLBLADDER ENLARGEMENT AFTER MAJOR SURGERY

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Background: Altered gallbladder motility has been implicated in the pathogenesis of gallstones in conditions such as pregnancy or during parenteral nutrition. An increased incidence of gallstones occurs after certain major surgical operations. Alterations in gallbladder motility have not previously been studied in the peri-operative period.

Aim: To measure gallbladder motility in subjects undergoing major non-gastrointestinal surgery in the peri-operative period.

Methods: Subjects undergoing aortic surgery (n=12) and cardiac surgery (n=19) had fasting gallbladder volumes measured immediately before surgery and again after being established on a normal diet.
before discharge from hospital. Ultrasound was used to make triplicate measures of gallbladder dimensions. The mean of each dimension was used to calculate gallbladder volume by the ellipsoid method.

**Results:** Mean fasting gallbladder volumes had increased by 270% in the aortic group and 290% in the cardiac group after surgery, despite the subjects taking diet (see table 1).

**Abstract 379, Table 1**

<table>
<thead>
<tr>
<th>Aortic</th>
<th>Cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op mean volume (standard deviation)</td>
<td>23.3 ml (8.0)</td>
</tr>
<tr>
<td>Median number of days USS performed after diet commenced (range)</td>
<td>3.0 (1-6)</td>
</tr>
<tr>
<td>Median number of days after surgery ultrasound performed (range)</td>
<td>8.0 (5-26)</td>
</tr>
<tr>
<td>Post-op mean volume (standard deviation)</td>
<td>63.5 ml (28.7)</td>
</tr>
<tr>
<td>Paired t-test (pre-op volume vs. post-op volumes)</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** Despite taking diet, fasting gallbladder volumes are increased in patients undergoing major non-gastrointestinal surgery until at least the time of discharge from hospital. Altered gallbladder motility following surgery may produce biliary stasis contributing to an increased incidence of gallstones in these patients.

**380 PREDICTING COMMON BILE DUCT STONES BEFORE PREOPERATIVE ERCP**

A. Li, P.G. Wheeler. Dept of Gastroenterology, William Harvey Hospital, Ashford, Kent, TN24 OLZ, UK

**Background:** A common indication for ERCP is to determine the presence of common bile duct (CBD) stones prior to laparoscopic cholecystectomy. Previous attempts have been made to avoid unnecessary ERCP using preoperative clinical and investigative parameters to select out patients with low probability of CBD stones. A retrospective audit was performed in a district hospital setting and selection criteria were applied to the data.

**Methods:** All patients undergoing ERCP prior to laparoscopic cholecystectomy over a 3-year period were included. Exclusion criteria were ERCP diagnoses of biliary stricture or hepatobiliary neoplasm. Only those with ultrasound reports and liver biochemistry results within 1 month prior to ERCP were included. 108 patients were included. Retrospectively, selection criteria were applied suggesting high probability of CBD stone prior to ERCP. These were: persistent as opposed to resolving jaundice within 1 month prior to ERCP; dilated CBD >7mm diameter, or CBD stone on ultrasound, history of pancreatitis or cholangitis.

**Results:** 63 out of 108 (58%) patients with CBD stones queried prior to laparoscopic cholecystectomy proved to have them on ERCP. Using retrospective selection criteria, 53 of these 63 (84%) patients with CBD stone were correctly identified as requiring preoperative ERCP. 31 out of the remaining 45 patients who did not have CBD stone but who were predicted to have them would have undergone unnecessary ERCP. Prediction of CBD stones thus has sensitivity (84%) but not specificity (31%). Individual predictors of CBD stones were: history of cholangitis, persistent jaundice and CBD dilatation or CBD stone on ultrasound. Age, sex, and history of pancreatitis were not predictive of CBD stones.

**Conclusions:** It is possible, using basic clinical parameters to predict the presence of CBD stone prior to laparoscopic cholecystectomy and reduce the numbers of preoperative ERCP.

**381 MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY VERSUS ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN THE DIAGNOSIS OF CHOLEDOCHOLITHIASIS**

N. Griffin1, M. Wastie1, K. Dunn1, S.D. Ryder1, I.J. Beckingham1. Depts of Surgery, Medicine and Radiology, Queen's Medical Centre, University Hospital, Nottingham, UK

**Background:** Over the last few decades, endoscopic retrograde cholangiopancreatography (ERCP) has become established as the gold standard in imaging of the biliary tree. More recently magnetic resonance cholangiopancreatography (MRCP) has been introduced as a new, non-invasive imaging modality for the detection of common bile duct stones and other pathology related to the biliary tract and pancreas.

**Methods:** A prospective study was carried out of 133 patients referred for both investigations to compare the results of ERCP and MRCP in determining the presence of common bile duct stones prior to laparoscopic cholecystectomy.

**Results:** 18 patients were excluded from the analysis as ERCP was unsuccessful in 8 patients and MRCP was not possible in a further 10 patients. There were 6 false negative results with MRCP and in 5 of these the calculi were less than 5 mm in diameter. MRCP showed a sensitivity of 84%, specificity of 96%, positive predictive value of 91% and negative predictive value of 93% when compared to ERCP as the gold standard.

**Conclusion:** MRCP has both high sensitivity and specificity for stones greater than 5 mm in diameter and should be the first line investigation in patients with gallstones and abnormal liver function tests. Adoption of this guideline at our institution would result in a 9% reduction in the number of ERCP's performed.

**382 RAPID ASSESSMENT OF THE JAUNDICED PATIENT: THE JAUNDICE HOTLINE**

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**Introduction:** In order to meet the challenge of increasing workloads and the governments “two week” rule, innovative reorganisation of existing health services may be required. These factors and a desire to improve our referral system for the acutely jaundiced patient, led to the establishment of an open access jaundice clinic; the Jaundice Hotline.

**Methods:** Referrals are made via a dedicated 24 hour phone line. Patients are assigned to the next available twice weekly clinic. Following a full history and examination, an ultrasound examination is performed by a consultant gastrointestinal radiologist. Appropriate blood tests are taken and the patient is then assigned to the next ERCP list, early outpatient review or direct admission.

**Results:** In the first year 107 patients were seen. 62 patients (58%) had biliary obstruction. The mean time between referral and consultation was 2.5 days. Patients who required an ERCP waited a mean time of 5.7 days. In the 69 patients who required hospital admission, the mean hospital stay was 6.1 days. The majority of these stayed 1 or two days for ERCP. This compares favourably with audit data from 1996 which showed a mean hospital stay of 11.5 days. 97% of patients and 95% of primary care practices rated the service as above average or excellent.

**Conclusions:** This approach to the jaundiced patient results in rapid assessment, diagnosis and treatment as well as reducing hospital stay. Novel reorganisation of existing health services at minimal extra cost will be important to high quality health service provision in the face of the UK governments “two week” cancer ruling.

**383 THE FREQUENCY OF SPONTANEOUS PASSAGE OF BILE DUCT STONES AND RELATION TO CLINICAL PRESENTATION**

S.E. Tranter, M.H. Thompson. Dept of Surgery, Southmead Hospital, Bristol, UK

**Aims:** Little is known about the spontaneous passage of bile duct stones. The aim of this study is to determine the rate of spontaneous stone passage and relate it to the clinical presentation of the bile duct stones.

**Methods:** Prospectively collected data was studied on a total of 1051 consecutive patients undergoing laparoscopic cholecystectomy with or without laparoscopic common duct exploration (LCDE). Comparisons were made between 142 patients with common bile duct stones (CBDs); 519 patients who had previous or current evidence of duct stones and 390 patients who had good evidence of previous duct stones but not present at the time of cholecystectomy. The evidence used for previous duct stones included a good history of jaundice, a raised serum alkaline, abnormal pre-operative liver function tests and/or a dilated common bile duct. We have assumed that this group underwent spontaneous passage of bile duct stones.
Results: 51% of patients undergoing laparoscopic cholecystectomy had a history of previous or current CBDS; 73% of these passed their ductal stones spontaneously prior to operation. Patients presenting with pancreatitis had a statistically significant 80% chance of passing their stones spontaneously (p<0.001). Those presenting with jaundice had only a 55% chance of spontaneous passage; the remainder in each group required LCDE or endoscopic sphincterotomy. All patients with cholangitis had CBDS at the time of operation.

