NESTED-POLYMERASE CHAIN REACTION (PCR) FOR THE DETECTION OF HELICOBACTER PYLORI IN GASTRIC BIOPSY SAMPLES.

MM Ormen, AC Gough, P Sarsfield* CD Johnson
University Surgical Unit, *Histopathology, Southampton General Hospital, Southampton.

H pylori is a fastidious organism strongly associated with gastric disease. A variety of protocols have been developed for its detection. Of these histology and culture have been considered the most specific, whereas the CLO-test is more sensitive. Nested-PCR is highly sensitive and specific for detection of small numbers of cells. The aim of this study was to compare the efficiency of nested PCR, CLO-test and histology in the diagnosis of H pylori infection.

41 dyspeptic patients (25M, 16F) median (range) age 54 (31-83) years, who had endoscopy were studied. No patient had peptic ulceration. All assays, CLO-test, histology and PCR were performed on biopsies obtained from the gastric antrum. The same sample was used for both CLO-test and nested PCR.

22 (54%), 19 (50%) and 35 (85%) samples were positive by CLO-test, histology (3 missing) and nested PCR respectively. 23 samples were positive by PCR and one or both of histology and CLO-test. 12 samples were negative to both histology and CLO-test, but positive to PCR. Six samples were negative on all three tests and no sample was negative to nested PCR and positive for another test. If CLO-test/histology is taken as the standard, nested PCR has a sensitivity of 100% and specificity of 65%. If nested PCR is the standard, CLO-test/histology has a sensitivity of 65% and a specificity of 100%.

False negative results with CLO-test and histology may result from scanty infection. The power of nested PCR to detect small numbers of organisms may explain positive results in these cases. However, minute amounts of contaminating material can give false positive results with PCR. Provided that care is taken to prevent contamination during sampling and DNA extraction, nested PCR seems a good candidate for gold standard status in the diagnosis of H pylori infection.

EVIDENCE FOR THE INVOLVEMENT OF INFLAMMATORY CYTOKINES AND HELICOBACTER PYLORI PRODUCTS IN PRODUCING TRANSGASTROINEA: EFFECTS IN A CELL CULTURE MODEL.

*Department of Internal Medicine, University of Michigan, Ann Arbor, USA, *Vanderbilt University, TN, USA and *Department of Gastroenterology, RPMs, London.

Patients infected with Helicobacter pylori (Hp) exhibit hypergastrinaemia. It has been proposed that inflammatory mediators could be responsible by altering G cell function. Aim. To test the ability of Hp products and tumour necrosis factor α (TNFα) and interleukin 8 (IL8), which are produced in Hp infected mucosa, to release gastrin from cultured G-cells.

Methods. Canine antral G-cells were isolated by collagenase–EDTA digestion and enriched by counterflow elutiation. After culture for 40 hours, the gastrin release in response to 2 hours stimulation with test substances was measured byRIA.

Results. Hp sonicates (0.5–50 μg/ml), water extracts (0.5–50 μg/ml) and purified lipopolysaccharide (0.5–50 μg/ml) had no significant effect on basal or stimulated gastrin release. IL8 1 nM and 10 nM released gastrin (4±16% and 43±24% above basal respectively; mean±SE; p<0.05). The effect of IL8 was inhibited by the somatostatin analogue octreotide (1 μM), TNFα (0.1–100 ng/ml) had no significant effect on basal or stimulated gastrin release. When tested in the presence of IL8, Hp pylori sonicates from 2 out of 4 strains stimulated gastrin release in a dose dependent manner: producing a maximal stimulation of 232±33% above basal (p<0.05). Viability was unimpaired.

Conclusions. The inflammatory cytokine IL8 can stimulate gastrin release from G-cells, this effect can be potentiated by Hp products. An interaction between cytokines and Hp products may contribute to the hypergastrinaemia seen in vivo.

A STUDY OF THE RELATIONSHIP BETWEEN ALCOHOL INTAKE AND GASTRIC LUMINAL ANTIOXIDANT CONCENTRATIONS. ZW Zhang, SE Patchett, D Perrett, MJG Farthing. Digestive Diseases Research Centre and Dept of Medicine, Medical College of St Bartholomew's Hospital, London, UK.

Epidemiological studies have suggested that there is a relationship between alcohol consumption and the development of gastric cancer. Adequate intake of anti-oxidants (vitamin C, E, and β-carotene) may be protective against gastric cancer and the levels in gastric juice may be particularly important. We therefore measured gastric luminal vitamins C, E, and β-carotene concentrations and examined whether they are influenced by alcohol intake. Anti-oxidant concentrations were determined in gastric juice obtained at upper gastrointestinal endoscopy in consecutive patients (vitamin C n=63, vitamin E n=68, β-carotene n=59). All values were measured in duplicate using HPLC/electrochemical detection and expressed as median [interquartile range]. Patients were interviewed with regard to their alcohol and cigarette consumption prior to endoscopy. Levels of alcohol consumed was graded as none, <21, 21-42 and >42 units/week. Cigarette consumption was similarly recorded as none, <10, 10-20 and >20 cigarettes/day.

The levels of each anti-oxidant in gastric juice were unaffected by the underlying endoscopic diagnosis. When controlled for age and sex, alcohol drinkers had significantly lower β-carotene in gastric juice than non-drinkers, 3.12nM [0.47-7.8] vs 3.92 [2.91-6.61], (p<0.01). The β-carotene level was inversely related to the amount of alcohol consumed (r=0.32, p<0.02). No relationship between alcohol consumption and vitamin C or E level was evident. Furthermore there was no association between smoking and the levels of any of these anti-oxidants regardless of the number of cigarettes smoked.

Alcohol intake would appear to be a determinant of gastric juice β-carotene concentration but not of vitamin C or E. The adverse effects of alcohol consumption on β-carotene levels may have implications for gastric cancer development particularly in subjects with high alcohol intake.

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TRANSDERMAL NICOTINE COMPARED WITH ORAL PREDNISOLONE FOR ACTIVE ULCERATIVE COLITIS. GAO Thomas, J Rhodes, K Raganath, V Mani, G Williams, R Newcombe, MAH Russell, C Feyerabend. Dept of Gastroenterology, UWH, Cardiff, Leigh Infirmary, Manchester. 1Institute of Psychiatry, Kings Hospital, London, 1

Ulcerative colitis (UC) is largely a disease of non-smokers. Controlled trials have shown benefit with transdermal nicotine (TN) given with 5-aminosalicylic acid (5-ASA) in active disease but not when given alone as maintenance therapy. We examined TN alone compared with prednisolone in active disease.

Methods. 61 patients with active UC were given either TN or 15 mg prednisolone for 6 weeks in a randomised, double-blind study. Incremental doses of TN were given for the first 9 days; patients tolerated 15 to 25 mg/16 hours. Most were taking 5-ASA at entry which was stopped at 9 days, a few taking topical steroids stopped these at the onset. Clinical, sigmoidoscopic and histological assessments were made at entry and at 6 weeks, or at premature withdrawal. Side-effects and serum nicotine and cotinine concentrations were monitored throughout.

Results. 43 completed the trial. Of these, 6 of 19 on TN achieved full sigmoidoscopic remission compared with 14 of 24 on prednisolone (p<0.08). In those who completed the study, there was significant improvement with both TN and prednisolone for the St Marks score (p<0.05 and p<0.001, respectively), Global Clinical Grade (p<0.01 for both), and sigmoidoscopic score (p<0.01 and p<0.001), differences between groups favour prednisolone, but none reach statistical significance. Those on TN had more withdrawals (11 vs 7 respectively, both for deterioration (6 vs 5) and for side-effects (5 vs 2). Side-effects were more frequent on TN than prednisolone (44 vs 19; p = 0.03), the most common of which were, nausea, light-headedness and tremor.

Conclusions. Nicotine alone was of benefit in acute colitis, but 15 mg of prednisolone was more effective.
BUTYRATE ENEMAS ARE LESS EFFECTIVE THAN PREDNISOLONE ENEMAS IN TREATING DISTAL OR LEFT SIDED ULCERATIVE COLITIS

Nightingale J M D, Barthoome B J, West K K, Mayberry J F, Wicks A C W

Butyrate, a short chain fatty acid readily metabolised by colonicocytes, has been proposed as treatment for diversion colitis and distal ulcerative colitis (UC) unresponsive to standard therapy. To compare butyrate enemas with prednisolone enemas and combined butyrate/prednisolone enemas, 21 patients with active distal or left sided UC were randomly allocated into 3 groups of 7. The enemas (all 100mL) were fed once daily at 8am or 8pm. The first group received butyrate enemas, the second group prednisolone 21-phosphate, 100 mmol sodium butyrate or the same amount of prednisolone and butyrate mixed together as one enema. After two weeks treatment, median stool frequency was significantly higher in the prednisolone group (9 stool/24hr) than in the butyrate group. At 2 weeks 7/21 patients receiving butyrate showed no improvement in their colitis and withdrew from the trial. No steroid treated patients withdrew. At 6 weeks the improvement in those receiving prednisolone was maintained, only 3 patients receiving butyrate had a reduction in stool frequency. There was no additional benefit in combining prednisolone and butyrate into one enema. Prednisolone enemas were successful in treating all patients while butyrate enemas only improved 3/7 patients. There was no advantage in combining both butyrate and prednisolone into one enema.

A RANDOMIZED CONTROLLED TRIAL OF ALBENDAZOLE FOR TREATMENT OF DIARRHOEA IN AFRICANS WITH AIDS

P Kelly, F Langs, E Kane, R Baggaley, F Kazembe, JOM Pophie, MJG Parfing. University of Zambia School of Medicine, Lusaka, Digestive Diseases Research Centre, Medical College of St Bartholomew's Hospital, London.

AIDS in sub-Saharan Africa is a major problem for health care services, but there are few effective treatments for patients with diarrhea. We have previously shown that intracellular enteropathogenic protozoa are found in the majority of HIV infected hospital patients with persistent diarrhoea in Zambia. We therefore carried out a randomised, double blind, placebo controlled trial of albendazole in the treatment of persistent diarrhoeas in HIV infected individuals in urban Zambia. 174 patients were randomised to receive albendazole (800mg twice daily for 14 days) or placebo, and followed up for six months. Treatment and monitoring was carried out by community orientated AIDS care teams working in three urban settings. 108 patients completed treatment and at least the first month of follow-up.

Albendazole reduced the number of days on which patients experienced diarrhoea by 29% compared to placebo (p<0.001). In patients with Karnofski scores of 50-70, diarrhoea was reduced by 50%, sustained over six months of follow up. Minimal adverse effects were noted. No benefit was detectable in moribund patients or in those who were still able to work. On an intention-to-treat basis, complete remission was obtained in 22% of all patients who received albendazole (p=0.004 against placebo), failing to 13% at 6 months. Albendazole had no effect on mortality.

