IBD/Colorectal/IBS Free Papers: 001-015

001 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.

002 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 $=+2.1\% \pm 4.8$, Group B $=+2.5\% \pm 3.4\%$, $p<0.05$. At the hip there was a significant gain of $+2.5\% \pm 3.1\%$, $p<0.05$ in Group B compared to a gain of $+1.1\% \pm 3.7\%$, $p=0.2$ 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.

003 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.

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 feed (AL110, Nestle, UK) were studied at day 0, 3, 7, 14, 21, 28, 56. Serum was collected and assessment of nutrition (weight for age Z score, triceps skinfold thickness, serum leptin) and clinical status (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-1 β (1ng/ml). After 24 hours the media was collected and assayed for IL-6, IL-8 and TNF- α . **Results:** In Caco2 cells IL-1 β leads to a marked inflammatory response with secretion of IL-6, IL-8 and TNF- α . Breast milk and Modulin decreased IL-6, IL-8 and TNF- α secretion by 50%. Boost decreased IL-6 and IL-8 secretion but had no effect on TNF α 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 vitro*. 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 modulation 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 (ESA) 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 ESA 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-1 β) and anti-inflammatory (IL-1 α) 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-1 α :IL-1 β compared to incubation with media alone. The median (interquartile range) ratio with media alone was 13.7 (9.91-23.60) compared with ratios of 64.17 (26.3-129.50) with 1:5 dilution ($p<0.03$), 51.12 (37.15-66.79) with 1:10 dilution ($p<0.03$) and 39.31 (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-1 α : IL-1 β ratio in 1:5 dilution only compared to media 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-1 α :IL-1 β ratio {media alone 22.77 (16.43-34.05) Vs 1:5 ESA 24.12 (13.4-93.6); $p=ns$, no difference with 1:10 or 1:20 dilutions}. In

UC, a non-significant decrease, rather than an increase in ratio of IL-1 α :IL-1 β 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. Differences in PUFA 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-analyses of elemental, peptide and whole protein feeds have shown a strong negative correlation between remission rate in CD 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 $\leq$ 150 and response as a fall in CDAI of $\geq$ 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 52% 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. The 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 3/29 LGD (10.3%) and in 4/97 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=25) 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 12-132). 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 proportion of patients initially treated with an IRA will require a subsequent rectal excision because of uncontrollable rectal polyps or rectal cancer. The aim of this study was to evaluate whether any particular genetic mutations were associated with an increased risk of rectal excision and to determine whether DNA analysis might be helpful in guiding management decisions.

Methods: FAP patients from a polyposis registry were included in this study. We identified all patients who had had an initial IRA and then early rectal excision; defined as within 5 years of original colectomy or at <30 years old. These patients were compared with those

who had had an IRA and had retained their rectum. APC gene mutations were identified by analysis of leucocyte DNA using direct sequencing techniques.

Results: 20 patients had required an early rectal excision and pouch formation. APC mutations have been identified in 12 (60%). 9 of these (75%) have a 5 base-pair deletion on exon 15 at codon 1309. There were two other mutations identified on exon 15 and one on exon 11. By comparison 240 patients have retained their rectum following colectomy and IRA. APC mutations have been identified in 108(45%). Only 6 (6%) have a mutation at codon 1309 and of these two patients have dense rectal polyposis which may require early rectal excision.

Conclusions: There is a significant association between an APC mutation at codon 1309 and the risk of early rectal excision after an IRA. This study demonstrates that the APC genotype may help predict outcome. Genetic mutation analysis may offer benefits beyond predictive screening and help guide surgical decision making in the future.

010 DUODENAL CANCER IN FAMILIAL ADENOMATOUS POLYPOSIS

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Background: Prophylactic colectomy in familial adenomatous polyposis (FAP) has decreased the incidence of colorectal cancer such that duodenal cancer and desmoid disease are now the leading causes of death. Management of the duodenal risk is complicated by the fact that despite over 95% of patients having identifiable adenomatous polyps in the duodenum only 5-10% go on to develop cancer.

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, table 1).

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

	No. of points (pts)		
	1	2	3
No. of polyps	1-4	5-20	>20
Polyp size (mm)	1-4	5-20	>10
Histology	tubulovillous	tubulovillous	villous
Dysplasia	mild	moderate	severe

Stage 0, 0pts; stage I, 1-4 pts; stage II, 5-6 pts; stage III, 7-8 pts; stage IV, 9-12 pts.