Conclusions: The majority of patients (almost 3 in 4) with CBDS passed their stones spontaneously. Four out of five patients with pancreatitis passed their stones spontaneously, in contrast to patients with jaundice who were less likely to undergo spontaneous resolution. Cholangitis always implied the presence of duct stones.

Abstract 384, Table 1

<table>
<thead>
<tr>
<th>Diverticulae Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number 83 261</td>
<td></td>
</tr>
<tr>
<td>Age 73 (26–89) 72 (51–93) N.S.</td>
<td></td>
</tr>
<tr>
<td>Sex 34 male, 49 fem 100 M, 155 F</td>
<td></td>
</tr>
<tr>
<td>Total with BDS 53 (64%) 86 (33%) P&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>BDS + gallstones 44 74 P=0.003</td>
<td></td>
</tr>
<tr>
<td>Primary BDS 7 2 P=0.005</td>
<td></td>
</tr>
<tr>
<td>BDS, previous cholecystectomy 2 10 P=0.19</td>
<td></td>
</tr>
<tr>
<td>Gallstones/cholecystecomes 56 (67%) 157 (60%) P=0.29</td>
<td></td>
</tr>
<tr>
<td>Biliary strictures 7 (8%) 45 (17%) P=0.07</td>
<td></td>
</tr>
<tr>
<td>H/O pancreatitis 8 (10%) 28 (11%) P=0.94</td>
<td></td>
</tr>
<tr>
<td>Cannulation 78/83 (94%) 249/261 (94%) P=0.82</td>
<td></td>
</tr>
<tr>
<td>Sphincterotomies 49/51 (96%) 85/87 (98%) P=0.98</td>
<td></td>
</tr>
<tr>
<td>Stone extraction 39/37 (94%) 61/69 (88%) P=0.49</td>
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</tbody>
</table>

Conclusions: Duodenal diverticulae are associated with an increased incidence of both primary and secondary bile duct stones. Duodenal diverticulae are not associated with pancreatitis. Duodenal diverticulae did not cause any technical difficulties at ERCAP.

Abstract 385, Oddi Manometry—Use and Safety

W. Jackson, K.R. Wedgwood. Dept of Upper GI Physiology, Castle Hill Hospital, Cottingham, Hull, UK

Introduction: The sphincter of oddi (SO) regulates the flow of pancreatic and biliary juice into the duodenum and prevents duodenal reflux. Sphincter of oddi manometry (SOM) can be used to diagnose dysfunction of the SO and the biliary tract. It is a common practice in Britain for ERCP films to be reviewed by radiologists. The risks of interpreting and treating SOD are such that alternative methods to predict the likely outcome of SOM and sphincterotomy are required. In combination with other techniques, psychological features may help indicate those patients for whom these procedures would be most beneficial.

Results: 32 Ps (20M, 12F-age range 19–91) entered the study. Mean duodenal pressure was 6mmHg (range 0–13). In 12 Ps SO function exhibited normal characteristics with mean SO basal pressure of 19nmHg (range 8–32), WA 128nmHg (range 99–163) and WF of 4/min (range 2–6), 20 Ps had abnormal characteristics. Combinations of 1 or more abnormalities were seen, high SO basal pressures in 5 Ps of 68mmHg (range 42–89). High WA in 3 Ps of 245mmHg (range 199–224). Low WA in 10 Ps of 72mmHg (range 42–93) and abnormal WF in 12 Ps of 12/min (range 7–23/min). Following sphincterotomy 82% of the Ps symptoms improved while 18% remained the same. No patient developed AP with a SSPTC.

Conclusion: The use of SSPTC for SOM reduces the inherent risks of AP caused by WPC. SOM may also identify Pts with abnormal motility resulting in symptoms which may benefit from sphincterotomy.

Abstract 386, Table 1

| Anxiety Depression | SOM (n=22) Normal (n=34) p |
|--------------------|--------------------------|---------|
| 5 (4–8) 8 (5–11) | 0.04 | |
| 2 (1–6) 4 (1–7) | 0.43 | |

Conclusion: Anxiety (but not depression) scores are significantly lower in those with definite SOM. The risks of investigating and treating SOM are such that alternative methods to predict the likely outcome of SOM and sphincterotomy are required. In combination with other techniques, psychological features may help indicate those patients for whom these procedures would be most beneficial.

Abstract 387, Interpretation of ERCP Spot Films by Radiologists—is it Necessary?

S.Z. Abbas, J.R. Lowes, D.K. George, J.L. Isaacs, R.H. Teague. Gastroenterology Dept, Torbay Hospital, Torquay, UK; Radiology Dept, Torbay Hospital, Torquay, UK

Background: It is a common practice in Britain for ERCP films to be reported by the endoscopist carrying out the procedure and also be interpreted by a radiologist afterwards. Its clinical value (and cost-effectiveness) has recently been challenged by an American tertiary centre (DDW 2000).

Aim: To determine the clinical impact of radiologist's post-procedure ERCP spot films interpretation at a DGH in Britain.

Methods: 140 consecutive ERCPs performed on 115 patients by 2 endoscopists and subsequently interpreted by a single radiologist in our unit were retrospectively analysed. Their reports were compared to the ones of the radiologist's (who had the endoscopists' report available at the time of reporting) and were divided into the following 3 categories: I) complete agreement, II) clinically insignificant findings reported by the radiologist but missed by the endoscopists, and III) clinically significant findings (that may have changed the patients' management) reported by the radiologist but missed by the endoscopists. A third gastroenterologist reviewed all the reports in the categories II and III.
Results: The mean age of the patients (65 males; 75 females) was 66 years (range = 27—96). The rate of cannulation of the duct of interest was 127 out of 140 cases (91%), and both endoscopists and radiologist’s reports were available in 118 of these.

Abstract 387, Table 1

<table>
<thead>
<tr>
<th>Categories n (%)</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>104</td>
<td>11</td>
<td>3</td>
<td>118</td>
</tr>
</tbody>
</table>

Conclusion: The role of radiologists’ interpretation of post-procedure ERCP spot films is small but significant. We believe this procedure should continue but be subject to further review.


388 THE ROLE OF SPIRAL CT CHOLANGIOGRAPHY IN PATIENTS WITH ABDOMINAL PAIN POST CHOLECYSTECTOMY

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Introduction: Patients (pts) with biliary type abdominal pain post cholecystectomy are often referred to gastroenterologists for ERCP. In view of the recognised risks associated with this procedure, the role of spiral CT cholangiography (sCTC), which has been shown to be highly sensitive for the detection of bile duct filling defects, in addition to ultrasound (US) and liver function tests (lfts), was examined to determine if all requests were appropriate.

Methods: 20 pts (7 male, 13 female, age range 32–83 yrs), in whom ERCP was not thought to be immediately indicated, were referred to sCTC. All had had a cholecystectomy within the last 5 years. No pt was jaundiced. After lfts and US had been performed, all patients had sCTC using i.v. bilioscopin, reported by one consultant radiologist. Only pts shown to have biliary stones by sCTC underwent ERCP.

Results: sCTC was successful in 18/20 pts (contract may not be excreted if there is abnormal liver function). 5 pts had biliary stones detected by sCTC (4 with normal calibre bile ducts on US); these were all confirmed at ERCP. 13 pts had a normal sCTC. Only 11 of these pts had had a previous US, each of which was normal. sCTC was normal in the 9 pts with normal lfts. 5 patients with abnormal lfts had a normal sCTC.

Conclusion: sCTC provides high resolution images of the biliary tree in the majority of patients. It is capable of picking up stones even in the presence of a non dilated biliary tree on US. sCTC should be considered in selected patients prior to ERCP and may prevent unnecessary procedures.

Liver Posters: 389–410

389 ORTHOTOPIC LIVER TRANSPLANTATION, PSC, IBD AND COLORECTAL CARCINOMA


Aim: We reviewed our centre’s experience of prevalence of IBD in patients undergoing transplantation for PSC, indication for colectomy and incidence of colorectal carcinoma.

Methods: Patients were identified from a prospectively maintained database then retrospective case note analysis was undertaken.