Thus, for HIV infected Zambians with diarrhoea of more than three weeks duration, albendazole offers substantial relief from symptoms and may be used empirically, without prior investigation. This is the first agent shown to be effective in a controlled trial for treatment of this disease in this setting.

INTRALESIONAL CHEMOTHERAPY IN THE TREATMENT OF GASTRIC KAPOSI'S SARCOMA IN AIDS

J A J Smithson, B G Gazzard (Introduced by B G Gazzard)
Dept of Gastroenterology, Hull Royal Infirmary, Anlaby Road, Hull.

Introduction: Gastric Kaposi's sarcoma is well described in patients with AIDS, as well a cause of mortality, it is an important cause of morbidity with symptoms of anorexia, abdominal pain and gastrointestinal haemorrhage. Gastric Kaposi's sarcoma is conventionally treated by systemic chemotherapy or radiotherapy with all the associated side effects.

Patients: Five patients with previous AIDS diagnoses were found to have gastric Kaposi's sarcoma, confirmed by histological samples taken at upper gastrointestinal endoscopy. All of the 5 patients had declined or were unable to have systemic treatment. The patient's symptoms were noted, and their gastric lesions mapped at endoscopy and recorded photographically. The gastric lesions were then injected with 1ml of bleomycin (0.2mg/ml) into each lesion or a total of 2mls at different sites if the lesion was greater than 2cm. A repeat endoscopy was performed at two weeks and again at one month if they required further treatment or if their symptoms had returned.

Results: At repeat endoscopy the lesions had diminished in size and number in all 5 patients. In 3 patients all of the lesions had resolved. All patients noticed an improvement in their symptoms after the first 3 days post treatment. This symptomatic improvement was particularly marked for anorexia resulting in weight gain for 4 of the patients. Longer term follow up showed that patients tolerated the treatment well and that the response was sustained with no recurrence at the sites initially responding to the injections. One patient remains lesion free at 14 months. One patient had a pyrpylocic lesion which was causing symptoms of obstruction this lesion resolved completely along with the symptoms.

CHARACTERISATION OF GLUTEN PEPTIDE/HLA DQ BINDING IN COELIAC DISEASE

RG Shidrawi, S Rosen-Bronson, A Wagner and PJ Cacciuri. Gastroenterology Unit, UMDS, St Thomas' Hospital, London, UK and ~Georgetown University Medical Center, Washington, DC.

Background: A peptide corresponding to amino acids 31-49 of A-gliadin, peptide A, has been shown to induce the histological features of coeliac disease (CD) both in vitro and in vivo (Sturgess, Lancet 1994; 343:758). Recent work has shown the binding affinity of this peptide to HLA DQ2 (a1*0501, b1*0201), the HLA restriction element of CD, correlates with its toxicity (Shidrawi et al., Gut 1995; 36 : A53).

Aims: We wished to characterise the binding of peptide A to HLA DQ2 by identifying which residues within this peptide are important in peptide/HLA binding.

Methods: Truncations and alanine point-substitutions for proline residues of peptide A were made using fmoc chemistry that were tested for >95% purity and identity using reverse phase HPLC and mass spectrometry. Lymphoblastoid B cell lines from coeliac patients homozygous for HLA DR17(3) and HLA DQ2, determined by PCR-RFLP typing, were used in peptide binding assays to compare the binding of these peptides with the binding of peptide A.

Results: Truncation of peptide 31-49 beyond residues 31-47 resulted in loss of binding. Alanine substitution for L31, Q33, P34, P35 and P36 also resulted in loss of binding, while alanine substitution for P32, P35 and P44 had no effect on binding. Alanine substitution for P39 improved binding affinity.

Conclusions: This data correlates with T cell proliferation work and identifies those residues in peptide 31-49 of A-gliadin that are important for binding to HLA DQ2 and therefore critical for coeliac toxicity.
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Th2 CYTOKINES INTERLEUKIN-4 AND INTERLEUKIN-10 IN THE SMALL INTESTINE OF PATIENTS WITH COELIAC DISEASE. Reckett C.G., Dell’Olio D, Nelufer J.M, Przemioslo R. and Ciclitira P.J. Gastroenterology Unit, UMDS, St.Thomas’ Hospital, London. SE1 7EH.

Aims: Our aim was to compare the level of production of IL-4 and IL-10 in villous and inflammatory infiltrate in jejunal biopsies from patients with untreated (CD/ND) and treated coeliac disease (CD/GFD) as well as disease controls (DC).

Methods: Biopsies from patients with CD (n=10, untreated n=7) and seven disease controls were studied. Cytokrotic sections from jejunal biopsies were incubated with monoclonal antibodies to IL-4, IL-10 and CD45, and stained with avidin-biotin immunoperoxidase immunohistochemistry. Sections were assessed blindly by two independent observers with epithelial staining recorded per 100 nucleated cells and a lamina propria counted with an eye-piece graticule (0.02mm²).

Results: No IL-4 or IL-10 positive cells were noted in the epithelium. In the lamina propria, the results of cytokine staining are expressed per 0.02mm²:

- **Th2 cytokine**
  - IL-4: median 3.63 range 2.63-10.63
  - IL-10: median 4.88 range 1.92-10.5

- **CD/GFD**
  - IL-4: 6.69 6.90
  - IL-10: 4.81

- **CD/ND**
  - IL-4: 7.11 7.35
  - IL-10: 5.75 5.83

- **DC**
  - IL-4: 8.69
  - IL-10: 4.81

There is a significant increase in CD45 staining between both CD/ND(p=0.003) and CD/GFD(0.008) compared to DC, as well as between a lamina propria is the site of production. There were no significant differences in IL-4 or IL-10 staining between the groups. When cytokine staining is expressed as a percentage of CD45 staining, there is a significant reduction in both IL-4(p=0.014) and IL-10(p=0.038) staining between CD/ND and CD/GFD.

Conclusions: These results demonstrate that in CD, there is no primary deficiency of the Th2 cytokines IL-4 and IL-10, and that the lamina propria is the site of production. The fall in the Th2 cytokine/CD45 ratio between CD/ND and CD/GFD along with the increase in inflammatory infiltrate in CD/ND confirm that the immune response in CD is predominantly Th1 driven.

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NITRIC OXIDE IN THE SMALL INTESTINAL MUCOSA OF PATIENTS WITH COELIAC DISEASE. Reckett C.G., Dell’Olio D, Nelufer J.M, and Ciclitira P.J. Gastroenterology Unit, UMDS, St.Thomas’ Hospital, London. SE1 7EH.

Introduction: Increased expression and production of proinflammatory cytokines such as interferon-gamma and tumour necrosis factor-alpha are found in the lamina propria of patients with untreated coeliac disease (CD). However, their precise role in the development of the mucosal lesion remains to be determined. It has been demonstrated in other disease states that these cytokines can mediate their effects via nitric oxide(NO).

Aims: Our aim was to use the NADPH-diaphorase activity of nitric oxide synthase(NOS), the enzyme that catalyses the production of NO, to indicate whether there is increased NOS in jejunal biopsies from patients with CD compared to disease controls.

Methods: Fifteen patients with CD (treated n=8, untreated n=7) and disease controls (n=8) were studied. Cytokrotic sections from jejunal biopsies were fixed in 4% paraformaldehyde, which inhibits all NADPH dependent enzyme systems except NOS. The sections were incubated in a solution of 100nmol/l Tris pH7.6 containing 0.3% Triton X, 1.12mmol/l NADPH and 0.24mmol/l nitro blue tetrazolium (NBT) at 37°C for 3.5 hours to allow the insoluble blue reaction product to form. After a final wash, the sections were mounted in glycero. Two independent observers assessed the sections and counted a 0.1mm² area of lamina propria on two sections from each patient using an eye-piece graticule.

Results: In the lamina propria, there was a significantly more NADPH-diaphorase staining of untreated CD(median:50.75, range:43.5-65.29) compared to treated CD(median:32.38, range:7.95-48.75)(p=0.003) and controls(median:14.38, range:3.75-22.25)(p=0.001) as well as between treated CD and controls p=0.046. The staining appeared to be almost entirely cellular in origin. In the epithelium, no staining was observed.

Conclusion: We have demonstrated, using NADPH-diaphorase as an indicator of NOS, significantly greater staining in the lamina propria of patients with untreated CD compared to treated patients and controls, thus for the first time implicating nitric oxide in the pathogenesis of the mucosal lesion in CD.

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FRACTIONAL CALCIUM ABSORPTION IS REDUCED IN TREATED COELIAC DISEASE. J M Subhani, P Beckett, M Pazianas, L Ang, C Collins, J D Maxwell, St George’s Hospital and Medical School, London SW17 ORE.

Metabolic bone disease and disordered calcium metabolism occur in coeliac disease. Though serum calcium levels return to normal on treatment, we and others have shown that reduced bone mineral density (BMD) persists. The mechanism is unknown. To study this we examined fractional calcium absorption in treated female coeliac disease patients and controls in relation to BMD.

We calculated fractional calcium absorption using a single ⁴²Ca isotope method. A lactose and gluten-free breakfast containing approximately 200mg calcium with 0.6 Mq of ⁴²Ca was given after an overnight fast. Blood was drawn at intervals, and ⁴²Ca concentration determined by liquid scintillation counting. Empirical measures of isotope content were obtained after correcting for serum calcium, height and weight (Heaney et al 1985). BMD was measured by Lunar DFX (dual energy Xray absorptiometry) densitometer.

22 coeliacs (47 yrs +/- SD 14) and 10 controls (41 yrs +/- SD 8) were studied. There was no significant difference between the groups in age, height, weight or serum calcium. Median time since diagnosis and gluten withdrawal was 4 years (range 1-12). Fractional calcium absorption was significantly reduced in coeliacs (40% v 57%, p=0.0005). Whole body BMD in 7 of 22 coeliacs was Z < -1 (expressed as Z scores i.e. variations from the mean by standard deviations SD), compared to only 1 of the 10 controls. Regression analysis revealed no significant relationship between age and calcium absorption (p= 0.18), or calcium absorption and BMD (p=0.79).

Treated, asymptomatic, biochemically normal coeliacs have markedly lower calcium absorption than healthy controls. However osteopenia in these patients is not completely explained by calcium malabsorption.

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BONE MINERAL DENSITY AND BONE TURNOVER IN TREATED COELIAC DISEASE. N A McFarlane1, J Dixey2, J Dumpy2, AK Bhalla2, DAF Robertson2, Dept of Gastroenterology, Royal United Hospital1, Bath, BA1 3NG. Bath Institute of Rheumatic Diseases2, BA1 1RL.

AIMS: To determine both bone mineral density [BMD] and bone turnover (bone formation and resorption) in patients with treated coeliac disease compared with healthy adults.