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.

Abstract 11, Table 1

Series	Literature	UK Case	Prospective Screen-Detected	
			HPP Cases	No HPP
No. of Patients	43	24	12	40661
Median Age M/F (years)	59/65	59/55	60/63	60/60
% Male	71%	54%	67%	50%
FHx colon cancer	3/24 (13%)	5/20 (25%)	0/12 (0%)	4430/40661 (11%)
Hx of smoking	-	11/15 (73%)	8/9 (89%)	10706/ 21256 (53%)
Cases with HP ≥ 10mm	21/31 (68%)	15/24 (53%)	4/12 (33%)	120/40661 (0.3%)
Sync. dysplasia:				
Cancer +/- adenoma	27/43 (63%)	13/24 (54%)	0/12 (0%)	124/40661 (0.3%)
Adenoma alone	8/43 (19%)	7/24 (29%)	6/12 (50%)	4950/40661 (11%)
Metac. dysplasia:				
Cancer +/- adenoma	2/6 (33%)	2/14 (14%)	1/7 (14%)	-
Adenoma alone	0/6 (0%)	8/14 (57%)	1/7 (14%)	-
FU (mean yrs/n)	4/6	6/14	2/7	-

011 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. Over 70% 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.

012 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.

013 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 diarrhoea (ID)^{1,2,3}. 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 cultures⁴. We hypothesised that patients who 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.

Results: The Odds Ratio for a case having a pre-existing FGID compared to a control is 4.74 (95% CI 2.75–8.13). Looking at IBS only, the Odds Ratio for a case having pre-existing IBS compared to a control is 5.04 (95% CI 2.63–9.63).

Abstract 13, Table 1

Number of:	Baseline FGID		IBS	
	Yes	No	Yes	No
Case	67	79	48	98
Control	24	134	14	144

Conclusions: Patients presenting to their GP with ID have a pre-existing high rate of FGID's, particularly IBS, compared to a matched community based control group. Studies that examine rates of new FGID's after ID need to carefully exclude patients with pre-existing FGID's. Because only a small percentage of patients with ID present to their GP, consultation behaviour is likely to mediate the results that we have.

1. McKendrick MW, Read NW *Journal of Infection* 1994
2. Neal KR et al *BMJ* 1997
3. Gwee KA et al *Lancet* 1996
4. Wheeler JG et al *BMJ* 1999

014 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 > 0.3 Hz. 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 500 μ s) was then delivered at frequencies of 0.1 Hz and 2 Hz. 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 0.1 Hz 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 2 Hz suggests that wind-up occurs via similar mechanisms in visceral and somatic tissues. However, the ability for wind-up to occur at lower thresholds in the oesophagus in comparison to the hand suggests that the viscerae may be more susceptible to develop central sensitization in response to repeated stimulation.

015 PROSTAGLANDIN E₂ 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.

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 10⁻⁶M PGE₂ 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 (±8%) of them responded to the first acid stimulus (n=10) with only 33±18% responding to the second stimulus (n=3). Addition of PGE₂ 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). Pre-incubation 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.

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016 INFLAMMATORY BOWEL DISEASE IN THE COMMUNITY: DISEASE PROFILE, HEALTHCARE UTILIZATION, IMPACT ON LIFESTYLE AND PRODUCTIVITY

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Aim: To ascertain demographic and clinical characteristics, health-care utilisation and impact of disease on lifestyle/productivity in community patients with inflammatory bowel disease (IBD).

Methods: Anonymised structured questionnaires were mailed to all NACC members in the Bromley and Dartford area with IBD in March 2000. Data was collected on demography, type of IBD, duration of IBD and nature of specialist care. Annual frequency of consultations in primary/secondary care, hospitalisations for IBD, frequency of radiological/endoscopic investigations, surgical operation rates, use of medications/complimentary therapy was also ascertained. The impact of IBD on lifestyle/productivity was also determined.