Results: 9/16 patients underwent orthotopic liver transplantation between January 1982 & February 1999 and subsequently followed up for >12 months. 105 were transplanted for PSC (with no evidence of cholangiocarcinoma), 78 men and 27 women with a mean age of 45.5 years were followed up for a median of 61 months (range 13–143). Pre-transplant 66 patients (62.9%) were diagnosed with UC and 4 (3.8%) with Crohns. Post-transplant this rose to 78 (74.3%) with UC and 5 (4.8%) with Crohns. Colectomy for non malignant indications: pre-transplant - 9 (2 dysplasia, 7 symptomatic), peri-operatively - 1 for dysplasia, post-operatively - 5 (1 dysplasia, 4 symptomatic). 7 patients, all with UC, developed colorectal adenocarcinoma and 1 caecal lymphoma. Incidence of colorectal adenocarcinoma in patients transplanted for PSC with an intact colon in the transplant was 7.4% compared with 0.8% for the rest of the transplant group (p<0.05) and 12.3% in patients with UC diagnosed prior to transplantation for PSC. Malignancy arose after a median of 4.5 yrs and all had colitis for >18yrs.

Conclusion: Patients with PSC and longstanding UC have a considerably increased risk of developing colorectal adenocarcinoma post liver transplantation and should be screened aggressively.

390 WORLDWIDE TRENDS IN MORTALITY RATES FOR HEPATOBIARY AND PANCREATIC TUMOURS, 1979–1997

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Background: The age-standardised mortality rate (ASMR) per 100,000 population for hepatocellular carcinoma (International Classification of Disease-9 155.0) is increasing in several countries including USA and Japan; but in England & Wales we previously reported an increase in ASMR for intrahepatic cholangiocarcinoma (ICD-9 155.1) only. To investigate this further we analysed mortality statistics from North America, Japan, Australia and Europe to compare ASMR of subcategories of hepatobiliary and pancreatic tumours.

Methods: ASMR for men and women for subcategories of liver tumours (ICD-9 155), tumours of the gall bladder and extrahepatic biliary tree (ICD-9 156) and pancreas (ICD-9 157) from 1979 to 1997 were obtained from the World Health Organisation mortality database.

Results: We confirmed increases in ASMR for hepatocellular carcinoma in those countries were previously reported, but also found significant rises in other countries, particularly France (2.4 to 7.6). There was also an increase in ASMR for intrahepatic cholangiocarcinoma in nearly all countries studied, with large rises seen in Scotland (0.2 to 1.0), Australia (0.1 to 0.7) and USA (0.2 to 0.6). There was a general downward trend in extrahepatic and pancreatic malignancies, with the exception of Southern European countries and Japan.

Conclusion: We confirm previous studies of rising death rates from hepatocellular in several countries, although the trends were not uniform amongst all countries. We also present a hitherto unreported rise in mortality rates for intrahepatic cholangiocarcinoma across 4 continents. This cannot readily be explained by diagnostic transfer from other tumour types, or by improved diagnosis and reporting. Future research on cholangiocarcinoma should include epidemiological studies to examine possible case-clustering and investigation of potential aetiological agents including environmental toxins. ASMR from hepatobiliary and pancreatic tumours are not static and require close future monitoring.

391 POSITIVE CRITERIA FOR PREDICTING MALIGNANCY IN BILIARY BRUSHING CYTOLOGY

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A total of 125 patients with biliary stricture and tumour masses had brushing cytology over a period of 3 years (1997–2000). One hundred and thirty five biliary brushing specimens with a known outcome were reviewed. On review an additional category of atypical probably benign was added (table). The review was carried out blind with no clinical or outcome information by two pathologists. On review the following criteria was considered indicative of malignancy: increased nuclear size, convoluted nuclear outline, abnormal chromatin pattern, increased nucleolar area and numbers, loss of cohesiveness and overlapping of nuclei. Only the negative for malignancy and malignant categories of test result were used to determine the value of the test. The results were as follows:
Both originally and on review the specificity and the predictive value of a positive result were 100%. However on review the accuracy increased from 60% to 89%, the sensitivity increased from 50% to 88% and the predictive value of a negative result increased from 34% to 43%.

Conclusion: The use of additional criteria has resulted in a marked improvement in the accuracy of malignant diagnosis in biliary brushing cytology.

Aim: To assess the haemodynamic effects and patients tolerability of the acute and chronic administration of low dose carvedilol.

Study design: 10 patients with mean age 54±12years were studied. Causes of cirrhosis were alcohol-7, primary biliary cirrhosis-1, and hepatitis C-1. Child's grade: A-1, B-6, C-3. 2 patients had ascites and 4 ascites in the past. Following baseline haemodynamic measurements patients were administered 12.5mg of oral carvedilol and the measurements repeated 1 hour later. The patients continued taking 12.5mg carvedilol daily for four weeks and the study was then repeated.

Results: Following acute administration of carvedilol, there was a 23% reduction in the hepatic venous pressure gradient (HVPG) from 16.37±2.14 to 12.56±3.91 mmHg (p<0.05), mainly due to a reduction in the wedged hepatic venous pressure (WHVP), with significant falls in the mean arterial pressure, pulse and cardiac output. Chronic administration resulted in a further fall in the HVPG from a reduction in the wedged hepatic venous pressure (WHVP), with significant improvement in the accuracy of malignant diagnosis in biliary brushing cytology.

Conclusion: The use of additional criteria has resulted in a marked improvement in the accuracy of malignant diagnosis in biliary brushing cytology.

Abstract 391, Table 1

<table>
<thead>
<tr>
<th>Result</th>
<th>Inadequate</th>
<th>Negative</th>
<th>Asymptomatic</th>
<th>Suspicious</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>7 (6%)</td>
<td>56 (47%)</td>
<td>19 (16%)</td>
<td>37 (31%)</td>
<td></td>
</tr>
<tr>
<td>Review</td>
<td>10 (8%)</td>
<td>14 (12%)</td>
<td>21 (18%)</td>
<td>13 (11%)</td>
<td>61 (51%)</td>
</tr>
</tbody>
</table>

Prospective study of liver dysfunction in pregnancy in south wales

C.L. Ch'ng, M. Morgan, I. Hainsworth, J.G.C. Kingham. Swansea NHS Trust, SA2 8QA, UK

Background and aims: Liver disease is uncommon in pregnancy but has serious consequences. Its frequency varies according to country, ethnic origin and not documented in Wales. We have prospectively determined incidence, causes and outcome of liver dysfunction in obstetric unit in South Wales.

Methods: A central laboratory identified all abnormal liver tests from patients in antenatal clinics and wards of an obstetric unit serving a population of 270,000. During the sixteen-month study, there were 4637 deliveries. Patients with abnormal tests (bilirubin >25µmol/L, aspartate transaminase (AST) >40U/L and/or gamma GT (GT) >35U/L) were studied prospectively on receipt of blood results and medical advice was provided to obstetricians. Clinical course of mother and fetus/infant was recorded.

Results: 140 patients had abnormal liver tests: elevation of AST in 115 (range 41–9299), GT in 58 (range 36–278) and bilirubin in 24 (range 26–155). Thrombocytopenia (<100 x 10^9/L) was seen in 33, raised bile acids in 18 (range 23–149 µmol/L) and hyperuricaemia in 32 (range 41–0.70 µmol/L). Hepatobiliary ultrasound scan (US) was abnormal in 8. There were 173 diagnoses amongst 131 patients: pre-eclampsia 63, obstetric cholestasis (OC) 21, HELLP syndrome 15, hyperemesis gravidarum 10, acute fatty liver 5, sepsis 12, post-Caesarean section 22, biliary duct stones 3, placental pathology 9, diabetes 6, drug toxicity 5, hepatic haematoma 1 and chronic hepatitis C 1. Elevation of AST was the predominant abnormality in OC. There were no maternal deaths but there was one intrauterine death at 30 weeks associated with pre-eclampsia. Sixty five patients required delivery by induction or Caesarean section to improve hepatic function. Thirty seven babies required admission to special care unit.

Conclusions: Liver dysfunction was seen in 140 of 4637 pregnancies (frequency 1 in 33) during a sixteen-month prospective study. Transient but sometimes serious effects on maternal and infant morbidity were observed but there were no maternal deaths and only one stillbirth.

Table 1

<table>
<thead>
<tr>
<th>Result</th>
<th>Inadequate</th>
<th>Negative</th>
<th>Asymptomatic</th>
<th>Suspicious</th>
<th>Malignant</th>
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<td>13 (11%)</td>
<td>61 (51%)</td>
</tr>
</tbody>
</table>

How well tolerated is day case liver biopsy?