METHODS: 75 adults (60 females) with coeliac disease (average age 52 years, median duration on gluten free diet [GFD] 3.4 years) had BMD measured at the lumbar spine and femoral neck using Hologic QDR dual energy X ray absorptiometry. 55 (45 females) of the above 75 patients underwent further detailed study of biochemical bone turnover markers. Bone formation was assessed by measuring two products of osteoblast activity, serum osteocalcin (Bone Gla protein) and procollagen 1 carboxyterminal peptide (PICP), and resorption assessed with the urinary collagen crossticks, pyridinoline (Pyr) and deoxypyridinoline (DPyr).

RESULTS. BMD in patients was significantly lower than in paired healthy controls matched for age and sex, at both spine (0.886 c.f 1.000 g.cm², p=0.001, Student's t test) and hip (0.721 c.f 0.76 g.cm², p=0.04). Compared with controls, patients had higher serum PICP (111.6 c.f 80.8 µg/ml, p<0.001), urinary Pyr (16.1 c.f 11.9 nmol/mmol creatinine, p=0.02) and DPyr (5.4 c.f 2.3 nmol/mmol, p<0.001). There was no difference in serum osteocalcin compared with controls (5.9 c.f 6.1 µg/l). There was no overall correlation between the bone turnover markers and BMD or rate of loss of BMD, however in the subgroup of postmenopausal coeliac patients (n=23) there was a significant negative correlation between %/year change in BMD and both Pyr (r=-0.722, p=0.001, Spearman's rank correlation) and DPyr (r=-0.69, p<0.005).

CONCLUSIONS: Reduced BMD is an important complication of coeliac disease, and increased bone turnover may be an important underlying pathophysiology mechanism. In particular, in postmenopausal patients high urinary collagen crossticks, which indicate increased resorption, are a marker of future bone loss, and in conjunction with a low initial BMD would indicate those patients most in need of intervention to preserve bone mass.
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TWO PHASE RANDOMISED CONTROLLED CLINICAL TRIAL OF ORAL DIETARY SUPPLEMENTS IN SURGICAL PATIENTS.
A.M. Keefe, M.J. Bray, P.W. Emery and D.B.A. Silk
1Department of Gastroenterology and Nutrition, Central Middlesex Hospital NHS Trust, London NW10 7NS and 2Department of Nutrition and Dietetics, King’s College, London W8 7AH.

It has previously been shown that the administration of oral dietary supplements (ODS) results in clinically significant short-term benefits in surgical patients. The aims of this study were (1) to re-evaluate the short-term clinical efficacy of ODS administered postoperatively to in-patients undergoing gastrointestinal surgery (phase 1), and (2) to investigate the clinical efficacy of ODS given during the first 4 months following hospital discharge (phase 2). 100 patients who were scheduled to undergone major gastrointestinal surgery entered the study. They were randomly assigned to receive a normal ward diet postoperatively, or the same diet supplemented ad libitum with ODS (Fortiap, Nutricia, 6.3 kcal/ml, 8 mg N/ml). The study period was from the day the patients started ingesting free fluids postoperatively (mean 5.3 days after surgery) until the day of hospital discharge. On discharge patients were further randomised to their usual home diet, or taking ODS in addition to their usual dietary intake for 4 months, resulting in the formation of 4 treatment groups in phase 2.

In phase 1, the mean daily energy and protein intakes were significantly higher in the treatment group than in the control group at study days 1, 2, 3 and 4 (by an average 1473±SEM 122 kcal, 13±1.3 g protein). Patients in the treatment group lost significantly less weight than control patients by discharge: 2.2±0.5 kg vs 4.2±0.4 kg, (p<0.001). Control patients showed a significant reduction in hand grip strength over their hospital stay, (p<0.02), whereas treatment patients maintained their hand grip strength. Significantly more patients in the control group (12) developed serious complications (wound infection,2, wound dehiscence 1, gastrointestinal perforation 1, septicemia 1, multiple complications 1) than in the treatment group (4; wound infection 2, wound dehiscence 1, multiplications 1; p<0.05). In phase 2, supplemented patients had significantly higher energy and protein intakes one month after discharge compared with controls. However, patients in the treatment group showed no significant differences in nutritional status and wellbeing between the groups.

We conclude that the prescription of oral dietary supplements postoperatively to patients undergoing moderate to major gastrointestinal surgery results in clinically significant benefits. These benefits, however, are restricted to the in-patient phase.

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A COMPARISON BETWEEN ORAL AND NASOGASTRIC (NG) NUTRITIONAL SUPPLEMENTS IN MALNOURISHED PATIENTS.
JP McWhirter, CR Pennington, Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee, UK.

Malnutrition is associated with increased morbidity and length of stay in hospital. Studies have shown that malnutrition is common and not recognised in the majority of affected patients. Most malnourished patients are not referred for nutritional support. There is a common perception that oral supplements are not taken, or reduce the consumption of oral diet, and that NG feeding is poorly tolerated. The aims of this study were: to assess the efficacy of supplemental enteral feeding on the nutritional status, to compare oral supplements (OS) with overnight supplemental NG feeding on nutritional outcome and to determine the influence of supplemental enteral feeding on oral diet. Patients malnourished on admission to hospital were randomised to one of 3 groups; control (C), OS or NG. All patients had access to hospital diet recorded on food record charts. In the treatment groups supplements were prescribed to meet estimated nutrient needs. Nutritional status was recorded at the start and the end of the feeding period. The total nutritional intake of all patients and tolerance of the feeding method was recorded. Eighty-six patients completed the study, (26C, 35 OS and 25 NG). 7 refused NG, 2 refused OS and 3 were withdrawn. More than 80% of energy requirements were achieved in 4 of the controls, 71% OS and 88% NG (p<0.001). Weight gain occurred in 2 (15%) C, 22 (63%) OS and 17 (68%) NG while weight loss occurred in 19 (73%) C, 9 (26%) OS and 6 (24%) NG (p=0.6). The mean weight changes were -2.5±C, -1.04±OS, +3.3% NG (p=0.001). The mean energy intake from food was 1250 C, 1090 OS, 1020 NG (p<0.05). There were no documented complications of OS. 3 complications of NG included 1 case of diarrhoea, 1 of bloating and 1 accidental removal of the tube. Thus without nutritional supplements, malnourished patients lose weight while nutritional supplements allow weight gain. NG feeding more effectively meets nutritional gaps. JP McWhirter is supported by Clintone Nutrition Ltd.

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METABOLIC MANIPULATION OF HYPERCATABOLIC CHRONICALLY SEPTIC PATIENTS USING RECOMBINANT HUMAN GROWTH HORMONE (rhGH), G.E.A. Betty*, C. Camacho-Hubner*, J.Powell-Tuck*, Department of Human Nutrition, The London Hospital Medical College, Whitechapel, London, E1 1BB. 2Department of Chemical Endocrinology, St Bartholomew’s Hospital, West Smithfield, London, ECIA 7BE.

Some gastronutritional patients remain septic and catabolic for long periods; feeding alone may not achieve positive nitrogen balance. Studies are difficult because stability of the septic state is required for meaningful measurements. 6 patients (4 m, mean age 52.7±20.5yrs with chronic stable sepsis receiving total parenteral nutrition (TPN) for gastrointestinal(GI) failure, pre-operative ileus or anastomotic leak was studied. Each patient was randomised to receive either 0.03 or 0.06mg/kg/day of rhGH (Nordisk Nordisk), given subcutaneously for 7 nights. Measurements included resting energy expenditure (REE) by indirect calorimetry to calculate TPN requirements, 12x hourly plasma samples (before first and after last dose of rhGH) for growth hormone (GH), to assess GH and continuous 24hr urine collections for urea nitrogen, full blood count and biochemical profile. Sepsis scores were calculated. Plasma was taken daily at 0900hrs for insulin-like growth factors (IGF-I,IGF-II), insulin-like growth factor binding protein (IGFBP-1,IGFBP-3) and insulin levels. Results were as follows:

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SUPPLEMENTAL ENTERAL NUTRITION IN PATIENTS UNDERGOING MAJOR RESECTIONAL SURGERY.
PM Murchan I Bradford D Palmer S Townsend CJ Mitchell J Macfie
Combined Gastroenterology Unit, Scarborough Hospital, UK.

We investigated the impact of supplemental enteral nutrition given in pre- and post-operative period on nutritional status and outcome of patients undergoing major excisional surgery.

Patients were randomised to receive normal diet or diet supplemented by a commercially available nutritional sip feed (20g protein 600 kcal/400 ml per day), for a minimum period of 14 days preoperatively and further randomised postoperatively. Parameters analysed: weight, hospital stay, POSSUM score, morbidity, serum proteins, anthropometric measurements and serial dynamometric assessment of muscle function. Group A, Pre- and postoperative supplements (n=12), Group B Pre-operative supplement only, (n=14), Group C Post-operative supplements only (n=11), Group D, No supplemental nutrition (controls) (n=13). Patients were well matched for age, sex and type of operation as well as standard home and in hospital patients. Patients receiving pre-operative nutritional support (groups A & B) showed a mean weight gain (0.14±0.09kg) from randomisation to day of surgery differing significantly with a weight loss of 1.2±0.74kg observed in controls (p < 0.05, ANOVA) While patients in all groups sustained some weight loss following surgery, control patients had a significantly greater weight loss than patients in any of the treatment groups (D of A, P < 0.01; D of B P < 0.05; D of C, P < 0.05). Duration of hospital stay was longer in patients not receiving any sip feeds (15±2 days) compared to patients receiving both pre- and post-operative nutrition (25±3 days) P 0.05. No differences were recorded in complication rates, POSSUM scores or biochemical indices of nutritional status. Pre- and post-operative supplemental nutrition reduces the inevitable weight loss associated with major excisional surgery and results in earlier hospital discharge.

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CIRCULATING IGA ANTIBODIES TO 60KDA BUT NOT 32KDA HEAT SHOCK PROTEINS ARE RAISED IN PATIENTS WITH HELICOBACTER PYLORI-RELATED GASTRIC ATROPHY.

SGRG Barton, ILP Beales*, VR Winrow, DS Rampton, J Calam*, London Hospital Medical College and *Hammersmith Hospital, London

Heat shock proteins (HSP’s) are ubiquitous, highly immunogenic intracellular molecules induced in vitro by inflammatory mediators and oxygen free radicals. It has been suggested that they may induce autoimmune phenomena in vivo. Helicobacter pylori (HP) causes varying gastroduodenal pathologies and it itself produces a 60kDa HSP and induces free radical stress. We have now assayed sera of patients with either gastritis (G), gastric atrophy (A), duodenal ulcer (DU) or gastric ulcer (GU), all with HP infection, as well as sera of HP-negative controls (N), for antibodies to the 60kDa and 32kDa HSP’s.