Results: 107 out of 266 patients with IBD responded (40% response rate). Mean duration of NACC membership 6.1yrs. Sex (M:F) 38:69. Age n(%): <40yrs 39(36%), 40–70yrs 47(44%), >70yrs 18(17%). 14(13%) smoked regularly. 60(56%) had ulcerative colitis(UC), 44(41%) had Crohn's disease (CD). Mean duration of illness was 12.6yrs [UC vs CD; 9.8 vs 16.7, p=0.0056]. 84(79%) were under Gastroenterologist care and 24(22%) under surgical care. In addition 10(9%) were under other specialities for complications. *Use of healthcare resources:* In previous 12 months, mean frequency of visits to GP was 2.2, (range 0–16) and to hospital specialists 2.2, (range 0–14). Frequency of Abdominal radiology and colonoscopies over previous 5 years was mean(range) 1.7(0–29) and 1.3(0–7) respectively. Hospital admission rate over the past 12 months was 18/107(17%)[UC vs CD, 12% vs 25%, NS] and Lifetime surgical operation rate 33/107(31%)[UC vs CD, 8% vs 65 p<0.0001]. *Medications:* Patients took a mean of 6.8 tablets per day[UC vs CD, NS]. 32/83(38%) had been non-compliant in past one month. Patients were on the following medications n(%): 23(21%) on prednisolone[UC vs CD, NS], 6(6%) on budesonide, 87(81.3%) on 5ASA[UC vs CD, NS], 22(21%) on Azathioprine[UC vs CD, NS], 18(17%) on calcium tablets, 13(12%) on acid suppressants. Only 7/23(31%) of patients on prednisolone were on calcium tablets. 6/22(27%) of patients on azathioprine were on prednisolone as well. 28/107(26%) had used complimentary therapy for IBD. *Effect on lifestyle:* 83(77%) patients with IBD over the previous one month had no or minimal limitation of lifestyle. In the previous 6 months, the mean days lost off work was 5.1 (range 0–99)[UC vs CD, NS].

Conclusion: IBD patients in the community place substantial pressures on healthcare but majority enjoy relatively good health with few limitations on employment and lifestyle.

017 AN ANALYSIS OF THE HOSPITAL COSTS OF INFLAMMATORY BOWEL DISEASE IN UK

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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.

Aim: To examine the total hospital costs of IBD patients over a year.

Methods: 100 consecutive IBD patients attending our multidisciplinary clinic were studied. Patient records were studied to collect data on the number of outpatient attendances, inpatient hospital days, cost of laboratory, radiological, endoscopic investigations and treatment costs incurred per patient over a 12-month period.

Results: 62 patients with ulcerative colitis and 38 with Crohns disease were studied. There were 44 male and 56 female patients. The mean age for both sexes combined were 47.8yrs (18–79) for UC and 46.5yrs (21–84) for Crohns. The median disease duration was 126.5 months (13–456) and 174 months (16–456) for UC and Crohns respectively. The mean total costs per patient per year for UC was £1096 (95%CI 855–1337) and £2184 (95%CI 1433–2935) for Crohns respectively. As the data was skewed the calculated median charges were lower than the mean, £903 (80–4644) for UC and £1276 (98–9534) for Crohns. The following table illustrates costs for UC and Crohns represented as mean with 95% CI intervals.

Abstract 17, Table 1

Costs	UC	Crohns
Inpatient (incl. Surgery)	£1755 (1297–2213)	£2738 (1802–3674)
Outpatient	£210 (176–244)	£267 (209–325)
Investigation	£258 (170–346)	£338 (210–466)
Medications	£487 (384–590)	£642 (478–806)

The percentage of total costs for ulcerative colitis and Crohns disease are 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 newer treatments, which are expensive but could reduce the inpatient hospital days and avoid surgery and thus prove to be cost effective.

327 DOES BETTER DISEASE RELATED EDUCATION IMPROVE QUALITY OF LIFE? A SURVEY OF IBD PATIENTS

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Background and aims: The importance of Health Related Quality of Life (HRQOL) assessment in patients with chronic disorders such as inflammatory bowel disease (IBD) is now acknowledged by researchers. Of the many factors which may influence HRQOL, patient knowledge of the condition and disease related information provision have hitherto not been studied.

Patients and methods: 250 patients with inactive IBD (UC=122, CD=128) were randomly chosen from our IBD clinic. Two sets of questionnaires (initially a standard questionnaire to assess level of disease related information (PIS), followed by a HRQOL questionnaire) were sent to each patient. In the PIS a score of 7 or more indicated satisfactory disease related knowledge and in the HRQOL a scores less than 51 suggested a normal QOL, and a score above 60 significantly impaired QOL.

Results: 168 patients (66%) returned both the questionnaires (UC=91, CD=77). The mean QOL in patients with UC and CD was 62.2 ± 8.3 and 63.9 ± 9.5 respectively, (p=ns). 99 patients (59%) had significantly impaired QOL (mean score 65 ± 7.6) with only 12