M Neilson, C Adams, T Joyce, I Akerdine, A.J. Stanley, A. Morris. Dept of Gastroenterology, Royal Infirmary, Glasgow, UK

It is recognised that day case liver biopsy is under-utilised in UK hospitals. Little is known about post discharge events in patients having this procedure.

Patients/methods: All patients satisfying BSG criteria for day case liver biopsy have been followed up to establish post discharge morbidity. Patients follow a structured protocol, identifying route for readmission if necessary. All patients are contacted by nursing staff 24 hours post procedure to establish the need for analgesia, GP visit and hospital admission. A total of 147 patients have been studied over 39 months (61 female 86 male) median age 40 years. Indication for
biopsy was Hepatitis C 0.4, Investigation of Abnormal Liver function 26, Autoimmune Hepatitis 5, Primary Biliary Cirrhosis 5, Methotrexate therapy 4, Haemochromatosis, Iron overload 7, Hepatitis B 2.

Biopsy method, Trucut needle n = 100, Trucore biopsy gun n = 47. Number of passes, 1 pass n = 119 (80.95%), two passes n = 25 (17%), three passes n = 3 (2.04%)

Results: 145 patients were discharged on the same day, 2 (1.36%) required overnight stay for observation. 139 of 145 were contacted by telephone the next day. 43 (29.25%) required analgesia at home. 4 (2.72%) called out GP. 3 (2.04%) returned to the hospital for review, one patient required readmission. (0.68%). 21% of patients biopsied with a trucore biopsy gun required analgesia at home while 33% biopsied by trucut needle required analgesia at home.

Conclusion: (1) Day case liver biopsy is safe in selected patients. A significant number of patients suffer post discharge pain requiring analgesia but little other morbidity was observed. (2) The use of the Trucore biopsy gun may reduce the need for analgesia post biopsy.

Abstract 397, Table 1

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=11) S.D.</td>
<td>(n=8) S.D.</td>
</tr>
<tr>
<td>Apparent amino acid conjugation [%]</td>
<td>40.83 ± 6.57</td>
<td>9.74 ± 13.36 ±16.9</td>
</tr>
<tr>
<td>Time to peak PDR [min]</td>
<td>53.5 ± 5.3</td>
<td>92.5 ±16.9</td>
</tr>
</tbody>
</table>

Conclusion: Apparent amino acid oxidation and time to peak PDR provide good discrimination between cirrhotic and non-cirrhotic individuals. The encouraging results of this pilot study warrant further investigation (a) to establish sensitive and specific cut-off values and (b) to assess the prognostic value of this new test.

Abstract 398, Table 1

<table>
<thead>
<tr>
<th></th>
<th>%5/96</th>
<th>%96/97</th>
<th>%97/98</th>
<th>%98/99</th>
<th>%99/00</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tests</td>
<td>1063</td>
<td>1380</td>
<td>1365</td>
<td>1168</td>
<td>1346</td>
</tr>
<tr>
<td>All +ve tests</td>
<td>319</td>
<td>362</td>
<td>403</td>
<td>358</td>
<td>440</td>
</tr>
</tbody>
</table>

*Pack-size change.

Conclusion: These results do not suggest that the incidence of paracetamol overdose has been affected by the over-the-counter pack size reduction at least in the Tayside region of Scotland. Further measures to reduce the burden of paracetamol overdose to the healthcare system must be considered.
indirect immunofluorescence, and for IgG- and IgA-gliadin antibod-
ies (AGA) by an ordinary ELISA. Ten serum samples from
biopsy-proven CD patients were served as methodological controls.

**Results:** AGA were detected with a significantly increased
frequency in patients with both PBC and AIC (21% and 35% vs 3% respec-
tively, P < 0.001). IgA-TTG were also found in 6 of 62 PBC
patients (10%), in 3 of 17 patients with AIC (18%), in all of 10 CD
patients, but not in blood donors. ARA and AMA were negative in
patients with PBC and AIC and in healthy controls. Intestinal biopsies
were performed in 47% of PBC and in 71% of the AIC patients with
at least one antibody positive. No evidence of coeliac disease was
found.

**Conclusions:** Our findings do not support the association between
PBC, AIC and CD. In liver disease gliadin and transglutaminase anti-
obodies are not useful in screening for CD, whereas the EMA test and
intestinal biopsy remain the gold standard.

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**400 THE INFLUENCE OF PRE-ADMISSION DIET UPON
LIVER FUNCTION TESTS OF PATIENTS WITH ACUTE
ALCOHOLIC HEPATITIS**

troenterology, Royal Infirmary, Glasgow, UK

Diet has been implicated in the development of alcoholic liver disease.
Epidemiological studies suggest a diet high in saturated fatty acid
(SFA) is associated with a lower mortality from alcoholic cirrhosis,
and polyunsaturated fatty acid (PUFA) is an important factor for the
development of alcoholic liver damage in rat models. The role of diet
in the aetiology of alcoholic hepatitis is unknown.

**Aim:** To assess the role of pre-admission diet on liver function
tests.

**Methods:** Nine patients presenting with acute alcoholic hepatitis
(AAH) diagnosed on clinical grounds were assessed. A detailed
history was obtained of their diet over the two weeks prior to admiss-
on.

**Results:** Patients were aged of 44.4 ± 2.8 years with admission
serum bilirubin of 200.1 ± 32.2. The energy intake was 2928 ±
423 kcal (49.5 ± 6.3% from alcohol). Patients with <8% of energy
from SFA had higher admission AST (342.7 ± 72.1 kcal of 128.6 ± 11.3;
p<0.02) and SB (280.8 ± 43.0 of 137.0 ± 18.1: p<0.02). Correlations of
admission AST, but not ALT, and SB were as follows:

<table>
<thead>
<tr>
<th>% kcal:</th>
<th>% kcal:</th>
<th>% kcal:</th>
<th>% kcal:</th>
<th>% kcal:</th>
<th>% kcal of</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>SFA</td>
<td>PolyE</td>
<td>Alcohol</td>
<td>RDI</td>
<td>Fat</td>
</tr>
<tr>
<td>AST</td>
<td>r = 0.796</td>
<td>r = 0.816</td>
<td>r = 0.712</td>
<td>r = 0.822</td>
<td>r = 0.796</td>
</tr>
<tr>
<td>SB</td>
<td>r = 0.763</td>
<td>r = 0.715</td>
<td>r = 0.736</td>
<td>r = 0.822</td>
<td>r = 0.796</td>
</tr>
</tbody>
</table>

Estimated dietary intake of vitamin C, selenium or vitamin B6 did
not appear to affect standard biochemical liver function tests, nor
did diet correlate with the prothrombin time or discriminant function.

**Conclusions:** AST activity and SB in AAH appear to be related to
the amount of fat, particularly SFA, and alcohol in the diet. As AST
derives from mitochondria, a low fat diet, especially if low in SFA,
with a high % caloric intake as alcohol may predispose to mitochon-
deral dysfunction. Pre-admission diet may therefore significantly
modify the expression of acute alcoholic hepatitis.

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**401 ALCOHOL CONSUMPTION PATTERNS IN HEAVY
DRINKERS WITH AND WITHOUT ALCOHOLIC LIVER
DISEASE (ALD)**

Gastroenterology and Liver Unit and Dept of Radiology, Royal Hallamshire
Hospital Sheffield, UK

**Background:** The risk of ALD increases with increasing alcohol
consumption; it is unclear whether the risk is also related to drinking
pattern or to type of alcoholic beverage consumed.

**Aim:** To compare patterns of lifetime alcohol intake in two previ-
ously characterised (Hepatology 2000 32:A20) cohorts of heavy
drinkers (>60U/wk/M) or 40U/wk (F) for >5yr): one with decompens-
ated ALD (patients: n=147, 107 M, age 48±SD10yr) and one with
no clinical, laboratory or ultrasound evidence of serious liver disease
(controls: n=101, 79M, age 48±SD9yr).

**Methods:** Lifetime total alcohol intake (LTA) and intake of
beer/lager, spirits, wine/sherry and cider to first decompen-
sation (patients) or to interview (controls) was assessed using the time-line
follow back method. Correlation of LTA between repeated testing and
between spouse estimates was 0.86 (n=9) and 0.81 (n=9) respectively.