Methods: All sera were tested for Iga, IgG and IgM antibodies against both 60kDa and 32kDa HSP antigens using established ELISA’s. Results are expressed as optical density ratios using a standard control.

Results: 32 kDa HSP serology results showed no differences between patient groups. 60 kDa HSP serology results are shown below (mean (SEM)).

<table>
<thead>
<tr>
<th></th>
<th>HP +ve</th>
<th>HP -ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iga</td>
<td>1.82(0.32)</td>
<td>1.03(0.09)</td>
</tr>
<tr>
<td>IgM</td>
<td>2.74(0.29)</td>
<td>2.24(0.29)</td>
</tr>
<tr>
<td>IgG</td>
<td>2.97(0.46)</td>
<td>1.13(0.12)</td>
</tr>
</tbody>
</table>

*p<0.005 from normal

*p<0.05 from gastritis (Mann-Whitney U)

Conclusions: Elevated Iga antibody levels to the 60kDa HSP in patients with HP-related gastric atrophy compared with HP-negative normal patients may reflect (a) a response to increased release of HSP from damaged gastric epithelial cells, and (b) generation of antibody cross-reacting with HP-derived and/or induced HSP. Elevated Iga antibody levels in atrophy patients compared to gastritis patients may indicate more HSP production and (2) contribute to gastric atrophy through an adverse effect on epithelial cell protection by HP’s.

H. PYLORI INFECTION IS ASSOCIATED WITH DECREASED GASTRIC JUICE β-CAROTENONE CONCENTRATION.

ZW Zhang, SE Patchett, D Perrett, P Dominzo, MJG Farthing. Digestive Diseases Research Centre, Depts of Medicine & Histopathology, Medical College of St Bartholomew’s Hospital, London, UK.

Previous studies suggest that β-carotene may be protective against gastric cancer. This is thought to be related to its ability to inhibit lipid peroxidation especially at low oxygen partial pressures. Factors decreasing gastric β-carotene concentration may increase the risk of gastric cancer. This study aimed to investigate effect of H. pylori infection on gastric luminal β-carotene concentration and relate this to the severity of histological changes in the stomach.

β-carotene concentrations were determined in gastric juice of 59 consecutive patients attending for upper endoscopy. H. pylori status was determined by rapid urease test, histology and culture. All specimens were examined ‘blind’ by the same histopathologist and both density of organisms and severity of histological changes were graded (0-3) according to the Sydney system. Measurements were performed in duplicate using HPLC/evanthroelectrical detection and expressed in µM (median [interquartile range]). There was no association between β-carotene levels and patient age or sex. H. pylori infected patients (77/59) had significantly lower β-carotene in gastric juice than uninfected patients, 3.12 [0.4-8.1] vs 4.33 [3.41-7.39], (p<0.02) and levels were inversely related to the density of organisms (r=0.28, p=0.03). Intestinal metaplasia was associated with significantly lower β-carotene than histologically normal mucosae 2.82 [2.0-3.96] vs 4.76 [3.5-6.88], (p<0.05). Increasing severity of inflammation and degree of atrophy were also associated with decreasing β-carotene levels though this failed to reach statistical significance.

H. pylori infection and its related histological changes are associated with decreased gastric luminal β-carotene concentrations. This may be relevant to the development of gastric neoplasia perhaps through impaired prevention of lipid peroxidation at low oxygen tensions found in the stomach.

SOMATOSTATIN RECEPTOR 1 (SSTR 1) mRNA IS REDUCED IN HELICOBACTER PYLORI (Hp) INFECTION.

Gibbons A.J., Legon S. and Calam J. Depts. of Medicine and Metabolic Medicine, Hammersmith Hospital, Du Cane Road, London, W12 ONN.

Introduction. 5 subtypes of somatostatin (SST) receptor have been identified so far. Northern blotting of SST mRNAs suggests that SST1 is the most abundant in human gastric mucosa. SST1 mRNA has not been studied extensively but is thought to mediate the inhibitory effect of SST on cell proliferation. As gastroepithelial proliferation and the risk of gastric carcinoma are increased in Hp infection we studied the abundance of SST1 mRNA in patients with and without this infection.

Method. Biopsies were taken from the gastric antrum of 6 Hp+ and 4 Hp- dyspeptic patients for total RNA extraction and Northern blotting. A 32P labelled cDNA probe for SST1 was used to detect the mRNA, the signals being quantified by phosphor imaging. GADPH mRNA levels were measured to correct for loading and transfer variations.

Results. The expression of SST1 mRNA in the gastric antrum was significantly reduced in Hp positive patients (p<0.005). The median antral SST1 mRNA in Hp+ mucosa was 0.3 (0.2-0.4) versus 0.6 (0.4-0.8) in Hp-mucosa. The ratio of expression was 0.5 in Hp+ patients. There are three SST gene duplications in human. Deficiency of this receptor may further decrease the expression of SST receptor in antral mucosa.

Conclusions. Elevated levels of SST1 mRNA in Hp negative patients suggest that SST1 is possibly protective against gastric cancer.
A COMPARISON OF OMEPRAZOLE 10MG AND 20MG OM WITH RANITIDINE 150MG BD FOR THE TREATMENT OF GORD IN PRIMARY CARE.

Venables T, Newland R, Patel AC, Hole J, Mulholland G, Turbitt M, Wright T, (introduced by PDI Richardson). Calvert Practice. St Wilfred's Sq, Calverton, Notts. NG16 4FP

Nine and forty patients with heartburn as the predominant symptom were endoscoped (only ulcerative oesophagitis excluded), then randomised double blind to omeprazole 10mg om, omeprazole 20mg om, or ranitidine 15mg bd for 4 weeks. The three groups were well matched at entry.

The primary efficacy variable of relief of heartburn (no more than 1 day of mild symptoms in the last 7 days) after 4 weeks treatment, was compared between treatment groups for all patients treated and for the subgroup with erosive oesophagitis. The costs of individual treatment success were also calculated.

Treatment groups

<table>
<thead>
<tr>
<th>Patients</th>
<th>Relief of Heartburn</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(N)</td>
</tr>
<tr>
<td>omepr 10 mg</td>
<td>330 (61%)</td>
</tr>
<tr>
<td>omepr 20 mg</td>
<td>338 (44%)</td>
</tr>
<tr>
<td>ranit 150 mg</td>
<td>326 (40%)</td>
</tr>
</tbody>
</table>

Erosive oesophagitis

| Omepr 20 mg | 101 (71%) |
| Omepr 10 mg | 102 (48%) |
| Ranit 150 mg | 113 (33%) |

Both 10mg and 20mg doses of omeprazole om provided relief of heartburn in significantly more patients than ranitidine 150mg bd (p<0.05, p<0.001 respectively). The omeprazole groups also showed greater symptom relief compared to ranitidine in those patients with erosive grade 2 and above oesophagitis (p<0.05, p<0.001 respectively). In all cases the costs of treatment success are lower with omeprazole.

MONITORING THE LOWER OESOPHAGEAL SPHINCTER - SPHINCTOMETER OR SLEEVE?

Nigel Trudgill, Faz Hussein, Stuart Riley. Northern General Hospital, Herries Road, Sheffield, S5 7AU

Lower oesophageal sphincter (LOS) function has been extensively studied using the Dent sleeve. Recently a solid state sphincter containing a sphinctometer and a perfused catheter, which measured gastric, oesophageal and LOS (via a Dent sleeve) pressures, submental EMG monitored swallowing and a pH probe was positioned 5 cm above the LOS. Following 20 minute accomodation and 30 minute basal recording periods, 200 kcal of long chain triglyceride (calogen) was infused into the stomach. Manometric and pH data was then recorded for a further 60 minutes.

Results: Sleeve and sphinctometer readings correlated well within individuals. Using the criteria proposed by Holloway (Gastroenterology 1991;A-205), 16 out of 16 tests gave a LOS present (LOS>4 cm H2 by 1 min end-tidal gas tension time). Following acidification and normal food intake, 13 of the 16 tests gave a LOS present, with 9 of these tests giving a sphinctometer reading abnormal by the criteria proposed by Holloway.
OESOPHAGEAL MOTOR RESPONSES TO GASTRO-OESOPHAGEAL REFLUX IN HEALTHY CONTROLS AND REFLUX PATIENTS.

A.Anggiansah, G Taylor, J Simpson, NF Bright, J Wang, WA Owen, AR Jones, WJ Owen. Dept of Surgery, Radiological Science and Public Health Medicine, Guy’s and St Thomas Hospital, London.

This study compared oesophageal motor responses to gastro-oesophageal reflux in 16 healthy controls (Group 1) and 25 reflux patients, of whom 15 were without (Group 2) and 10 with oesophagitis (Group 3).

All subjects had 24-hour ambulatory oesophageal pH measurements (5cm above the lower oesophageal sphincter (LOS)) combined with pressure monitoring (5, 10 and 15cm above the LOS). Motor activities occurring during reflux episodes (pH>4) were analysed semi-automatically. Contraction patterns (peristaltic, simultaneous, segmental and mixed-type including reverse peristaltic) and also the peristaltic contraction characteristics (amplitude, duration and velocity) were compared between the 3 groups. The total reflux episodes (RE), associated total motor activities (MA), total reflux duration (RD), average motor activities per minute (AMA), and medians of the total percentage of reflux (PR) in the 3 groups were:

<table>
<thead>
<tr>
<th>Group</th>
<th>RE MA RD (mins)</th>
<th>AMA PR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>459 706 465.6</td>
<td>2.1* 1.35*</td>
</tr>
<tr>
<td>Group 2</td>
<td>794 1923 2623</td>
<td>0.9 10.7</td>
</tr>
<tr>
<td>Group 3</td>
<td>579 1263 1482.6</td>
<td>1.0 9.1</td>
</tr>
</tbody>
</table>

AMA was significantly higher and PR was significantly lower in Group 1 (*p<0.05) but no differences were found in other groups. In all groups, the most common contraction patterns of motor activities was peristaltic. The ¾ of peristaltic activity per subject was significantly higher in Group 1 (*p<0.05). There were no significant differences in other patterns of contraction in the 3 groups (p>0.5). Of the peristaltic contraction characteristics there were no significant differences in any parameters (amplitude, duration and velocity) in the 3 groups (p>0.05).

Motor responses to reflux were more frequent in controls than in reflux patients. Contractions in response to reflux was found to be predominantly peristaltic. The motor activities were similar in all groups except that the peristaltic activity was stronger in healthy controls.

CHARACTERISTIC OF REFLUX IN RELATION WITH SYMPTOM EVENT IN PATIENTS WITH GASTRO-OESOPHAGEAL REFLUX RESISTANT TO OMEPRAZOLE THERAPY.


Omeprazole is successful in producing relief from symptoms of gastro-oesophageal reflux (GOR) but it has been suggested between 10-20% fail to get symptom relief.