**Results:** LTA was higher in controls (median 138840U, IQR
100776–190424) than in patients (median 114712, IQR 80262–
165984); p<0.02 by Mann-Whitney (M-W). Spirit, wine and cider
consumption increased with time in both cohorts; in contrast,
beer/lager consumption either did not change (patients) or fell (con-
trols). Controls drank more beer/lager (median 103064, IQR 41912
to 156312) than did patients (median 61,152, IQR 21658–109733);
M-W p<0.01. In contrast, spirit consumption tended to be higher in
patients (median 0U, IQR 0–54080) than in controls (median 0U,
IQR 0–25688); whilst this difference was not significant by M-W,
the distribution of patients tended towards higher levels of spirit
consumption than did that of the controls (2x Chi2 16.9; p<0.05).
Cider and wine consumption did not differ between the cohorts.
The proportions of time spent in constant drinking (≥5 days/wk),
weekend-only drinking, binge drinking and abstinence were similar in
the two cohorts.

**Conclusion:** These data point towards the existence of factors
other than total alcohol consumption in the development of ALD.

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**402 EVIDENCE A REDUCTION IN HEPATIC PERFUSION
DURING EARLY ABSTINENCE IN ACUTE ALCOHOLIC
HEPATITIS**

troenterology and Nuclear Medicine, Royal Infirmary, Glasgow, UK

**Background:** It has been noted that patients with acute alcoholic
hepatitis (AAH) often worsen several days after admission to hospital
and abrupt cessation of alcohol. The reason for this deterioration
is unknown.

**Aim:** We aimed to assess hepatic perfusion and uptake of colloid
by Kupffer cells in 10 patients with AAH within 3 days of alcohol cessa-
tion.

**Methods:** Each patient underwent paired liver sulphur colloid
scans: early (day 1–3) and late (day 7–9) after admission. First-pass hepatic arterial (G1) and portal venous gradients (G2) were measured
and the hepatic perfusion index (HPI%) was calculated using the for-
ula G1/G1+G2*100%. Overall uptake in the liver was assessed relative
to that of the vertebral bodies (L/V ratio).

**Results:** The patients had a mean Discriminant Function (DF) of
45.4 ± 6.8. All patients survived the episode of AAH. Changes seen
between early and late scans are shown:

<table>
<thead>
<tr>
<th>L/V ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
</tr>
<tr>
<td>44.5 ± 28.0</td>
</tr>
<tr>
<td>0.8 ± 12.8</td>
</tr>
<tr>
<td>98.9 ± 27.8</td>
</tr>
<tr>
<td>1.4 ± 0.88</td>
</tr>
<tr>
<td>Late</td>
</tr>
<tr>
<td>34.6 ± 17.5</td>
</tr>
<tr>
<td>0.7 ± 8.0</td>
</tr>
<tr>
<td>82.9 ± 18.3</td>
</tr>
<tr>
<td>1.6 ± 0.89</td>
</tr>
</tbody>
</table>

**Conclusion:** Kupffer cell function is impaired at the time of
admission with AAH and this dysfunction persists throughout the first
7–10 days. Hepatic perfusion however diminishes during this period
of time and may explain why patients who are ill on admission often
become more so during the second week of hospitalisation.

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**403 STUDY OF ACUTE LIVER FAILURE IN SCOTLAND**

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Plevris, P.C. Hayes, K.J. Simpson. Liver Unit, Royal Infirmary of Edinburgh
EH3 9YW, UK

**Introduction:** Acute liver failure (ALF) is a devastating condition
which although rare retains a high mortality. New information on its
incidence and outcome are important in planning for this condition.
Aims: (1) To accurately describe the incidence and outcome of ALF in Scotland. (2) To determine the contribution that social deprivation has in determining outcome in patients with ALF.

Methods and patients: Data was prospectively collected for 227 ALF admissions to the Scottish Liver Transplant Unit (SLTU) from 1992–2000. Trey and Davidson’s definition of ALF was used. Information was collected on outcome, consideration for transplant and markers of social deprivation (DEPCAT score).

Results: The incidence of all cause ALF and paracetamol-induced ALF (POD) in Scotland in 1999 was 0.588/100,000 and 0.4/100,000 population respectively and has not changed. The mean age of patients was 36.9 +/-0.93 years; 39.2% were male and 60.8% female. The causes of ALF were paracetamol (74.0%), Non-A-E hepatitis (6.1%), idiopathic (7.3%) & idiosyncratic drug reactions (4.8%). Of the 168 POD patients, 80 met the King’s College Poor Prognosis Criteria (KCPCP criteria) and 39 were listed for OLT. Of these 25 were transplanted and 14 died before OLT. Of the 41 patients not considered suitable transplant candidates 1 spontaneously recovered. Of the 88 patients who did not meet the King’s College poor prognosis criteria 18 died. The common reasons for not listing POD patients were ongoing alcohol dependence (29.3%), patients were too sick for transplant (24.4%) or significant psychiatric illness (22%). The commonest cause of death in POD patients was multi-organ failure (70.8%) and refractory elevations of ICP (23.6%). The POD group contains a greater proportion of patients with higher DEPCAT and DEPCAT scores compared with all cause ALF (p=0.04). There is no relationship between DEPCAT score and other outcomes such as meeting of KCPCP criteria, listing for OLT or death.

Conclusion: (1) Paracetamol remains the commonest cause of ALF in Scotland and has not decreased after legislative changes. (2) Only 51.2% of POD patients meeting KCPCP criteria were listed for OLT. (3) Whilst social deprivation in Scotland is associated with a higher rate of paracetamol-induced ALF, there was no difference (by DEPCAT score) in outcomes such as ALF severity, consideration for transplant or death.

The true size of the problem of chronic viral hepatitis is becoming apparent, the real costs in population terms have only so far been modelled. This study examined the heath resource use and costs associated with chronic viral hepatitis from diagnosis, compared with the general population. Cause of death was also examined.

Methods: A purpose-built register of liver disease in Tayside, ELDIT, was used. The study population comprised residents of Tayside, Scotland in the study period 1991 to 1997. Subjects HCV or HBsAg positive were identified from ELDIT. Two comparators from the general population were allocated by age (5 year band)-sex. This study examined the heath resource use and costs associated with HBV-specific CD8+ cell response in hepatitis B virus infection.

Distinct functional patterns of HBV-specific CD8+ cell response in hepatitis B virus infection

G.J.M. Webster, S. Reijn, F. Malacarne, D. Brown, G. Ogg, M. Lascar, R. Williams, G.M. Duheiko, A. Bertolletti. Centre for Hepatology, and Institute of Hepatology, Royal Free and University College Medical School, London; Institute of Molecular Medicine, Oxford, UK

Introduction: The range of manifestations of HBV infection suggests a degree of variability in host/virus interaction. We analysed longitudinally the frequency and function of HBV-specific CD8+ cells in different disease profiles of hepatitis B.

Methods: 15 HLA-A2+ subjects were studied longitudinally for 9–24 months, with 3 subjects in each group: resolved acute hepatitis B: Gp A (HBV DNA undetectable, ALT normal); chronic hepatitis B: Gp B (HBV DNA<10pg/ml, ALT<40IU/L); Gp C (HBV–10, ALT 40–80); Gp D (HBV>100, ALT<80); Gp E (HBV–00, ALT>80). Core, envelope, and polymerase-specific CD8+ cells were directly analysed by flow cytometry, after staining with HLA-A2/HBV peptide tetramer complexes. In parallel, expansion capacity and γIFN production of CD8+ cells specific for 11 HLA-A2 restricted epitopes was tested. Frequency of intrahepatic HBV-specific CD8+ cells was obtained at liver biopsy in all patients in groups C–E.

Results: Differences in direct cell frequency were seen in liver, where HBV-specific CD8+ cells were virtually undetectable in groups D and E (0.02–0.3% of CD8+), but clearly detectable in group C (0.9–1.4% of CD8+), whereas the frequency of these cells was usually not above background frequency. In contrast, different patterns of circulating HBV-specific CD8+ were demonstrable when expansion capacity and γIFN production of expanded CD8+ cells was tested. Gp A showed greatest potential for multispecificity (at least 3 of 11 HLA-A2 restricted epitopes). Although HBV-specific CD8+ cells in chronic HBV patients showed a reduced ability to expand in vitro, a multispecific CD8+ response was repeatedly present in Gp C patients, whereas this pattern was present only during a flare of disease (ALT 1200 U/L) in one patient in Gp D, and was entirely absent in Gp E. Of interest, patients in Gp B, who control HBV without clinical liver injury, demonstrated only a mono/oligoclonal response.