We investigated thirty-four patients (18 male, 16 female), age range 29-73 years (mean 40.3) with GORD with persistent heartburn and chest pain, who did not respond to omeprazole therapy. Mean duration of symptom was three years and period of treatment was between 1-5 months with omeprazole 20-40 mg daily. Omeprazole was stopped seven days prior to the study.

All patients underwent 24 hour simultaneous oesophageal and gastric pH monitoring. Oesophageal pH was recorded 5 cm above the lower oesophageal sphincter determined manometrically and gastric pH was monitored at 15 cm below the oesophageal sphincter.

A symptom event was defined as secondary to an acid reflux episode when oesophageal pH<4 or alkaline reflux when oesophageal pH>7 with associated rise in gastric pH>4 for longer than 20 seconds (2 minutes before and after the onset of symptom). The latter was analysed during inter-prandial periods only.

A total of 147 symptom events occurred during 24 hour pH monitoring in 34 patients.

<table>
<thead>
<tr>
<th>Pathological acid reflux</th>
<th>49/147</th>
<th>33.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological alkaline reflux</td>
<td>26/147</td>
<td>19.0%</td>
</tr>
</tbody>
</table>

Symptoms but no reflux | 70/147 | 47.6% |

This study shows 33.3% symptoms were associated with acid reflux and 19.0% symptoms were associated with alkaline reflux whereas 47.6% symptoms were not associated with reflux. This suggests acid sensitive oesophagus and alkaline reflux are important factors which may contribute to failure of omeprazole therapy in this group of patients. Symptoms without reflux suggests these patients may have altered perception of pain or may have anxiety.

DOES INTOLERANCE OF pH MONITORING CAUSE FALSE NEGATIVE RESULTS?

Mckeen, I.A, Douglas, S, Heading, R.C. Centre for Liver and Digestive Disorders, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh.

Several centres report that among patients undergoing diagnostic oesophageal pH monitoring, a small proportion show a positive symptom index (SI) with normal acid exposure time (AET). There is still doubt about whether these patients represent a distinct group within the GORD clinical spectrum or whether these findings are false negative results, perhaps related to intolerance of the test.

We invited 207 consecutive patients undergoing pH monitoring to record their deviation from normal eating patterns and degree of distress on visual analogue scales (VAS) on completion of the test. Regression analyses and Chi square tests were used to compare VAS results with demographic and clinical features, looking particularly for associations with distress or failure to eat normally during the test.

Only 27% of patients recorded a degree of distress in the upper half of the VAS. In patients with positive SI, no associations were found between eating pattern or distress during the test and symptoms of heartburn or dysphagia, presence or absence of oesophagitis or AET. However tolerance of the test was less good in young patients.

Patients showing a positive SI and normal AET have not been especially intolerant of the test. This suggests that the results cannot be categorised simply as "false negatives" and that the patients represent a distinct group with symptomatic reflex disease.


Previous studies have shown that various regions of the gut, in particular the colon and rectum, are abnormally sensitive to balloon distension in patients with IBS. However, these studies have only examined up to two anatomical regions in the same patient at any one time and thus it is not known whether all or just specific areas of the gut are abnormally sensitive. Sensory and motility responses to balloon distension of the oesophagus (O), duodenum (D), jejunum (J), ileum (I) and rectum (R) were therefore evaluated in random order in 20 patients with diarrhoea predominant IBS (aged 22-57, 11 females) and compared with 20 matched healthy volunteers (aged 20-57, 10 females).

All patients had loose stools (>3 bowel movements per day) and fulfilled the Rome criteria for IBS. In addition, patient anxiety scores were evaluated using the Hospital Anxiety and Depression questionnaire (abnormal > 10). Results: In accordance with previous studies, IBS patients had significantly lower sensory thresholds in the R [vol to discomfort (mL): IBS 109(60,225) geometric mean (range) v controls 175(30,325); p<0.001] and C (100(50,180) v166(60,500); p=0.03) compared with controls. Furthermore, IBS patients exhibited significantly lower thresholds for discomfort, provoked by distension of the O (106(20) v 208,110; p=0.002), D (145(15,170) v 120(15,150); p=0.002), J (380(20,150) v 370(10,170); p<0.001), and I (38(15,120) v 55(30,150); p=0.03). However, these sensory changes were not associated with any change in cmH2O at mean volume to discomfort: O, 0.45(0.25,0.96) v 0.49(0.22,2.38); D, 3.41(4.79,6.3) v 3.21(5.92,8.28); J, 2.44(1.9,8.13) v 2.11(1.8,12.6); I, 1.76(0.99,1.45) v 1.49(0.92,5.5); and C, 3.4(0.8,6.3) v 3.4(1.6,6.2); R, 5.92(8.2,12.5) v 5.92(3.2,10.3). In addition, although patients had higher anxiety scores (92(19), median [range]) than controls (4.5(2,7); p<0.001), there was no correlation between their anxiety score and sensory threshold in the D (r = 0.21; p=0.39; I = 0.23; p = 0.28; C = -0.28; p=0.38) and R (r = -0.41; p=0.08), with the exception of the O (r = -0.54; p=0.027). Conclusion: This is the first study to confirm the suspicion that IBS represents a generalized disorder of visceral sensation. Furthermore, although these results do not exclude a sensory defect at a local level within the gut, they lend some support to the concept of there being an abnormality of the visceral afferent nervous system or in central modulation.
GUT 1995; 37 (suppl 2)

ANXIETY, DEPRESSION AND INTESTINAL TRANSIT.
DA Gorard, JE Gombrone, GW Libby, MIG Farthing. Digestive Diseases Research Centre, Medical College of St. Bartholomew's Hospital, London.

Patients with anxiety and depression often have bowel symptoms, but there have been no objective measurements of intestinal transit in patients with psychiatric illness. This study measured intestinal transit times in 21 psychiatric outpatients (5 M, median age 27y, range 17-45y) fulfilling DSM-III-R criteria for major depression and/or generalised anxiety disorder. These patients were taking no drugs and bowel symptoms were not necessary for study entry. 21 healthy controls, 6 M, 24 (19-45y) were also studied. All subjects had a structured clinical interview and completed the Beck Depression Inventory (BDI), and Hospital Anxiety (HAD-A) and Depression (HAD-D) scale. Orocecal transit time (OCCT) was measured by lactulose hydrogen breath test. Whole gut transit time (WGGT) was measured by abdominal radiography after ingestion of radio-opaque markers on 3 consecutive days.

Results: median (range)

<table>
<thead>
<tr>
<th>Anxiety</th>
<th>Depresson</th>
<th>Anx. &amp; depression</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI</td>
<td>11.5 (7-19)</td>
<td>25 (10-41)</td>
<td>19.5 (18-22)</td>
</tr>
<tr>
<td>HAD-A</td>
<td>15 (11-17)</td>
<td>12 (7-18)</td>
<td>15 (11-16)</td>
</tr>
<tr>
<td>HAD-D</td>
<td>5.2 (5-10)</td>
<td>11 (9-18)</td>
<td>13 (10-15)</td>
</tr>
<tr>
<td>OCCT (min)</td>
<td>60 (10-70)</td>
<td>110 (60-180)</td>
<td>70 (60-90)</td>
</tr>
<tr>
<td>WGGT (b)</td>
<td>14 (6-29)</td>
<td>49 (35-71)</td>
<td>14 (18-43)</td>
</tr>
</tbody>
</table>

The anxiety group had shorter transit times than both the depressed group (OCCT, p<0.01; WGGT, p<0.001) and the controls (OCCT, p=0.05; WGGT, p<0.001). Prolongation of transit time in depression compared to controls did not reach statistical significance (OCCT, p = 0.08; WGGT, p=0.09). However in the total patient group, WGGT correlated positively with BDI (r = 0.59, p<0.01) and HAD-D (r = 0.66, p<0.001).

These measurements of transit in affective disorders are consistent with clinical impressions that anxiety is associated with increased bowel frequency, and depressed patients tend to be constipated. The findings demonstrate that mood has a direct effect on the enteric nervous system.

WGA8

DO AMBULATORY POUCH AND ANAL MOTILITY PATTERNS IN COLON POUCHES EXPLAIN POOR FUNCTIONAL RESULTS?
J Romanos, S Humphreys, NJ McC Mertesken
Department of Colorectal Surgery, John Radcliffe Hospital, Oxford

Colonic anastomosis with a J-colon pouch formed from the descending colon is a relatively new operative approach to tumours of the middle and lower third of the rectum. This may avoid the functional problems of increased frequency, urgency, incontinence and nocturnal soiling associated with rectal excision. The aim of this study was to record the motility pattern of the neorectum, its coordination with anal canal motor activity and its relation to functional outcome.

Fourteen patients (9 male, 5 female; median age 62, range 43-71) were assessed clinically and studied using ambulatory manometry (Gaeltec 4 transducer system) for a median duration of 6 hours (range 6-24). Twelve patients had a functional pouch for a median period of 32 months (range 11-25) and two patients with a pouch formed 7 and 12 months previously still had their neoanal canal. Seven healthy controls (5 male, 2 female; median age 40, range 33-50) were studied for a similar period.

Median day and night time stool frequency in 12 patients with a functioning pouch, was 3.3 (1-6) and 0.3 (0-2) respectively. Four patients complained of minor faecal leakage and 7 of incomplete evacuation. Compared with the controls the pouch group had lower resting anal pressures, median 73 (44-118) vs 100 (45-120) cmH2O and higher pouch pressures, median 25 (4-74) vs 15 (5-29) cmH2O. Proximal canal pressure gradient was as high as 60 (4-114) cmH2O in pouch patients and 85 (32-100) cmH2O in the control group (NS). Incontinent patients even lower pressure gradients than continent patients (p<0.005). Slow wave activity in the anal sphincter (median frequency 7 cps; controls 16 cps, p<0.001) was present in 12 patients (85%). "Sampling episodes" were seen in 7 patients (50%). Two incontinent patients (14%) showed spontaneous anal relaxation with a reversed pressure gradient. Large isolated contractions (>30 cmH2O and >20 sec) were seen in 10 patients (83%). Rythmic contractions were seen in 7 (50%) patients.

These motility patterns tended to be more prominent in poor function (incomplete emptying, incontinence) pouches. Apart from a few rhythmic low amplitude contractions, no other activity was observed in non functioning pouches.

Colonic pouches represent a very promising alternative to the excised rectum, acting as reservoirs which preserve a high pressure gradient against the already compromised anal canal. In poor function pouches a lower pressure gradient and more prominent motility pattern was noted.

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COLONIC DISTRIBUTION OF DAILY DOSED, RADIO-LABELLED RESIN : RIGHT-SIDED RESERVOIR & LEFT-SIDED CONDUIT.
Hebdon JW, Gilchrist PJ, Blackshaw PE, Perkins AC, Wilson CG, Spiller RC. Dept of Medicine, University Hospital, Nottingham & Dept of Pharmacology, Strathclyde University

Early radiological studies of regional colonic residence used radio-opaque pellets which give a poor colonic image especially for regions containing few pellets. We have used repeated dosing with radio-labelled resin to provide a clear colonic outline allowing accurate assessment of regional distribution of resin.

Methods: On 4 consecutive mornings 10 healthy female volunteers ingested a Eudragit-coated gelatin capsule containing In111-labelled amebrite resin. Subjects were scanned in the morning immediately prior to dosing and at 4, 8, 12 and 16h later. The distribution of label in ascending (AC), transverse (TC), descending colon (DC), and rectosigmoid region (RS) was measured in a total colonic activity. Results (mean±SEM, n=10).

Similar activity distributions were obtained in each of the 4 scans. Averaging the 4 scans activity was as follows: AC 30±8, DC 36±6, DC 15±4 & RS 19±5%. The mean % in the distal colon (DC+RS) was 34, the 95% Confidence Interval 45±23 did not overlap 50%, p<0.05.

Conclusions: During the day 2/3rds of a daily dose, enteric coated formulation lies within the proximal colon with only 1/3rd in the distal colon and only 15% in the DC. Compared with the proximal colon's reservoir function the distal colon appears to behave more like a conduit.

The descending colon appears to be the most difficult area of the colon to target with locally acting drugs.

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WITHDRAWN
Liver perfusion F189-F192

Indocyanine Green Clearance reflects the degree of reperfusion injury and accurately predicts graft function following orthotopic liver transplantation.

JN Plevris, K Rajadhyaksha, H Smith, M Rollins, A Lee, NDC Finlayson, PC Hayes
Scottish Liver Transplant Unit, The Royal Infirmary Edinburgh, Scotland.

Introduction: Primary graft dysfunction remains difficult to predict. We have previously shown that indocyanine green clearance (ICCG) measured at 24hrs following orthotopic liver transplantation (OLT) accurately predicts graft survival and outcome.

Aims and Materials: We evaluated the use of ICCG as a marker of graft function following OLT in 46 liver transplants (41 patients; 16 males, 25 females) and investigated its relationship with the markers of reperfusion injury during OLT. In all patients ICCG was measured at 24hrs; in 4 patients ICCG was measured at the end of operation and 4-8 hours for 48hrs. In 24 patients repeated blood samples were taken before, during the anhepatic and reperfusion phase and up to 12 hrs following OLT to measure the levels of neutrophil elastase and reactive oxygen intermediates (ROI). All patients had normal hepatic artery Dopplers post-OLT.

Results: a) All patients with ICCG >200 ml/min (N=38) recovered following OLT and remained well. Eight patients had an ICCG <200 ml/min, four were retransplanted for graft failure, 2 died and 2 survived after prolonged hospitalisation. b) ICCG significantly correlated with ROI production and neutrophil elastase during OLT (R= -0.74, p<0.01 and R= 0.70, p<0.01 respectively) c) Repeated ICCG’s did not change during the first 48 hrs post-OLT.

Conclusion: ICCG at 24hrs post OLT reflects the degree of reperfusion injury and accurately predicts primary graft function and outcome.

ROLE OF GMP ON HAEMODYNAMIC CHANGES DURING LIVER TRANSPLANTATION.

K. Basta, N. Henderson, J. Dillon, A. Lee, P. Hayes
Scottish Liver Transplant Unit, Edinburgh Royal Infirmary.

During liver transplantation haemodynamic instability particularly upon reperfusion often occurs. Profound pulmonary hypertension, systemic hypotension and cardiac arrest have been reported. Changes in vascular tone due to humoral factors released upon reperfusion of the graft has been suggested as a possible mechanism. In this study we looked at the changes in cGMP, a marker of nitric oxide (NO) activity before and upon reperfusion, and investigated its possible role in the haemodynamic changes.

Methods: Measurements of cGMP by radioimmunoassay were performed on blood samples taken through a right atrial catheter from 14 patients at pre-anhepatic, anhepatic phase and post reperfusion at 30 minutes, one and two hours. Haemodynamic data were recorded mean systemic and pulmonary arterial pressures (MAP, MPAP), cardiac output (CO), pulmonary and systemic vascular resistances (PVR, SVR).

Results: cGMP decreased to 3.19 ± 0.88 nmol (Mean ± SEM) upon reperfusion from a baseline level of 5.33 ± 0.73 nmol/L (p<0.01). It decreased further to 1.63 ± 0.90 nmol/L two hours post-reperfusion. MAP decreased on reperfusion to 74 ± 9.8 from 88 ± 5.4 mmHg (p<0.05), MPAP increased to 23 ± 7 mmHg, from 17 ± 4 mmHg (p<0.02), and PVR to 135 ± 4.6 from 62.8 ± 9.6 dyn-s-cm⁻¹ (p<0.01). CO decreased to 8.72 ± 0.84 L/min, from 10.3 ± 1.6 L/min (NS), and SVR to 571 ± 76.2 from 632 ± 105 dyn-s-cm⁻¹ (NS). The changes in cGMP correlated with MPAP (p<0.01), and PVR (p<0.01) when compared at equivalent time points.

Conclusion: The haemodynamic alterations seen in this study were comparable to those reported in literature. The significant increase in pulmonary pressure and vascular resistance correlated with the reduction in NO activity following reperfusion. This could be the initiating mechanism of further potential haemodynamic deterioration.


HAEMODYNAMIC CHANGES IN TOXIC HEPATIC INJURY.

A.L. Makin, R.D. Hughes and Roger Williams. Institute of Liver Studies, King’s College School of Medicine and Dentistry, London SE5 8RS, U.K.

The hyperdynamic circulatory changes induced by acute hepatic failure are associated with multiple organ failure and a high mortality. Aims: To determine to what extent the changes in systemic haemodynamics affected hepatic haemodynamics. Methods: Experiments were performed at different times over the course of severe toxic liver injury induced in rats by galactosamine (1.1 g/kg, i.p.). Liver injury was confirmed by a prolonged INR and elevated AST. The animals (n=6-10) were subjected to hepatic vascular occlusion (HVO) and portal venous (PVBF) blood flow were measured using the radioisotope microsphere technique. Hepatic arterial (DhaO₂) and portal venous (DpvO₂) oxygen delivery were calculated from blood flow values and direct measurements of arterial and portal venous blood oxygen content. Results: MAP fell from a baseline value of 115 ± 6 mmHg (± SEM) to 99 ± 1.3 mmHg at 12 hours and 84 ± 1.5 mmHg at 24 hours (p<0.05), recovering to 90 ± 3.5 mmHg by 48 hours. Cardiac output did not alter from a baseline value of 240 ± 13 ml/min until after 12 hours and peaked at 404 ± 18 ml/min (p<0.05) by 48 hours. Within 12 hours of galactosamine administration total hepatic blood flow increased by 60% from 3.3 ± 0.3 ml/min to 5.3 ± 0.8 ml/min (p<0.05), mainly due to increased PVBF. Over the next 12 hours HABF increased by 450% from 0.1 ± 0.2 ml/min to 4.5 ± 0.7 ml/min (p<0.01). Between 24 and 48 hours PVBF increased by a further 100%, from 2.6 ± 0.5 ml/min to 5.3 ± 2.1 ml/min (p<0.05). At 48 hours total hepatic blood flow had increased by 500% from baseline with 44% of the cardiac output passing via the hepatic circulation compared to a control value of only 21%. In control animals DpvO₂ is twice DhaO₂ (3.2 ± 0.1 and 1.5 ± 0.1 ml O₂/min/kg, respectively) but within 24 hours the hepatic artery became the dominant source of delivered oxygen. (5.7 ± 0.6 vs 9.2 ± 1.0 ml O₂/min/kg). By 48 hours oxygen delivery to the liver was split equally between the portal venous and arterial circulations (9.7 ± 1.2 and 9.9 ± 1.3 ml O₂/min/kg). Systemic and hepatic haemodynamics returned to control values by 72 hours. Conclusion: These changes in the hepatic circulation may have important implications for the management of fulminant hepatic failure. The inotropic agents used to maintain the MAP are vasoconstrictors and may thus impair arterial blood flow and oxygen delivery at a stage when the artery is the main source of delivered oxygen further compromising cellular function and exacerbating the hepatic injury.

Clinical vs haemodynamic response to drugs in portal hypertension
PA McCormick, D Patch, L Greenslade, J Chen, N McIntrye, AK Burroughs University Department of Medicine. Royal Free Hospital School of Medicine, London, UK.

Introduction: Up to now success of drug therapy in individual patients has been based on the occurrence of variceal bleeding. Recently it has been suggested that drug induced changes in the hepatic venous pressure gradients (HVPG) may reliably predict rebleeding, and that an absolute value of 10-12 mmHg or a reduction of ≥ 20% from baseline should be used as haemodynamic indices to target drug therapy. This approach has been reported to be successful for both primary and secondary prophylaxis. Method: We investigated this prospectively in 62 patients with cirrhosis and variceal bleeding who were treated with a combination of propranolol and isosorbide mononitrate. Mean age was 52 years (range 20-80), 46 male, 62% alcoholic. We used the same haemodynamic criteria as above. Drug doses were increased if the haemodynamic criteria of response were not fulfilled. 9 patients had three measurements of HVPG 19 patients were excluded from the analysis 7 because initial measurements were not available, 11 because repeat measurements not performed (including some whobled) and 1 because of very low initial HVPG, leaving 43 patients for analysis Results: There were 27 haemodynamic responders, 10 non-responders. Rebleeding occurred in 9/27 (33%) responders at a mean of 226 ± 59 days and in 4/16 (25%) non-responders at a mean of 575 ± 154 days. Two patients bled shortly after stopping drug therapy, one in the responder and one in the non-responder group. Conclusion: In this cohort, measurement of portal venous pressure did not predict likelihood of rebleeding. Therefore, further prospective studies need to be done, to establish the predictive value of repeated HVPG measurement.
Clinical practice  F193–F199

BISMUTH CARBOMER ENEMAS IN TREATMENT OF CHRONIC UNREMITTING POUCHTIS

Antibacterial drugs are the mainstay of treatment of pouchitis, especially metronidazole which is the only drug with efficacy shown in a controlled study. However 15% of patients have chronic unremitting pouchitis despite medical treatment, with high incidence of side-effects, and recurrence within one week after discontinuation of therapy.