Conclusion: This study shows that patients chronically infected with HBV possess a heterogeneous pattern of virus-specific CD8+ response, suggesting that the understanding that most HCV-infected patients may be characterised by a failure to expand a multispecific CD8+ cell response merits reappraisal.

Precore HBV mutant infection is more common than expected among HBV carriers in Scotland

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Background: Chronic Hepatitis B is uncommon and HBV precore mutant infection is presumed to be low in Scotland.

Aims: (1) Compare HBeAg(+) with AntiHBe(+) carriers 2) Analyse virological characteristics of AntiHBe(+) carriers

Methods: Review of 109 chronic HBsAg(+) patients referred to our centre from Jan’89 to Dec’98. PCR (qualitative and semi-quantitative) for HBV DNA in Anti e (+) patients and molecular sequencing of DNA(+) samples for the HBV precore mutant.

Results: 1) 65(60%) patients were Anti e (+) and 44(40%) e Ag(+). No difference was found in epidemiological and clinical features except sexual transmission being more common in the e Ag(+) group (p<0.001). 35(65%) of Anti e (+) patients had raised ALT, the mean of which was 4x ULN and this did not differ significantly from that in the e Ag(+) group. Liver histology results were also similar between e (+) and Anti e (+) patients with >90% showing features of chronic hepatitis +/- cirrhosis. 2) 27/35 (80%) Anti e (+) patients with raised ALT levels had liver biopsies and all were abnormal; 18(51%) showed features of chronic hepatitis +/- cirrhosis. 47/65 serum samples were analysed and 39/47(83%) found positive for HBV DNA (>50 copies/ml serum). 29/37(79%) had the A1896 precore HBV mutant. 10/29 (34%) were British patients. 21/29(72%) had HBV DNA levels >5000 copies/ml. Quantitated DNA was also found to correlate positively and significantly with ALT. (Pearson 2-tailed correlation: r=0.7, p<0.001).

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Conclusions: 1) HBV carriers, whether eAg(+)- or Anti e(-)+, were comparable in epidemiological, clinical, biochemical and histological characteristics. 2) 54% Anti e(-)+ patients presented with raised ALT; of these virtually all had chronic hepatitis +/- cirrhosis. 3) Ongoing viraemia was detected in >80% of Anti e(-)+ patients. 4) 74% of Anti e(-)/DNA+ patients had the classical precore HBV mutant. 5) Quantitative HBV DNA levels correlated positively and significantly with ALT levels.

407 NEURAL NETWORKING IN HEPATITIS C PATIENTS TO PREDICT KNO德尔 SCORES

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Hepatitis C is a relatively common disease and prone to chronicity. Liver biopsy and grading by the Knodell method in a patient with chronic Hepatitis C provides valuable information regarding treatment but is associated with a certain degree of risk. Recently published work [Tharakan] proposes clinical algorithms to predict the Knodell score in Hepatitis C patients. It is anticipated that accurate predictions of the score could make liver biopsies obsolete.

We aimed to test this hypothesis by building and training suitable neural networks and prospectively validating our predictions in a single blinded manner. Our system builds and validates training, evaluates them, selects the top networks, throws in a few mutations and goes back into the training/testing cycle back again. Data from 20 Hepatitis C patients were used as input variables. Neural networks were built and trained from these data with the best networks chosen to predict the Knodell score. The data from 25 Hepatitis C patients including genotype, AST level, age and past medical history of blood transfusions, operations, and tattooing were forwarded to us from two different centres, which formed a set of variables. Prediction of the Knodell score was elaborated for each individual patient using the best neural networks. Predictions of the Knodell score were then compared with the actual values obtained from two independent Histopathologists. We used student t-tests to compare the group of predicted versus actual values of the Knodell score. Predicted versus actual values of the Knodell score correlated highly significantly (p<0.0001). Predictions of the Knodell score were possible at an over 95% accuracy level. It is concluded that neural networks may be useful to predict the Knodell score with a high level of accuracy. Liver biopsies for the assessment of Hepatitis C patients in order to make treatment decisions may therefore be avoided.

408 ACUTE AND CHRONIC EFFECTS OF INTERFERON ALPHA THERAPY ON MOOD AND THE HYPOTHALAMIC PITUITARY ADRENAL (HPA) AXIS IN PATIENTS WITH CHRONIC HEPATITIS C

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Background: Fatigue and depression are common sequelae of interferon alpha therapy. The pathogenesis of this is unclear. Interferon at low doses (+/- 5 million units) is known to stimulate the HPA axis. Dysregulation of this axis occurs in up to 60% of patients with major depression secondary to Interferon a/Ribavirin.

Aims: (1) To determine if low dose Interferon a / Ribavirin combination effects the HPA axis and (2) To determine if major depression secondary to Interferon a was associated with chronic hypercortisolaemia.

Methods: 10 patients with chronic Hepatitis C were assessed before treatment [with Interferon a and Ribavirin], 30mins following 3 million units of interferon a, and after 1 month of combination treatment. Serum cortisol was evaluated by estimation of the mean cortisol value of 10 sequential sampled taken between 1pm to 4pm, at twenty minute intervals, on the test days as outlined above (Halbreich method).

Results: There was a significant increase in fatigue and depression scores measured by both BDI, (±0.7+/- 4.8 before compared to 15.3 +/- 5.0) after one month of treatment, and by HAM, (3.8 +/- 1.8 before compared to 11.8 +/- 2.8) after one month of treatment with combination therapy (Interferon a /Ribavirin). 30% of patients fulfilled criteria for DSM-IV major depression after one month of treatment. None of the patients demonstrated demethasone supression at baseline or on follow up and there was no significant change in mean cortisol [271.7 +/- 39.9 vs 260.6 +/- 28.5 nmol/l,p=0.81]. Serum cortisol did not change during the first 3.5 hours following low dose Interferon a.

Conclusion: In contrast to high dose Interferon a, low dose Interferon a does not stimulate the HPA axis either acutely or chronically. Depression, which we observed in 30% of subjects taking the combination e(+) / Ribavarin, may occur via other mechanisms eg. Proinflammatory cytokine activation and we are currently investigating this possibility.

409 VALIDATION OF THE REVISED INTERNATIONAL AUTOIMMUNE HEPATITIS GROUP (IAHG) SCORING SYSTEM: EXPERIENCE IN THE NORTH OF ENGLAND

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Introduction: Autoimmune hepatitis (AIH) is a chronic necroinflammatory liver disease of unknown aetiology. Diagnosis demands exclusion of other causes of liver disease. The IAHG has recently established a revised scoring system to define definite & probable AIH (J Hepatol 1999; 31: 929–38). We aimed to apply this revised scoring system to a series of patients diagnosed as AIH from the North of England, in order to verify its sensitivity and specificity.

Methods and methods: 10 patients diagnosed as AIH between June 1972 - March 2000 from 11 hospitals in our region were enrolled in this retrospective study (87 F, 19 M; mean age at presentation 49.27 yrs ± 16.57, mean follow-up 6.64 yrs ± 5.3). The medical records of all patients were reviewed, data required for the IAHG score were entered onto an anonymous database, and the score was calculated for each patient (pre-treatment: definite AIH >15, probable AIH 10–15, post-treatment: definite AIH >17, probable AIH 12–17).

Results: At presentation 43 (41%) patients had cirrhosis. 91 (85%) patients had “classic” Type 1 AIH with +ve antinuclear antibody (ANA) and/or smooth muscle antibody (SMA). 8 patients presented <20 yrs of age, 9 at 21–30 yrs, 14 at 31–40 yrs, 19 at 41–50 yrs, 40 at 51–65 yrs and 16 at >65 yrs of age. Pre-treatment mean IAHG score was 18.4 ± 3.7, 81 with definite, 22 with probable, 3 with score <10 [One with +ve ANA but history of exposure to Diclofenac, one with +ve SMA but histology compatible with autoimmune cholangiopathy, one with +ve ANA but histology compatible with PBC]. Post-treatment mean IAHG score was 21.4 ± 3.5, 85 with definite, 18 with probable, 3 with score <12. During follow-up 10 patients have received a liver transplant, & 4 patients have died, one with hepatocellular carcinoma.