We report the results of an open trial of bismuth retention enemas in patients with chronic unremitting pouchitis. 12 patients (4 females, 8 males; median age 36 years, range 21-47) were studied. All of them discontinued chronic antibacterial or anti-inflammatory therapy on entry to the study. The median follow up time after pouch surgery was 48 months (range 6-104). Diagnosis of pouchitis and its response to treatment were evaluated with the Pouchitis Disease Activity index (PDAI), which includes clinical, endoscopic and histological criteria. Patients were treated with enemas of bismuth citrate mixed with a polycarbophil carboxer (Tillotts Pharma AG Ziefen, Switzerland) for 45 days, and they were monitored for evidence of relapse at monthly intervals for 1-6 months. The median PDAI score decreased from 12 (range 9-15) to 6 (range 4-15) (p<0.002) with decreases in either the clinical symptoms and endoscopic and histologic PDAI scores (p<0.002 for all variables). Of the 10 patients who responded to the treatment (83%), only two experienced an early relapse after discontinuation of therapy (within 2 months). No side-effects were reported. Our findings suggest that a randomized, double blind trial of bismuth citrate/carboxer enemas is warranted in patients with pouchitis.

LONG TERM SEQUELAE AFTER SPHINCTEROTOMY FOR ANAL FISSURE
J N Land, N C Armitage, J H Schotefield.
Dept. of Surgery, University Hospital, Derby Road, Nottingham, NG7 2UH.

Internal sphincterotomy is the standard treatment for anal fissure. It has recently been reported that this procedure may have long term sequelae such as impaired continence in up to 30% of patients.

This study investigated the long term outcome following internal sphincterotomy for anal fissure in one Hospital. Outcome was assessed by postal questionnaire, followed by consultation where requested by respondents. Questionnaires were sent to 128 patients, Ninety nine (78%) were returned. Thirty five patients (33%) had experienced anal pain for more than 1 month post operatively. Twenty eight (28%) complained of persistent mucus discharge, 18% had ongoing difficulty in controlling flatus, 19% had difficulty holding liquid stool.

Ten (10%) patients who replied to the questionnaire wished to be reviewed to discuss ongoing symptoms. Five of these had a recurrent fissure, all of whom were successfully treated with topical GTN cream.

Although sphincterotomy is standard treatment for fissure, a large proportion of these patients will experience either a recurrence of their fissure or a disturbance in their continence mechanism. In view of these findings, non-surgical treatment of anal fissure should be investigated.

Treatment of Corticosteroid Resistant Ulcerative Colitis with Heparin - A report of 9 cases
Richard C Evans and Jonathan M Rhodes
Department of Medicine
University of Liverpool
Liverpool L69 3BX

Heparin, a sulphated proteoglycan, inhibits thrombin formation and neutrophil elastase and binds chemokines. It has potential as an anti-inflammatory agent by inhibition of neutrophil activation, adhesion and endothelial penetration through these mechanisms. The long half-life of endothelial bound heparin may permit intermittent treatment. Previous reports have shown a beneficial anti-inflammatory effect of heparin in Ulcerative Colitis (Geffe et al Lancet 91:337-238-239).

Aims: To assess the role of heparin as a therapeutic agent in Ulcerative Colitis in an open study.

Methods: Hospitalised patients in relapse from Ulcerative Colitis and unresponsive to high dose corticosteroid therapy were treated with intravenous heparin, the dose adjusted to provide standard anticoagulant activity. This continued as subcutaneous injections on discharge, with a gradual reduction in the frequency of doses.

Results: Within one week of starting heparin 6/9 patients had shown a considerable reduction in stool frequency. After two weeks of heparin therapy stool frequency had improved from 7/day (3-11) [median (range),pre treatment] to 3/day (1-15) and by 4 weeks 7/9 were in clinical remission although one subsequently relapsed at 8 weeks while still receiving heparin. Three of the patients required elective colectomy but six remain well. Apart from bruising at s/c injection sites no complications were seen due to the anticoagulant activity.

Conclusion: The response to heparin in patients with UC resistant to standard therapy is encouraging and supports the previous uncontrolled evidence for a therapeutic effect. A controlled trial of heparin in UC is clearly indicated.

CURRENT PRACTICE - USE AND ABUSE OF CHEMICAL Faecal OCCULT BLOOD TESTS
MORAN*, JONES AFI#, CHESSLER IM.
Depts of Clinical Chemistry and Gastroenterology, Birmingham Heartlands Hospital, and Dept of Medicine*, Bristol Royal Infirmary

INTRODUCTION. Chemical faecal occult blood (FOB) tests are liable to interference by dietary peroxidases and faecal degradation, but are routinely used by many clinicians. The aim of this audit was to assess which FOB tests were being used, the laboratory recommendations on use, and the perceived clinical indications and diagnostic value.

DESIGN. Questionnaires were posted to laboratories and consultant physicians and surgeons with an interest in gastroenterology in the West Midlands, and also to GPs in a local hospital catchment area.

RESULTS. Sixteen of the laboratories replied (80%), using a total of >20,000 tests in 1993. Seven different FOB tests were being used, and all but one were gastric tests, with the most commonly used test being Perohex 40C (BDH) (38%). Three-quarters requested 3 faecal samples, 38% advised dietary restriction, 25% advised avoidance of oral iron supplements, and 25% reported grades of positivity. Twenty-two GP's and 32 of the consultants replied (40%). The clinical indications for routine use of FOB tests favoured by the highest proportion of GP's were (a) men with iron deficiency anaemia (IDA) (81%), (b) post-menopausal women with IDA (63%) and (c) altered bowel habit in patients > 50 years (62%). The majority of the consultants requesting FOB tests for the above indications stated that a negative test result would not influence decisions on arranging further investigations. The clinical indications for routine use of FOB's favoured by the highest proportion of consultants were (a) men with IDA (45%), (b) post-menopausal women with IDA (43%) and (c) post-menopausal women with IDA (42%). The majority of the consultants requesting FOB tests for the above indications stated that a negative result would not influence decisions on arranging further investigations. FOB tests were never requested by 42% of the consultants.

CONCLUSION. The wide discrepancies in the routine use of FOB tests indicates that these tests are often used inappropriately. The optimum use of each FOB test requires evidence-based definition.
CLINICAL PATTERNS OF FAMILIAL INFLAMMATORY BOWEL DISEASE: EVIDENCE FOR GENETIC ANTICIPATION?

J Satsangi, C Grossarth-Mat 宾, H Holt, DP Jewell
Gastroenterology Unit, Radcliffe Infirmary, Oxford

Introduction About 15-20% of patients with ulcerative colitis or Crohn’s disease will have another family member affected, usually a first-degree relative. Both genetic and environmental factors may be pertinent. Clinical patterns of disease within families remain poorly documented, but may be valuable in understanding disease heterogeneity, and inheritance of susceptibility.

Subjects Over 200 multiply-affected families resident in the United Kingdom have been identified. Clinical details were obtained from the family members and from their physicians. 54 families in whom 1 parent and at least one child were affected (a total of 77 parent-child pairs), and 155 families in whom at least 2 siblings were affected (a total of 190 affected sibling pairs) were involved. Clinical characteristics were compared in these pairs of affected relatives - disease type (CD, UC or indeterminate), extent, age of onset, need for surgery and presence of extra-intestinal manifestations.

Results Parent-child pairs Parent and child were concordant for disease type in 58 of 77 pairs (75.3%), for extent in 63.6%, extra-intestinal manifestations in 70.1%, and smoking history in 85%. However the median age of onset in parents was significantly higher than in offspring (p<0.05). In 40 pairs, 60.6%, the parent was at least 10 years older than the child at diagnosis.

Sibling pairs Siblings were concordant for disease type in 81.6% of pairs, extent in 76.0%, extra-intestinal manifestations in 83.8% and smoking history in 81.3%. In contrast to the parent-child pairs, in 68.1% (111 sibling pairs), siblings were diagnosed within 10 years of each other. The median age of onset was 24.0 years.

Conclusions Consistent clinical patterns are evident in many families with familial inflammatory bowel disease. The differences in age of onset between parents and children are not readily explained by a simple cohort effect or reporting bias, and may reflect the effect of genetic factors, producing anticipation between generations.

MOTILITY F200–F205

COMPUTERISED RECORDING AND DISPLAY OF OESOPHAGEAL MANOMETRY WITH VIDEO BARIUM SWALLOW

Haylett KR, Vales F, Lee SH, McIlroy RF
University of Birmingham Department of Surgery, Radcliffe Infirmary, Birmingham, M13 9QD.

Aim: To develop a technique, using ambulatory pressure monitoring and digital video recording equipment such that combined oesophageal manometry and barium fluoroscopy can be performed as a one step investigation in patients with suspected swallow disorders. Method: The technique uses a computerised synchronous "WINDOWS" display of the results. The manometry recording was made using a Gaetec MPF2 ambulatory pressure recorder while the barium swallow was recorded from a Philips Diagnostic 66 X-Ray system connected to a personal computer (PC) with a digital acquisition system. The PC controlled both the ambulatory recorder and the digital video system enabling a synchronous review of the combined test. The examination involved intubating the patient with a 4 sensor catheter tip pressure transducer. The profile of the lower sphincter was determined and the transducers located in the oesophagus. This was followed by the combined oesophageal manometry and barium swallow test. The "WINDOWS" display of the two sets of data allowed accurate step forward/backward analysis of the relationship between bolus transit and pressure contractions. Results: The instrument system developed proved able to synchronously display the recorded digital video and manometric recordings; the ambulatory recorder and catheter tip transducer were well tolerated by the patient; the test was not difficult to incorporate into the standard barium swallow examination and the transducer did not interfere with visualisation of bolus transit. Conclusion: Those patients who had been combined test have one less hospital visit than normal and benefit from having the two related investigations performed at the same stage of medical treatment. The integrated review is providing new insight into the relationship between oesophageal bolus transit and synchronous pressure contractions. It also helps clarify previously poorly understood motility data and enables more appropriate therapeutic measures to be initiated.

Motility F200–F205

The nitrile oxide (NO) pathway may influence gallbladder function. Postprandial gallbladder emptying (GBE) was measured on separate occasions in 6 healthy volunteers during infusions of normal saline (P;3ml/min), NO donors nitroglycerine (NG; med dose 30mcg/min) and sodium nitroprusside (SNP;1mcg/kg/min). hydralazine (H,200mcg/min) as a control hypotensive agent and the NO synthase inhibitor L-NMA (1,3mg/kg over 20 minutes). NG, SNP and H were infused in doses sufficient to reduce systolic blood pressure by 10%; I significantly increased baseline. Infusion was started before and maintained for 90 minutes after ingestion of a fatty meal (two egg omelette). Gallbladder volume was measured by ultrasound.

Results: Fasting volumes were similar with all infusates. Both N and S caused significant impairment of GB function.