Conclusions: This study demonstrates that the revised IAHG criteria will be generally applicable in clinical practice in defining disease groups. Patients with the “classic” condition can be distinguished from those with variant forms of AIH.

410 INTEGRIN RECEPTOR EXPRESSION CHANGES IN DISEASED HEPATIC STELLATE CELLS

H.L. Reeves, A.D. Burt, C.P. Day. University of Newcastle-upon-Tyne, UK

The extracellular matrix (ECM) is now recognised as exerting a powerful influence on cell phenotype. Hepatic stellate cells are the principal effector cells of liver fibrosis. If isolated and maintained in vitro on a normal basement membrane-like matrix such as matrigel, they remain quiescent, poorly proliferative cells, producing small amounts of normal basement membrane proteins, such as type IV collagen and fibronectin. If, however, the cells are cultured on type I collagen, representing the 'scrat' matrix of cirrhosis, they rapidly transform into a highly proliferative myofibroblast-like phenotype, producing greatly increased quantities of type I collagen. The communication between cells and their ECM is through cell surface receptors called integrins. These are heterodimeric transmembrane protein complexes composed of a α and a β subunit, whose ligands are matrix molecules rather than cytokines. In this study stellate cells have been isolated from normal rat liver and been allowed to transform in culture. In addition, cells have been isolated from normal and diseased human livers. Integrin subunit expression has been detected immunohistochemically.
**Abstract 410, Table 1**

<table>
<thead>
<tr>
<th>Cell type</th>
<th>$\beta_1$</th>
<th>$\alpha_1$</th>
<th>$\alpha_2$</th>
<th>$\beta_2$</th>
<th>$\alpha_3$</th>
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<tbody>
<tr>
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<td>+</td>
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<td>+</td>
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<td>+</td>
</tr>
<tr>
<td>Transformed rat cells</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Normal human quiescent</td>
<td>++</td>
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<td>-</td>
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<td>+</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Normal human transformed primary bile duct cirrhosis</td>
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<td>+</td>
<td>-</td>
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<td>+</td>
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<tr>
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<tr>
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</table>

The results are summarised in the table above. In rat stellate cells, $\beta_1$, $\alpha_1$, $\alpha_2$, $\alpha_3$, $\alpha_4$, and $\alpha_5$ are all weakly expressed by quiescent cells, and their expression is increased in activated cells. In contrast, $\alpha_5$ is strongly expressed in both quiescent and activated rat stellate cells. The repertoire of integrins expressed by human stellate cells resembles that of rat stellate cells. As human stellate cells transform, they upregulate the expression of $\alpha_5$ and $\alpha_1$, with de novo expression of $\alpha_3$, $\alpha_4$, and $\alpha_5$. The integrin expression in stellate cells isolated from diseased human livers resembles activated rather than quiescent cells. In conclusion, chronic liver injury is associated not only with modifications to the components of the ECM, but also with changes in the expression of ECM receptors. Thus, manipulation of integrin expression or function may lead to new antifibrotic therapies.

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**411 THE PREVENTION AND TREATMENT OF MURINE COLITIS USING GENE THERAPY WITH ADENOVIRAL VECTORS ENCODING INTERLEUKIN-10**

J.O. Lindsay, C.J. Ciesielski, T. Scheinin, F. Brennan, H.J.P. Hodgson. The Division of Medicine and The Kennedy Institute of Rheumatology Division, Imperial College School of Medicine, London, UK

**Background:** Interleukin-10 knockout (IL-10 -/-) mice spontaneously develop Th1 T cell mediated colitis with many similarities to Crohn’s disease. Daily injections of IL-10 are able to prevent disease onset but do not induce remission in established disease.

**Aims:** To investigate the therapeutic efficacy and mechanism of action of gene therapy using adenoviral vectors encoding IL-10 (AdvmuIL-10) in the IL-10 -/- mouse model of colitis.

**Results:** A single systemic injection of AdvmuIL-10 was able to prevent the onset of colitis for at least 10 weeks, but was also sufficient to induce remission in IL-10 -/- mice with established disease (p<0.001 by ANOVA compared to saline or empty vector (Advo) treated controls). Histological scores were significantly lower in AdvmuIL-10 treated mice than controls (p=0.05). In addition, AdvmuIL-10 therapy reduced the elevated serum amyloid protein levels and stool IL-1B concentrations characteristic of this disease (p<0.05). IL-10 protein was present in colonic homogenates of AdvmuIL-10 treated IL-10 -/- mice, and the effects of secreted IL-10 were detectable by a sensitive bioassay for at least 10 weeks after injection. The immunoregulatory effect of a single AdvmuIL10 injection was manifest both by a reduction in TNF-α, IFN-γ and RANTES release from stimulated spleen cell cultures (p<0.005 compared to saline treated controls) and also by a change in the pattern of CXC-RP (x, y, z, ..., A, B, C) lymphocytes in the spleen compared to control mice (p<0.05 compared to saline treated controls). The delivery of IL-10 appeared to diminish the host anti adenosinergic response as serum from IL-10 -/- mice treated with AdvmuIL-10 contained significantly lower titres of neutralising anti-adenosinergic antibodies than mice that had received either empty vector or a virus encoding an irrelevant protein - Advyfial (p<0.05).

**Conclusion:** Gene therapy strategies using adenoviral vectors encoding immunoregulatory cytokines may prove to be a potent approach for the treatment of chronic inflammatory diseases such as Crohn’s disease.

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**412 ACID 1 STUDY: RESULTS OF A RANDOMISED TRIAL OF H. PYLORI ERADICATION IN PATIENTS ON MAINTENANCE ACID SUPPRESSION IN THE COMMUNITY**

A.J. Morris, C. Craig, C. Morran, K. Harden, H. Burns, A. Power, D. Walsh, R.C. Stuart. ACID 1 Study Group, Digestive Disease Centre, Glasgow Royal Infirmary, Glasgow, UK

**Objective:** The assessment of community intervention in dyspepsia (ACID1) study investigates the effect of H pylori (Hp) eradication in a large community based dyspeptic population irrespective of underlying diagnosis.

**Patients/methods:** 11,149 of 176,268 patients receiving HRA or PPI from 40 general practices were identified. After exclusions those receiving maintenance therapy (≥3 scripts/year) were randomised to active (n=4003) or control (n=1707) groups. Active patients were divided according to diagnostic groups: investigated ulcer n=1143 (28.5%); investigated non-ulcer n=1772 (44.3%); and uninvestigated n=1088 (27.2%). Active patients were invited to a nurse led community dyspepsia clinic and received health information, 7C Urea Breath Test (UBT) and, where possible, were prescribed Hp eradication. Glasgow Dyspepsia Severity Score (GDSS) and Digestive Disease Quality of Life (DDQol) data (0, 6 months) and prescription data(0, 6, 12 months) were collected. Patients receiving Hp eradication had repeat 7C UBT at 6 months.

**Results:** 1213 of 2393 (51.6%) patients attending clinic were Hp positive. Per protocol eradication rate achieved was 766/937 (80.4%) patients. Mean changes in score for GDSS and DDQ are presented.

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**413 TGF-α INDUCES A β-CATENIN/TCF MEDIATED TRANSCRIPTION EVENT IN BARRETT’S OESOPHAGUS**

C. Tselipis, I. Perry, D. Wakein, R. Hardy, D. Garrod. Epithelial Laboratory, Dept of Medicine, University of Birmingham, Birmingham, UK

In Barrett’s Oesophagus one of the earliest identified events is the up-regulation of the EGF-receptor, and its associated ligand TGF-α. Previous reports have identified a number of alterations in the expression and localisation of cell-cell adhesion molecules, such as E-cadherin and β-catenin of the adherans junction, in the transition from a normal stratified squamous to the metaplastic mucosa of Barrett’s Oesophagus. Relocalisation of β-catenin from the membrane to the nucleus induces oncogene expression (a process termed β-catenin / TCF mediated transcription).

In this study we assessed whether the elevated levels of TGF-α could direct the metaplastic-remodeling event observed in the initiation of Barrett’s Oesophagus.