<table>
<thead>
<tr>
<th>Time</th>
<th>% Fasting GB volumes SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100±0</td>
</tr>
<tr>
<td>15</td>
<td>81±5</td>
</tr>
<tr>
<td>30</td>
<td>57±7</td>
</tr>
<tr>
<td>60</td>
<td>25±14</td>
</tr>
<tr>
<td>90</td>
<td>15±5</td>
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</table>

*p<0.05 (ANOVA)

Conclusion: Pharmacological doses of NO donors impair postprandial GB.

VISCERAL SENSATION AND EMOTION: A STUDY USING HYPNOSIS
LA Houghton, NA Jackson, P Cooper, PJ Whorwell. Department of Medicine, University Hospital of South Manchester, Manchester, U.K.

We have previously shown that hypnosis can be used to study the effect of different emotions on the physiology of the gastrointestinal tract. These studies showed that both anger and excitement increase colonic motility, whilst happiness led to its reduction (Lancet 1992; 340: 69-72). The purpose of this study was to investigate the effect of hypnosis and relaxation between the emotional states of happiness, anxiety and depression on the motility and function of the human colon. This study was also designed to test the interaction between these emotional states and the effect on the rectal sensation.

Vagal nerve activity. Vagal nerve activity was assessed by the measurement of rectal afferent activity during hypnosis in comparison with a waking state.

Instrumental test. The test was designed to assess the effect of the emotional state on the voluntary control of rectal afferent activity following a sham procedure. This involved the administration of a colonic distention with water, followed by a sham procedure (hypnosis or relaxation). The effect of the emotional state on the rectal afferent activity was then assessed by measuring the changes in rectal afferent activity during hypnosis.

Conclusions. The results of this study suggest that hypnosis can be used to study the effect of different emotions on the physiology of the gastrointestinal tract. These studies also showed that both anger and excitement increase colonic motility, whilst happiness led to its reduction. The purpose of this study was to investigate the effect of hypnosis and relaxation between the emotional states of happiness, anxiety and depression on the motility and function of the human colon. This study was also designed to test the interaction between these emotional states and the effect on the rectal sensation.

F024
**Oesophagus F206-F210**

**REFLUX CONTROL AT FLEXIBLE ENDOSCOPY USING ENDOULMINAL SUTURING IN AN ‘IN-VIVO’ MODEL. SS Kadickzamanahton, E Yang, CC Hepworth, F Gong, DP Evans, CJ Swan. Gastrointestinal Science Research Unit, The London Hospital Medical College, London.**

This study was designed to test the efficacy and safety of a new anti-reflux procedure called endoscopic gastropasty (EG), performed at flexible endoscopy without laparotomy or laparoscopy.

Six large white, male, female pigs (median weight 24 kg) underwent preliminary endoscopy and station pull-through manometry under anaesthesia. A pH sensitive radio-telemetry capsule was then sewn into the oesophageal wall 5 cm above the manometrically defined lower oesophageal sphincter (LOS) using the endoscopic sewing machine (ESM). Following recovery 48-96 hour pH recordings were obtained in an amphibian setting by a data logger worn by the pig in the jacket over an aerial. This recording revealed that the pigs naturally refluxed acid (median 4% time pH < 4 -9.3%). After one week, using the ESM, endoscopic gastropasty (EG) was performed by placing 2 rows of sutures just below the gastro-oesophageal junction to create a neo-oesophagus of 1-2 cm in length. Post-operative manometry was performed and following recovery, post-operative ambulant pH recordings (48-96 hours) were carried out. Endoscopy performed one week after the procedure revealed that the stitches were intact.

There were no complications or deaths due to the procedure. Following EG, the median LOS pressure increased from 3 (range 2.3-6) to 6 (range 4.5-16) mmHg (p=0.03) and LOS length increased from 3 (2.5) to 3.75 cm (range 3.4-5) [p=0.04]. The median (range) % time pH < 4 decreased significantly from 9.3% (6-11.1) to 0.2 (0-2.9) [p=0.04]. (Wilcoxon rank test)

EG was safe with no serious complications and significantly increased LOS pressure and length and decreased acid reflux in the oesophagus compared to the animal model. EG is now under assessment in human patients with GORD.

**OESOPHAGEAL ACIDIFICATION DOES NOT AFFECT SALIVARY SECRETION, BUT STIMULATED SALIVARY FLOW DECREASES ACID CLEARANCE TIME L.Y. Schindel, M. Hector, D.F. Evans, D.L. Wrigge. GI Science Research Unit, and Dept of Child Dental Health, London Hospital Medical College, UK.**

Waterbrash is commonly experienced by patients with gastro-oesophageal reflux (GOR) and is generally attributed to an increase in salivary secretion, suggesting an oesophago-salivary reflux link. This study was designed to assess the effect of oesophageal acid on salivary secretion and the role of saliva in acid clearance.

After oesophageal manometry, a pH probe was placed 5 cm above the lower oesophageal sphincter (LOS) in 10 healthy volunteers, aged 21-38 years. An additional paediatric feeding tube was placed 10 cm above the LOS to allow infusion of either 20 ml of water or 0.1N hydrochloric acid. Acid clearance time was measured in the upright position with one swallow every 45 s, modifying the quality of the swallows (wet vs. dry), the quality of the material swallowed (saliva vs. water) and salivary flow (basal vs. stimulated by a chewing gum base). Volume, protein concentration and pH of the expectorated saliva were measured. A portable digital recorder was used for acquisition of oesophageal pH data at a sampling frequency of 0.15 Hz. (Mean ± SE)

Gutt-stimulated salivary flow was higher than basal flow (26.0 ± 3.4 vs. 13.2 ± 2.0 ml/15 min; p=0.005). The presence of acid in the lower oesophagus did not affect salivary flow, its protein concentration or pH. This was true both for resting and post-acid stimulated secretion. Acid clearance depended on the quality of swallows and salivary flow.

**ACID CLEARANCE TIME (min)**

<table>
<thead>
<tr>
<th>Quality of swallows</th>
<th>Basal salivation</th>
<th>Stimulated salivation</th>
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<tbody>
<tr>
<td>Dry swallows</td>
<td>12.6±2.6</td>
<td>9.1±2.3</td>
</tr>
<tr>
<td>Wet swallows (saliva)</td>
<td>6.9±1.9</td>
<td>2.3±0.2</td>
</tr>
<tr>
<td>Wet swallows (water)</td>
<td>7.8±1.8</td>
<td>p&lt;0.02</td>
</tr>
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</table>

We conclude that acidification of the lower oesophagus does not affect salivary flow in healthy volunteers. The act of chewing, however, markedly decreases acid clearance time and this may be useful as a non-pharmacological treatment option in the relief of symptoms due to gastro-oesophageal reflux.

Saliva contains several protease inhibitors, but the role played by these in protecting the normal oesophagus against damage by refluxed gastric pepsins has never been investigated. Such activity would be of particular importance if significant quantities of saliva were present in the lower oesophageal refluxate, but failed to raise the oesophageal pH above 4. The effect of saliva was studied over a range of ratios where such conditions could exist.

Whole and parotid saliva samples, from healthy volunteers were snap frozen in liquid nitrogen and stimulated gastric juice samples collected onto ice following injection of pentagastrin 8 μg/kg.

Proteolytic activity was assessed using a modified haemoglobin digestion assay. To assess its pH independent ability to inhibit gastric pepsins, saliva, buffered to pH 3 or 4, was added to the assay system. Results are expressed as percentages of the activity measured in control assays to which saliva was not added, medians and (ranges), n=10.

<table>
<thead>
<tr>
<th>ASSAY TYPE</th>
<th>RATIO OF SALIVA TO GASTRIC JUICE</th>
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<tbody>
<tr>
<td>SALIVA</td>
<td>pH 25:1</td>
</tr>
<tr>
<td>Whole</td>
<td>pH 4</td>
</tr>
<tr>
<td>Parotid</td>
<td>pH 4</td>
</tr>
<tr>
<td>Whole</td>
<td>pH 3</td>
</tr>
<tr>
<td>Parotid</td>
<td>pH 3</td>
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These results demonstrate that neither parotid nor whole saliva has a pH independent effect on proteolysis by gastric juice (Wilcoxon signed rank test p=0.5, p=0.2-0.5; p=0.2-0.06***). We conclude that abnormalities of salivary antiproteases are unlikely to be important in the component of reflux oesophagitis caused by peptic digestion. However, a possible role in the control of damage caused by leukocytes remains.

MECHANISM OF GASTRO PROTECTION BY EPIDERMAL GROWTH FACTOR IN THE RAT: INFLUENCE OF CAPSAICIN DESENSITISATION AND CLOSE ARTERIAL INFUSION OF A CALCITONIN GENE-RELATED PEPTIDE ANTAGONIST ON GASTRIC MUCOSAL BLOOD FLOW

JY Kang, Teng CH, Chen FC*, Wee A**, Division of Gastroenterology, Department of Medicine and the Departments of Physiology* and Pathology**, National University of Singapore.

The gastro protective effect of capsaicin occurs via stimulation of afferent nerves, release of calcitonin gene-related peptide (CGRP) and consequent gastric hyperaemia. How epidermal growth factor (EGF) protects the stomach is not entirely clear but a gastric hyperaemic effect has also been described. The present studies aim to clarify the underlying mechanism of gastro protection by EGF. Gastric mucosal injury was induced by 2 ml absolute ethanol 1/2 hour after intragastric administration of solvent, capsaicin 5 mg or EGF 25 µg in adult male Sprague Dawley rats, half of which have undergone sensory ablation. Damage was assessed macroscopically and microscopically. In an ex vivo gastric chamber preparation the effects of subcutaneous capsaicin and topical EGF on gastric mucosal blood flow was examined with or without close arterial infusion with hCGRP8-37, a CGRP antagonist. Both capsaicin and EGF reduced ethanol-induced damage in animals with intact innervation, macroscopic damage being 26.7±5.6%, 0.2±0.2%* and 8.4±1.6%* in the solvent, capsaicin and EGF groups. In capsaicin desensitized animals macroscopic damage scores were 22.2±3.2%, 19.6±2.8% and 33.6±8.7%. Microscopic evaluation showed a similar trend. Both capsaicin and EGF induced gastric hyperaemia provided sensory nerves were intact (areas under the curve were 594.8±20.9, 829.8±64.5* and 760.2±33.6* for the solvent, capsaicin and EGF groups but 608.1±32.5, 610±29.8 and 571.4±22.7 in capsaicin desensitized animals). hCGRP8-37 abolished the hyperemic effect of both capsaicin and EGF. The area under the curve was 605.4±18.9, 863.2±26.7* and 812.5±26.1* in the solvent, capsaicin and EGF groups in the control experiment but were 565.3±245.1, 549.2±222.7 and 556.7±233.3 when hCGRP8-37 was infused. Conclusion: EGF may exert its effect via capsaicin sensitive afferent neurone leading to release of CGRP and gastric hyperaemia.

* p<0.05 versus control