Stimulation of both primary and established oesophageal cell cultures with TGF-α for 3 hr resulted in the transition of β-catenin from a membranous to nuclear localisation, as assessed by immunofluorescence. We further identified this transition was associated with tyrosine phosphorylation of β-catenin. Using the TOPFLASH luciferase reporter construct, a measure of β-catenin / TCF mediated transcription, TGF-α stimulation induced a 5 fold increase in TCF-β-catenin mediated transcription. This could be inhibited by use of an EGF-receptor kinase inhibitor, tyrphostin.

This data has identified that TGF-α, which is up regulated in the majority of human epithelial cancers, may induce tyrosine phosphorylation of β-catenin by receptor-ligand activation. This results in its migration to the nucleus where it can participate in the activation of β-catenin / TCF mediated transcription, the target genes of which

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**A109**
include oncocenes such as Cyclin D1 and c-myc. Such changes in adhesion molecule localisation and oncogene expression may be important in the metaplastic-remodeling events observed in Barrett’s Oesophagus.

**414** SWITCHING ON SWALLOWING, SWITCHING ON THE BRAIN—A NEW APPROACH FOR THE TREATMENT OF DYSPHAGIA

C. Fraser1, M. Power1, S. Hamdy1, D. Hobday1, I. Hollander1, A. Hobson1, P. Tyrell1, S. Williams1, J. Rothwell1, D.G. Thompson1. University of Manchester; Manchester; Institute of Neurology, London, UK

**Background/aims:** Animal studies demonstrate that stimulation of both the cerebral cortex and brainstem can provoke swallowing. Peripheral, sensory input is also important for normal swallowing, since altered sensation can affect swallowing performance. Our aim was to identify, in healthy adults, the physiologic changes in cortical and brainstem activity that occur during normal swallowing, and then examine the effect of altered sensation (either sensory stimulation or topical anaesthesia of the swallowing musculature) on this activity. We then show that sensory stimulation can be applied to stroke patients with dysphagia (difficulty swallowing) and produce a quantifiable improvement in swallowing performance.

**Methods:** Techniques involved water swallowing; electrical sensory stimulation of swallowing musculature by intraluminal catheter with ring electrodes; topical anaesthesia by lidocaine spray; transcranial magnetic stimulation (TMS), functional magnetic resonance imaging (fMRI) and videofluoroscopy (VFS).

**Results:** Normal subjects (as recorded with TMS): (i) An increase in both cortical and brainstem activity occurred during water swallowing. (ii) Sensory stimulation, depending on the stimulus parameters, provoked either long-lasting suppression, or enhancement of activity within cortex but not brainstem. (iii) Topical anaesthesia suppressed cortical activity. Normal subjects (as recorded with fMRI): (iv) Sensory stimulation at the optimal parameters leading to enhancement of cortical activity, prior to swallowing, resulted in stronger, bilateral, hemispheric activation compared to swallowing alone. Dysphagic stroke patients: (v) Sensory stimulation both enhanced cortical activity within the undamaged (but not damaged) hemisphere and at the same time produced a clear improvement in swallowing performance compared to sham.

**Conclusions:** Normal swallowing leads to activation within brainstem and cortex. Altered sensation may suppress or enhance this activity. “Beneficial” sensory stimulation at the optimal parameters, leads to greater activation of areas of brain functionally important for swallowing. When this is applied to dysphagic stroke patients, cortical activity is also enhanced, predominantly in the undamaged hemisphere, and a clear improvement in swallowing performance is produced. Sensory stimulation therefore provides us with a new and exciting, physiologic technique for managing dysphagia, particularly after stroke.

**415** ADMISSION BLOOD LACTATE IS PREDICTIVE OF OUTCOME IN PARACETAMOL INDUCED ACUTE LIVER FAILURE

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**Background:** The Kings College (KCH) criteria select patients with paracetamol induced acute liver failure (ALF) for transplantation (OLT) but have limited sensitivity and may identify patients too late for successful OLT. In a large cohort of ALF patients we have determined threshold values of blood lactate to best identify non-survivors and have applied these to a second prospective sample of patients, comparing prognostic accuracy and speed of identification with the KCH criteria.

**Patients and Methods:** L-lactate was determined in whole arterial blood using an automated analyser. In the initial sample of 103 patients (35 non-survivors, 10 OLT) threshold values of blood lactate 4 and 12 hours after admission were determined by ROC techniques and logistic regression. These were applied to the validation sample of 107 consecutive patients (21 non-survivors, 8 OLT) and diagnostic performance compared to the KCH criteria. Assessment of prognostic accuracy of utilised standard measures and likelihood ratios (LR).

**Results:** Initial sample blood lactate was higher in non-surviving patients at 4 hours (9.3 mMol/l (range 1.7–21) vs. 1.4 mMol/l (0.33–7.9), p<0.0001) and 12 hours (5.5 (1.3–18.6) vs. 1.3 mMol/l (0.26–3.2), p<0.0001). 4 hour level with maximal sensitivity and specificity was 3.5 mMol/l, and 12 hour 3.0 mMol/l. Application to the validation sample identified non-surviving patients earlier (4 versus 12 hrs p<0.0001) and with equivalent accuracy to the KCH criteria. The addition of 12 hour lactate of >3 mMol/l to KCH criteria raised sensitivity from 76% to 91%.

**Abstract 415, Table 1**

<table>
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<tr>
<th>Indicator</th>
<th>n</th>
<th>died</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PLR</th>
<th>NLR</th>
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<tbody>
<tr>
<td>A. 4 hr Lactate &gt;3.5</td>
<td>18</td>
<td>14</td>
<td>67</td>
<td>95</td>
<td>89</td>
<td>13</td>
<td>0.35</td>
</tr>
<tr>
<td>B. 12 hr lactate &gt;3</td>
<td>18</td>
<td>16</td>
<td>76</td>
<td>97</td>
<td>93</td>
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<td>0.24</td>
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<td>C. Either A or B</td>
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<tr>
<td>Kings and B</td>
<td>24</td>
<td>19</td>
<td>91</td>
<td>94</td>
<td>93</td>
<td>14</td>
<td>0.1</td>
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</table>

**Conclusions:** Blood lactate levels rapidly and accurately identify non survivors of ALF, and their measurement is likely to improve the speed and accuracy of selection of appropriate candidates for transplantation.

**416** THE PREVALENCE OF COELIAC DISEASE IN PATIENTS fulfilling the ROME 2 CRITERIA FOR IRRITABLE BOWEL SYNDROME: A CASE CONTROL STUDY

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**Background:** European studies suggest that up to 20% of the population suffer with irritable bowel syndrome (IBS). The diagnosis is made by fulfilling symptom based criteria and the exclusion of organic pathology. Coeliac disease (CD) is thought to affect 1 in 2–300 individuals. CD can present with GI symptoms but alternative manifestations are increasingly recognised. No published studies have assessed the prevalence of CD in IBS.

**Aim:** To determine the prevalence of CD in patients fulfilling the ROME 2 criteria for IBS.

**Methods:** Data was collected prospectively from a single university centre, from January 99 to October 2000. 300 patients who fulfilled the Rome 2 criteria had their IgG/IgA antigliadin and antidiomysial (EMA) antibodies checked. Patients with any positive antibody were offered duodenal biopsy. 300 healthy volunteers without IBS served as age and sex matched controls (C). In this cohort individuals positive for IgA gliadin or EMA were biopsied.

**Results:** IBS group: n=300 (214 female. Mean age 45.4 Median 56. Range 18–87). Controls (214 female. Mean age 45.4 Median 56).

**Abstract 416, Table 1**

<table>
<thead>
<tr>
<th></th>
<th>IgG only</th>
<th>IgA only</th>
<th>IgA IgG</th>
<th>EMA</th>
<th>EMA/IgG</th>
<th>EMA/IgA</th>
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<tbody>
<tr>
<td>C</td>
<td>256</td>
<td>41</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
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</table>

Of the 66 IBS patients with positive antibodies. There were 14 cases of CD (11/12 EMA positive, 1 EMA positive patient declined a biopsy). 3 patients with CD were lost to follow-up/declined biopsy and 43 had normal duodenal mucosa. There were 2 EMA positive cases of CD from the controls (p=0.004, Odds ratio 7.3 [95 CI 1.32–4] chi-squared test for independence).

**Conclusion:** This is the first study to assess the prevalence of CD in patients with IBS (4.7%). Patients with IBS should be routinely screened for CD. Using only EMA 20% of cases would have been missed.